J. Am. Chem. Soc. **1984**, *106*, 183-186

Electrostatic Stabilization of the Transition State in Proton Transfer from Carbon

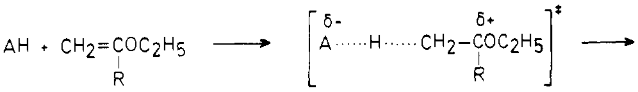
Alf Thibblin

Contribution from the Institute of Chemistry, University of Uppsala, P.O. Box 531, S-751 21 Uppsala, Sweden. Received May 11, 1983

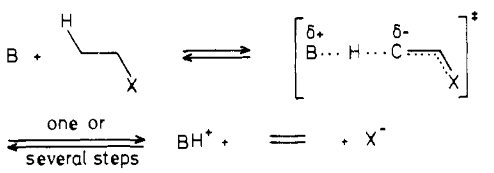
Abstract: The base-promoted reactions of 2-(p-nitrophenyl)ethyl chloride (**1**), 9-(chloromethyl)fluorene (**2**), 1-(2-chloro-2-propyl)indene (**3**), and 1-(2-acetoxy-2-propyl)indene (**4**) have been studied in 28 mol % Me_2SO-H_2O. They all exhibit rate-limiting proton transfer. Quinuclidine (Q) was found to be a more effective general base "catalyst" than hexafluoro-2-propanol anion (P^-) in these reactions. Thus, after correction for the small difference in thermodynamic basicity, the following rate constant ratios k_Q/k_{P^-} were obtained: 1.2, 4.4, 3.6, and 16, respectively. The small ratio for **1** indicates that partial desolvation of P^- is responsible for not more than a minor part of the rate differences between Q and P^- in these reactions. It is concluded that the reactions of **2**, **3**, and **4** are accelerated by electrostatic interaction between the developing positive charge on the tertiary amine and the partial negative charge on the carbon atom in the transition state. This favorable electrostatic interaction seems to be considerably larger in methanol.

Deviations from structure–reactivity correlations of the Brønsted type may occur in reactions where specific interactions are involved in the transition state, e.g., electrostatic interaction or steric hindrance to proton transfer, or in reactions where partial desolvation of the catalyst takes place prior to proton transfer. The requirement for partial desolvation is most important for basic oxygen anions, and this usually is manifested in curved Brønsted plots.[1-3] Accordingly, the comparably low rate constants for H_2O and HO^- in proton transfers to and from carbon have been explained by desolvation effects.

Studies by Kresge and co-workers[4,5] on general acid catalyzed hydrolysis of vinyl ethers in water have shown that positively charged acids give negative deviations from a Brønsted relation based upon neutral carboxylic acids and that the former gave a good Brønsted correlation of their own. On the other hand, negatively charged acids were found to be more efficient catalysts than the carboxylic acids. These effects were attributed to energy-increasing and energy-lowering electrostatic interactions, respectively, between the catalyst and the cationic center developing on the substrate in the transition state. For example, acids of the type RPO_3H^- were found to be better catalysts than neutral carboxylic acids of the same pK_a by about one order of magnitude in specific rate.[5]



In a similar way, a carbanionic center, developing in a reaction involving rate-limiting proton transfer to or from carbon, may interact favorably with the catalyst, e.g., in an elimination reaction



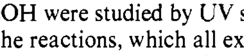
In a recent paper I reported that the ionization of 1-(2-acetoxy-2-propyl)indene (**4**) in methanol proceeds about 1600 times faster with quinuclidine as base than with p-$NO_2C_6H_4O^-$.[6] Since the thermodynamic basicities are about the same, this may indicate a considerable electrostatic stabilization of the transition state with the former base. However, as was pointed out in that paper, a significant part of the rate difference possibly comes from solvation effects. Steric hindrance may also contribute to the large rate difference.

Distinguishing an electrostatic effect from a desolvation effect is usually very difficult. In the present paper, the estimation of the magnitude of the energy-lowering electrostatic effect is based upon comparison with a reference reaction that shows a much smaller rate-acceleration effect owing to delocalization of the negative charge away from the carbon atom.

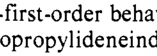
The reaction used as a reference is the elimination from 2-(p-nitrophenyl)ethyl chloride (**1**) in 28 mol % Me_2SO-H_2O.[7] The reaction has been found by Gandler and Jencks to undergo general base "catalysis" by oxyanions with a Brønsted coefficient of β = 0.67. Since the present work has found that the efficiency of quinuclidine and hexafluoro-2-propanol anion in promoting the reaction is similar (after correction for the small pK_a difference of the conjugate acids), this should be an ideal reference when the role of electrostatic stabilization of the transition states of related base-promoted elimination reactions is estimated.

Results

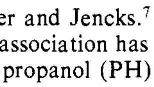
Reactions of 1, 2, and 3. The kinetics of reaction of 2-(p-nitrophenyl)ethyl chloride (**1**), 9-(chloromethyl)fluorene (**2**), and 1-(2-chloro-2-propyl)indene (**3**) with base in Me_2SO-H_2O or MeOH were studied by UV spectrophotometry. The sole products of the reactions, which all exhibit pseudo-first-order behavior, are p-nitrostyrene, dibenzofulvene, and 1-isopropylideneindene, respectively, as found by HPLC analyses. A small amount of buffer acid was added to the reaction solutions to suppress reaction by lyate ion. The ionic strength in 28 mol % Me_2SO-H_2O was 0.30 M; i.e., the reaction medium was exactly the same as that used by Gandler and Jencks.[7]



1



2



3 (X = Cl)
4 (X = OAc)

Buffer association has been found to be significant with hexafluoro-2-propanol (PH) buffers ($K_{assoc} \approx 4.8$).[7]

$$RO^- + ROH \overset{K_{assoc}}{\rightleftharpoons} RO^-{\cdot}HOR$$

---

[1] Jencks, W. P.; Brant, S. R.; Gandler, J. R.; Fendrich, G.; Nakamura, C. *J. Am. Chem. Soc.* **1982**, *104*, 7045-7051.

[2] Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1962**, *84*, 2910-2913.

[3] Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451-464.

[4] Kresge, A. J.; Chiang, Y. *J. Am. Chem. Soc.* **1973**, *95*, 803-806.

[5] Chwang, W. K.; Eliason, R.; Kresge, A. J. *J. Am. Chem. Soc.* **1977**, *99*, 805-808.

[6] Thibblin, A. *J. Am. Chem. Soc.* **1983**, *105*, 853-858.

[7] Gandler, J. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 1937-1951.

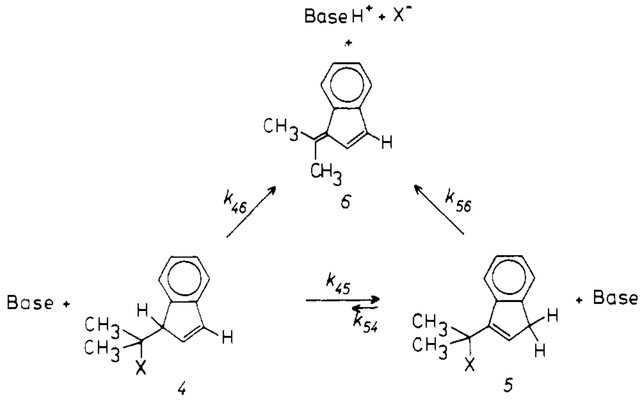
0002-7863/84/1506-0183$01.50/0

Table I. Rate Constants and Acceleration Effects for the Reactions of **1**, **2**, **3**, and **4** in 28 mol % Me_2SO-H_2O or in MeOH

substrate	solvent	base	[base], mM	[base H$^+$], mM	temp, °C	10^3k, M^{-1} s^{-1}	rate acc^a
1	Me_2SO-H_2O	P^-			40	6.8^b	1.2
	Me_2SO-H_2O	Q	100	7.0	40	2.79	
	MeOH	MeO^-	116		25	1.64	
	MeOH	Q	118	6.2	25	0.0035	
2	Me_2SO-H_2O	P^-	4.80	0.38	25	1740	4.4
	Me_2SO-H_2O	Q	10.0	0.70	25	3410	
	MeOH	MeO^-			25	640^c	
	MeOH	Q	118	6.2	25	42.5	
3	Me_2SO-H_2O	P^-	4.80	0.38	25	953	3.6
	Me_2SO-H_2O	Q	10.0	0.70	25	1450	
	MeOH	MeO^-			30	184^d	
	MeOH	Q	118	6.2	30	$\sim56^e$	
4	Me_2SO-H_2O	P^-	24.0	1.9	25	19.4^i	16
	Me_2SO-H_2O	Q	10.0	0.70	25	130^i	
	MeOH	MeO^-			30	$16.0^{f,i}$	
	MeOH	$p-NO_2C_6H_4O^-$			30	$0.0040^{g,i}$	~1600
	MeOH	Q			30	$\sim6.3^{h,i}$	

[a] See text. [b] Reference 7. [c] Reference 9. [d] Reference 8e. [e] After converting the rate constant measured at 25 °C: 36.0×10^{-3} M^{-1} s^{-1}. [f] Reference 8e. [g] Reference 6. [h] After converting the rate constant measured at 20 °C (ref 8f) using a factor of 2.5. [i] The rate constant for the total reaction, i.e., elimination and rearrangement.

Scheme I



However, only a very small correction has to be done at the low concentration of PH used in the present work. Thus the observed rate constants have to be increased by about 1%. The corrected rate constants as well as those measured in methanol are reported in Table I.

Reactions of 4. The reaction of 1-(2-acetoxy-2-propyl)indene (**4**) with hexafluoro-2-propanol anion (P^-) or with quinuclidine (Q) in 28 mol % Me_2SO-H_2O or in MeOH in the presence of the conjugate acid (PH or QH^+) provides the products 3-(2-acetoxy-2-propyl)indene (**5**) and 1-isopropylideneindene (**6**) (Scheme I), the latter being the only product after long reaction times. The kinetics of **4** as well as of **5** were studied by a calibrated sampling-quench HPLC procedure (Table I). When **5** is the substrate, the exclusive product is **3-h**. The reaction system of Scheme I has been studied thoroughly in this laboratory.[6,8]

The reactions follow the rate laws:

$$\frac{d[4]}{dt} = \{-(k_{45} + k_{46})[4] + k_{54}[5]\}[\text{base}] \qquad (1)$$

$$\frac{d[5]}{dt} = \{k_{45}[4] - (k_{54} + k_{56})[5]\}[\text{base}] \qquad (2)$$

$$\frac{d[6]}{dt} = \{k_{46}[4] + k_{56}[5]\}[\text{base}] \qquad (3)$$

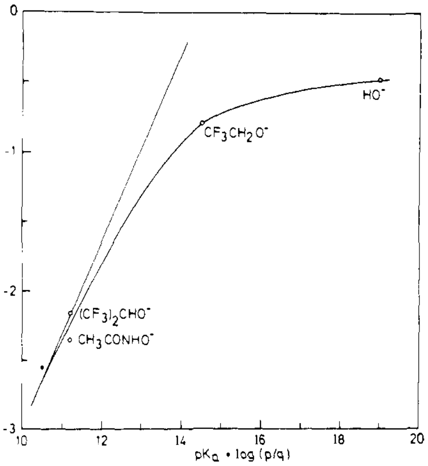


Figure 1. Brønsted plot for base-promoted elimination reactions from 2-(*p*-nitrophenyl)ethyl chloride (**1**) in 28 mol % Me_2SO-H_2O at 40 °C: oxyanions, ○ (data from ref 7); quinuclidine, ●.

The concentration of the base decreases slightly during the reactions, and at infinite time about 1% or less of the base has been consumed. The base concentrations therefore can be considered to be approximately constant during the kinetic runs, and near first-order behavior is expected.

The tautomeric equilibrium constant $[4]_{eq}/[5]_{eq}$ has been determined in methanol with pyridine as catalyst at 20 and 30 °C.[8f] The average value (20.4) is used for evaluation of the rate constants in the aqueous medium since it is likely to be a good approximation. The pseudo-first-order rate constants were determined by a simple computer simulation of the reactions using the integrated expressions of eq 1–3. The rate constants and reaction conditions are collected in Table I.

Discussion

The elimination reactions studied have rate-limiting transition states that are positioned near the E1cB–E2 borderline. Thus the indene **4** has been shown to react stepwise via an irreversibly formed carbanion intermediate which is tightly hydrogen bonded to the conjugate acid of the catalyst, i.e., an *E1cB$_I$–HBA* mechanism.[6] There are also strong indications that the reaction of the corresponding chloride **3** is of the same mechanistic type.[8e] Jencks and co-workers have argued that **1** reacts via a carbanion-like E2 mechanism,[7,10] but a stepwise irreversible mechanism involving a significant amount of hyperconjugative stabilization (weakening of the bond to the chloride in the transition state) is a viable alternative. The same objection is valid for More O'Ferrall's

---

(8) (a) Ahlberg, P. *Chem. Scr.* **1973**, *3*, 183–189. (b) *Ibid.* **1973**, *4*, 33–39. (c) Ahlberg, P.; Bengtsson, S. *Ibid.* **1974**, *6*, 45–46. (d) Thibblin, A.; Ahlberg, P. *Acta Chem. Scand., Ser. B* **1976**, *30*, 555–561. (e) Thibblin, A.; Ahlberg, P. *J. Am. Chem. Soc.* **1977**, *99*, 7926–7930. (f) Thibblin, A.; Bengtsson, S.; Ahlberg, P. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1569–1577. (g) Thibblin, A.; Ahlberg, P. *J. Am. Chem. Soc.* **1979**, *101*, 7311–7318. (h) Thibblin, A. *Chem. Scr.* **1980**, *15*, 121–127. (i) Thibblin, A.; Onyido, I.; Ahlberg, P. *Ibid.* **1982**, *19*, 145–148. (j) Thibblin, A. *Ibid.* **1983**, *22*, 70–73. (k) *Ibid.* **1983**, *22*, 182–187.

assignment of the E2 mechanism to the reaction of **2**.[9-12]

However, the question of whether there is a barrier to expulsion of the chlorine or not in these reactions is not of significance for the following discussion. The important thing is that all these reactions have carbanion-like transition states that give the possibility of electrostatic interaction between the catalyst and the developing negative charge on the carbon.

The amount of proton transfer in these reactions can be approximated with the Brønsted coefficients. Gandler and Jencks have measured β for compound **1** with oxyanions in Me_2SO–H_2O as 0.67 (Figure 1).[7] For compound **2** in 90% H_2O–EtOH, Spencer and co-workers have found β to be 0.50.[13] A Brønsted slope of 0.53 has been measured for **4** in methanol.[6] There are indications that the β value for **3** is close to this figure. Similar values are expected in Me_2SO–H_2O. Thus the reactions of all the substrates should have transition states with approximately half-transferred protons, which is also indicated by the kinetic deuterium isotope effects[6,8f] and the kinetic solvent isotope effects measured for other 2-(*p*-nitrophenyl)ethyl derivatives.[7]

The rate accelerations given in Table I are calculated from the rate constants measured with quinuclidine (Q) and hexafluoro-2-propanol anion (P^-) as $k_Q/k_{P^-}{}^{cor}$, where $k_{P^-}{}^{cor}$ is the rate constant of the P^--promoted reaction after correction for the higher basicity of P^- (0.7 pK_a unit)[7] utilizing the Brønsted equation and the above β values.

The accelerations should be a combination of favorable electrostatic interaction between the developing charge on the initially uncharged catalyst and the developing carbanionic center, difference in desolvation between the two bases (P^- should be considerably more solvated), and steric hindrance to proton transfer. Jencks and co-workers have concluded that steric hindrance is not significant for proton abstraction from 2-(*p*-nitrophenyl)ethyl compounds since the rate constants for the anions of fluorinated *tert*-butyl alcohols fall on the same Brønsted line as those of other oxyanions.[1] It is reasonable that the same is true also for the 9-(X-methyl)fluorene system.

As indicated by the small acceleration effect on the reaction of **1**, the contribution from desolvation should be less than 20% in any of the rate accelerations in the aqueous solvent reported in Table I. Moreover, since the solvation of basic oxyanions should be weaker in methanol, it is reasonable to assume that the desolvation contribution is even less in this solvent.

When the leaving group is Q^+ instead of Cl, the reaction producing *p*-nitrostyrene ($\beta = 0.67$) is unquestionably irreversible stepwise and there is no acceleration effect at all. The data of Gandler and Jencks[7] yield $k_Q/k_{P^-}{}^{cor} = 0.9$.

Despite the large Brønsted slope of $\beta = 0.67$ for substrate **1**, the electrostatic stabilization effect is very low. This can be rationalized by delocalization in the transition state of negative charge away from the carbanionic center into the nitro group.[22] Thus electron delocalization does not lag behind proton abstraction. In contrast, according to Bordwell and co-workers,[14] ionization of nitroalkanes has a rate-limiting transition state involving only a small amount of delocalization. However, Jencks and Jencks[21] and others have concluded that there is a great deal of delocalization in the transition state.

The pK_a of the substrates should be rather similar since the pK_a in Me_2SO of p-$NO_2C_6H_4CH_3$,[10,16] fluorene,[15,16] and indene[15,16] change, i.e., delocalization of the electron density away from the carbon to the nitro group. The slow proton abstraction from **1** consequently has a steep energy barrier like that of the ionization of nitroalkanes.

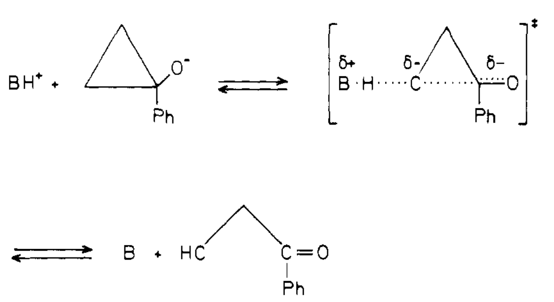
Recently, a method was presented for correlating rate constants of irreversible stepwise base-promoted elimination reactions with has been determined to be 20.5, 22.6, and 20.1, respectively. Notwithstanding, the reaction of **1** is considerably slower than the reactions of the other substrates. This behavior is consistent with a proton transfer involving a significant amount of structural the leaving group according to the equation

$$\log (k/k_0) = \rho^*\sigma^* + lL \qquad (4)$$

where σ^* is the polar (Taft) substituent constant of CH_2X and L is the leaving-group ability of X.[11] The parameter l is a measure of the sensitivity of the reaction system to a change in leaving-group ability. The 9-(X-methyl)fluorene system in NaOMe/MeOH at 25 °C is used as a reference ($\rho^* = 2.25$, $l = 1$).[11] The reactions of 1-(2-X-2-propyl)indene, e.g., are well approximated by the above equation ($\rho^* = 1.7$, $l = 1.2$).[11] Also the reactions of 1-X-2-(*p*-nitrophenyl)ethane[7] can be correlated with eq 4 ($\rho^* = 1.3$, $l = 0.98$). The low ρ^* of the latter reactions indicate a low sensitivity to the polarity of the leaving group consistent with the conclusion in the present paper that the electron density at C_β is low and that the delocalization is extensive. The degree of bond breaking to the leaving group is small according to the small l parameter. There seems to be a correlation between ρ^* and the rate accelerations for **1**, **2**, and **3**.

In the previous study of the reaction of **4** in methanol with oxyanion bases,[6] it was found that the base set p-$NO_2C_6H_4O^-$, $C_6H_5O^-$, and MeO^- (the pK_a of the conjugate acids in methanol are 11.50, 14.46, and 18.31)[17] yields a good Brønsted correlation with $\beta = 0.53$. The rate constant of the MeO^--promoted reaction does not deviate. This suggests that strongly basic oxyanions are much less solvated in methanol than in water. It also suggests that the rate constants of the MeO^--promoted reactions of **1** and **2** can be utilized to estimate the rate constants for reaction with an oxyanion base of the same basicity as that of Q (p$K_{QH^+} \approx 11.5$). Calculations employing the same β values as in the aqueous medium (0.67 and 0.50, respectively) then yield rate constants which together with the measured rate constants for the Q-promoted reactions provide rate acceleration effects of 78 and 169, respectively. These estimates are, of course, very uncertain. Curvature of the Brønsted plots decreases these values. On the other hand, greater Brønsted slopes imply larger effects. The electrostatic stabilization is expected to be larger in methanol than in Me_2SO–H_2O in accord with the different polarity of the media. Consistently, the rate acceleration effect for **4** (as well as for **1**, **2**, and **3**) is considerably greater in methanol.

The general acid catalyzed cleavage of 1-phenylcyclopropanol anion, which represents proton removal in the reverse direction,



is related to the elimination reactions.[18] It was found for this S_E2 reaction that 2,2,2-trifluoroethanol, as well as H_2O, is a less effective catalyst in water than protonated tertiary amines for a given pK. The Brønsted slope of $\alpha = 0.25$ for this reaction indicates a rather large positive charge on the catalyzing tertiary

---

(9) More O'Ferrall, R. A.; Warren, P. J. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1920–1927.

(10) Keeffe, J. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1983**, *105*, 265–279.

(11) Thibblin, A. *Chem. Scr.* **1980**, *15*, 121–127.

(12) More O'Ferrall, R. A.; Warren, P. J.; Ward, P. M. *Acta Univ. Ups., Symp. Univ. Upsaliensis* **1977**, *12*, 209–218 and references therein.

(13) Spencer, T. A.; Kendall, M. C. R.; Reingold, I. D. *J. Am. Chem. Soc.* **1972**, *94*, 1250–1254.

(14) (a) Bordwell, F. G.; Boyle, W. H., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 3907–3911. (b) Bordwell, F. G.; Bartmess, J. E.; Hautala, J. A. *J. Org. Chem.* **1978**, *43*, 3107–3113.

(15) Matthews, W. E.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. S.; Drucker, G. E.; Margollin, Z.; McCollum, R. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006–7014.

(16) (a) Bordwell, F. G.; Algrim, D.; Vanier, N. R. *J. Org. Chem.* **1977**, *42*, 1817–1819. (b) Bordwell, F. G. *Pure Appl. Chem.* **1977**, *49*, 963–968.

(17) Parsons, G. H.; Rochester, C. H. *J. Chem. Soc., Faraday* Trans. *1* **1975**, 1058–1068.

(18) Thibblin, A.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 4963–4973.

amine in the transition state that could interact favorably with the developing negative charge on the carbon atom.

1-Phenyl-2-arylcyclopropanol anions, which react 10^5 times faster, also show general acid catalysis, with $\alpha \leq 0.1$.[18] The differences in catalytic efficiency between H_2O and tertiary amines are much larger in this reaction, probably in part due to the larger charge on the protonated tertiary amine indicted by the small α value.

Theoretically, a change in pK_a of a catalyst results in a change in transition-state structure. Thus a weaker base corresponds to a transition state with more proton transfer. This means that the transition state has a greater possibility for electrostatic interaction. It also means strong hydrogen bonding between the protonated catalyst and the carbanionic center provided that the charge is not delocalized away from the carbon atom. This is inferred from the conclusion that the pK_a of the catalyst determines the strength of the hydrogen bond in reaction-intermediate complexes between a carbanion and the protonated base.[6]

Experimental Section

General. The ^1H NMR analyses were made with a JEOL FX 100 spectrometer equipped with a 5-mm dual probe (^1H, ^{13}C). The high-performance liquid chromatography analyses were carried out with a Hewlett-Packard 1084B liquid chromatograph/variable wavelength detector on a C8 reversed-phase column (4.6 × 130 mm). The mobile phase was a solution of 46 vol % ethanol in water. The apparatus used for the UV kinetics was a Varian Cary 118 spectrophotometer.

The kinetic runs were performed at constant temperature in a HETO 01 PT 623 thermostat or in a jacketed cuvette of quartz (Hellma 160B, 10 mm) thermostated with water from the bath. The temperature was measured with a calibrated mercury thermometer with an absolute accuracy of ±0.02 °C. Since the temperature of the bath did not deviate more than 0.01 °C from the average value (t), the absolute temperature of the bath was $t \pm 0.03$ °C.

Materials. Methanol (Fluka, for UV spectroscopy) stored over 0.3-nm molecular sieves was used without further purification. A stock solution of NaOMe was prepared by adding pure-cut pieces of sodium to methanol. The concentration was determined by titration of aliquots of this stock solution with 0.1 M HCl. Dimethyl sulfoxide (Merck, for spectroscopy) was used without further purification. The dimethyl sulfoxide-water mixture was prepared by adding 0.4 vol of distilled water to a volumetric flask and then filling to the mark at 25 °C. This mixture, as analyzed gravimetrically, corresponds to 28 mol % Me_2SO.[7]

Quinuclidine hydrochloride (Aldrich, 97%) was recrystallized twice from 99.5% ethanol. Quinuclidine (EGA-Chemie) was purified by recrystallization twice from hexane and sublimed at reduced pressure. 1,1,1,3,3,3-Hexafluoro-2-propanol (EGA-Chemie, >99%) was distilled through a short Vigreux column.

The syntheses and purification of 1-(2-chloro-2-propyl)indene and 1-(2-acetoxy-2-propyl)indene have been reported previously. Nitration of 2-phenylethyl chloride gave 2-(*p*-nitrophenyl)ethyl chloride, which was purified by recrystallization three times from pentane-diethyl ether.[19] 9-(Chloromethyl)fluorene was prepared from the corresponding alcohol by reaction with $SOCl_2$.[20] The melting point after three recrystallizations from 99.5% ethanol was 69-70 °C (lit. 66.5-67.5 °C).[20] The purity of all substrates was checked by HPLC.

Kinetics. The reactions in Me_2SO-H_2O were carried out at ionic strength 0.30 M, maintained with potassium chloride. In the UV kinetics, the absorbance change was followed at 331 nm (*p*-nitrostyrene), 255 nm or 293 nm (dibenzofulvene), and 308 nm (1-isopropylideneindene), respectively, in tightly stoppered, jacketed 10-mm cells. After thermostating the base solution for at least 30 min, the reaction was started by injection of 1-3 μL of a concentrated substrate solution (CH_3CN). Pseudo-first-order rate constants were evaluated from plots of ln ($A_\infty - A$) versus time. The slow reaction of **1** with Q in methanol was followed by measurements of the initial rate of reaction (~2% reaction, $\Delta A \approx 0.3$) after the addition of 5 μL of 0.63 M substrate to 1 mL of base solution. The infinity absorbance A_∞ was determined in a separate experiment with NaOMe. Thus 50 μL of the former reaction solution was added to 1 mL of thermostated NaOMe solution in a second cuvette and the infinity value was used to calculate A_∞ for the parallel initial-rate experiment. The rate constant was then obtained from the relationship $k = (\Delta A/t)/(A_\infty - A/2)$.

The sampling-quench HPLC procedure was used to measure the kinetics of **4**. The kinetic runs were performed in the following way. A reaction flask equipped with a tight TFE septum was filled with 5 mL of base solution. After thermostating, 1 μL of 0.6 M substrate (CH_3CN) was injected with a syringe. During the run, aliquots (500 μL) were withdrawn with a syringe and rapidly transferred to a standard 2-mL bottle equipped with a TFE septum and containing enough of a quench solution (prepared by diluting 15.6 mL of 2 M sulfuric acid with 40% ethanol-water to 250 mL) to neutralize the base solution. This mixture was then analyzed by HPLC. The areas under the separated peaks of starting material (**4**), olefin (**6**), and the small amount of rearrangement material (**5**), together with the relative extinction coefficients (response factors) at 254 nm, which were determined by using several standard mixtures, prepared by weighing, of pure **4**, **5**, and **6**, gave the composition in mol %. Samples were taken at least four times from the reaction mixture and every quenched sample was analyzed three times. To obtain accurate rate constants from the computer simulation it was necessary to run kinetics also with the rearrangement product **5**.

Evaluation of Rate Constants. The rate constants of the reactions of **4** and **5** were evaluated by using a combination of manual treatment, which gave approximative values of the pseudo-first-order rate constants from plots of ln (mol % starting material) vs. time, and computer simulation. The latter method has been described previously.[8e,f]

When starting from pure **4** the concentrations of **4**, **5**, and **6** are described by the following:

$$\text{mol \% } \mathbf{4} = ae^{-m_1t} + (100 - a)e^{-m_2t}$$

$$\text{mol \% } \mathbf{5} = be^{-m_1t} - be^{-m_2t}$$

$$\text{mol \% } \mathbf{6} = 100 + ce^{-m_1t} - (100 + c)e^{-m_2t}$$

where

$$a = 100(k_{45} + k_{46} - m_2)/(m_1 - m_2)$$

$$b = 100\ k_{45}/(m_2 - m_1)$$

$$m_1 = [(k_{45} + k_{46} + k_{54} + k_{56})^2/4 - k_{45}k_{56} - (k_{54} + k_{56})k_{46}]^{1/2} + \tfrac{1}{2}(k_{45} + k_{46} + k_{54} + k_{56})$$

$$m_2 = -[(k_{45} + k_{46} + k_{54} + k_{56})^2/4 - k_{45}k_{56} - (k_{54} + k_{56})k_{46}]^{1/2} + \tfrac{1}{2}(k_{45} + k_{56} + k_{54} + k_{56})$$

Acknowledgment. I am indebted to Professor Per Ahlberg for helpful discussions and to the Swedish Natural Science Research Council for financial support.

Registry No. 1, 20264-95-3; **2**, 36375-77-6; **3**, 64909-94-0; **4**, 42271-88-5; quinuclidine, 100-76-5; hexafluoro-2-propanol anion, 44870-01-1.

---

(19) Beeby, M. H.; Mann, F. G. *J. Chem. Soc.* **1949**, 1799-1803.

(20) Wawzonek, S.; Dufek, E. *J. Am. Chem. Soc.* **1956**, *78*, 3530-3533.

(21) Jencks, D. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7948-7960.

(22) **Note Added in Proof**: This is consistent with the conclusion that the ionization of 2-nitropropane involves a smaller development and concentration of charge in the transition state than the detriation reaction of chloroform: Dahlberg, D. B.; Kuzemko, M. A.; Chiang, Y.; Kresge, A. J.; Powell, M. F *J. Am. Chem. Soc.* **1983**, *105*, 5387-5390.