

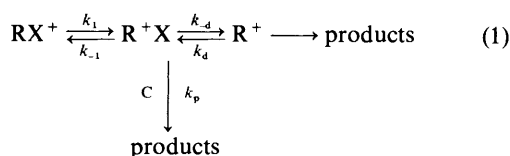
Acid-catalysed Solvolysis of 1,1-Diphenylethyl Methyl Ether in Highly Aqueous Media. Reaction *via* Ion-Molecule Pairs?¹

Alf Thibblin

Institute of Chemistry, University of Uppsala, PO Box 531, S-751 21 Uppsala, Sweden

The acid-catalysed solvolysis of 1,1-diphenyl-1-methoxyethane (**1-OMe**) to 1,1-diphenylethanol (**2**) and 1,1-diphenylethene (**3**) has been studied in aqueous solvents. Iodide ion accelerates the solvolysis. The twofold increase in rate observed in 20 vol% DMSO in water in the presence of 0.8 mol dm⁻³ I⁻ instead of Cl⁻ may be explained by nucleophilic attack on a carbocation intermediate of ion-molecule type that undergoes significant internal return, or by a specific salt effect. The addition of water to the carbocation, generated by solvolysis of the *p*-nitrobenzoate **1-PNB**, is catalysed to a small extent by general bases. The acid-catalysed hydrolysis of **1-OMe** is accelerated slightly by formic acid buffer.

The present work is part of an investigation into the role of ion pairs and ion-molecule pairs as intermediates in heterolysis reactions in water and highly aqueous media. The equilibrium constant $K_{as} = [R^+X^-]/([R^+][X^-])$ for formation of ion pairs from singly-charged ions in water is generally $< 1 \text{ dm}^3 \text{ mol}^{-1}$.² The equilibrium constant $K_{as} = k_d/k_{-d} = [R^+X^-]/([R^+][X^-])$ for formation of ion-molecule pairs [eqn. (1)] should be even



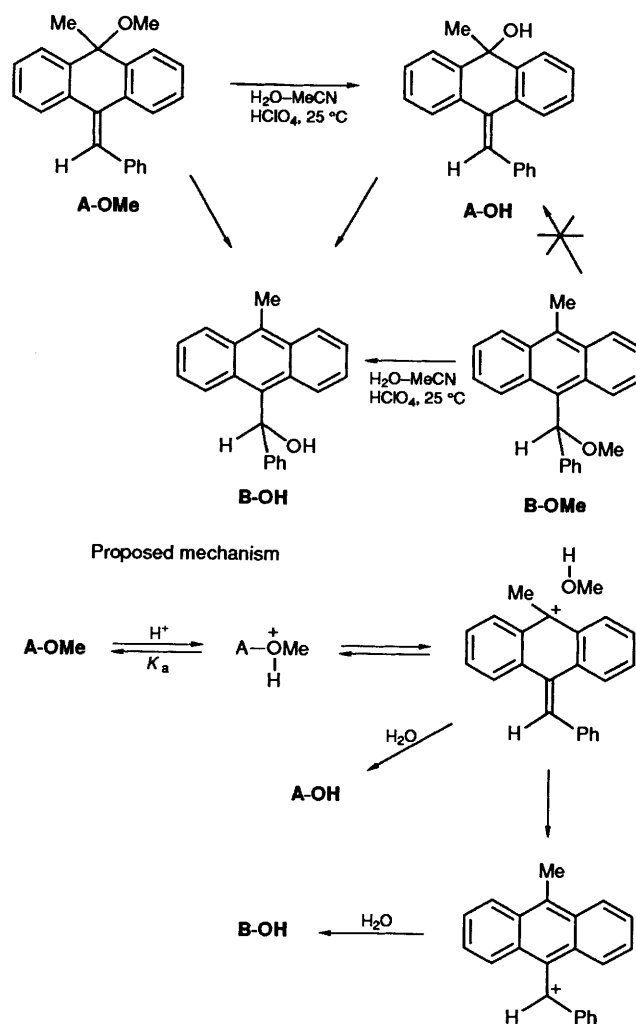
smaller. Accordingly, a substantial fraction of reaction products is not likely to originate from the reaction of the ion-molecule pair with a dilute reactant since the lifetime of the intermediate should be too short to allow it to encounter, and react with, other reactants than those that are already close to the ion-molecule pair when it is formed.³ Thus, a substantial k_p/k_{-d} ratio [eqn. (1)] requires a pre-association mechanism whereby the dilute reactant C assumes a reaction position before the R-X⁺ bond is ruptured, or reaction with the solvent.

However, if there is a specific interaction between the carbocation and the leaving group that increases the barrier for separation, equivalent to a larger equilibrium constant K_{as} , substantial reaction from the ion-molecule pair may occur.

The very few examples of ion-molecule pairs reported in the literature include reaction of R⁺X with solvent or added nucleophile,⁴⁻⁷ and rearrangement of R⁺X, followed by collapse to form an isomeric product.⁸

For example, it was concluded that the acid-catalysed reaction of the anthranyl derivative **A-OMe** proceeds *via* an ion-molecule pair intermediate in water-acetonitrile as well as in alcoholic solvents (Scheme 1).⁶ It was found that, compared with its dissociation to a 'free' solvent-equilibrated carbocation, the ion-molecule pair reacts more rapidly with a solvent molecule. The free carbocation is assumed to give the rearrangement product exclusively, which is supported by the fact that acid-catalysed hydrolysis of the corresponding anthracene ether **B-OMe** does not give any anthranyl alcohol **A-OH**, but yields **B-OH** as the sole product.

The observed trapping of the ion-molecule pair with solvent suggests that return is significant. Is it possible to trap this intermediate by an added dilute strong nucleophile? Is the acid



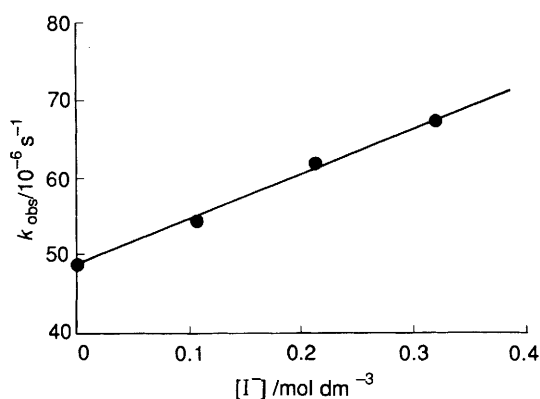
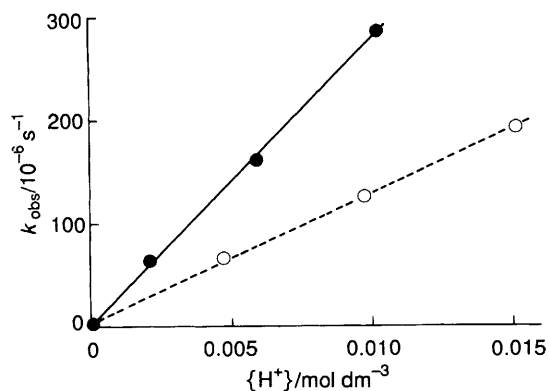
Scheme 1

catalysis of specific or general type? These questions are of great interest and the aim of the present work is to investigate them by employing the structurally related, but less reactive, diphenyl ethyl system. This system has the advantage that negatively-charged leaving groups can also be studied⁹ and the data pertaining to them can be compared with the data pertaining to uncharged leaving groups.

Table 1 Rate constants for the acid-catalysed reactions of **1-OMe** in 20 vol% DMSO in water at 25 °C

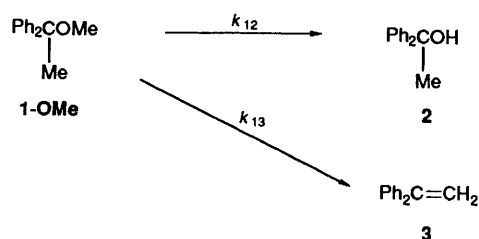
Salt 0.32 mol dm ⁻³	$(k_{12} + k_{13})/10^{-3}$ dm ³ mol ⁻¹ s ⁻¹	$10^3 k_{13}/k_{12}$
none	9.5 ^a	15
KCl	7.9 ^b	
KBr	9.1 ^b	
NaClO ₄	9.3 ^b	
KI	11.0 ^b	

^a From slope of plot of k_{obs} vs. $[\text{HClO}_4]$, 0.01–0.05 mol dm⁻³; ionic strength maintained constant at 0.05 mol dm⁻³ with NaClO₄. ^b From k_{obs} and the measured pH.

**Fig. 1** Acceleration by iodide anion of the acid-catalysed reaction of **1-OMe** in 20 vol% DMSO in water at constant pH and at ionic strength 0.32 mol dm⁻³ maintained with KCl**Fig. 2** Acid catalysis of the reaction of **1-OMe** in 20 vol% DMSO in water in the presence of KCl and KI, respectively. The hydron activity $\{H^+\}$ is measured by a pH meter equipped with a glass electrode: ●, 0.80 mol dm⁻³ KI; ○, 0.80 mol dm⁻³ KCl.

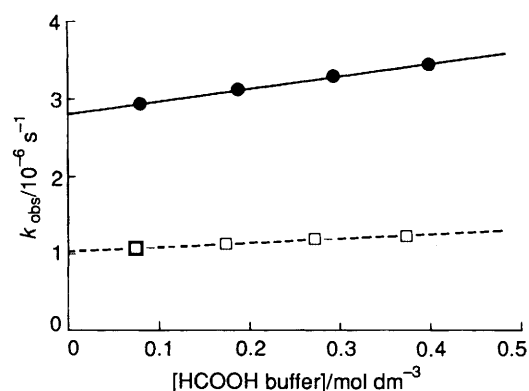
Results

The solvolysis of 1,1-diphenyl-1-methoxyethane (**1-OMe**) in 20 vol% DMSO in water produces mainly the alcohol **2**, as well as some olefin, 1,1-diphenylethene (**3**) (Scheme 2).



Scheme 2

There is a significant salt effect on the acid-catalysed reaction

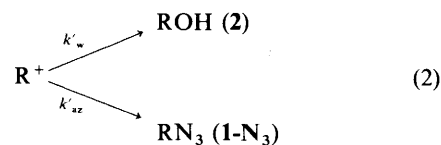
**Fig. 3** Formic acid-buffer catalysis of the reaction of **1-OMe**; buffer ratio 3:1 (HA:A⁻): ●, 20% DMSO; □, 25% MeCN

of the ether **1-OMe** (Table 1). The reaction rate at constant pH is more rapid in the presence of Br⁻ than Cl⁻, and I⁻ increases the rate even more. Fig. 1 shows the effect of KI on the observed rate at constant pH and constant ionic strength maintained with KCl. Extrapolation shows that the reaction is 2.0 times faster with 0.8 mol dm⁻³ KI than with 0.8 mol dm⁻³ KCl. Plots of observed rate constants vs. H⁺ activity are shown in Fig. 2 at a constant salt concentration of 0.8 mol dm⁻³ KCl and KI, respectively. These plots also demonstrate that the presence of I⁻ is more favourable than Cl⁻ to the promotion of a fast reaction. The rate ratio of 2.2 agrees with that obtained at constant pH (Fig. 1).

The carbocationic intermediates show very similar nucleophilic selectivities with different types of leaving group.⁹ For example, the second-order ratio for reaction of the acetate **1-OAc** in aqueous acetonitrile with azide ion and water was measured as $k_{\text{az}}/k_{\text{w}} = 1235$. A very similar rate ratio was expected for the reaction of **1-OMe**. Attempts have been made to measure this ratio of azide and alcohol product as well as the solvolysis rate of the reaction of **1-OMe**. However, the reaction is very slow in HN₃-N₃⁻ buffers and the azide product **1-N₃** is not stable for such long reaction times, therefore, no reliable results were obtained.

The reaction of **1-OMe** is accelerated to a small extent by general acids, as shown in Fig. 3 for formic acid. Catalysis by acetic acid is very small (plot not shown). Formic acid accelerates the reaction in MeCN-water to a smaller extent than in DMSO-water. This may be the result of a negative medium effect of the added buffer, which partly counteracts a positive slope of the catalysis; a negative effect on solvolysis rate by added acetate anion has been found previously for diphenylethyl substrates.⁹

The partitioning of the carbocation intermediate formed in the solvolysis of the *p*-nitrobenzoate **1-PNB** in MeCN-water between reaction with solvent water and azide ion [at a concentration of 0.1 mol dm⁻³; eqns. (2) and (3)] is dependent



$$k'_w = k'_{\text{az}} / ([1\text{-N}_3]/[2]) = k_{\text{az}}[\text{N}_3^-] / ([1\text{-N}_3]/[2]) \quad (3)$$

on the concentration of added AcO⁻ and, to a smaller extent, on the concentration of added CF₃COO⁻, as shown in Fig. 4. This decrease in k'_{az}/k'_w may be interpreted as general base catalysis on the rate of reaction of the carbocation intermediate with water (with first-order rate constant k'_w) or to a decrease in the

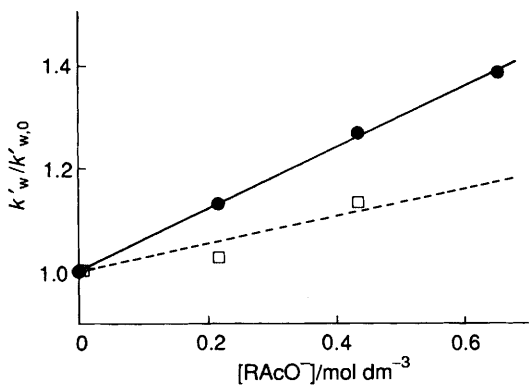


Fig. 4 General-base catalysis by carboxylate anions of the reaction of the carbocation generated from **1-PNB** with water in 25 vol% acetonitrile in water at ionic strength 0.75 mol dm^{-3} . The azide anion concentration is 0.10 mol dm^{-3} . The rate constant $k'_{w,0}$ is the rate constant for the reaction of the carbocation with water in the absence of azide anion. ●, CH_3CO_2^- ; □, CF_3CO_2^- .

diffusional rate of azide anion (with pseudo-first order rate constant k'_{az}). Fig. 4 is based upon the assumption of an unchanged diffusion rate constant for azide ion. The slope of the trifluoroacetate-catalysed reaction is approximate since the HPLC peak area of the product alcohol **2** had to be corrected due to an unknown impurity.

The olefin **3** is stable in DMSO–water and in MeCN–water at pH 2 for at least several hours.

Discussion

The solvolysis of **1-X** is expected to be of $\text{S}_{\text{N}}1$ -type. Experimental support for this mechanism has been reported recently.⁹ Despite the fact that the reactivity of an azide ion is much greater than that of solvent water molecule toward the acetate **1-OAc** in 20% DMSO–water, the observed reaction rate is constant, within the limits of experimental error, up to an azide concentration of 0.8 mol dm^{-3} , at which the yield of **1-N₃** is over 90%. Thus, the azide ion is not involved in the rate-limiting transition state.

The leaving group X in the substrate **1-X** does not have a significant effect on the selectivity of the carbocationic intermediate toward different nucleophiles.⁹ However, this does not prove that the substitution products are formed *via* the free solvent-equilibrated carbocation since it has been found that an intramolecular ion pair with sulfonate leaving groups behaves in very much the same way as the free carbocation in reactions with nucleophiles.¹⁰ The olefin **3** has been concluded to be formed mainly by elimination from the ion pair.⁹

The acid-catalysed reaction of **1-OMe** exhibits a nucleophilic selectivity value of $k_{\text{EtOH}}/k_{\text{w}} = 3.0$ in water–ethanol mixtures. A considerably larger selectivity, $k_{\text{EtOH}}/k_{\text{w}} = 13$, has been measured for the structurally related anthranil ether **A-OMe** (Scheme 1).⁶ A larger selectivity of the latter reaction is consistent with the reactivity–selectivity principle since the anthranil carbocation intermediate should have a lower energy than the diphenylethyl carbocation. Consistently, the anthranil ether **A-OMe** reacts about 1000 times faster than **1-OMe**. The reactivity difference is probably the result of the cyclic structure of the anthranil system, which produces very minor steric and entropic inhibition of resonance stabilization of the carbocation by the phenyl groups.^{11,12}

The kinetics of the acid-catalysed reaction of **1-OMe** were studied in DMSO–water in order to minimize special salt effects. Thus, specific solvation has been shown to be insignificant in DMSO–water mixtures in contrast to acetonitrile–water mixtures¹³ and salt effects on solvolysis of alkyl chlorides in 70% and 80% aqueous DMSO have been found to

be small.¹⁴ Solvolysis of the *p*-nitrobenzoate **1-PNB** in 20% DMSO–water exhibits very small salt effects.⁹ The relative rates at a salt concentration of 0.80 mol dm^{-3} were measured as 1 (no salt), 0.9 (NaClO_4), 1.0 (NaCl), 1.1 (NaI) and 1.0 (NaN_3).⁹ The acceleration of the solvolysis that is seen by addition of the iodide anion (Figs. 1 and 2) may therefore be caused by nucleophilic attack on the initially formed carbocation–methanol pair. The iodide anion has a very high nucleophilicity and presumably reacts with the intermediate at a diffusion-controlled rate. This interpretation requires the internal return from the ion–molecule pair to be fast and the reaction between I^- and the intermediate to proceed at a rate comparable to that of diffusional separation. The product **1-I** is expected to react very fast to yield the final products **2** and **3**. Rate-limiting attack of iodide ion on a benzyl carbocation–dimethyl sulfide ion–molecule pair has been suggested previously.⁴

Perchlorate anion also has a positive rate effect as compared with chloride (Table 1). The reason may be that large, soft anions decrease the internal return of the initially formed ion–molecule pair by assisting in its separation to give a free, solvent-equilibrated carbocation. It has been seen that formation of tri-*p*-anisylmethyl carbocation from the alcohol is accelerated by perchlorate anion.¹⁵ For example, it was found that substitution of 0.5 and 1 mol dm^{-3} NaCl with the same concentrations of NaClO_4 increases the rate by 14% and 60%, respectively.

The attack of MeOH on the carbocation should involve a significant activation energy since $k_{\text{MeOH}} \approx 5 \times 10^7 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ (assuming $k_{\text{az}} = 5 \times 10^9 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$, $k_{\text{az}}/k_{\text{w}} = 660$, and $k_{\text{MeOH}}/k_{\text{w}} = 6.4$).⁹ Accordingly, if the formation of the ion–molecule pair [k_{d} in eqn. (1)] is diffusion controlled, it may be concluded that the collapse of the ion–molecule pair [k_{-1} in eqn. (1)] is slow. However, the formation of the ion–molecule pair from the free carbocation should involve substantial changes in solvation and geometry. It is likely that these processes account for a considerable part of the activation energy of formation of the ether from the carbocation.

In contrast to the fast return of the carbocation–methanol pair suggested by this work, the ion pair formed from **1-OAc** has been estimated to return only to a small extent (*ca.* 4%).⁹ This estimation was based upon the assumption that the substitution product **2** is formed *via* the free carbocation. If this assumption is correct, the reason for this difference may be a larger ‘nucleophilicity’ of MeOH, compared with AcO^- in the intermediate. Solvent-equilibrated acetate anion and methanol have about the same nucleophilicity toward the carbocation ($k_{\text{OAc}}/k_{\text{MeOH}} = 2$)⁹ but this not necessarily relevant for how fast the ion pair and ion–molecule pair undergo internal return. It is conceivable that the ion–molecule pair collapses faster due to more favourable geometric and solvation requirements.¹⁶

It has been found that AcO^- as a potential leaving group in an allylic ion pair gives rise to a greater collapse of rearrangement products relative to formation of alcohol than MeOH as leaving group.⁸ However, this was attributed to the bifunctional nature of AcO^- , which lowers the barrier for formation of the rearranged acetate product.

The slopes of Fig. 4 combined with the assumption that the carbocation reacts with azide anion with a diffusion-controlled rate that does not change with buffer concentration suggest catalysis.¹⁷ Accordingly, the reaction of water with the carbocation generated from the *p*-nitrobenzoate **1-PNB** in MeCN–water is catalysed by acetate anion, and to a smaller extent, by trifluoroacetate anion. The slopes of the plots in Fig. 4 yield the rate constants for the catalysis by AcO^- and CF_3COO^- as 2.3×10^6 and *ca.* $1.1 \times 10^6 \text{ dm}^6 \text{ mol}^{-2} \text{ s}^{-1}$, respectively. A very approximative Brønsted parameter of β *ca.* 0.07 is estimated from these rate constants. A negative deviation of *ca.* $10^{0.9}$ is calculated for the water-catalysed

reaction based upon a rate constant for the catalysis by water of *ca.* $9.4 \times 10^4 \text{ dm}^6 \text{ mol}^{-2} \text{ s}^{-1}$. A similar Brønsted value, $\beta = 0.08$, and negative deviation by water of $10^{1.2}$ have been reported for the catalysis of the reactions of trifluoroethanol with 1-(4-methoxyphenyl)ethyl carbocation in 50:45:5 water-trifluoroethanol-methanol.¹⁷

The indications for general base catalysis given in Fig. 4 are in accord with the interpretation that the increase in the rate of the acid-catalysed reaction of **1-OMe** with increasing formate buffer concentration (Fig. 3) reflects general acid catalysis. The catalysis of formic acid is apparently very small compared with catalysis of the hydron. The small β value indicates that the Brønsted parameter α should have a value of *ca.* 0.9. If the general acid catalysis is significant, the formation of the ion-molecule pair is a concerted reaction.

A concerted S_N2 reaction is of course an alternative to a stepwise reaction with iodide anion and it is not possible to exclude this possibility by the experimental results. Assistance from iodide or azide anion has not been detected in the solvolysis of diphenylethyl substrates with other, less efficient, leaving groups.⁹ Moreover, in the light of the results with the anthranil ethers,⁶ a concerted reaction seems less likely.

Conclusions

The methyl ether **1-OMe** solvolyses to a carbocation-molecule pair which may be trapped by iodide anion. The internal return is faster than diffusional separation. The solvolysis is catalysed by H_3O^+ , but only to a very small, or possibly insignificant, extent by general acids.

Experimental

General.—The ¹H-NMR analyses were performed with a Varian XL 300 spectrometer equipped with a 5 mm dual probe (¹H, ¹³C). The HPLC analyses were carried out with a Hewlett-Packard 1090M liquid chromatograph equipped with a diode-array detector and a C8 reversed-phase column (3.0 × 200 mm). The mobile phase was a solution of acetonitrile in water. The reactions were studied at constant temperature in an HETO 01 PT 623 thermostat or in an aluminium block thermostated with circulating water from the thermostat.

Materials.—Acetonitrile, dimethyl sulfoxide (DMSO), methanol and ethanol were of spectroscopic quality and were used as solvents without further purification. All other chemicals were of reagent grade. A stock solution of sodium perchlorate was prepared from perchloric acid and sodium hydroxide solution. 1,1-Diphenylethanol (**2**) was purified by recrystallization of commercially available material (Aldrich) from pentane. The synthesis of 1,1-diphenyl-1-methoxyethane (**1-OMe**) has been described previously.^{9,18}

Kinetics and Product Studies.—The reactions were run at constant ionic strength in solutions prepared by mixing a water solution of the salt(s) with the organic solvent(s) at room temperature, *ca.* 22 °C. The reaction vessel was a 2 cm³ HPLC flask, sealed with a tight PTFE septum, which was placed in an

aluminium block in the water thermostat or, in the faster reactions, directly in the HPLC apparatus in an aluminium block held at constant temperature with circulating water from the thermostat. The reactions were initiated by addition of a few mm³ of the substrate dissolved in acetonitrile by means of a spring-loaded syringe. The concentration of the substrate was <0.1 mmol dm⁻³. The reaction solution was analysed at appropriate intervals on the HPLC apparatus. The mol% of the starting material and each of the products were measured by means of the relative response factors, which were determined in separate experiments. The rate constants were calculated from plots of ln(area starting material) or ln(mol%) *vs.* time and product compositions. The response factor of the azide **1-N₃** was assumed to be the same as that of **2**. Corrected total peak areas in experiments in which the half life of the substrate was a few hours or less with and without azide did not differ significantly, indicating similar response factors. In the slow reactions of **1-OMe** with formic acid buffers, fluorene was used as an internal standard; the rate constants were calculated from plots of ln(area substrate/area reference) *vs.* time.

Acknowledgements

The Swedish Science Research Council has supported this work financially.

References

- 1 Presented in part at the *Third European Symposium on Organic Reactivity* (ESOR III), Göteborg, Sweden, 1991.
- 2 C. W. Davies, *Ion Association*, Butterworths, London, 1962, pp. 77 and 168.
- 3 W. P. Jencks, *Chem. Soc. Rev.*, 1981, **10**, 345.
- 4 R. A. Sneen, G. R. Felt and W. C. Dickason, *J. Am. Chem. Soc.*, 1973, **95**, 638.
- 5 A. R. Katritzky and B. E. Brycki, *J. Phys. Org. Chem.*, 1988, **1**, 1, and references therein.
- 6 A. Thibblin, *J. Chem. Soc., Chem. Commun.*, 1990, 697.
- 7 I. Szele and H. Zollinger, *J. Am. Chem. Soc.*, 1978, **100**, 2811; Y. Hashida, R. G. M. Landells, G. E. Lewis, I. Szele and H. Zollinger, *J. Am. Chem. Soc.*, 1978, **100**, 2816.
- 8 A. Thibblin, *J. Chem. Soc., Perkin Trans. 2*, 1987, 1629.
- 9 A. Thibblin, *J. Phys. Org. Chem.*, 1992, in the press.
- 10 C. D. Richie and T. C. Hofelich, *J. Am. Chem. Soc.*, 1980, **102**, 7039.
- 11 A. Streitwieser, *Solvolytic Displacement Reactions*, McGraw-Hill, New York, 1962.
- 12 D. R. Boyd, R. A. S. McMordie, N. D. Sharma, R. A. More O'Ferrall and S. C. Kelly, *J. Am. Chem. Soc.*, 1990, **112**, 7822.
- 13 T. R. Stengle, Y.-C. E. Pan and C. H. Langford, *J. Am. Chem. Soc.*, 1972, **94**, 9037.
- 14 R. Anantaraman and K. R. Ramaswami Iyer, *Indian J. Chem.*, 1975, **13**, 1075.
- 15 C. A. Bunton and S. K. Huang, *J. Am. Chem. Soc.*, 1972, **94**, 3536.
- 16 C. Paradisi and J. F. Bunnett, *J. Am. Chem. Soc.*, 1985, **107**, 8223.
- 17 J. P. Richard and W. P. Jencks, *J. Am. Chem. Soc.*, 1984, **106**, 1396.
- 18 K. Ziegler and B. Schnell, *Ann. Chem.*, 1924, **437**, 242.

Paper 1/06053H

Received 29th November 1991

Accepted 7th April 1992