Rate and Product Analytical Study of the Solvolysis of 3-Chlorobenzyl Arenesulfonates in Aqueous 2,2,2-Trifluoroethanol

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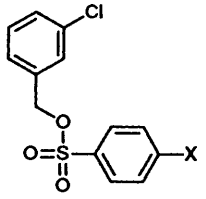
The rates of solvolysis of 3-chlorobenzyl 4-methyl-, 4-methoxy-, and 4-bromo-benzenesulfonates at different temperatures in 1:1 (v/v) 2,2,2-trifluoroethanol–water have been measured and the activation parameters determined. Qualitatively, the rate constants show the expected dependence upon the substituent in the benzenesulfonate leaving group, and the toluenesulfonate is 42 times less reactive (at 25 °C) than benzyl toluenesulfonate itself. In the product analytical study, the ratio of the 3-chlorobenzyl alcohol to the 3-chlorobenzyl trifluoroethyl ether was determined in each of the three cases, and shown to be independent of the nature of the nucleofuge. Introduction of the 3-chloro substituent into the electrophile, however, causes the selectivity for water as opposed to trifluoroethanol to be increased by *ca.* 50%. The results are discussed in terms of a substitution reaction which is concerted but not synchronous, a solvent-induced, largely uncoupled S_N2 mechanism.

The solvolysis of benzyl arenesulfonates has been investigated over many years, and both S_N1 and S_N2 mechanisms have been invoked to account for kinetics and product analytical results.[1–3] More recently, there has been a developing consensus that these reactions occur by a solvent-induced S_N2 mechanism, and the bond making and bond breaking processes, though concerted, may be synchronous to a variable degree depending upon the particular substrate and reaction conditions. There appears to be no firm evidence that these substrates react by a fully stepwise S_N1 mechanism involving an intermediate benzylic carbenium ion that can be intercepted by nucleophilic solutes. With hard nucleophiles such as hydroxylic solvents, bond making and breaking are largely uncoupled, whereas with soft nucleophilic solutes such as iodide and thiocyanate, the two aspects of the reaction are coupled.[4] It was necessary to extend our earlier investigation of the solvolysis of the parent benzyl toluene-*p*-sulfonate in aqueous trifluoroethanol in order to provide data essential for the interpretation of subsequent studies on the solvolysis of doubly substituted benzyl azoxyarenesulfonates.[5] We report here results of a limited investigation of the effects of substituents upon rates and selectivity in the solvolysis of compounds **1** in 1:1 (v/v) trifluoroethanol–water.



1a; X = CH_3
b; X = CH_3O
c; X = Br

Experimental

Methods.—All rate and product studies were of reactions carried out in aqueous trifluoroethanol made by mixing equal volumes of the two purified solvents. Rates of solvolysis of thermostatted reaction mixtures were measured by monitoring the decrease in UV absorbance with time. A calibration curve was constructed from the analysis of standard solutions of pure 3-chlorobenzyl alcohol in aqueous methanol by high performance liquid chromatography (HPLC). Reaction mixtures in aqueous trifluoroethanol were then analysed directly to give the absolute yields of the 3-chlorobenzyl alcohol product. In the solvolysis of the parent benzyl toluenesulfonate,[4] determination of absolute yields of both alcohol and ether products, and the absence of any other peaks in the chromatograms, established that these were the only two products. In the present study also, only two products were detected and shown to be the alcohol and trifluoroethyl ether. Consequently, the yield of the ether was taken to be (100% minus the measured absolute percentage yield of the alcohol).

2,2,2-Trifluoroethanol was heated under reflux over polyphosphoric acid then distilled onto molecular sieves (type 3 A) from which it was fractionally distilled (b.p. 74–75 °C). Water was distilled before being used in the solvolytic medium.

3-*Chlorobenzyl Toluene*-p-*sulfonate.*—Sodium hydride (0.178 g, 7.43 mmol) was added to 3-chlorobenzyl alcohol (1.06 g, 7.43 mmol) in dry diethyl ether and the reaction was stirred at room temperature for *ca.* 14 h then cooled to −25 °C. An ether solution of toluene-*p*-sulfonyl chloride (recrystallised; 1.42 g, 7.43 mmol) was added and the reaction mixture was maintained below 0 °C for a further 14 h before being filtered with minimum exposure to air. The filtrate was evaporated to leave a crystalline product which was recrystallised twice from pentane (0.38 g, 1.18 mmol, 16%, m.p. 79–81 °C, lit.,[6] 81.5–82 °C).

3-*Chlorobenzyl* 4-*Methoxybenzenesulfonate.*—This compound was made by the same method as the toluenesulfonate [18%, m.p. (recrystallised from diethyl ether) 49–51 °C; δ_H($CDCl_3$, 60 MHz) 7.90–6.75 (4 H, AB system), 7.12 (4 H, m), 4.89 (2 H, s) and 3.54 (3 H, s) (Found: C, 53.6; H, 4.2. Calc. for $C_{14}H_{13}ClO_4S$: C, 53.76, H, 4.19%)].

3-*Chlorobenzyl* 4-*Bromobenzenesulfonate.*—This compound was also made by the same method [22%, m.p. (recrystallised from diethyl ether–pentane) 51–53 °C; δ_H($CDCl_3$, 60 MHz) 7.76–7.45 (4 H, AB system), 7.25–6.98 (4 H, m) and 4.99 (2 H, s) (Found: C, 43.2; H, 2.80. Calc. for $C_{13}H_{10}BrClO_4S$: C, 43.18, H, 2.80)].

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Table 1 Rate constants and activation parameters for the solvolysis of 3-chlorobenzyl arenesulfonates in 1:1 (v/v) trifluoroethanol–water[a]

T/°C	k/10^{-5} s^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}
1a			
68.7	276	78	−67
59.7	135		
50.4	58.6		
29.9	7.41		
25.0	4.48[b]		
1b			
64.5	169	82	−57
51.7	48.1		
41.8	20.3		
34.5	8.52		
25.0	3.08[b]		
1c			
56.0	347	80	−51
42.7	100		
32.2	34.8		
21.4	10.2		
25.0	15.6[b]		

[a] Standard deviations on individual rate constant calculations were always <1%; the correlation coefficients on the Eyring calculations were always >0.999; estimated errors in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are 4 kJ mol^{-1} and 8 J K^{-1} mol^{-1}, respectively. [b] Calculated from the results at other temperatures.

Table 2 Product analysis for solvolysis of 3-chlorobenzyl arenesulfonates in 1:1 (v/v) trifluoroethanol[a]

Substrate	Alcohol[b] (%)	Ether[c] (%)
1a	87.9	12.1
1b	87.9	12.1
1c	89.2	10.8

[a] Averaged results; each reaction was carried out twice and each reaction mixture was analysed at least five times. [b] 3-Chlorobenzyl alcohol. [c] 3-Chlorobenzyl trifluoroethyl ether.

Product Analysis.—HPLC was carried out using Gilson instrumentation including a UV detector set at 257 nm and a Rheodyne 7125 valve incorporating a 20 mm^3 injection loop. A standard 25 cm, 5 μm Spherisorb C-18 reverse-phase column was used, and the water and HPLC grade methanol of the eluting medium were separately filtered before use. Each of a set of standard solutions of 3-chlorobenzyl alcohol (redistilled under reduced pressure) of concentrations 2.4 × 10^{-3}–18.6 × 10^{-3} mol dm^{-3} in 50% aqueous methanol was analysed at least five times to give a calibration correlation. Accurately weighed amounts of *ca.* 15 mg of the 3-chlorobenzyl arenesulfonate were then dissolved in 4.00 cm^3 of 1:1 (v/v) trifluoroethanol–water and, after *ca.* ten half-lives, the reaction mixture was analysed directly using the same analytical conditions as had been used in the calibration. Each reaction was carried out twice and each reaction mixture was analysed at least five times. The alcohol was analysed using 65:35 methanol–water as the eluent; the trifluoroethyl ether was also analysed in separate injections using 78:22 methanol–water as the eluent in order that the detector's alcohol–trifluoroethyl ether response factor could be determined. The pumping speed was 1.5 cm^3 min^{-1} in all analyses.

Kinetics.—Rates of solvolyses were measured by monitoring the decrease in UV absorbance at a wavelength between 230 and 260 nm (depending upon the compound) in the thermostatted cell compartment of a Pye Unicam SP8-300 spectrophotometer under the control of an Apple II microcomputer as previously described.[4,5] All reactions were monitored for *ca.* five half-lives, and rate constants were calculated automatically at the end of each run using a non-linear least-squares routine. Reactions were carried out at four temperatures covering at least 30 °C, then activation parameters and rate constants at a common temperature, 25 °C, were computed using the Eyring equation.[7]

Results

Rate results are given in Table 1. Whilst there is a good (though limited) Hammett correlation of rate constants at 25 °C, ρ = 1.37 (r > 0.999), there is no obvious trend in either the standard enthalpies or entropies of activation.

Absolute alcohol yields were determined from the calibration correlation obtained using standard solutions of purified 3-chlorobenzyl alcohol. The corresponding trifluoroethyl ether was not available in a sufficiently pure state to allow the same strategy to be followed for it. However, only the alcohol and ether were detected in these product mixtures, and it had been previously established that, in the parent case, the alcohol and ether together were the total product. Consequently, the absolute yield of the alcohol allowed the ether yield to be calculated by difference and the results are given in Table 2. (From the data leading to these results, the relative molar response factor of the detector towards alcohol and ether was determined since analyses for the ether had been carried out. This gave an average value of 1.10 ± 0.02 in good agreement with the value of 1.12 obtained earlier for the parent system by a different method. This was an important result for a subsequent product analytical study of solvolyses of a series of substituted benzyl azoxyarenesulfonates.)

Discussion

Introduction of the 3-chloro substituent into benzyl toluenesulfonate causes the rate constant to be reduced by a factor of 42 at 25 °C in this solvent. As far as the substituent effect upon the nucleofuge is concerned, a three-point Hammett plot is clearly insufficient to warrant any extended interpretation. Suffice it to state that the appreciably positive ρ value of 1.37 for this reaction in aqueous trifluoroethanol indicates the development of negative charge in the arenesulphonate nucleofuge in the activated complex. It may be compared with the result of 1.86 for the ethanolysis of 2-adamantyl arenesulfonates,[8] reactions which involve a stepwise mechanism and a fully developed negative charge in the nucleofuge in the rate-determining activated complex.[9] The present result indicates that the nucleofuge is largely but not wholly unbonded from the benzylic residue in the activated complex, and that this phase of the reaction is ahead of the formation of the new bond between the benzylic residue and the incoming nucleophile (solvent). This is fully in accord with other results for benzylic systems and the current view that benzyl arenesulfonates react with hard nucleophiles such as hydroxylic solvents by an uncoupled concerted S_N2 mechanism. The activation parameters support such an interpretation. The enthalpies of activation are large indicating that the bond making is lagging behind the bond breaking phase, and the substantially negative entropies of activation are as expected of a bimolecular reaction in which there is a loss of translational degrees of freedom in the formation of the activated complex. Comparable but authentic unimolecular reactions in this same medium do not have such negative entropies of activation.[4,10]

Perhaps the strongest evidence from the present study that the S_N2 mechanism of solvolysis of benzyl arenesulfonates is towards the uncoupled extreme comes from the product analyses. The yields, not surprisingly, indicate a selectivity of the

3-chlorobenzylic electrophile in favour of reaction with water rather than trifluoroethanol. This selectivity factor is 7.3 for 3-chlorobenzyl toluenesulfonate (**1a**) and should be compared with 4.9 for the reaction of the parent benzyl toluenesulfonate in the same medium,[4] an increase of *ca.* 50%. Clearly, the less reactive electrophile is appreciably more selective in partitioning between water and trifluoroethanol in accordance with expectation. Remarkably, the selectivity is the same within experimental error for **1a–c**; in other words, it is virtually independent of the nature of the nucleofuge. This indicates that the nucleofuge is only very weakly bonded in the transition state which is, therefore, towards the uncoupled end of the S_N2 range ('S_N1-like').

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