A Relationship between Selectivity and Solvent Composition for Nucleophilic Attack on Carbocations in Alcohol–Water Mixtures

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Rate constants and products of solvolyses of *p*-methoxybenzyl chloride **1**, chlorodiphenylmethane **2** (Y = Z = H), chloro(4-chlorophenyl)phenylmethane **2** (Y = H, Z = Cl) and chlorobis(4-chlorophenyl)methane **2** (Y = Z = Cl) are reported in ethanol– and methanol–water mixtures at 25 °C. Product selectivities (*S*), defined by:

$$S = [\text{ether product}][\text{water}]/[\text{alcohol product}][\text{alcohol solvent}]$$

are related to four rate constants for reactions involving one molecule of solvent as nucleophile and another molecule of solvent as general base catalyst (*e.g.* k_{wa} involves water as nucleophile and alcohol as general base, and k_{ww}, k_{aw} and k_{aa} are defined similarly). A linear relationship between $1/S$ and molar ratios of solvent

$$1/S = (k_{wa}/k_{aw})([\text{alcohol solvent}]/[\text{water}]) + k_{ww}/k_{aw}$$

is derived theoretically and validated experimentally for solvolyses of the above substrates from water up to 70% alcohol–water—in this range of solvents, the contribution from k_{aa} can be neglected. For solvolyses of *p*-methoxybenzyl chloride, *S* is independent of pH between pH 2 and 12, *S* decreases when acetone is added but increases if acetonitrile is added and for 90% ethanol–water *S* increases with added LiCl and $LiClO_4$ and increases further if acetonitrile is also present.

Solvolytic reactions in alcohol–water mixtures lead to alcohol and ether products from which selectivities can be calculated using eqn. (1).[1,2]

$$S = ([\text{ether product}]/[\text{alcohol product}]) \times ([\text{water}]/[\text{alcohol solvent}]) \quad (1)$$

Although considerable amounts of data are available on selectivities for solvolyses in alcohol–water mixtures,[3] systematic studies of individual substrates over a wide range of aqueous binary solvents are relatively rare. Reliable results in highly aqueous mixtures are difficult to obtain because of the increased rates of solvolysis and decreased solubilities,[4] but solubility problems can be flagged either visually or by deviations from first order kinetics at the start of a reaction (*e.g.* in conductimetric studies of $< 10^{-4}$ mol dm^{-3} solutions[4]). After establishing satisfactory mixing procedures from kinetics, parallel product studies can then be carried out at the same very low substrate concentrations by high performance liquid chromatography (HPLC).

From the wider range of selectivity data now becoming available, we are establishing relationships between selectivity and solvent composition in aqueous binary mixtures. Recent work was focussed on mechanistic changes which are observed in solvolyses of benzoyl[5] and benzenesulfonyl[6] chlorides because there are two competing reaction channels differing in sensitivity to solvent polarity. One of the reaction channels for solvolyses of benzoyl chloride is similar to the concerted reactions of *p*-nitrobenzoyl chloride in alcohol–water mixtures, which can be dissected into four competing reactions and a rate–product correlation can be observed.[7] The other reaction channel is similar to solvolyses of *p*-methoxybenzoyl chloride, which show a constant and low selectivity probably due to an S_N1 reaction *via* a solvent-separated ion pair;[8] *S* is < 1 for ethanol–water mixtures,[8a] probably because water inserts more easily than ethanol between the cation and the leaving group, and the leaving group then acts as a general base catalyst for nucleophilic attack by solvent on the cation.[1b,8]

We have now examined some other stepwise reactions, and we report rate constants and product data for four substrates which are known from kinetic evidence for common ion rate depression to be prone to solvolyse by S_N1 mechanisms *via* 'free' cations. The results provide sufficient data on alcohol–water selectivities (*S*) to support a new relationship between *S* and solvent composition for these S_N1 reactions. The solvent dependence of *S* values has the potential to provide a probe for the presence of cationic intermediates, complimenting the usual experiments involving added nucleophilic traps which have the disadvantage that they may induce mechanistic changes. If, in addition to the essentially constant selectivities for S_N1 reactions *via* solvent-separated ion pairs,[8] a well-defined solvent dependence of *S* could be established for product formation *via* 'free' carbocations, reactions *via* the two types of carbocations could be distinguished. Following earlier studies concerned mainly with the reactivity–selectivity debate,[1,2] the wider range of data now accessible and current interest in carbocations generated by laser-flash photolysis[9] encouraged further work on the solvent dependence of selectivities for solvolyses in aqueous alcohols.

Theory

Nucleophilic attack on carbocations may be general base catalysed,[10] and *S* values for S_N1 solvolyses in aqueous alcohols are often solvent-dependent,[3] contrary to simple expectations based on single solvent molecules competing to attack the carbocation intermediate. Nucleophilic attack may occur on 'free' carbocations, on solvent-separated ion pairs or possibly on contact ion pairs, and the solvent-dependence of *S* may be

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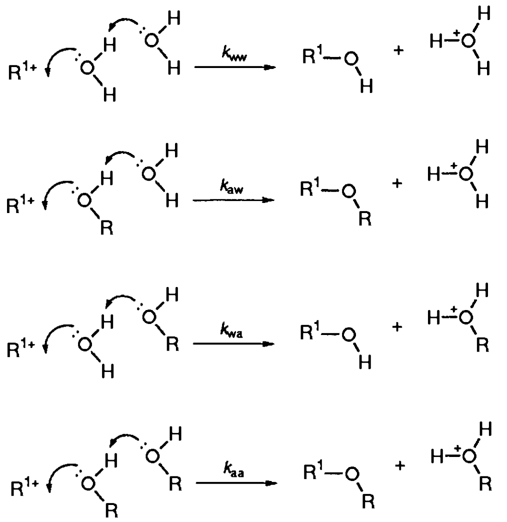
due to changes in the nature of the ion pair leading to product.[11] An alternative explanation involving nucleophilic attack solely on 'free' carbocations is given below to account for the solvent dependence of S for S_N1 reactions.

If nucleophilic attack by one solvent molecule were assisted by a second molecule of solvent acting as general base, in alcohol–water mixtures there will be four competing product-determining steps (Scheme 1) defined by the following third order rate constants: k_{ww} in which water is both nucleophile and general base; k_{aw}, the alcohol solvent (ROH) acts as nucleophile and water acts as general base; k_{wa}, water acts as nucleophile and alcohol acts as general base; k_{aa}, alcohol acts as both nucleophile and general base. These product-determining steps (Scheme 1) are irreversible under typical reaction conditions, and so the product ratios are determined by the rate constants multiplied by appropriate terms expressing the second order dependence on solvent (see below). For reactive carbocations, nucleophilic attack by solvent will be rapid relative to heterolysis, but the relative rates of irreversible product-determining steps *via* free carbocations should be independent of the rate constants determining the overall rate of the S_N1 reaction. Scheme 1 is of the same kinetic form as the one we have previously derived for acyl[7a,7b] and sulfonyl[7c] transfer reactions, and so the present work can be related directly to our previous studies.[7] However, for S_N1 reactions, there would not be any connection between the observed first order solvolysis rate constants and the third order rate constants controlling the selectivity values.



Scheme 1 General base catalysed reactions for nucleophilic attack of carbocations

We have previously shown that the molar (stoichiometric) concentrations of solvent lead to a quantitative relationship between derived third order rate constants and observed first order rate constants for solvolyses of *p*-nitrobenzoyl chloride[7b] and of *p*-nitrobenzenesulfonyl chloride.[7c] Although considerable attention has been paid to complex solvation effects,[3] the factors influencing reactivity are the very rapid microscopic effects which arise between the initial state and the transition state of a reaction. Our proposal is that the molar concentration of solvent is a good measure of the availability of the solvent in the dynamic situation accompanying a reaction. Consequently, we assume that the rates of reactions shown in Scheme 1 are given by third order rate constants multiplied by the appropriate molar concentrations of solvent. If, in highly aqueous media, k_{aw}[water][ROH] $\gg$ k_{aa}[ROH]^2, the relationship given in eqn. (2) can readily be derived.[7b,7d]

$$1/S = (k_{wa}/k_{aw})([\text{alcohol solvent}]/[\text{water}]) + k_{ww}/k_{aw} \quad (2)$$

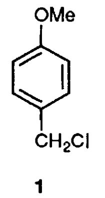
The intercept of eqn. (2) implies that the maximum S value in highly aqueous media is determined by the ratio of third order rate constants k_{aw}/k_{ww}; this ratio represents the rate of nucleophilic attack by alcohol compared with the rate of nucleophilic attack by water, in water as solvent and with water acting as a general base catalyst. A similar ratio can be determined in alcohol because, in highly alcoholic media if k_{wa}[water][ROH] $\gg$ k_{ww}[water]^2, the relationship given in eqn. (3) can be derived.[7b]

$$S = (k_{aw}/k_{wa})([\text{water}]/[\text{alcohol solvent}]) + k_{aa}/k_{wa} \quad (3)$$

The intercept of eqn. (3) implies that the minimum S value in highly alcoholic media is determined by the ratio of third order rate constants k_{aa}/k_{wa}, *i.e.* nucleophilic attack by alcohol or water occurring in alcohol with alcohol acting as the general base catalyst. Eqns. (2) and (3) lead to acceptable agreement between independent measures of k_{aw} and k_{wa} for solvolyses of *p*-nitrobenzoyl chloride[7b] and of *p*-nitrobenzenesulfonyl chloride,[7c] providing strong support for the concept of stoichiometric solvation.

The main purpose of the work described in this paper is to test whether there is a linear relationship between $1/S$ and the alcohol/water molar ratio, as predicted by eqn. (2). This would provide necessary evidence for the validity of the above theory, and also show that eqn. (2) was a valid empirical relationship. However, the success of eqn. (2) would not alone verify the theory, and would not imply that polar effects were absent from the product-determining step of S_N1 reactions of carbocations; eqn. (2) would fit the data if the third order rate constants were solvent-dependent, but the ratio of rate constants k_{aw}/k_{wa} were independent of solvent composition.

Suitable substrates on which to test eqn. (2) are those which react only by substitution pathways *via* 'free' carbocations. Also, the substrates should permit rapid mixing in highly aqueous mixtures, and should not be so reactive that their solvolyses are interfacial.[8a] We chose *p*-methoxybenzyl chloride **1**, which shows common ion rate depression in 50% v/v trifluoroethanol–water,[12] chlorodiphenylmethane **2** (Y = Z = H) which shows common ion rate depression in 80% acetone–water,[13] chloro(4-chlorophenyl)phenylmethane **2** (Y = H, Z = Cl), and chlorobis(4-chlorophenyl)methane **2** (Y = Z = Cl), which shows common ion rate depression in ethanol–trifluoroethanol mixtures.[14]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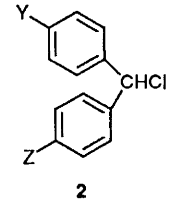

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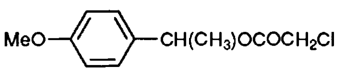
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Results

Rate constants for solvolyses chlorodiphenylmethane **2** (Y = Z = H) at 25 °C are summarised in Table 1 and results at various temperatures are given in Table 2 along with the corresponding Arrhenius parameters. Rate constants for solvolyses of chloro(4-chlorophenyl)phenylmethane **2** (Y = Cl, Z = H) are given in Table 3 and chlorobis(4-chlorophenyl)-

methane **2** (Y = Z = Cl) are given in (Table 4). At very low substrate concentrations (< 10^{-5} mol dm^{-3}) in highly aqueous media, it was necessary to remove carbon dioxide from the solvent to avoid a buffering effect.[20] Kinetic data for the chlorobis(4-chlorophenyl)methane **2** (Y = Z = Cl) in highly aqueous mixtures was more difficult to obtain because of its lower solubility.

Selectivity data were obtained from product analyses as soon as possible after completion of 10 half-lives of reaction. Data for chlorodiphenylmethane **2** (Y = Z = H) are given in Table 5, for chloro(4-chlorophenyl)phenylmethane **2** (Y = H, Z = Cl) in Table 6 and chlorobis(4-chlorophenyl)methane **2** (Y = Z = Cl) in Table 7. Selectivity data for *p*-methoxybenzyl chloride **1** was investigated in a wide range of alcohol–water mixtures (Table 8), at various pH values for 20% ethanol and 80% ethanol (Table 8), and in the presence of added acetone or acetonitrile without (Table 9) or with (Table 10) added salts.

Discussion

The kinetic data (Tables 1–4) show a 2–3 fold deactivating effect of each of the 4-chloro-substituents in solvolyses of **2** (Y = Z = H), **2** (Y = H, Z = Cl) and **2** (Y = Z = Cl). It was hoped that reliable selectivity data for the more aqueous solvents could be obtained for the less reactive substrates **2** (Y = Cl, Z = H) and **2** (Y = Z = Cl), but substitution of hydrogen by chlorine significantly increases hydrophobicity, as shown by HPLC retention times and by the difficulties in obtaining reliable kinetic data in highly aqueous media. Consequently, our studies of diphenylmethyl derivatives **2** are limited to solvolyses in 20 or 30% alcohol–water mixtures or solvents of higher alcohol contents. Solvolyses of **2** (Y = Z = H) in 30% methanol–water and **2** (Y = H, Z = Cl) in 20% ethanol–water give lower *S* values than expected, and solvolyses of the chloroacetate **3** in 10–30% methanol–water also show a decrease in *S* as the water concentration is increased;[21] however, the effects are small (< 10%) and azide ion was also present in solvolyses of **3** (*S* is influenced by the presence of anions—see discussion below). Also, solvolyses of *p*-methoxybenzyl chloride **1** show a consistent trend of increasing *S* as water is added to dilute the alcohol down to as low as 10% v/v alcohol–water (Table 8).

Table 1 Rate constants (k/s^{-1}) for solvolyses of chlorodiphenylmethane **2** (Y = Z = H) in aqueous alcohol mixtures[a] at 25 °C

Solvent composition[b]	k/s^{-1} Ethanol–Water	k/s^{-1} Methanol–Water
100	5.41×10^{-5} [c]	8.33×10^{-4} [c]
95	1.92×10^{-4} [c]	
90	4.87×10^{-4} [c]	3.74×10^{-3} [c]
80	1.72×10^{-3} [c]	$(1.38 \pm 0.01) \times 10^{-2}$
70	6.90×10^{-3} [d]	$(4.55 \pm 0.02) \times 10^{-2}$
60	1.77×10^{-2} [e]	1.59×10^{-1} [d]
50	$(5.90 \pm 0.10) \times 10^{-2}$	$(3.40 \pm 0.15) \times 10^{-1}$
40	2.26×10^{-1} [d,e]	1.10 ± 0.02
30	1.8 [f]	3.5 [f]
20	7.0 [f]	

[a] Determined conductimetrically in duplicate with the kinetic apparatus having a turbo-stirrer, except where stated otherwise; errors shown are average deviations. [b] % v/v Alcohol–water. [c] Data from ref. 15. [d] Data from ref. 16. [e] Data from ref. 17. [f] Calculated from data lower temperatures (see Table 2).

Selectivity values for solvolyses of *p*-methoxybenzyl chloride (Table 8) are in very good agreement (< 3% error) with our previously-published data,[19] showing the good reproducibility of the HPLC data. Also, the selectivity data in 70–90% ethanol–water (Tables 5–7) are in good agreement with independent studies of buffered solutions analysed by gas chromatography,[2] except for solvolyses of **2** (Y = H, Z = Cl) in 90% ethanol–water (Table 6). The lack of dependence of selectivities on pH is supported by studies of *p*-methoxybenzyl chloride **1** in 20 and 80% ethanol–water (Table 8), providing that excessive reaction times are avoided. For solvolyses of **1** in 20% ethanol–water at pH 2, *S* increases slowly for at least 30 h, but such reaction times correspond to thousands of half-lives. A control experiment showed that after 40 h in 20% ethanol–water at pH 2, *p*-methoxybenzyl alcohol reacts to give 3% ether.

Selectivity data from different investigators have in the past shown some surprisingly large variations. Selectivities could depend on the method of mixing and on the adequacy of buffering (*e.g.* the earlier studies[1a] of solvolyses of chlorodiphenylmethyl derivatives **2** in 70% ethanol–water are not in agreement with later work; Tables 5–7).

Plots of $1/S$ *versus* the molar ratio of alcohol/water [eqn. (2)] are linear from 30% to at least 70% alcohol–water mixtures (Table 11), and thereafter curvature is significant (Figs. 1–4) consistent with increasing contributions from the k_{aa} term. Selectivities for methanol–water are significantly greater than for ethanol–water, and the slopes of $1/S$ plots are lower for methanol–water than for ethanol–water (Table 11). These

Table 2 Rate constants (k/s^{-1}) for solvolyses of chlorodiphenylmethane **2** (Y = Z = H) in aqueous alcohol mixtures[a]

Solvent[b]	T/°C	k/s^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}
50% EtOH	0.0 [d]	$(2.87 \pm 0.01) \times 10^{-3}$	19.0	−0.4
50% EtOH	25.0 [d]	$(5.91 \pm 0.02) \times 10^{-2}$		
30% EtOH	−10.0 [e]	$(2.97 \pm 0.02) \times 10^{-2}$	17.8	2.2
30% EtOH	0.0 [e]	$(1.07 \pm 0.02) \times 10^{-1}$		
30% EtOH	25.0 [c]	1.8 [c]		
20% EtOH	−10.0 [f]	$(9.70 \pm 0.09) \times 10^{-2}$	18.6	7.6
20% EtOH	0.0 [f]	$(3.69 \pm 0.05) \times 10^{-1}$		
20% EtOH	25.0 [c]	7.0 [c]		
40% MeOH	10.0 [e]	$(2.43 \pm 0.03) \times 10^{-1}$	16.3	−3.6
40% MeOH	25.0 [d]	1.10 ± 0.02		
30% MeOH	−10.0 [f]	$(7.00 \pm 0.09) \times 10^{-2}$	17.0	0.8
30% MeOH	0.0 [f]	$(2.38 \pm 0.04) \times 10^{-1}$		
30% MeOH	25.0 [c]	3.5 [c]		

[a] Determined conductimetrically at least in duplicate with the turbo-stirrer apparatus; errors shown are average deviations and the kinetic runs were performed by injecting a dilute solution of chlorodiphenylmethane in dry acetonitrile after removing carbon dioxide from highly aqueous alcohols (20% EtOH, 30% MeOH, 30% EtOH, 40% MeOH) either by using an ultrasonic bath for 15 min or by adding 5 mm^3 of 1% chlorodiphenylmethane in dry acetonitrile to each solvent (5 mm^3) before the kinetic run to remove the buffering effect (*i.e.* double injection). [b] % v/v alcohol–water. [c] Calculated from Arrhenius plots. [d] Injected 25 mm^3 of 1% (v/v) substrate in dry acetonitrile. [e] Injected 25 mm^3 of 0.3% (v/v) substrate in dry acetonitrile. [f] Injected 25 mm^3 of 0.2% (v/v) substrate in dry acetonitrile.

Table 3 Rate constants (k/s^{-1}) for solvolyses of chloro(4-chlorophenyl)phenylmethane **2** (Y = Cl, Z = H) in aqueous alcohol mixtures[a] at 25 °C

Solvent composition[b]	k/s^{-1} Ethanol–Water	 Methanol–Water
100	2.06×10^{-5}[c]	2.97×10^{-4}[c]
90	$(2.05 \pm 0.01) \times 10^{-4}$[e]	$(1.42 \pm 0.01) \times 10^{-3}$[e]
80	$(7.28 \pm 0.05) \times 10^{-4}$[e]	$(5.18 \pm 0.02) \times 10^{-3}$[e]
70	$(2.20 \pm 0.01) \times 10^{-3}$[e]	$(1.71 \pm 0.01) \times 10^{-2}$[e]
60	$(6.11 \pm 0.03) \times 10^{-3}$[f]	$(4.91 \pm 0.03) \times 10^{-2}$[f]
50	$(1.95 \pm 0.01) \times 10^{-2}$[d,g]	$(2.41 \pm 0.08) \times 10^{-1}$[d,g]
40	$(9.28 \pm 0.04) \times 10^{-2}$[d,h]	$(5.1 \pm 0.2) \times 10^{-1}$[d,i]
30	$(6.51 \pm 0.06) \times 10^{-1}$[d,j]	1.11 ± 0.07[d,k]

[a] Determined as described in Table 1 (footnote *a*). [b] % v/v Alcohol–water. [c] Data from ref. 18*a*. [d] Repeated three times. [e] Injected 10 mm^3 of 10% (v/v) substrate in dry acetonitrile. [f] Injected 10 mm^3 of 3% (v/v) substrate in dry acetonitrile. [g] Injected 10 mm^3 of 1% (v/v) substrate in dry acetonitrile. [h] Injected 25 mm^3 of 0.5% (v/v) substrate in acetonitrile. [i] Injected 20 mm^3 of 0.2% (v/v) substrate in dry acetonitrile after a preliminary injection of 5 mm^3 of a 1% solution. [j] Injected 25 mm^3 of 0.3% (v/v) substrate in dry acetonitrile; other data at 25 °C, $k = (7.85 \pm 0.05) \times 10^{-2}\,s^{-1}$, $\Delta H^{\ddagger} = 16.9$ kcal mol^{-1}, $\Delta S^{\ddagger} = -2.78$ cal K^{-1} mol^{-1}. [k] Injected 20 mm^3 of 0.2% (v/v) substrate in dry acetonitrile after a preliminary injection of 5 mm^3 of a 2% (v/v) solution.

Table 4 Rate constants (k/s^{-1}) for solvolyses of chlorobis(4-chlorophenyl)methane **2** (Y = Z = Cl) in aqueous alcohol mixtures[a] at 25 °C

Solvent composition[b]	k/s^{-1} Ethanol–Water	 Methanol–Water
100	8.07×10^{-6}[c]	1.15 ± 10^{-4}[c]
90	$(8.11 \pm 0.20) \times 10^{-5}$[e]	$(5.37 \pm 0.10) \times 10^{-4}$[e]
80	$(2.85 \pm 0.01) \times 10^{-4}$[e]	$(1.97 \pm 0.01) \times 10^{-3}$[e]
70	$(8.03 \pm 0.06) \times 10^{-4}$[e]	$(6.76 \pm 0.03) \times 10^{-3}$[e]
60	$(2.01 \pm 0.02) \times 10^{-3}$[d,f]	$(1.72 \pm 0.03) \times 10^{-2}$[d,g]
50	$(6.53 \pm 0.10) \times 10^{-3}$[d,g]	$(5.58 \pm 0.10) \times 10^{-2}$[d,h]
40	$(3.30 \pm 0.02) \times 10^{-2}$[d,i]	$(1.90 \pm 0.02) \times 10^{-1}$[d,j]
30	$(1.89 \pm 0.02) \times 10^{-1}$[d,j]	$(5.0 \pm 0.02) \times 10^{-1}$[d,k]
20	1.06 ± 0.03[d,l]	

[a] Determined as described in Table 1 (footnote *a*). [b] % v/v Alcohol–water. [c] Data from ref. 18*b*. [d] Repeated three times. [e] Injected 10 mm^3 of 10% (w/w) substrate in dry acetonitrile. [f] Injected 10 mm^3 of 3% (w/w) substrate in dry acetonitrile. [g] Injected 15 mm^3 of 1% (w/w) substrate in dry acetonitrile. [h] Injected 25 mm^3 of 0.5% (w/w) substrate in dry acetonitrile. [i] Injected 25 mm^3 of 0.3% (w/w) substrate in dry acetonitrile. [j] Injected 25 mm^3 of 0.2% (w/w) substrate in dry acetonitrile. [k] Injected 20 mm^3 of 0.1% (w/w) substrate in dry acetonitrile. [l] Injected 15 mm^3 of 0.1% (w/w) after a preliminary injection of 5 mm^3 of 0.2% substrate in dry acetonitrile.

trends can be explained by the k_{aw} term, which compared with the k_{wa} term, is greater for methanol–water than for ethanol–water.

The intercepts of eqn. (2) (Table 11) are determined by the ratio of third order rate constants k_{ww}/k_{aw}, so nucleophilic attack by methanol assisted by water is 7–8 times more favourable than nucleophilic attack by water assisted by water. Similarly, attack by ethanol is about 4–5 times faster than attack by water. S values in 90–95% alcohol–water correspond approximately to the intercepts of eqn. (3) (k_{aa}/k_{wa}). Consequently, nucleophilic attack by methanol in methanol is about 4 times faster than nucleophilic attack by water in methanol, whereas attack by ethanol in ethanol is only twice as fast as attack by water in ethanol. Hence a change in solvent from water to alcohol approximately halves the rate ratios for nucleophilic attack by alcohol compared with attack by water.

Table 5 Product selectivities [S; eqn. (1)] for solvolyses of chlorodiphenylmethane **2** (Y = Z = H) in alcohol–water mixtures[a] at 25 °C

Solvent composition[b]	S Ethanol–Water	 Methanol–Water
95	(2.32)[c]	4.2
90	2.5 (2.54)[c] (2.16)[d]	4.5
80	2.8 (2.78)[c] (2.60)[d]	5.2
70	3.3[e] (3.25)[c] (3.02)[d]	5.7[e]
60	3.7[e] (3.20)[d]	6.3[e]
50	4.0[e] (3.76)[d]	6.8[e]
40	4.4[f]	7.7[f]
30	4.6[f]	7.4[f]

[a] Determined after 10 half-lives by response-calibrated reversed-phase HPLC at least in duplicate and usually four times for each two independent samples; typical errors 2–5%; relative response factor: 0.997 (ethanol–water), 0.960 (methanol–water). [b] Volume percent (v/v %). [c] Data from ref. 2*a*. [d] Data from ref. 2*b*. [e] 10% substrate in dry acetonitrile (14 mm^3) was injected into the turbo-stirrer apparatus containing alcohol–water mixtures. [f] 1% substrate (14 mm^3) were injected into the turbo-stirrer apparatus containing aqueous alcohol solvent mixtures.

Table 6 Product selectivities [S; eqn. (1)] for solvolyses of chloro(4-chlorophenyl)phenylmethane **2** (Y = H, Z = Cl) in alcohol–water mixtures[a] at 25 °C

Solvent composition[b]	S Ethanol–Water	 Methanol–Water
95	(2.03)[c]	
90	1.5[d] (2.14)[c]	3.3
80	2.6 (2.49)[c]	4.3[e]
70	3.1[e] (2.84)[c]	5.7[e]
60	3.5[f]	6.4[f]
50	4.0[g]	7.0[g]
40	4.1[g]	7.5[g]
30	4.3[h]	7.8[h]
20	3.8[i]	

[a] Determined as described in Table 5 (footnote *a*); relative response factor at 230 nm, 260 nm: 1.36, 1.07 (ethanol–water), 1.33, 1.07 (methanol–water); performed by injecting a dilute solution of substrate in dry acetonitrile (14 mm^3) into the turbo-stirrer apparatus containing alcohol–water (7 cm^3), except 90% methanol–water and 80% ethanol–water mixtures where 10 mm^3 of 10% substrate in dry acetonitrile was injected into ampoules containing alcohol–water mixtures (5 cm^3). [b] % v/v Alcohol–water. [c] Data from ref. 2*a*. [d] $S = 1.4$ after 500 half-lives. [e] Injected 10 mm^3 of 10% substrate in dry acetonitrile (λ 260 nm). [f] Injected 14 mm^3 of 3% substrate in dry acetonitrile (λ 260 nm). [g] Injected 14 mm^3 of 1% substrate in dry acetonitrile (λ 230 nm). [h] Injected 14 mm^3 of 0.5% substrate in dry acetonitrile (λ 230 nm). [i] Double injection of 14 mm^3 of 0.1% substrate in dry acetonitrile (λ 230 nm).

Studies of alcohol–alcohol selectivities in ternary solvent systems containing 50 vol% water[22] could involve three general base catalysts (water and the two alcohols) for each nucleophile; the observed selectivities probably represent mainly nucleophilic attack by alcohol with water as the general base catalyst.

Addition of acetone (Table 9) decreases selectivities for solvolyses of *p*-methoxybenzyl chloride **1**, in agreement with previous work on solvolyses of derivatives of **2**.[2] In contrast, addition of acetone to solvolyses of diphenylmethyl *p*-nitrobenzoate leads to an increase in S.[2b] Addition of acetonitrile leads to increases in S for solvolyses in 90% alcohol–water, but S decreases for 30% alcohol solvents (Table 9). Hence the effect of cosolvent is complex, and cannot be explained solely by a reduction in solvent polarity

Table 7 Product selectivities [S; eqn. (1)] for solvolyses of chlorobis(4-chlorophenyl)methane **2** ($Y = Z = Cl$) in alcohol–water mixtures[a] at 25 °C

	S	
Solvent composition[b]	Ethanol–Water	Methanol–Water
95	(1.93)[c]	
90	2.1[d] (2.03)[c]	3.6
80	2.4 (2.41)[c]	4.1
70	3.0 (2.75)[c]	4.8[d]
60	3.5[e]	5.4[e]
50	3.9[e]	6.2[e]
40	4.4[f]	6.8[f]
30	4.6[g]	7.1[g]

[a] Determined as described in Table 5 (footnote *a*); relative response factor at 230 nm, 268 nm: 0.99, 0.89 (ethanol–water), 1.05, 1.05 (methanol–water); performed by injecting dilute solutions of substrate in dry acetonitrile (14 mm³) into the turbo-stirrer apparatus containing alcohol–water (7 cm³), except 90% E, 80% E, 70% E, 60% E, 90% M and 80% M (E = ethanol–water, M = methanol–water); 10 mm³ of 10% substrate in dry acetonitrile was injected into ampoules (5 cm³) containing alcohol–water mixtures. [b] % v/v Alcohol–water. [c] Data from ref. 2*a*. [d] Injected 10 mm³ of 10% substrate in dry acetonitrile (λ 268 nm). [e] Injected 14 mm³ of 3% substrate in dry acetonitrile (λ 268 nm). [f] Injected 14 mm³ of 1% substrate in dry acetonitrile (λ 230 nm). [g] Injected 14 mm³ of 0.3% substrate in dry acetonitrile (λ 230 nm).

Table 8 Product selectivities [S; eqn. (1)] for solvolyses of *p*-methoxybenzyl chloride **1** in alcohol–water mixtures[a] at 25 °C

	S	
Solvent composition[b]	Ethanol–Water[c]	Methanol–Water[c]
90	1.7 (1.7)	3.6 (3.6)
80	2.0[d] (2.0)	3.7 (3.8)
70	2.3	4.0
60	2.7 (2.7)	4.8 (4.8)
50	3.2	5.3
40	3.7 (3.6)	5.7 (5.8)
30	4.1	6.3
20	4.3[e,f] (4.4)	6.3[e] (6.4)
10	4.8[e]	7.2[e]

[a] Determined as described in Table 5 (footnote *a*); relative response factor: 1.00 (ethanol–water), 1.06 (methanol–water). [b] % v/v Alcohol–water. [c] Performed by injecting 10% substrate in dry acetonitrile (14 mm³) into either a sample tube or an ampoule (prior to sealing) containing alcohol–water mixtures (5 cm³); values in parentheses are from ref. 19. [d] At pH 2, S is 2.0 and at pH 12, S is 1.9. [e] Performed by injecting 10% substrate in dry acetonitrile (14 mm³) into the turbo-stirrer apparatus containing alcohol–water mixtures (7 cm³). [f] At pH 2, S is 4.3 and at pH 12, S is 4.2.

Table 9 Effect of aprotic solvents on selectivities [S; eqn. (1)] for solvolyses of *p*-methoxybenzyl chloride **1** in alcohol–water mixtures[a] at 25 °C

Protic solvent (% v/v)	Added cosolvent		
	None	50% $(CH_3)_2CO$	50% CH_3CN
90% EtOH	1.7	1.6	2.5
30% EtOH	4.1	2.6	3.6
90% MeOH	3.6	2.5	4.0
30% MeOH	6.3	3.3	4.4

[a] Determined as described in Table 5 (footnote *a*).

caused by the addition of the aprotic cosolvent[2a] or by changes in solvent activities.[23]

The effect of added salts is to increase S values (Table 10), consistent with a preferential dehydrating effect of the added salt. Significant changes in S are observed when 1 mol dm⁻³ lithium chloride or lithium perchlorate are added to 90% alcohol–water. Under these conditions, water is in a 5.5-fold molar excess compared to salt. If each ion preferentially bound

Table 10 Effect of added salts on selectivity [S; eqn. (1)] for the solvolyses of *p*-methoxybenzyl chloride **1** in aqueous alcohol mixtures[a,b] at 25 °C

	S			
Salt	90E	90E + AN[c]	90M	90M + AN[c]
None[d]	1.7	2.5	3.6	4.0
0.1 mol dm⁻³ LiCl	1.7	2.5	3.4	3.9
1.0 mol dm⁻³ LiCl	2.1	3.7	3.9	4.8
0.1 mol dm⁻³ $LiClO_4$	1.9	2.7	3.3	3.8
1.0 mol dm⁻³ $LiClO_4$	2.9	3.9	4.1	4.6

[a] Determined as described in Table 5 (footnote **a**); AN = acetonitrile, 90E = ethanol–water (90:10 v/v %), 90M = methanol–water (90:10 v/v %). [b] Concentration of salts were made up by mixing a calculated amount of salt and aqueous alcohol after vacuum drying at 100 °C. [c] Mixed aqueous alcohol (+ salt if any) with an equal volume of acetonitrile (50:50 v/v %), so the molarity of salt is then half of the value given in column 1.[d] From Table 9.

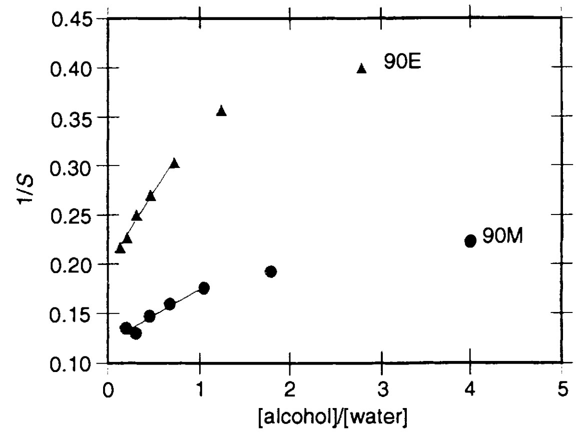

Fig. 1 Plot of $1/S$ *vs.* alcohol/water molar ratio [eqn. (2)] for solvolyses of chlorodiphenylmethane **2** ($Y = Z = H$); the symbol (▲) refers to ethanol–water mixtures and (●) refers to methanol–water mixtures; S values from Table 5 and statistical data given in Table 11

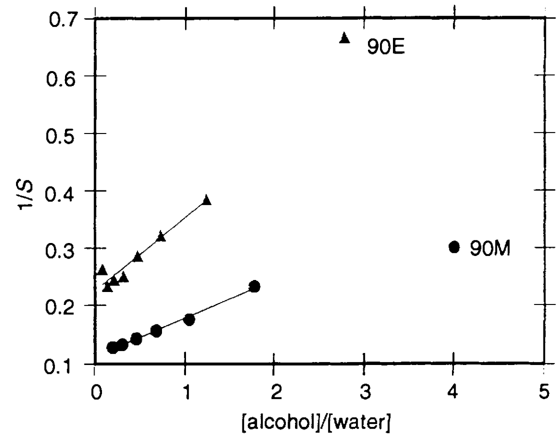

Fig. 2 Plot of $1/S$ *vs.* alcohol/water molar ratio [eqn. (2)] for solvolyses of chloro(4-chlorophenyl)phenylmethane **2** ($Y = H, Z = Cl$); the symbol (▲) refers to ethanol–water mixtures and (●) refers to methanol–water mixtures; S values from Table 6 and statistical data given in Table 11

Table 11 Correlations between 1/*S* and molar ratio of alcohol/water [eqn. (2)]

Substrate	Solvents	Slope	Intercept	Correl. coeff.
2 (Y = Z = H)[a]	30–70% EtOH	0.147 ± 0.008	0.199 ± 0.004	0.995
2 (Y = Z = H)[a]	30–70% MeOH	0.053 ± 0.007	0.121 ± 0.004	0.973
2 (Y = H, Z = Cl)[b]	20–80% EtOH	0.127 ± 0.015	0.226 ± 0.009	0.967
2 (Y = H, Z = Cl)[b]	30–80% MeOH	0.065 ± 0.003	0.113 ± 0.002	0.997
2 (Y = Z = Cl)[c]	30–70% EtOH	0.201 ± 0.008	0.190 ± 0.003	0.997
2 (Y = Z = Cl)[c]	30–70% MeOH	0.082 ± 0.005	0.125 ± 0.003	0.994
1[d]	10–70% EtOH	0.334 ± 0.014	0.203 ± 0.005	0.996
1[d]	10–60% EtOH	0.370 ± 0.012	0.198 ± 0.003	0.998
1[d]	10–70% MeOH	0.105 ± 0.006	0.141 ± 0.003	0.993

[a] See Fig. 1. [b] See Fig. 2. [c] See Fig. 3. [d] See Fig. 4.

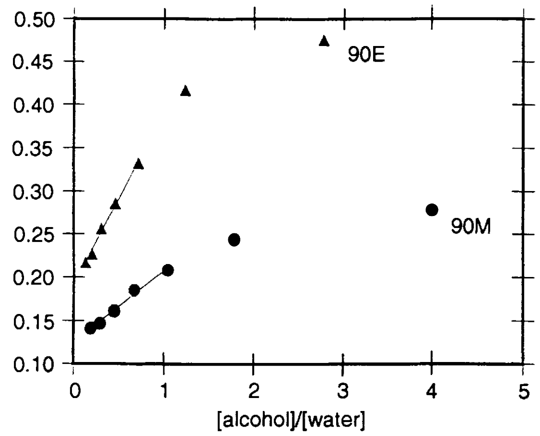

Fig. 3 Plot of 1/*S* *vs.* alcohol/water molar ratio [eqn. (2)] for solvolyses of chlorobis(4-chlorophenyl)methane **2** (Y = Z = Cl); the symbol (▲) refers to ethanol–water mixtures and (●) refers to methanol–water mixtures; *S* values from Table 7 and statistical data given in Table 11

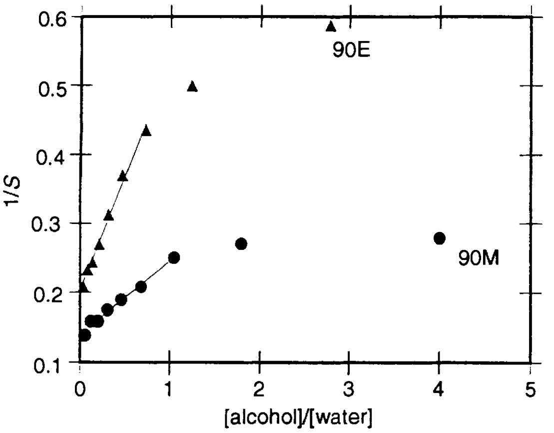

Fig. 4 Plot of 1/*S* *vs.* alcohol/water molar ratio [eqn. (2)] for solvolyses of *p*-methoxybenzyl chloride **1**; the symbol (▲) refers to ethanol–water mixtures and (●) refers to methanol–water mixtures; *S* values from Table 8 and statistical data given in Table 11

several water molecules, and only free solvent could react, the sharp increase in *S* can be explained. Hence, alcohol–water selectivities are likely to be affected significantly by the presence of anions such as azide ion,[3,10c,21] and it will be difficult to use *S* values as a probe for salt-induced changes in product-determining steps.

Counteranions from the leaving group may influence selectivity of carbocations, if their departure from the reaction site is not achieved before the nucleophile attacks. Similar results were obtained for derivatives of **2** with chloride and *p*-nitrobenzoate leaving groups at different temperatures,[2b] but bromodiphenylmethane is reported[2a] to give higher selectivities than the chloride **2** (Y = Z = H). Further work is needed on this aspect of selectivities.

Conclusion

Given the selectivity (*S*) defined by eqn. (1), there is a linear relationship between 1/*S* and the molar solvent ratio [eqn. (2)] for S_N1 solvolyses within the solvent range water to 60% alcohol–water mixtures for the following substrates: *p*-methoxybenzyl chloride **1**, chlorodiphenylmethane **2** (Y = Z = H), chloro(4-chlorophenyl)phenylmethane **2** (Y = H, Z = Cl), and chlorobis(4-chlorophenyl)methane **2** (Y = Z = Cl). In addition to being useful for interpolations, as the Grunwald–Winstein equation is for rate data, eqn. (2) may be applicable to many other substrates. As *S* is approximately constant for solvolyses *via* solvent-separated ion pair intermediates,[8a] eqn. (2) may help to identify the nature of cationic intermediates, and so may help to identify changes in product-determining steps. Nucleophilic attack occurs in the rate order: MeOH > EtOH > water, with larger rate differences in water than in alcohol.

Experimental

Materials.—*p*-Methoxybenzyl chloride **1**, chlorodiphenylmethane **2** (Y = Z = H), and chloro(4-chlorophenyl)phenylmethane **2** (Y = H, Z = Cl), obtained from Lancaster MTM, were distilled under reduced pressure and were checked for purity by HPLC of the compound and/or of the corresponding methanolysis product; both diphenylmethane derivatives **2** showed an impurity peak which could not be removed by repeated distillation but which did not interfere with the peaks of interest. Chlorobis(4-chlorophenyl)methane **2** (Y = Z = Cl), obtained from the corresponding alcohol (Lancaster MTM) by stirring with conc. hydrochloric acid,[24] was recrystallised from light petroleum–chloroform m.p. 62 °C (lit.,[18b] 63 °C), and was also shown to be pure by HPLC of the alcoholysis products. Acetonitrile (Fisons, HPLC grade), acetone (AR grade), ethanol and methanol for solvolyses were dried by standard methods,[7b] and aqueous mixtures were prepared by mixing appropriate volumes at ambient temperatures. Methanol for HPLC was AR grade.

Kinetic Methods.—The rapid response conductimetric method was employed, as described recently.[7b] Product studies for the fastest reactions were carried out in a similar apparatus.[7b]

Chromatography.—A Spherisorb S5 ODS2 column (15 cm × $\frac{1}{4}''$), having about 8500 theoretical plates, was used with an HPLC system consisting of a Perkin-Elmer ISS 101 autosampler; LDC Milton Roy Constametric 3000 solvent pump; LDC Milton Roy Spectromonitor 3100 variable wavelength UV detector (usually set between 260 and 274 nm but reduced to 230 nm for studies of the most dilute solutions), and a Hewlett Packard 3395 integrator/plotter. Eluents were 70% methanol–water for **2** (Y = Z = H), 80% methanol–water for **2** (Y = H, Z = Cl), and 85% methanol–water for **2** (Y = Z = Cl). Relative response factors (Tables 5–8) refer to peak areas (ether/alcohol).

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