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Kinetics and mechanisms of solvolysis of 3-chloro-3-ethylpentane in alcohols as solvents. Application of multiparametric equations and factor analysis to the solvolytic reactions of *tert*-alkyl halides

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ABSTRACT: This paper introduces a new set of rate constants for solvolysis of 3-chloro-3-ethylpentane in eight monoalcohols, from methanol to 2-methylbutan-1-ol, and in 10 dialcohols, from ethane-1,2-diol to pentane-1,5-diol, and also in diethylene and triethylene glycol. These results together with previous obtained data for several solvolytic reactions of *tert*-alkyl halides (2-iodo-2-methylpropane, 2-bromo-2-methylpropane, 2-chloro-2-methylpropane, 2-bromo-2-methylbutane, 2-chloro-2-methylbutane and 3-chloro-3-methylpentane) in the same mono- and dialcohols were studied by means of a standard multiparametric approach and by target factor analysis (TFA). TFA provides an open criterion for selecting the quantity and nature of the possible causes of the variation in the rate constants. The results allow one to identify and quantify the dominant solute–solvent interaction mechanisms affecting the reactions. Solvent dipolarity, polarizability and hydrogen bond donor acidity are the main influences on reactivity, although mono- and dialcohols behave differently. Copyright © 2001 John Wiley & Sons, Ltd.

KEYWORDS: solvolytic reactions; *tert*-alkyl halides; linear solvation relationships; target factor analysis

INTRODUCTION

New experimental values of rate constants were determined for the solvolysis of 3-chloro-3-ethylpentane in hydroxylic solvents, mono- and dialcohols, in order to identify the main interactions which take place between solvent and solute molecules using linear solvation energy relationships (LSER). Multiparameter correlations of the logarithm of the rate constants, log k, or of the Gibbs energy of activation, $\Delta\ddagger G$, with empirical solvent parameters have already been reported, previously.[1–4]

This study is extended here to solvolytic reactions on a wider range of substrates: 2-iodo-2-methylpropane, 2-bromo-2-methylpropane, 2-chloro-2-methylpropane, 2-bromo-2-methylbutane, 2-chloro-2-methylbutane, 3-chloro-3-methylpentane and 3-chloro-3-ethylpentane. All the solvents studied were alcohols, eight mono- and ten dialcohols. The behaviour of each reaction was fitted to a previously proposed model. As most suitable for evaluation of the medium effects, we chose the Gonçalves, Albuquerque and Simões (GAS) empirical equation[4] together with the Taft, Abboud, Kamlet and Abraham (TAKA) equation.[5]

In addition, we opted for target factor analysis (TFA), which provides a less arbitrary criterion for identifying the possible causes of variations in the data. This avoids some *a priori* tendentious hypotheses.[6,7] To the best of our knowledge, this is the first time that TFA methodology has been applied to such kinetic results.

Experimental

All the mono- and dialcohols used are listed in the second column of Table 1. They were obtained from BDH and Merck with 99% purity or better and were carefully dried over appropriate molecular sieves to keep the content of water $<0.02\%$ before use. The substrate 3-chloro-3-ethylpentane was synthesized by us and purified by distillation under reduced pressure. Its purity was tested by gas chromatography and mass spectrometry.

Conductance measurements were carried out with a Wayne–Kerr B905 bridge regulated and controlled by a computer. The temperature control in the reaction cells was always better than $\pm 0.01\,^{\circ}C$.[1]

At least three different runs were carried out to obtain a mean value for each rate constant. Good agreement was found, the mean deviation always being $<2\%$.

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Table 1. Rate constants, $10^6 k$ (s^{-1}), for the solvolysis of 3-chloro-3-ethylpentane (3-Cl-3-EtPe) in alcohols at 25.00 °C

No.	Solvent	3-Cl-3-EtPe
1	Methanol	7.773
2	Ethanol	1.491
3	Propan-1-ol	1.907
4	Propan-2-ol	2.053
5	Butan-1-ol	1.797
6	Butan-2-ol	2.144
7	2-Methylpropan-1-ol	1.417
8	2-Methylbutan-1-ol	1.129
9	Ethane-1,2-diol	63.73
10	Propane-1,2-diol	5.247
11	Propane-1,3-diol	16.36
12	Butane-1,2-diol	1.908
13	Butane-1,3-diol	2.944
14	Butane-1,4-diol	4.574
15	Butane-2,3-diol	1.482
16	Pentane-1,5-diol	2.259
17	Diethylene glycol	5.616
18	Triethylene glycol	2.510

Results and Discussion

A new collection of rate constants, *k*, for the solvolysis of 3-chloro-3-ethylpentane (3-Cl-3-EtPe) in eight monoalcohols, from methanol to 2-methylbutan-1-ol, and 10 dialcohols, from ethane-1,2-diol to pentane-1,5-diol, and also diethylene and triethylene glycol, were determined experimentally at 25.00 °C.

The reactions follow first-order kinetics and conductance values, *G*, obtained at regular intervals of time, were analysed with the Kezdy–Swinbourne method.[8]

$$G_t = G_{t\infty}(1 - e^{k\Delta t}) + e^{k\Delta t} G_{t+\Delta t} \qquad (1)$$

Where the subscripts t, t_∞ and $t + \Delta t$ denote the conductance at time t, infinite time and $t + \Delta t$, where Δt is a constant period of time. A computer program yields the k values from the best statistically determined straight line obtained from the pairs of points (G_t, $G_{t+\Delta t}$).

All the observed kinetics show an experimental error of <1% in k (s^{-1}). The mean values of the rate constants are presented in the third column of Table 1. In Table 2, we give all the available experimental data (log *k*) for the solvolytic reactions of *tert*-alkyl halides obtained in our laboratory for the same range of solvents. Both methodologies, the classical multiparametric approach and TFA, were performed based on the data matrix. Table 2 also shows the best data submatrix (**A** to **D**) used in TFA.

Linear solvation energy relationships

In their pioneering multiparameter approach to the influence of solvents, Koppel and Palm[10] suggested that

Table 2. Values of $-\log k$ for the solvolysis of *tert*-alkyl halides in alcohols (25.00 °C), with data submatrices **A**, **B**, **C** and **D** used in TFA methodology

		Substrate						
No.	Solvent	*t*-BuI[a]	*t*-BuBr[a]	*t*-BuCl[a]	2-Br-2-MeBu[b]	2-Cl-2-MeBu[b]	3-Cl-3-MePe[b]	3-Cl-3-EtPe
		A			**B**			
1	Methanol	3.91	4.46	6.06	4.05	5.65	5.34	5.11
2	Ethanol	4.65	5.36	7.07	4.87	6.41	6.04	5.83
3	Propan-1-ol	4.86	5.44	7.33	5.09	6.70	6.39	5.72
4	Propan-2-ol	5.05	5.67	7.80	5.25	6.16	6.11	5.69
5	Butan-1-ol	4.95	5.61	7.52	5.30	6.14	5.78	5.75
6	Butan-2-ol	5.40	5.78	8.10	5.58	5.69	5.52	5.67
7	2-Methylpropan-1-ol	5.19	5.68	8.30	5.38	6.09	5.99	5.85
8	2-Methylbutan-1-ol	–	–	–	5.46	6.13	6.18	5.95
		C			**D**			
9	Ethane-1,2-diol	2.55	3.03	4.61	2.85	4.30	4.14	4.20
10	Propane-1,2-diol	3.56	4.03	5.51	3.81	5.43	5.31	5.28
11	Propane-1,3-diol	2.95	3.71	5.29	3.42	5.15	4.83	4.79
12	Butane-1,2-diol	4.16	4.57	6.14	4.36	5.88	5.69	5.72
13	Butane-1,3-diol	4.05	4.50	6.05	4.19	5.68	5.60	5.53
14	Butane-1,4-diol	3.81	4.27	5.99	4.01	5.57	5.42	5.34
15	Butane-2,3-diol	4.48	4.88	6.21	4.68	5.97	5.87	5.83
16	Pentane-1,5-diol	4.19	4.68	6.32	4.42	5.95	5.76	5.65
17	Diethylene glycol	3.16	3.84	5.69	3.75	5.49	5.44	5.25
18	Triethylene glycol	3.30	4.14	6.07	3.99	5.88	5.52	5.60

[a]Values from Ref. 2.
[b]Values for monoalcohols from Ref. 9 and for dialcohols from Ref. 1.

Table 3. Selected properties of the solvents (25.00 °C)[a]

No.[b]	$f(\varepsilon)$	$g(\eta)$	E_T^N	$10^3\delta_H^2$ (MPa)	π^*	α	β
1	0.477	0.203	0.762	0.887	0.60	1.09	0.73
2	0.470	0.221	0.654	0.703	0.55	0.88	0.80
3	0.464	0.235	0.617	0.590	0.53	0.79	0.85
4	0.463	0.230	0.546	0.552	0.48	0.68	0.93
5	0.458	0.242	0.602	0.485	0.54	0.74	0.84
6	0.456	0.241	0.506	0.488	0.54	0.54	0.91
7	0.459	0.240	0.552	0.516	0.50	0.71	0.92
8	0.454	0.247	0.534	0.482	0.51	0.64	0.93
9	0.480	0.259	0.790	0.887	0.89	0.88	0.72
10	0.474	0.260	0.722	0.881	0.76	0.83	0.78
11	0.479	0.263	0.747	0.847	0.84	0.90	0.77
12	0.467	0.262	0.676	0.600	0.71	0.80	0.71
13	0.474	0.264	0.682	0.562	0.75	0.76	0.74
14	0.467	0.267	0.704	0.738	0.93	0.63	0.68
15	0.466	0.259	0.651	0.602	0.75	0.68	0.88
16	0.473	0.268	0.654	0.603	0.76	0.70	0.82
17	0.477	0.267	0.713	0.615	0.92	0.72	0.67
18	0.469	0.272	0.704	0.480	0.88	0.66	0.69

[a]Values of the solvent parameters, defined in eq. (1) and (2), are from Ref. (3, 4, 13, 14);
[b]Solvents are numbered as in Table 1.

a complete description of all solute–solvent interactions must include both non-specific and specific effects.

To describe the main significant solvent properties, different sets of parameters have been proposed, each being claimed to be suficient for such a purpose.[11] In our work, to analyse solvent effects by means of LSER, each set of rate constants, corresponding to one substrate reacting in the whole range of solvents, was correlated with several properties of the solvents based on adequate correlation models. Among the most suitable empirical equations for evaluation of the medium effects, we chose a modified version of the (GAS) equation.[2,4]

$$\log k = a_0 + a_1 g(\eta) + a_2 E_T^N + a_3\beta + a_4\delta_H^2 \qquad (2)$$

and the TAKA equation.[5]

$$\log k = a_0 + a_1\pi^* + a_2\alpha + a_3\beta + a_4\delta_H^2 \qquad (3)$$

In Eqn. (2), $g(\eta)$ is the function for the refractive index $(\eta^2 - 1)/(\eta^2 + 2)$, E_T^N is the normalized Dimroth and Reichardt value of $E_T(30)$, β is the Kamlet–Taft hydrogen bond acceptor (HBA) basicity parameter and δ_H^2 is the cohesive energy density (related to the Hildebrand parameter).[11] In Eqn. (3), β and δ_H^2 have the same meaning and π^* and α are the well-known Kamlet–Taft microscopic solvatochromic parameters related to the solvent dipolarity/polarizability and the hydrogen bond donor (HBD) acidity, respectively.[12] A compilation of the values of the empirical solvent parameters for the set of studied solvents is given in Table 3.

For each equation, the effect of the different parameters on the variation of log k values (the dependent variable) was first analysed using a stepwise procedure, in which the significance of the independent variables was tested. The decision for the selection and elimination of variables was performed taking into account the significance level (*SL*) of each regression coefficient (better than 95%), the multiple linear correlation coefficient (R), the standard deviation of the fit (s) and the Fisher statistical parameter (F). A least squares fit was then performed to obtain the best model for each set of rate constants.

Table 4 summarizes the statistically significant results of the application of the GAS equation [Eqn. (2)] and Table 5 the application of the TAKA equation [Eqn. (3)] When the GAS equation is applied, the 'hidden' parameter, a_0, is always smaller than when the TAKA equation is used. For *t*-BuCl solvolysis, the difference between the a_0 values is of the same order as the standard deviation of this coefficient. The value of log $k = -19.5$, at 25 °C, reported by Koppel and Palm[10] seems to confirm that the set of GAS equation descriptors are adequate to describe solute–solvent interactions. However, when the set of data is split, the a_i values should not change outside the limits of error, although errors could increase, but this is not the case for 2-Br-2-MeBu (Table 5). The value of a_2 changes significantly for mono- and dialchols, which may be due to their specific properties and/or to the fact that the set of adjustable parameters is non-ideal. The former hypothesis is supported by the different nature of the submatrix in Table 7 concerning the two sets of alcohols when considered separately. However, in the latter hypothesis, when the solvent nucleophilicity (β parameter) was explicitly included, we observed that this descriptor has no statistical meaning.

The results of the application of both equations show

Table 4. Correlation of rate constants for solvolysis of *tert*-alkyl halides in alcohols (25.00 °C), with applicaton of the GAS equation: $\log k = a_0 + a_1 g(\eta) + a_2 E_T^N + a_3\beta + a_4\delta_H^2$

Substrate	$a_0 \pm$ sd[a] (%*SL*)[f]	$a_1 \pm$ sd (%*SL*)	$a_2 \pm$ sd (%*SL*)	$a_3 \pm$ sd (%*SL*)	N[b]	F[c]	R[d]	s[e]
t-BuI	−13.01 ± 0.91 (>99.99%)	11.87 ± 3.53 (99.54%)	8.88 ± 0.78 (>99.99%)	–	17	74.0	0.96	0.26
t-BuBr	−13.50 ± 0.81 (>99.99%)	12.70 ± 3.16 (99.87%)	8.49 ± 0.78 (>99.99%)	–	17	87.5	0.96	0.24
t-BuCl[g]	−20.92 ± 2.05 (>99.99%)	15.88 ± 3.17 (99.98%)	13.24 ± 1.26 (>99.99%)	2.13 ± 1.21 (>89.83%)	17	112	0.98	0.22
t-BuCl	−17.56 ± 0.82 (>99.99%)	13.99 ± 3.20 (99.94%)	11.44 ± 0.79 (>99.99%)	–	17	145	0.98	0.24
2-Br-2-MeBu	−12.15 ± 0.69 (>99.99%)	8.67 ± 2.74 (99.36%)	8.39 ± 0.63 (>99.99%)	–	18	115	0.97	0.20
2-Br-2-MeBu	−12.66 ± 0.45 (>99.99%)	–	12.37 ± 0.64 (>99.99%)	–	10[h]	369	0.99	0.08
2-Cl-2-MeBu	−13.42 ± 1.02 (>99.99%)	–	11.20 ± 1.45 (99.99%)	–	10[h]	59.6	0.94	0.18
3-Cl-3-MePe	−13.58 ± 0.84 (>99.99%)	–	11.67 ± 1.19 (>99.99%)	–	10[h]	97.0	0.96	0.15
3-Cl-3-EtPe	−13.12 ± 0.88 (>99.99%)	–	11.08 ± 1.24 (>99.99%)	–	10[h]	79.2	0.95	0.16

[a]Standard deviation of the coefficient.
[b]Number of points.
[c]Fisher statistical value.
[d]Multiple linear correlation coefficient.
[e]Standard deviation of the fit.
[f]Percent significance level.
[g]This correlation was included for comparative purposes.
[h]Dialcohols.

conclusively that, for the set of solvolytic reactions under study, the factors that dominate the activation process are the dipolarity/polarizability, described by $g(\eta)$ or π^*, and the HBD acidity, described by E_T^N or α, of the solvent. All these effects contribute to accelerating the solvolytic process.

The TAKA equation leads to the conclusion that, for the particular case of *t*-BuCl solvolysis, a further term

Table 5. Correlation of rate constants for solvolysis of *tert*-alkyl halides in alcohols (25.00 °C), with application of the TAKA equation: $\log k = a_0 + a_1\pi^* + a_2\alpha + a_3\beta + a_4\delta_H^2$

Substrate	$a_0 \pm$ sd[a] (%*SL*)[f]	$a_1 \pm$ sd (%*SL*)	$a_2 \pm$ sd (%*SL*)	$a_3 \pm$ sd (%*SL*)	N[b]	F[c]	R[d]	s[e]
t-BuI	−9.50 ± 0.51 (>99.99%)	4.73 ± 0.41 (>99.99%)	2.70 ± 0.53 (99.98%)	–	17	75.6	0.96	0.26
t-BuBr	−9.88 ± 0.45 (>99.99%)	4.65 ± 0.36 (>99.99%)	2.55 ± 0.46 (99.99%)	–	17	95.9	0.97	0.23
t-BuCl	−17.57 ± 1.97 (>99.99%)	7.22 ± 0.76 (>99.99%)	4.65 ± 0.74 (>99.99%)	3.16 ± 1.46 (>95.05%)	17	88.5	0.98	0.24
2-Br-2-MeBu	−9.49 ± 0.39 (>99.99%)	4.13 ± 0.32 (>99.99%)	2.87 ± 0.42 (>99.99%)	–	18	106	0.97	0.21
2-Br-2-MeBu	−12.11 ± 0.59 (>99.99%)	5.14 ± 0.48 (>99.99%)	5.29 ± 0.48 (>99.99%)	–	10[g]	95.8	0.98	0.11
2-Cl-2-MeBu	−12.92 ± 0.96 (>99.99%)	4.15 ± 0.77 (99.90%)	5.35 ± 0.78 (99.98%)	–	10[g]	30.9	0.95	0.18
3-Cl-3-MePe	−12.85 ± 1.05 (>99.99%)	4.31 ± 0.85 (99.90%)	5.30 ± 0.86 (99.98%)	–	10[g]	26.0	0.94	0.20
3-Cl-3-EtPe	−12.61 ± 0.92 (>99.99%)	4.36 ± 0.74 (99.94%)	4.99 ± 0.75 (99.97%)	–	10[g]	31.7	0.95	0.18

[a]Standard deviation of the coefficient.
[b]Number of points.
[c]Fisher statistical value.
[d]Multiple linear correlation coefficient.
[e]Standard deviation of the fit.
[f]Percent significance level.
[g]Dialcohols.

Table 6. Summary of target test (*SPOIL* <6) using two factors based on covariance

Submatrix	Target	*AET*[a]	*EDM*[b]	*SPOIL*[c]	*F*[d]	*df1*[e]	*df2*[e]	*%SL*[f]
A	$g(\eta)$	0.0091	0.0030	2.83	3.75	5	1	37.2
	E_T^N	0.1343	0.0303	4.32	8.20	5	1	25.9
	β	0.0293	0.0056	5.10	11.23	5	1	22.3
B	$g(\eta)$	0.0055	0.0029	1.67	1.52	6	2	44.7
	E_T^N	0.0780	0.0193	3.91	6.58	6	2	13.8
	δ_H^2	0.1239	0.0294	4.10	7.18	6	2	12.7
	α	0.1268	0.0382	3.17	4.45	6	2	19.5
	β	0.0345	0.0132	2.41	2.74	6	2	29.1
C	$f(\varepsilon)$	0.0405	0.0075	5.34	13.09	8	1	21.1
	$g(\eta)$	0.0171	0.0042	3.93	7.31	8	1	27.9
	E_T^N	0.0853	0.0150	5.59	14.32	8	1	20.2
	π^*	0.0830	0.0215	3.73	6.62	8	1	29.2
	I	0.0791	0.0149	5.21	12.49	8	1	21.6
D	$f(\varepsilon)$	0.0351	0.0117	2.83	3.87	8	2	22.2
	$g(\eta)$	0.0152	0.0062	2.23	2.55	8	2	31.2
	E_T^N	0.0708	0.0265	2.48	3.05	8	2	27.0
	π^*	0.0862	0.0345	2.29	2.67	8	2	30.1
	I	0.0691	0.0225	2.90	4.01	8	2	21.5

[a]Apparent error in the target.
[b]Error from data matrix
[c]*SPOIL* associated to the target.
[d]Fisher statistical value.
[e]Degree of freedom.
[f]Percent significance level.

should be considered, the HBA basicity parameter described by β. This means that, at least in this case, nucleophilic assistance during the activation process is important. We must point out that although the significance level (*SL*) of the regression coefficient β for the GAS equation does not achieve the stipulated minimum level it is nevertheless partly high at 89.83% (Table 4).

Bentley and co-workers[15,16] suggested that solvolyses of *tert*-butyl halides are sensitive to solvent nucleophilicity assistance during heterolysis of the carbon–halogen bond by an S_N2 (intermediate) mechanism; however, nucleophilic solvation may occur at both the α-carbon and the β-hydrogen. Kevill and D'Sousa[17] also reported that there is an appreciable contribution from rearside nucleophilic solvation of the developing carbocation on the rates of *tert*-butyl chloride solvolysis. Abraham[18] first concluded that inclusion of the β term did not improve the goodness of the statistical fit for *t*-BuCl. However, with a more extensive set of reaction rates, the nucleophilic assistance term becomes statistically significant.[19] Recent work by Takeuchi *et al.*[20,21] and Liu *et al.*[22] carefully examined extended Grunwald–Winstein-type relations involving a nucleophilicity parameter when applied to various crowded alkyl derivatives. They obtained good straight lines and concluded that the solvolytic reactivity was influenced by nucleophilic solvent participation.

Catálan *et al.*[23] showed that the solvolysis of *tert*-butyl chloride is favoured by an increased basicity of the medium. In addition, Abboud and co-workers[24,25] recently reported that the *tert*-butyl derivatives solvolyse faster than expected on the grounds of the stability of the bridgehead carbenium ions. This should be ascribed to nucleophilic solvent participation in the case of the *tert*-butyl derivative.

Our results show that nucleophilic assistance does not influence *t*-BuBr and *t*-BuI solvolysis rates to any significant extent. However, for *t*-BuCl solvolysis the HBA basicity parameter has a moderate contribution, which is consistent with a process assisted by increased solvent basicity.

The analysis through the GAS and TAKA equations concerning the substrates 2-Cl-2-MeBu, 3-Cl-3-MePe and 3-Cl-3-EtPe shows that they only have statistical meaning for the set of dialcohols. The parameters π^* and α are the most relevant for the TAKA equation and only E_T^N should be considered in the GAS equation. This agrees with $E_T^N(30)$ is a linear combination of the π^* and α parameters. There is, in fact, a superior non-colinearity between any two solvent parameters for TAKA compared to GAS, for the all set of studied alcohols. The correlation coefficient between E_T^N and β, for instance, is 0.850, and that between α and β is only 0.374. This makes the use of the TAKA equation more discriminatory and less ambiguous.

Target factor analysis

The use of FA and TFA allows a better understanding of the variations in the data sets, log *k* in our case, without prior assumptions of any model or any kind of behaviour. As far as we know, this is the first application of such a

Table 7. Factor loadings based on covariance ($NF^a = 2$) using values of log*k*

Substrate	Submatrix	$g(\eta)$	E_T^N	$g(\eta)$	β
t-BuI	**A**	-26.55 ± 2.33	2.08 ± 0.90	-4.51 ± 9.51	-4.48 ± 2.56
t-BuBr		-24.72 ± 2.95	0.43 ± 1.13	-20.19 ± 9.36	-0.92 ± 2.52
t-BuCl		-46.75 ± 7.99	5.52 ± 3.07	11.63 ± 17.44	-11.87 ± 4.69
		$RMS^b = 0.26$		$RMS = 0.21$	
		$g(\eta)$	E_T^N	$g(\eta)$	α
2-Br-2-MeBu	**B**	-26.33 ± 0.93	16.73 ± 0.36	-24.97 ± 0.62	0.90 ± 0.19
2-Cl-2-MeBu		-15.21 ± 3.47	-4.36 ± 1.35	-18.75 ± 2.25	-2.34 ± 0.19
3-Cl-3-MePe		-16.77 ± 3.46	-3.41 ± 1.35	-19.54 ± 2.22	-1.83 ± 0.67
3-Cl-3-EtPe		-20.64 ± 1.50	-1.51 ± 0.59	-21.87 ± 0.98	-0.81 ± 0.30
		$RMS = 0.26$		$RMS = 0.24$	
		$g(\eta)$	E_T^N	I	π^*
t-BuI	**C**	-72.86 ± 20.53	22.25 ± 7.72	-10.91 ± 2.23	8.88 ± 2.71
t-BuBr		-62.56 ± 13.45	17.59 ± 5.06	-9.82 ± 1.96	6.88 ± 2.39
t-BuCl		-56.89 ± 5.89	13.14 ± 2.21	-9.78 ± 2.07	4.84 ± 2.53
		$RMS = 0.44$		$RMS = 0.49$	
		$g(\eta)$	E_T^N	I	E_T^N
2-Br-2-MeBu	**D**	-52.17 ± 7.11	13.98 ± 2.67	-12.87 ± 0.48	12.65 ± 0.68
2-Cl-2-MeBu		-49.02 ± 4.37	10.53 ± 1.64	-12.08 ± 1.17	9.29 ± 1.66
3-Cl-3-MePe		-51.14 ± 5.25	11.58 ± 1.97	-12.60 ± 0.94	10.28 ± 1.34
3-Cl-3-EtPe		-49.93 ± 5.58	11.18 ± 2.09	-12.31 ± 0.96	9.91 ± 1.36
		$RMS = 0.22$		$RMS = 0.14$	

[a]Number of factors.
[b]Root mean square error.

'hypothesis-free' method to a dynamic process of this type. The present work introduces the method in order to improve our knowledge about the interaction mechanisms acting in the solvent-dependent solvolytic processes.

Data were first analysed using FA. The number of eigenvectors or factors necessary to explain the main variance of the results was obtained through application of the IND function and cross validation techniques.[6,26,27] Once the number of abstract factors had been decided unambiguously, TFA was applied to identify the nature of each.

We started with the complete, free from 'holes' original data matrix of seven substrates and 17 solvents. To improve the absolute fit of the data, four submatrices were selected. These submatrices ensure a clear physicochemical interpretation. The solvent parameters checked as possible targets in a future model were $f(\varepsilon)$, $g(\eta)$, E_T^N, δ_H^2, π^*, α, β and I (the unitary vector). This set of tested solvent parameters is included in the set of 'pure fundamental' solvent parameters defined by the FA and the SMIRC procedure performed by Palm and Palm.[28] All the data treatment was performed with the TARGET 90 program.[6,29]

Each of the eight targets was tested and the apparent error (*AET*) together with the error from the data matrix (*EDM*) served to calculate the *SPOIL* value associated with the target and the corresponding statistical parameter *F*. Targets that are real factors should have values of *SPOIL* below 6 and significance levels (*SL*) above 5%.[30,31] Table 6 gives a summary of target testing using two factors based on the covariance for each data submatrix. An increase in this number of factors can, on the one hand, improve the absolute fit of the data but, on the other, decrease the number of statistical degrees of freedom. Therefore, to preserve this, the number of factors (*NF*) should be equal to or less than the value represented by the ratio $(n \times m)/(n + m)$, n and m being the number of columns and rows, respectively.[28]

Those solvent parameters confirmed as possible real factors, or the targets, which lie in the factor space, were subsequently used for the calculation of their loadings and for reproduction of the data matrix. The best combination of solvent parameters yields the lowest error on the estimation of the factor loadings and/or the lowest root mean square error, (*RMS*), in reproduction of the data matrix. Table 7 shows the factor loadings and the associated errors and the *RMS* of the best results submatrix. Although the associated *RMS* errors in the reproduction of the data submatrix **A** are acceptable, as they have the same magnitude as the values of the standard deviation obtained using the LSER methodology, some factor loadings show large associated errors. This can be explained by the small submatrix dimension, since when the product of the rows and columns increases the errors tend to decrease. The application of TFA to the solvolytic reactions of all halides allowed us to differentiate between the behaviour of mono- and dialcohols. For *tert*-butyl halides (*t*-BuX; X = Cl, Br or I) the most important parameters are $g(\eta)$ and E_T^N. However, the pairs $g(\eta)$ and β and I and π^* are also possible real factors for mono- and dialcohols, respectively (Table 7). If we compare the results of TFA application to the submatrix **A** and **C**, and the submatrix

B and **D**, we can see that for the pair $g(\eta)$, E_T^N there is, in general, a significant increase in the absolute value of the factor loadings for the dialcohols. This is most probably a consequence of a stronger solute–dialcohol interaction than the solute–monoalcohol interaction during the activation process. When we choose the pair of parameters $g(\eta)$ and β for the submatrix **A**, we verify that the basicity parameter is more relevant for the substrate *t*-BuCl than for the other halides, as already verified through LSER methodology (Tables 4 and 5). For solvolysis of 2-Br-2-MeBu, 2-Cl-2-MeBu, 3-Cl-3-MePe and 3-Cl-3-EtPe in dialcohols, the statistical analysis of the results shows that the dominant solvent interaction is the HBD acidity, E_T^N, as concluded before through the application of LSER methodology (Table 4). However, use of the TFA statistical method indicates that the parameter $g(\eta)$ can also be important. It should be noted that when the pair of parameters I and E_T^N is considered (submatrix **D**, Table 7), the factor loadings show the same nature, magnitude and sign as the LSER regression coefficients obtained for the same substrates (Table 4). With respect to the solvolytic reactions of 2-Br-2-MeBu, 2-Cl-2-MeBu, 3-Cl-3-MePe and 3-Cl-3-EtPe in the eight monoalcohols, the TFA methodology provides further information since through the LSER methodology all hypotheses were statistically meaningless. In this case the relevant solvent parameters are $g(\eta)$ and α or $g(\eta)$ and E_T^N.

Reasonable correlations obtained using TFA only on subsets of the original data matrix can be explained by a different kinetic behaviour of mono- and dialcohols and also by the nature of the alkyl group attached to the tertiary carbon. We emphasize that LSER methodology can provide estimations of the effects of solvent on reaction rates. The results obtained from the multivariate TFA method are in good agreement with those obtained from LSER. It has already been emphasized that the application of the TFA approach is innovative in the context of the chemical systems studied here.

Further studies using more heavily congested tertiary alkyl substrates are in progress and also the application of the methodology of transfer thermodynamic functions in order to analyse solvent nucleophilic effects in the transition state in more detail.

Increasing the total number of selected basic columns and rows of the starting matrix for the TFA treatment can result in a highly useful tool for additional information concerning reaction processes in solution.

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