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The quaternisation reaction of phosphines and amines in aliphatic alcohols. A similarity analysis using the isokinetic, isosolvent and isoselective relationships †

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Received 22nd December 2003, Accepted 1st March 2004
First published as an Advance Article on the web 22nd March 2004

Accurate second-order rate constants were measured at 5 K intervals in the temperature range 298.15–328.15 K for the quaternisation reaction of triethylphosphine with iodoethane in methanol, ethanol, propan-1-ol and butan-1-ol. These data are complemented previously reported rate constants for the quaternisation reaction of triethylamine with iodoethane in the same solvents and at similar temperatures. Each of these two reaction series is analysed in terms of the isokinetic relationship (IKR) with respect to solvent variation and of the isosolvent relationship (ISoR) with respect to temperature variation, using in the latter case five different empirical solvent scales. Statistically validated IKR and ISoR have been found for both reaction series. The resulting isokinetic temperatures of 347 K (phosphine series) and of 730 K (amine series) are discussed in terms of Linert's theory of the isokinetic relationship. The best ISoR correlation is obtained using the Dimroth–Reichardt E_T^N solvent scale for the phosphine series and the Kamlet–Taft a_{KT} solvent scale for the amine series. It is demonstrated that no real solvent can be envisaged as having the characteristics of an isokinetic solvent. The selectivity of the nucleophiles triethylphosphine and triethylamine in the attack on iodoethane is examined by treating together both reaction series in terms of the isoselective relationship (ISeR). The isoselective temperature with respect to solvent is found to be 289 K, which is close to the value of 302 K predicted by Exner and Giese's formula on the basis of the individual isokinetic temperatures. A novel ISeR analysis with respect to temperature is performed. It reveals that the a_{KT} scale is the most appropriate solvent scale for describing this selectivity series, and that it is feasible to find an isoselective solvent. A new equation is developed for predicting the isoselective solvent parameter from individual isosolvent parameters and is shown to yield realistic values. The present similarity analysis shows that there are significant differences between the courses of these quaternisation reactions. On the basis of the experimentally determined isoparameter values, in liquid alcohols as solvent it is proposed that the reaction between triethylphosphine and iodoethane follows a classic bimolecular nucleophilic substitution pathway, whereas the desolvation of triethylamine molecules has to be taken into account to describe the mechanism of the original Menshutkin reaction.

Introduction

The Menshutkin reaction leading to the quaternisation of tertiary amines has been considered as the classic example of a S_N2 ionogenic reaction.[1] This mechanism is well understood, now being described as a concerted A_ND_N reaction in which the nucleophilic substitution at a saturated carbon atom takes place in a single step.[2] This notwithstanding, from a similarity analysis of literature data for the quaternisation reaction of a series of aliphatic amines with iodomethane in aqueous solution, Bel'skii[3] proposed a stepwise reaction mechanism involving the formation of a short-lived ion-pair intermediate. In addition, Parker and co-workers[4] have recently found kinetic evidence for a two-step mechanism in displacement reactions at a primary carbon atom using an anionic nucleophile. Therefore, these recent investigations[3,4] suggest that an $A_N{*}D_N$ mechanism may be operating in certain bimolecular nucleophilic substitution reactions in solution.

In the chemistry of phosphorus, the analogue of the Menshutkin reaction is the formation of quaternary phosphonium salts from tertiary phosphines and haloalkanes. The kinetics of these reactions[5] have not received as much attention as for the formation of quaternary ammonium halides. In fact, since the exploratory kinetic study by Davies and Lewis[6] and the first systematic research on structural effects by Henderson and Buckler,[7] not many reports have been published addressing the effects of temperature and solvent on the rates of quaternisation of phosphines.[8–12] Moreover, the reaction between triethylphosphine and iodoethane, which is the very analogue of the original century-old Menshutkin reaction,[1,13,14] does not seem to have been used in any systematic study. It is therefore of interest to explore the similarities between these two simple nucleophilic substitution reactions.

We report here rate constants for the quaternisation reaction of triethylphosphine (Et_3P) by iodoethane (EtI) (Scheme 1) in the series of aliphatic alcohols methanol (MeOH), ethanol (EtOH), propan-1-ol (PrOH) and butan-1-ol (BuOH), in the temperature range 298.15–328.15 K at ambient pressure. These

$$(CH_3CH_2)_3P: + CH_2ICH_3 \rightarrow (CH_3CH_2)_4P^+ + I^-$$

$$(CH_3CH_2)_3N: + CH_2ICH_3 \rightarrow (CH_3CH_2)_4N^+ + I^-$$

Scheme 1

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† Electronic supplementary information (ESI) available: Table S1 containing literature values of solvent parameters for alkan-1-ols in five different scales and Table S2 with rate constants for the quaternisation of triethylamine by iodoethane at different temperatures in methanol, ethanol, propan-1-ol and butan-1-ol. See http://www.rsc.org/suppdata/ob/b3/b316556f

DOI: 10.1039/b316556f

Table 1 Rate constants and mean deviations for the quaternisation of triethylphosphine by iodoethane at different temperatures in methanol (MeOH), ethanol (EtOH), propan-1-ol (PrOH) and butan-1-ol (BuOH)[a]

	$k \times 10^5$/dm^3 mol^{-1} s^{-1}			
T/K	MeOH	EtOH	PrOH	BuOH
298.15	14.95 ± 0.02	8.585 ± 0.012	6.881 ± 0.009	6.172 ± 0.033
303.15	19.88 ± 0.06	12.77 ± 0.02	11.12 ± 0.02	8.905 ± 0.010
308.15	26.82 ± 0.14	18.16 ± 0.01	16.04 ± 0.02	12.90 ± 0.02
313.15	37.35 ± 0.11	26.51 ± 0.12	23.52 ± 0.06	21.65 ± 0.02
318.15	52.04 ± 0.14	37.61 ± 0.16	36.50 ± 0.08	34.68 ± 0.06
323.15	79.39 ± 0.29	53.56 ± 0.31	56.19 ± 0.10	45.95 ± 0.24
328.15	96.13 ± 0.04	71.36 ± 0.47	71.69 ± 0.10	76.63 ± 0.42

[a] Rate constants are given in temperature-independent units.

data are analysed together with published kinetic data obtained in our laboratory for the quaternisation reaction of triethylamine (Et_3N) with iodoethane (Scheme 1) in the same set of solvents and similar temperatures.[15] Taking the differing solvent as the changing variable for the purpose of similarity analysis, the isokinetic relationship (IKR)[16–19] with respect to solvent and a new approach for the isosolvent relationship (ISoR) with respect to temperature are tested for both quaternisation reactions. The isoselective relationship (ISeR)[20] is also examined for the attack of different nucleophiles on a common substrate with respect to solvent and temperature variation. The isoparameter values thus obtained are used to analyze the effect of changing nucleophile on the reaction pathway. We conclude that the reaction between triethylphosphine and iodoethane is a much better model for a concerted A_ND_N reaction than the original Menshutkin reaction.

Results and discussion

Quaternisation of triethylphosphine by iodoethane

Rate constants, k, for the reaction between Et_3P and EtI in four lower straight-chain alkanols are presented in Table 1. Accurate second-order rate constants at seven different temperatures in each solvent were derived from conductivity data as described in the Experimental section. Rate constant values are expressed in temperature-independent concentration units[21] referred to solvent densities at 298 K.

Isokinetic relationship

The IKR is an important tool[16] for the similarity analysis of organic reactivity. In this method patterns in kinetic data for a reaction series as a function of temperature T are tested according to eqn. (1).

$$\log (k_{ij}/T_j) = a_{IKR} + b_i\,(T_j^{-1} - \beta_{IKR}^{-1}) \qquad (1)$$

In a plot of $\log (k/T)$ against T^{-1} the latter equation describes a set of straight lines having slopes b_i, which will eventually intersect at a common point. Then the corresponding temperature is designated as the isokinetic temperature, β_{IKR}. In such a case there is proportionality between increments in standard activation enthalpies $\Delta^{\neq}H°$ and in standard activation entropies $\Delta^{\neq}S°$ along the reaction series, the proportionality constant being β_{IKR};[16–19] eqn. (2).

$$\delta\Delta^{\neq}H° = \beta_{IKR}\,\delta\Delta^{\neq}S° \qquad (2)$$

Similarity analyses in terms of the IKR are frequently carried out for reaction series in which slight structure changes are introduced in the substrate or in the reagent. On this occasion we have constructed a reaction series by changing the solvent, the associated β_{IKR} parameter being termed by Whalley and co-workers[22] as the isokinetic temperature with respect to solvent. The data in Table 1 were fitted by eqn. (1) using a recent programme for least-squares linear regression with a common point of intersection[18] implemented on a Microsoft EXCEL97 spreadsheet, which is available on the Web.[23] The occurrence of an isokinetic relationship in this reaction series is accepted at 95% confidence level, the F-test giving $F = 3.53$ and standard deviations being $s_{00} = 0.0221$ for unconstrained lines in terms of eqn. (3) and $s_0 = 0.0245$ for straight lines constrained by eqn. (1).

$$\log (k_i/T) = a_i + b_i\,T^{-1} \qquad (3)$$

Fig. 1 shows the resulting isokinetic plot from which the isokinetic temperature is found to be 347 K. This value for β_{IKR} clearly falls above the experimental temperature range. According to eqn. (1) the common value for $\log (k_{ij}/T_j)$ at temperature β_{IKR} is given by parameter a_{IKR}, which is calculated to be −5.123. As pointed out by other authors,[3,24] both β_{IKR} and a_{IKR} values are needed for the full description of a given reaction series.

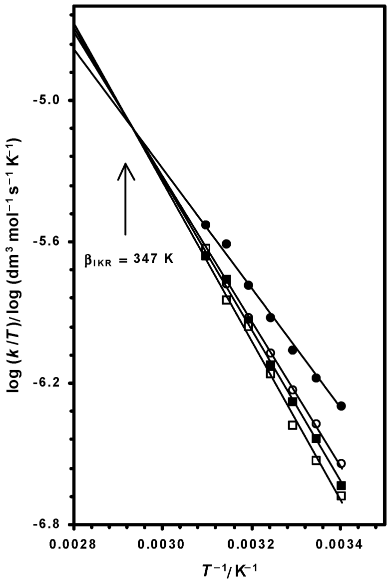

Fig. 1 Isokinetic plot according to eqn. (1) of the data in Table 1 for the quaternisation reaction of Et_3P with EtI in different solvents: (●), MeOH; (○), EtOH; (■), PrOH; and (□), BuOH.

The IKR-constrained values for standard enthalpies and entropies of activation are given in Table 2 along with the unconstrained values obtained in terms of the Eyring equation, eqn. (3).

We observe that the constrained values for activation parameters calculated by the IKR are generally within the standard deviation of the corresponding unconstrained values obtained by the Eyring equation.

Table 2 Standard enthalpies of activation $\Delta^{\neq}H^{\circ}$ and standard entropies of activation $\Delta^{\neq}S^{\circ}$ derived from eqns. (1) and (3) for the reaction Et_3P + EtI in a series of solvents

	$\Delta^{\neq}H^{\circ}$/kJ mol^{-1}		$\Delta^{\neq}S^{\circ}$/J K^{-1} mol^{-1}	
Solvent	Eqn. (1)	Eqn. (3)	Eqn. (1)	Eqn. (3)
MeOH	48.64	49.75 ± 1.73	−155	−152 ± 6
EtOH	58.62	55.25 ± 0.48	−127	−137 ± 2
PrOH	61.26	61.91 ± 1.43	−119	−117 ± 5
BuOH	64.48	66.09 ± 2.14	−110	−104 ± 7

The finding of this isokinetic temperature indicates that the quaternisation rate of Et_3P by EtI in a series of alkan-1-ols at 347 K would be fairly independent of the solvent chain length, provided that activation enthalpies and entropies remain unchanged at temperatures up to β_{IKR}. A further cautionary limitation is the boiling of methanol at 338 K and ambient pressure.

The chemical significance to be attached to the occurrence of isokinetic temperatures in reaction series was much debated for a long time.[16] However, in the late 1980's Linert[25–27] developed an appealing theory for interpreting experimental values of isokinetic temperatures. Resorting to a stochastic theory of reaction rates, Linert has shown that solvents act as heat baths towards activated processes in solution. For the link between active vibrational frequencies of the molecules of a given solvent, $\nu_{heat\ bath}$ and β_{IKR}, Linert[25,26] proposes eqn. (4) where h is the Planck constant and k_B is the Boltzmman constant.

$$\beta_{IKR} = h\ \nu_{heat\,bath}/k_B \qquad (4)$$

From the latter expression we readily derived eqn. (5), which is a more practical formula in terms of wavenumbers $\tilde{\nu}$.

$$\tilde{\nu}_{heat\,bath}/cm^{-1} = 0.695\ (\beta_{IKR}/K) \qquad (5)$$

On the other hand Linert's theory explains why isokinetic relationships in a series of solvents are far less common than for reaction series in a single solvent.[19,27–29] From eqn. (5) we calculate $\tilde{\nu}_{heat\ bath}$ to be 241 cm^{-1} for the reaction Et_3P + EtI in alkan-1-ols. Hence chemically similar solvents may possess a common vibrational frequency, which in the present case lies in the far infrared region of the electromagnetic spectrum. The far infrared spectra of a homologous series of aliphatic alcohols were investigated in detail by Lake and Thompson,[30] who associate low-frequency vibrations with hydrogen bonding in the liquid phase and with torsional modes in the monomers. At ambient temperature, wavenumbers increasing from 110 cm^{-1} in EtOH up to 148 cm^{-1} in BuOH are assigned to the stretching of hydrogen bonds in the liquid alcohol, the corresponding value for MeOH being believed to be lower than[30] 80 cm^{-1}. Since on raising temperature these rather different values are expected to be displaced to lower wavenumbers, they do not seem likely to be responsible for the observed isokinetic temperature. This notwithstanding, all of these alcohols in the vapour state show a band near 200 cm^{-1} (MeOH, 197 cm^{-1}; EtOH, 199 cm^{-1}; PrOH, 201 cm^{-1}; BuOH, 200 cm^{-1}), which Lake and Thompson[30] assigned to torsion in the hydroxyl group of monomeric forms. This absorption band, which is not found with the liquid alcohols, is likely to be displaced to higher frequencies in the case where weak interactions arise.[30] It can therefore be safely assumed that $\tilde{\nu}_{heat\ bath}$ at 241 cm^{-1} for the reaction Et_3P + EtI in alkan-1-ols is associated with infrared active vibrational transitions involving the hydroxyl group in solvating molecules of primary alcohols. This key information points to a strong participation of the solvent in the formation of activated complexes.

Isosolvent relationship

In the foregoing IKR analysis we used different solvents for perturbing the basic reaction. In fact, the straight lines in Fig. 1 are isosolvent lines. Although this approach has been termed an isosolvent relationship by Linert and his colleagues,[19,28,29] we prefer to keep the latter designation for similarity analyses in which empirical solvent parameters[31–33] (SP) are used to describe solvent effects on reaction rates at different temperatures. In these terms the ISoR is given by eqn. (6), which is formally similar to eqn. (1) for the IKR.

$$\log (k_{ij}/T_j) = a_{ISoR} + b_j\ (SP_i - SP_{ISoR}) \qquad (6)$$

In eqn. (6) subscript i identifies the solvent and subscript j the experimental temperature. Hence in the analysis of data in Table 1 i = MeOH, EtOH, PrOH and BuOH, and eqn. (6) will contain a total of nine fitting parameters, namely a_{ISoR}, b_j and SP_{ISoR}. The latter adjustable parameter, which is named the isokinetic-solvent parameter, gives the value at which the seven isotherms tie in a bundle (point of intersection). In turn, parameter a_{ISoR} would give the constant value for log (k_{ij}/T_j) at different temperatures in a solvent having the value of SP_{ISoR} in a given solvent scale. Such solvent for the reaction under examination would then be most appropriately designated as the isokinetic solvent with respect to temperature. However, the question arises whether there can be found a real liquid solvent with these properties. According to the Transition State Theory, activation enthalpies for reactions in a given solvent i are calculated by eqn. (7).

$$\Delta^{\neq}H_i^{\circ} = -R\ [\partial \ln (k_i/T)/\partial T^{-1}]_p \qquad (7)$$

Hence, in a reaction series complying with the ISoR expressed by eqn. (6), $\Delta^{\neq}H_i^{\circ}$ are related to SP_i by eqn. (8).

$$\Delta^{\neq}H_i^{\circ} = -2.303\ R\ (\partial\ b/\partial\ T^{-1})_p\ (SP_i - SP_{ISoR}) \qquad (8)$$

The latter equation indicates that the enthalpy of activation would vanish in a solvent characterised by SP_{ISoR}. However, this eventuality is not allowed by the principles of chemistry for single-step activated processes. Thus, contrary to the possible experimental attainment of an isokinetic temperature, we have demonstrated that the concept of an isokinetic solvent is purely hypothetical. Its usefulness consists only in providing a method for similarity analysis of chemical reactions in a family of solvents. For example, numerical values for the parameters a_{IKR} in eqn. (1) and a_{ISoR} in eqn. (6) should be very close to each other in the case of a given reaction series obeying both IKR and ISoR.

In order to perform the ISoR analysis of our kinetic data, we examined a number of solvent parameters.[31–33] The hint provided by the value for β_{IKR} and the fact that the reagent (Et_3P) and the emerging iodide ion in the activated complex are strong electron-pair donors, directed our attention to empirical scales describing the ability of a solvent to interact with donors. Thus for the alcohols we consider: (i) the Kamlet–Abboud–Taft π^* scale[34] for measuring non-specific dipolarity–polarisability effects which stabilise electric charges and dipoles; (ii) the Mayer–Gutman–Gerger AN scale[32] for describing a blend of polarity and electron-pair accepting properties; (iii) the Dimroth–Reichardt E_T scale, in fact the E_T^N scale,[35] also to describe a blend of solvent polarity and its capability of donating a proton in a solvent-to-solute hydrogen bond (HBD); (iv) the Kamlet–Taft α_{KT} scale[36] for describing solvent HBD properties in relation to a general solute and, finally, (v) Abraham and colleagues[37] α_2^H scale[36] which is an equilibrium thermodynamics scale of hydrogen-bond acidity of solvent

Table 3 Isosolvent relationship (ISoR) parameters in eqn. (6) for the quaternisation of triethylphosphine by iodoethane at different temperatures in methanol, ethanol, propan-1-ol and butan-1-ol, using different solvent scales

			Standard deviation		
Solvent scale	SP_{ISoR}	a_{ISoR}	s_{00} unconstrained	s_0 ISoR	F^a
E_T^N	1.305	−5.129	0.0248	0.0241	0.79
α_2^H	0.587	−5.148	0.0289	0.0271	0.55
AN	57.63	−5.072	0.0323	0.0298	0.42
π^*	0.980	−5.176	0.0405	0.0372	0.41
α_{KT}	1.632	−5.194	0.0437	0.0397	0.34

[a] F-test value at 95% confidence level.

molecules as solutes in an inert solvent. In contrast to the latter scale, we note that the former four scales describe bulk solvent properties. In ISoR calculations we used the selected literature[32,34–36] SP values at 298 K presented in Table S1 † for the four alcohols in the above mentioned five empirical dimensionless scales.

Results of the five ISoR analyses using the IKR-80-20 programme[23] are summarised in Table 3. They show that there is an isosolvent relationship for the quaternisation reaction of triethylphosphine by iodoethane in a series of primary alcohols, which holds for any of the selected scales. In addition to the results reported in Table 3, for every solvent scale examined coefficients b_j in eqn. (6) are found to be positive at all experimental temperatures. This feature reveals that reaction rates are enhanced by increasing the solvent capability for solvating electric charges, for accepting electron pairs and for donating hydrogen bonds. These interactions are therefore stronger with developing charges in activated complexes than with neutral reactant molecules. As theoretically predicted above, the extremely high estimates reported in Table 3 for SP_{ISoR} in different solvent scales (*cf.* Table S1 †) evidence that no isokinetic solvent with respect to temperature can be chemically devised.

Solvent effects on reaction rates cannot generally be described using a single solvent parameter. However, the correlation of rates of a Menshutkin reaction in a variety of mono- and dialcohols was achieved using a single-parameter equation.[38,39] It is therefore interesting that our ISoR analysis suggests a single solvent parameter to be sufficient for correlating reaction rates in a homogenous set of solvents. Furthermore, the statistical data in Table 3 allow us to point out which is the most appropriate scale. On the basis of both unconstrained and ISoR-constrained standard deviations (Table 3), solvent effects are best described by the solvatochromic E_T^N scale, the latter being closely followed by the thermodynamic α_2^H scale. This sequence is confirmed when matching of a_{ISoR} and a_{IKR} values is appreciated. The relationship between IKR and ISoR(E_T^N) is shown in Fig. 2 using the form of an open-book double-diagram.[40] In particular, it evidences a very good agreement between regression values obtained for the parameters a_{IKR} and a_{ISoR}. We recall that E_T^N values for protic solvents describe their hydrogen-bond donor acidity and that α_2^H values will measure the power of non-associated alcohol molecules for establishing hydrogen bonds with activated complexes. The insight thus gained from the ISoR analysis is therefore in accordance with the information provided by the value of the isokinetic temperature with respect to solvent.

It should be noted that the present discussion is conditioned by the reliability of numerical values used for solvent parameters. Thus, had we used the values determined by Gonçalves *et al.*,[41] for the solvatochromic parameter α_{KT} of the alcohols, the latter scale would jump from fifth to second position in this comparison.

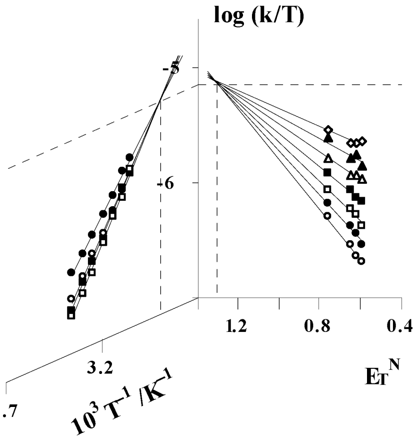

Fig. 2 Combined isokinetic [eqn. (1)] and isosolvent [E_T^N solvent scale, eqn. (6)] plots for the quaternisation reaction of Et_3P with EtI. Kinetic data from Table 1. Left, in different solvents using the same symbols as in Fig. 1. Right, at different temperatures: (○), 298.15 K; (●), 303.15 K; (□), 308.15 K; (■), 313.15 K; (△), 318.15 K; (▲), 323.15 K; and (◇), 328.15 K.

Quaternisation of triethylamine by iodoethane

The Menshutkin reaction is one of the best investigated chemical reactions in solution.[1,42] It is therefore a good choice as a reference reaction for comparison purposes. The effects of temperature and alcohols as solvent on the kinetics of reaction between triethylamine and iodoethane (Scheme 1) were studied in our laboratory and published elsewhere.[15,43] On those occasions second-order rate constants k_2 were expressed using the units (mole fraction)$^{-1}$ s^{-1}. In dilute solutions, these units can be converted to the conventional concentration scale by means of eqn. (9) where V_A* stands for the molar volume of the pure solvent. Actually, we used the values for molar volumes determined at 298.15 K in our laboratory,[44] thus obtaining the rate constants in temperature-independent units[21] reproduced for convenience in Table S2 †. Except for two pairs of temperature–solvent, namely at the highest temperature in methanol and at the lowest temperature in butan-1-ol, the kinetic data in Table S2 † for the triethylamine as nucleophile were obtained in the same solvents and experimental temperatures as in the case where triethylphosphine is the reagent (Table 1).

$$k_2\ /\mathrm{dm^3\ mol^{-1}\ s^{-1}} = (V_A{}^*/\mathrm{dm^3\ mol^{-1}}) \times k_2/(\text{mole fraction})^{-1}\ \mathrm{s^{-1}} \quad (9)$$

The aforementioned units conversion is important on two inter-linked grounds. For one, numerical values for standard entropies of activation depend on the units used for expressing rate constants.[45] For another, since the conversion factor varies with the nature of the solvent, then the value for the isokinetic temperature with respect to solvent in a given series of second-order reactions will also be dependent on the composition scale in which rate constants are expressed. These remarks can be better understood with reference to eqn. (2). Because a change in standard state will affect the values of activation entropies but not those of activation enthalpies, the isokinetic temperature for these reaction series will depend on the choice of

Table 4 Standard enthalpies of activation $\Delta^{\neq}H^{\circ}$ and standard entropies of activation $\Delta^{\neq}S^{\circ}$ derived from eqns. (1) and (3) for the reaction Et_3N + EtI in a series of solvents

	$\Delta^{\neq}H^{\circ}$/kJ mol^{-1}		$\Delta^{\neq}S^{\circ}$/J K^{-1} mol^{-1}	
Solvent	Eqn. (1)	Eqn. (3)	Eqn. (1)	Eqn. (3)
MeOH	75.02	73.65 ± 0.69	−97	−101 ± 3
EtOH	76.03	76.78 ± 0.57	−95	−93 ± 2
PrOH	77.65	78.92 ± 1.01	−93	−89 ± 4
BuOH	78.61	76.75 ± 0.98	−92	−98 ± 4

standard state and hence on the units for second-order rate constants.

Isokinetic relationship

Analysing the kinetic data in Table S2† for the quaternisation reaction of triethylamine by iodoethane in terms of the IKR using eqn. (1) and the IKR-80-20 programme,[23] and of Eyring equation using eqn. (3) leads to the activation parameters reported in Table 4.

Although the IKR-constrained values for enthalpies and entropies of activation deviate moderately from their free Eyring-plot values, the isokinetic relationship is statistically accepted ($F = 4.87$, $s_{00} = 0.0106$, $s_0 = 0.0125$). The best fitting parameters in eqn. (1) are $a_{IKR} = -0.108$ and $\beta_{IKR} = 730$ K, the resulting isokinetic plot being shown on the right[40] of Fig. 3. The isokinetic temperature with respect to solvent is thus well above the experimental range. In terms of Linert's theory, eqn. (5) yields $\tilde{\nu}_{\text{heat bath}} = 507$ cm^{-1} for this reaction. Having examined the infrared spectrum of the solvents, we found that all of the four alcohols show up a broad band that includes the estimated common heat-bath wavenumber for the solvents. The peak of this band for the different alkan-1-ols used as solvent lies in the narrow interval 650–647 cm^{-1}. For the interpretation of infrared spectra of alcohols, Coates[46] refers to a group frequency in the range 720–590 cm^{-1} originated in the hydroxyl group, which is assigned to O–H out-of-plane bend. Using this information, we tentatively relate the isokinetically important vibrational absorption at about 507 cm^{-1} to some disturbance in the solvent hydrogen-bond network caused by energy transfer during the activation process.

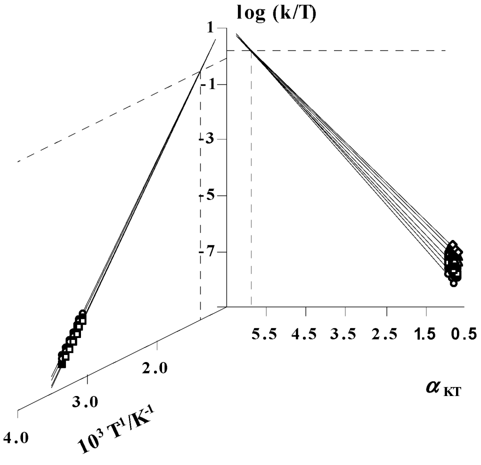

Fig. 3 Combined isokinetic [eqn. (1)] and isosolvent [a_{KT} solvent scale, eqn. (6)] plots for the quaternisation reaction of Et_3N with EtI. Kinetic data from Table S2†. Right, in different solvents using the same symbols as in Fig. 1. Left, at different temperatures using the same symbols as in Fig. 2.

In a reanalysis of literature data for the reaction between iodomethane and a series of primary, secondary and tertiary aliphatic amines in aqueous solution, Bel'skii[3] found this series to be described by an IKR with $\beta_{IKR} = -1232$ K. The large negative isokinetic temperature is then appropriately interpreted in terms of Schmid and Han's rationalisation of the anti-compensation effect.[47,48] On this basis Bel'skii[3] proposed a two-step reaction mechanism consisting of a reversible equilibrium between reactants and ion pairs, followed by dissociation into separated ions. In modern usage[2] this mechanism is described as an $A_N{*}D_N$ reaction. Apparently, the change of solvent from the high electric permittivity water to the much lower electric permittivity alkan-1-ols, will disfavour the formation of ion pairs. Also of interest is Bel'skii's finding of $\beta_{IKR} = 6145$ K for a numerous series of displacement reactions using anionic nucleophiles in water.[3]

At this stage we highlight the striking variation in isokinetic temperature, and therefore in the fine details of the activation process, following the change in nucleophile from triethylphosphine to triethylamine. We note further that both isokinetic temperatures are positive, as in the case of anionic reagents in similar reactions in solution.[3] Also, on comparing Table 2 for Et_3P as nucleophile with Table 4 for Et_3N, it is clear that activation enthalpies and entropies are much more solvent dependent in the case when Et_3P is the nucleophile than in the case of Et_3N. This aspect, however, will be analysed later as it belongs to the realm of isoselective relationships.

Isosolvent relationship

The ISoR analysis done above for the phosphine series is now reproduced for the solvent effect on the original Menshutkin reaction in a series of alcohols at different temperatures. Table 5 summarises the results obtained by fitting the data in Table S2† to eqn. (6) using the IKR-80-20 programme[23] and different solvent scale parameters in Table S1†. Although the isosolvent relationship is statistically accepted for all of the solvent scales examined, chemical intuition will cast doubts regarding the appropriateness of the a_2^{H}, E_T^{N} and AN scales for correlating the amine series. Indeed, the corresponding regression values for the parameter $a_{ISoR}(Et_3N)$, which should match the value of −0.108 found for $a_{IKR}(Et_3N)$, are abnormally high. Interestingly, comparison of Tables 3 and 5 reveal that the order of best fitting solvent scales according to their quality of fit, is effectively reversed between these two apparently similar quaternisation reaction series. In addition, we observe that the best solvent scales for correlating the amine reaction series are those designed for describing average capabilities of a solvent in establishing hydrogen bonds with solute molecules (a_{KT} scale) and in non-specific stabilisation of electric charges and dipoles (π^* scale). The ISoR plot obtained using the a_{KT} scale is shown on the right[40] of Fig. 3. As displayed in this figure the matching between parameter values for a_{IKR} and a_{ISoR} is only fair for the amine reaction series. Present findings are in general agreement with previous studies using multiparametric equations for establishing linear solvation energy relationships. Thus, for the original Menshutkin reaction in a large set of hydroxylic solvents constituted mostly by aliphatic mono- and dialcohols, the empirical π^* scale was found to be the statistically most significant single descriptor of solvent effects on reaction rates[38] and on initial state Gibbs energies,[49] both at 298 K.

Summing up the similarity analysis of the Menshutkin reaction series, we evidenced the IKR revealing a high positive isokinetic temperature which, besides suggesting a non-specific energy exchange between solvating alcohol molecules and the reactants, runs together with the best solvent scales selected by the ISoR.

Isoselective relationship

The isoselective relationship (ISeR) is an important method for the similarity analysis of two different reaction series.[20] Using our kinetic data in Tables 1 and S2†, the selectivity of two different nucleophiles (Et_3P and Et_3N) towards a common substrate (EtI) can be appreciated in a series of solvents at different

Table 5 Isosolvent relationship (ISoR) parameters in eqn. (6) for the quaternisation of triethylamine by iodoethane at different temperatures in methanol, ethanol, propan-1-ol and butan-1-ol, using different solvent scales

			Standard deviation		
Solvent scale	SP_{ISoR}	a_{ISoR}	s_{00} unconstrained	s_0 ISoR	F^a
α_{KT}	5.856	0.188	0.0440	0.0386	0.21
π^*	3.780	1.560	0.0550	0.0474	0.13
α_2^{H}	8.14×10^3	38.5×10^3	0.0571	0.0509	0.30
$E_{\mathrm{T}}^{\mathrm{N}}$	26.8×10^3	56.4×10^3	0.0653	0.0584	0.32
AN	553×10^3	34.5×10^3	0.0897	0.0810	0.38

[a] *F*-test value at 95% confidence level.

temperatures. By convention, selectivities are expressed using the ratio fast-to-slow reaction rates. The corresponding selectivity relationship is given by eqn. (10), which is an analogue of eqn. (1).

$$\log\,[k(\mathrm{Et_3P})/k(\mathrm{Et_3N})]_{ij} = a_{\mathrm{ISeR}} + b_i\,(T_j^{-1} - \beta_{\mathrm{ISeR}}^{-1}) \qquad (10)$$

In eqn. (10) the fitting parameter β_{ISeR} is designated as the isoselective temperature with respect to solvent. At this temperature the selectivity is given by a_{ISeR}, the latter value remaining unchanged upon solvent variation.

An interesting consequence arises when an ISeR links two reaction series. Thus for corresponding reactions in the two series, differences in their activation enthalpies are linearly related to differences in their activation entropies, the slope being the isoselective temperature.[20,50] This similarity consequence, which may be observed even if the IKR does not hold for individual reaction series,[51] is described by eqn. (11).[20,50]

$$\Delta^{\neq}H_i^{\circ}(\mathrm{Et_3N}) - \Delta^{\neq}H_i^{\circ}(\mathrm{Et_3P}) = \mathrm{constant} + \beta_{\mathrm{ISeR}}\,[\Delta^{\neq}S_i^{\circ}(\mathrm{Et_3N}) - \Delta^{\neq}S_i^{\circ}(\mathrm{Et_3P})] \qquad (11)$$

Using the versatile IKR-80-20 programme,[23] the existence of an ISeR among these reaction series is statistically validated ($F = 9.72$, $s_{00} = 0.0192$, $s_0 = 0.0263$) and the adjustable parameters in eqn. (10) are found to be $a_{\mathrm{ISeR}} = 1.614$ and $\beta_{\mathrm{ISeR}} = 289$ K. The former value is therefore the predicted common selectivity to be observed in different primary alcohols at 289 K. The fact that $\beta_{\mathrm{ISeR}} = 289$ K is closer to $\beta_{\mathrm{IKR}}(\mathrm{Et_3P}) = 347$ K than to $\beta_{\mathrm{IKR}}(\mathrm{Et_3N}) = 730$ K is readily understood in terms of the structure of eqn. (11). Since variations in activation parameters along the phosphine series (Table 2) are steeper than along the amine series (Table 4), then eqn. (11) will give a bias towards to the reaction series exhibiting the steepest changes in activation enthalpies and entropies. The ISeR evidencing the competition of $\mathrm{Et_3P}$ and $\mathrm{Et_3N}$ in the nucleophilic attack on EtI is shown on the left of the open-book diagram[40] depicted in Fig. 4. The isoselective temperature is only 9 K below the lowest experimental temperature. It can thus be expected that a reversal in the selectivity order will be observed at temperatures below 289 K. According to eqn. (11), the temperature dependence of selectivity is linked to the value found for β_{ISeR}. As a general rule,[20] low β_{ISeR} values signal dominant entropic contributions which can be associated with early transition states. In the case under examination, an isoselective temperature slightly below the experimental conditions should indicate balanced contributions of activation enthalpies and entropies between the reaction series being compared.

The isoselective temperature with respect to solvent can be independently estimated from the previously determined isokinetic temperatures with respect to solvent for both reaction series. Exner and Giese[50] give this relationship in the form of eqn. (12), where a_H is the slope for the linear variation of $\Delta^{\neq}H_i^{\circ}(\mathrm{Et_3N})$ against $\Delta^{\neq}H_i^{\circ}(\mathrm{Et_3P})$.

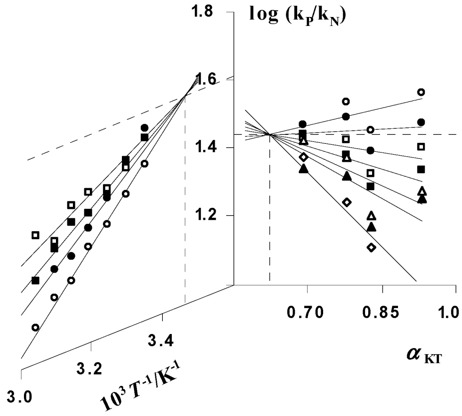

Fig. 4 Combined isoselective plots according to eqn. (10) and to eqn. (13) with the α_{KT} solvent scale. Selectivity data for the attack of $\mathrm{Et_3P}$ and $\mathrm{Et_3N}$ on EtI constructed with the kinetic data in Tables 1 and S2†. Left, in different solvents using the same symbols as in Fig. 1. Right, at different temperatures using the same symbols as in Fig. 2.

$$\beta_{\mathrm{ISeR}}(\mathrm{calc}) = (a_H - 1)\,\beta_{\mathrm{IKR}}(\mathrm{Et_3P})\,\beta_{\mathrm{IKR}}(\mathrm{Et_3N})/[a_H\beta_{\mathrm{IKR}}(\mathrm{Et_3P}) - \beta_{\mathrm{IKR}}(\mathrm{Et_3N})] \qquad (12)$$

Using the data in Tables 2 and 4 for activation enthalpies derived in terms of eqn. (1), we obtained $a_H = 0.2183$ and eqn. (12) yields $\beta_{\mathrm{ISeR}}(\mathrm{calc}) = 302$ K, which is in fair agreement with $\beta_{\mathrm{ISeR}}(\mathrm{exp}) = 289$ K. This small difference may in part be ascribed to the fact that the value for $\beta_{\mathrm{IKR}}(\mathrm{Et_3P})$ used in eqn. (12) is based on two more experimental data points than the other quantities.

Similarity analyses in terms of selectivities can be taken a step forward. Seemingly for the first time, we examine the relationship at different temperatures between selectivity and solvent parameter. In the event of an isoselective relationship being obeyed, it will be described by eqn. (13), which is similar to eqn. (6).

$$\log\,[k(\mathrm{Et_3P})/k(\mathrm{Et_3N})]_{ij} = a_{\mathrm{ISeR}} + b_j\,(SP_i - SP_{\mathrm{ISeR}}) \qquad (13)$$

We keep the designation ISeR for similarity analyses based on eqn. (13), in which the fitting parameter SP_{ISeR} identifies the isoselective solvent with respect to temperature. The selectivity will therefore be temperature-independent when competing reactions are run in the isoselective solvent. No thermodynamically awkward situation is likely to arise in this solvent. Since solvent scales are assumed to be temperature independent, differentiating eqn. (13) with respect to the inverse of temperature leads to eqn. (14).

$$\Delta^{\neq}H_i^{\circ}(\mathrm{Et_3P}) - \Delta^{\neq}H_i^{\circ}(\mathrm{Et_3N}) = -2.303\,R\,(\partial\, b/\partial\, T^{-1})_p\,(SP_i - SP_{\mathrm{ISeR}}) \qquad (14)$$

Hence the special condition imposed by an isoselective solvent is that activation enthalpies will be the same for competing

Table 6 Isoselective relationship (ISeR) parameters in eqn. (13) and values calculated by eqn. (16) for the competing quaternisation of triethylphosphine and triethylamine by iodoethane at different temperatures in methanol, ethanol, propan-1-ol and butan-1-ol, using different solvent scales

Solvent scale	SP_{ISeR}	a_{ISeR}	Standard deviation s_{00} unconstrained	 s_0 ISeR	F^a	a_b	SP_{IseR} (calc)
α_{KT}	0.622	1.440	0.0635	0.0577	0.41	0.3417	−0.561
π^*	0.435	1.433	0.0663	0.0603	0.41	0.1198	0.599
α_2^{H}	0.273	1.432	0.0686	0.0646	0.61	4.19×10^{-5}	0.246
$E_{\mathrm{T}}^{\mathrm{N}}$	0.525	1.425	0.0695	0.0665	0.71	3.20×10^{-5}	0.449
AN	33.84	1.418	0.0738	0.0742	1.03	4.70×10^{-5}	31.60

[a] F-test value at 95% confidence level.

reactions. Nevertheless, their entropies of activation will differ by an amount that can be estimated with the help of eqn. (11). In other words, in isoselective solvents selectivities are entirely entropy controlled.

This novel ISeR analysis is done using again the IKR-80-20 programme[23] for correlating our experimental selectivity data with solvent empirical parameters. Taking the appropriated data from Tables 1, S1 † and S2 †, the results of the selectivity analysis in terms of the new eqn. (13) are summarised in Table 6. The ISeR with respect to temperature is statistically accepted for each of the five solvent scales employed to describe solvent effects. In Table 6 these scales are ordered by decreasing quality of fitting. Comparison of Table 6 with Tables 3 and 5 indicates that the ISeR with respect to temperature is dominated by the effect of solvent on the Menshutkin reaction, which is the slower and more selective of the two competing reactions. The values for SP_{ISeR} in the different scales point to a higher alkan-1-ol as the isoselective solvent for this pair of reactions. Indeed, for hexan-1-ol[30] $\alpha_{\mathrm{KT}} = 0.65$ and $\alpha_2^{\mathrm{H}} = 0.29$, these values being slightly above the corresponding experimental SP_{IseR} values of 0.62 and 0.27, respectively. It seems therefore to be realistic to run these quaternisation reactions under experimental conditions of isoselectivity. However, our results for the ISeR with respect to temperature led to standard deviations (Table 6) which are about twice as large as the value of 0.0263 obtained for the ISeR with respect to solvent. In addition, there is also an imperfect matching between the values for a_{ISeR} derived from the two alternative representations for ISeR as exemplified in Fig. 4 when using the α_{KT} scale.

In the case where an ISeR with respect to temperature holds for two reaction series that obey the ISoR, there should exist a relationship among the corresponding three isosolvent parameters. This link can be established by noting that, for example, the parameter SP_{ISoR} in eqn. (6) plays the same formal role as $\beta_{\mathrm{IKR}}{}^{-1}$ does in eqn. (1). We start by rearranging Exner and Giese's[50] eqn. (12) into the form of eqn. (15).

$$\beta_{\mathrm{ISeR}}(\mathrm{calc})^{-1} = [a_H\, \beta_{\mathrm{IKR}}(\mathrm{Et_3N})^{-1} - \beta_{\mathrm{IKR}}(\mathrm{Et_3P})^{-1}] / (a_H - 1) \quad (15)$$

By making isosolvent parameters, SP fill the place of their analogue β^{-1} parameters in eqn. (15), we obtain eqn. (16) in which a_b is the slope for the linear dependence of $b_{\mathrm{j}}(\mathrm{Et_3N})$ on $b_{\mathrm{j}}(\mathrm{Et_3P})$.

$$SP_{\mathrm{ISeR}}(\mathrm{calc}) = [a_b\, SP_{\mathrm{ISoR}}(\mathrm{Et_3N}) - SP_{\mathrm{ISoR}}(\mathrm{Et_3P})] / (a_b - 1) \quad (16)$$

Given the novelty of the present analysis, we tested eqn. (16) numerically using SP_{ISoR} values from Tables 3 and 5. The slope a_b in the different solvent scales was obtained from linear regression of the fitting parameters b_{j} for the constrained ISoR equations. Results of this exercise are reported in the last two columns of Table 6. The values of empirical parameters for the isoselective solvent calculated in accordance to eqn. (16) generally agree with the corresponding experimental values. The notable exception is for the α_{KT} solvent scale. However, as noted in Table 3 this scale is the least appropriated for expressing the ISoR in the case of the quaternisation reaction of triethylphosphine.

Desolvation and reaction mechanism

Since at least 1976 the term 'desolvation'[52] has become increasingly used in the chemical literature[11,52–67] to describe the releasing of solvent molecules in reactant solvation shells which needs to take place before activated complexes can be formed. This destruction of specific solvation structures is particularly marked for anionic nucleophiles as reagents in displacement reactions. Nonetheless, the concept of desolvation, but not the term itself had already been used in the context of Menshutkin reactions in solution as early as in 1964 by Tokura and Kondo.[68] Also, Johnson *et al.*[69] even considered pyridine molecules hydrogen-bonded to methanol molecules to be non-reactive towards iodoethane.

As suggested by Linert,[29] isokinetic temperature values shed light on the energy transfer between reactant and solvent molecules, the latter acting as a molecular heat bath. In turn, values for the a_{IKR} parameter allow insights into the reaction pathway. For the quaternisation reactions under examination, we note that isokinetic temperatures are both positive being much higher for the nucleophile triethylamine (730 K) than for triethylphosphine (347 K), a pattern also observed for their a_{IKR} negative values (−0.11 and −5.12, respectively). The latter comparison indicates that the energy requirement is greater for $\mathrm{Et_3N}$ than for $\mathrm{Et_3P}$. This difference can be confidently ascribed to the need for desolvation of the amine. However, the desolvation step does not appear to be kinetically independent. In effect a negative isokinetic temperature would be expected[47,48] for a truly two-step reaction following the $A_{\mathrm{N}}{*}D_{\mathrm{N}}$ mechanism. Otherwise, the reaction between $\mathrm{Et_3P}$ and EtI has all of the characteristics associated with the $A_{\mathrm{N}}D_{\mathrm{N}}$ mechanism, being free from desolvation effects.

Conclusions

From the foregoing comprehensive similarity analysis of the quaternisation reaction of triethylphosphine and triethylamine with iodoethane in a series of aliphatic alcohols at different temperatures, we draw the following main conclusions.

(i) Within the framework of Linert's theory for the isokinetic relationship,[25–27] we raise the possibility for isokinetic temperatures being determined by infrared-active heat-bath vibrational frequencies that do not show up in the spectra of pure liquid solvents. It is therefore of interest to explore the vibrational properties of solvating molecules for extending the applicability of Linert's theory.

(ii) For a given second-order reaction in a series of solvents, the numerical value of the isokinetic temperature will depend on the choice of standard state as implied by the composition scale used to express reaction rates. Although we simply preferred using the concentration scale, it is not clear how this variable affects isokinetic temperatures and thereby their significance.

(iii) In the case where a reaction in different solvents behaves in accordance with the isosolvent relationship, we demonstrate that the enthalpy of activation would vanish in the isokinetic solvent. This finding implies that no real solvent can be envisaged having the characteristic of an isokinetic solvent, *i.e.* in which rate constants would be directly proportional to the temperature.

(iv) By analogy with Exner and Giese's equation for predicting isoselective temperatures, we obtained eqn. (16) for the prediction of isoselective solvent parameter values from the knowledge of individual isosolvent parameter values. We also show that it is generally possible to select an isoselective solvent, *i.e.* a solvent in which both competing reactions have equal rate constants.

(v) We found the IKR-80-20 programme[23] to be both reliable and versatile in the similarity analysis of kinetic data.

(vi) Finally, we collected evidence supporting the view that, in aliphatic alcohols as solvent, the quaternisation of triethylphosphine by iodoethane is a much better model reaction for the A_ND_N mechanism than the classic original Menshutkin reaction between triethylamine and iodoethane. The desolvation of reactants plays an important part in the latter reaction, the mechanism of which having some characteristics of the $A_N{*}D_N$ mechanism. Similarity analysis is thus an efficient tool for elucidating the mechanism of chemical reactions in solution.

Experimental

Materials

Triethylphosphine (≥97%) and iodoethane (≥99.5%) were obtained from Fluka, the purity of iodoethane being controlled by gas-phase chromatography. Tetraethylphosphonium iodide (≥97%) was purchased from Aldrich and used as received; its purity was verified by argentimetry titration. Alcohols were obtained from Merck (≥99.5%) and their water content was kept lower than 0.02%. Spectrophotometric analysis confirmed that solvents contained no organic impurities. Solvents were stored under dry-nitrogen, their purity being periodically checked by density and conductivity measurements. Tetraethylphosphonium iodide was kept over P_2O_5 in a desiccator and its purity was verified by argentimetry titration.

Apparatus

A Wayne Kerr B 905 bridge (accuracy ±0.05%) and commercial conductivity cells (980-K19/120) were used to obtain the conductimetric data from which rate constants and calibration curves were calculated. Cells constants ranged from 0.9 to 1.0 cm^{-1}. Kinetic experiments were performed in a thermostated bath as described previously.[15,70] The temperature was kept constant to within ±0.01 K.

Kinetic measurements

All solutions were prepared by weight in the four solvents dried with oxygen-free nitrogen. Reacting solutions with equal initial concentrations in both reactants (approximately 0.03 mol dm^{-3}) were followed conductimetrically up to 15–30% conversions (depending on the reaction). Five kinetics runs were made at each temperature and solvent, approximately 100 experimental data points being obtained for each kinetic run. Concentration–time plots for the ionic reaction products were based on standard curves relating concentration to experimental conductance. As described elsewhere,[15,70] this calibration method is constructed on duplicate measurements for ten calibrating solutions in the concentration range 0.0002–0.010 mol dm^{-3} for each working temperature and solvent. After thermal equilibration conductance readings for the solutions were made at regular time intervals, the latter being chosen according to the reacting mixture. Rate constants were then calculated from the slope of linear plots describing the integrated second-order rate law for equal initial concentration in both reactants, which gave good correlation coefficients.

Acknowledgements

We thank Dr Luís F. Gouveia for supplying the computer programme used to draw the appealing open-book double-diagrams. We also thank the financial support by Fundação para a Ciência e a Tecnologia.

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