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ALKYLATION OF PYRIDINIUM-*N*-PHENOXIDE BETAINE DYES WITH IODOMETHANE: SUBSTITUENT, SOLVENT AND TEMPERATURE DEPENDENCE

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The rate constants of the pseudo-first-order methylation reaction of seven substituted pyridinium-*N*-phenoxide betaine dyes by iodomethane, were determined by UV–visible spectrophotometry in nine different solvents. The influence of substituents on the position of the long-wavelength, intramolecular charge-transfer absorption band of the unsubstituted betaine dye can be described by a modified Hammett equation. The solvent-dependent absorption constant ρ_A correlates satisfactorily with the acceptor properties of the nine solvents used. The substituent-dependent alkylation rate constants ($\ln k$) correlate linearly with the Hammett substituent constants, whereas the solvent-dependence of $\ln k$ follows a more complicated pattern. Temperature-dependent measurements of the rate of alkylation exhibit an isoenthalpic behaviour for all the betaines in all the solvents investigated, i.e. the Arrhenius activation energy is almost constant for all differently substituted betaines in a given solvent. Temperature-dependent measurements of the alkylation rate of the unsubstituted betaine in different solvents led to an isosolvent relationship, i.e. the corresponding Arrhenius plots show a common point of intersection. According to the theory of isokinetic relationships, this isosolvent behaviour is interpreted in terms of a resonant energy exchange between the reacting species and the surrounding heat-bath system, which in this particular case seems to be the betaine molecule itself.

INTRODUCTION

In recent years, many solvent parameters for the empirical description of solute–solvent interactions have been proposed, but only few of them have survived the application test and are now commonly accepted.[1,2] Amongst them are the $E_T(30)$ values of Reichardt and co-workers[1,3] and the acceptor numbers (*AN*) of Gutmann and co-workers.[4,5]

$E_T(30)$ values are defined as molar transition energies (in kcal mol^{-1}) for the longest wavelength, intramolecular charge-transfer UV–visible absorption band of the dissolved standard betaine dye **1a** (Scheme 1). They are known for more than 300 solvents[1,6–8] and numerous binary solvent mixtures,[1,9] and they have found many applications, e.g. in analytical chemistry.[10]

Acceptor numbers (*AN*) are derived from the relative ^{31}P NMR chemical shift of triethylphosphane oxide in a given solvent relative to the shift of the 1 : 1 adduct $Et_3PO \rightarrow SbCl_5$ with *n*-hexane ($AN = 0$) as reference solvent. They are known for about 50 solvents and some binary solvent mixtures.[4,5,11]

Both probe molecules, the solvatochromic betaine dye **1a** and triethylphosphane oxide, possess with the $N^+{-}O^-$ and $P^+{-}O^-$ groups a negatively charged oxygen atom capable of specific interactions with hydrogen-bond donor (HBD) and electron-pair acceptor (EPA) solvents. Thus, in addition to the non-specific solute–solvent (i.e. van der Waals) interactions,[12] both probe molecules are particularly suitable for the registration of the solvent Lewis acidity, i.e. the acceptor properties of the surrounding solvent molecules.[12,13] Therefore, a satisfactory linear correlation exists between $E_T(30)$ and *AN* for a set of selected solvents.[5]

The $E_T(30)$ values are strongly temperature dependent (they increase with decreasing temperature) and

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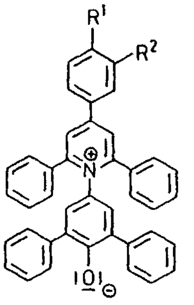


Scheme 1.

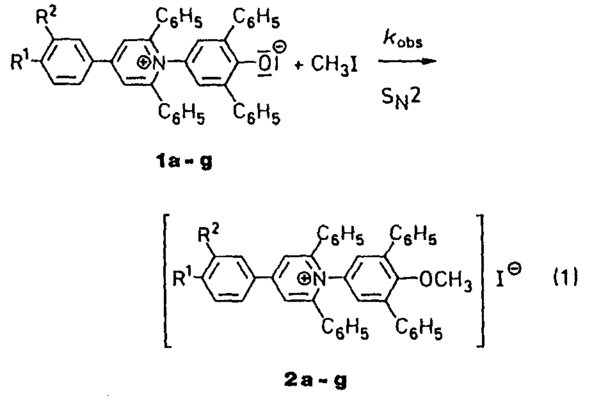
Betaine	R^1	R^2	σ^a
1a	H	H	0·000
1b	CH_3	H	−0·170
1c	H	OCH_3	0·115
1d	Cl	H	0·227
1e	H	Cl	0·373
1f	CF_3	H	0·54
1g	H	NO_2	0·710

[a] Hammett substituent constants taken from reference 17.

the corresponding thermochromism of solutions of **1a** is, in contrast to *AN*, easily measurable.[14]

The often linear correlation between empirical solvent parameters and other solvent-dependent properties (e.g. logarithms of rate and equilibrium constants, absorption energies) can be considered as manifestations of general linear free-energy relationships (LFERs).[1,15,16] Since LFERs and the so-called isokinetic relationships (IKR)[16] are closely related by theory, it seemed of interest to compare the thermochromism of the solvatochromic betaine dyes used to establish the $E_T(30)$ scale with their kinetic behaviour at different temperatures in different solvents.

Previous work has already shown that the alkylation of the pyridinium-*N*-phenoxides **1a**–**g** by iodomethane according to equation (1) follows a simple S_N2 mechanism in many solvents.[18] With an excess of iodomethane, pseudo-first-order kinetics can be observed, which can easily be followed by UV/visible spectrophotometry, since with increasing alkylation of **1a**–**g** to the (methoxyphenyl)pyridinium salts **2a**–**g**, the long-wavelength absorption band of **1a**–**g** gradually disappear. In this way, the rate constants of the methylation reaction (1) for seven differently substituted betaine dyes **1a**–**g** were determined at various temperatures in nine solvents.



EXPERIMENTAL

The rate of reaction (1) was determined using the stopped-flow technique with a stopped-flow UV–visible spectrophotometry (Tracor Northern, TN-1705) which was combined with a multi-channel analyser (Tracor Northern, TN-1710), both supplied by Applied Photophysics (London). This instrument permits the registration of 1016 data points between 400 and 900 nm. The measurements showed clearly that reaction (1) proceeds without the formation of coloured intermediates or side-products. Further kinetic measurements were performed with a Durrum D-110 stopped-flow spectrophotometer at the wavelength of maximum absorption of the betain dyes **1a**–**g** in the solvent under investigation. For that purpose, their UV–visible spectra were recorded beforehand with a Cary 17-D spectrophotometer. The cell temperature was kept constant with a Haake F4/k or Lauda TUK 30D thermostat within the limits of ±0·05 and ±0·1 K, respectively. The far-IR spectra were recorded with a model 20F Fourier-transform spectrometer (Nicolet Instruments).

The betaine dyes **1a**–**g** were synthesized according to published procedures.[3,10,18] Iodomethane (Merck, Darmstadt) was used as obtained. Acetone (AC), methyl acetate (MeOAc) and ethyl acetate (EtOAc) were dried dynamically with molecular sieve 3 Å. Acetonitrile (An) was refluxed with sodium hydroxide pellets for 48 h, distilled, refluxed twice over P_4O_{10} and redistilled. Chloroform was purified by passing it through a column filled with aluminium oxide. Dimethyl sulfoxide (DMSO) was refluxed with calcium hydride, distilled under reduced pressure and stored over molecular sieve 3 Å. Nitromethane (NM) and nitroethane (NE) were washed with water, dried with anhydrous calcium chloride and distilled under reduced pressure. Propane-1,2-diol carbonate (PDC) was dried with molecular sieve 4 Å and distilled twice under reduced pressure. Trimethyl phosphate (TMP) was refluxed over calcium hydride and distilled twice under reduced pressure. Tetrahydrofuran (THF) was refluxed over sodium and distilled. 1,2-Dichloroethane (DCE) was of general grade and used as received. All solvents had a water content of less than 100 mg l^{-1} as determined by Karl Fischer titration (except AC). The influence of traces of water on the rate was studied by varying the water content in An by mixing known amounts of water-rich and water-poor An, the water content of which had previously been determined by Karl Fischer titration.

Solutions of iodomethane were prepared by dissolving accurately weighed amounts of CH_3I to give concentrations of 0·3–0·5 mol l^{-1}. These solutions were used within 2 days because decompositions occurred in some solvents after 1–2 weeks. Under these circumstances, the reaction kinetics were strictly first order, so that the determination of betaine concentrations was not necessary. However, according to their molar absorptivities, the required concentrations of **1a**–**g** must be between 1×10^{-4} and 2×10^{-4} mol l^{-1}. Great care was taken to avoid traces of acids in the solvents used, because otherwise the betaine dyes are decolourized by protonation.[18]

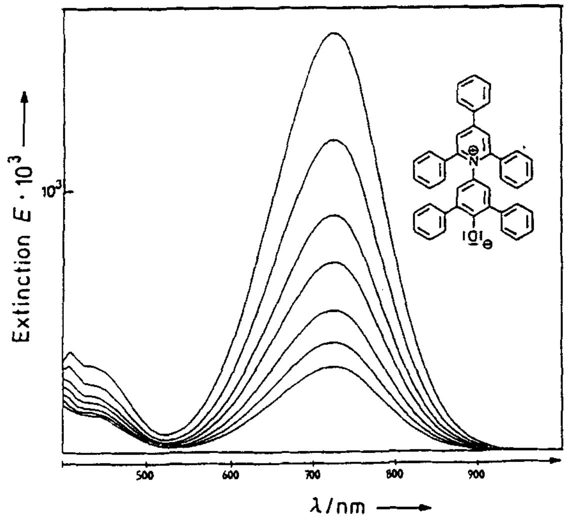


Figure 1. Decrease of the solvatochromic, long-wavelength UV–visible absorption band of betaine **1a** during methylation with iodomethane in chloroform at 19·9°C. *c*(betaine) = $2 \cdot 5 \times 10^{-4}$ mol l^{-1}; $c_0(CH_3I) = 0 \cdot 50581$ mol l^{-1}. Time interval between two spectra, 200 s; first spectrum recorded 60 s after reaction start

RESULTS

The mechanism of alkylation reaction (1), as proposed by Reichardt and Müller,[18] was confirmed by the observed strict pseudo-first-order behaviour and the absence of any other coloured intermediate, as can be seen in Figure 1, showing the decrease in the betaine UV–visible absorption with increasing methylation. Typical values of the pseudo-first-order rate constants $k[= k_{obs}/c_0(CH_3I)]$ are given in Table 1. In some solvents, however, deviations from this behaviour occurred: in DMSO, reaction of iodomethane with the solvent itself takes place and the *k*-values are no longer independent of the initial iodomethane concentration, yielding an apparently higher order in iodomethane. In nitroethane, the betaine dyes decompose. In methyl acetate, the reaction is not pseudo-first-order, with the concentration–time curves showing a distinct maximum. In trimethyl phosphate, the betaines eventually decompose. Despite this, linear pseudo-first-order plots could be obtained up to three half-lives, enabling us to obtain approximate rate constants in this case.

Because of preferential solvation of the betaine molecules by the more polar component of binary solvent

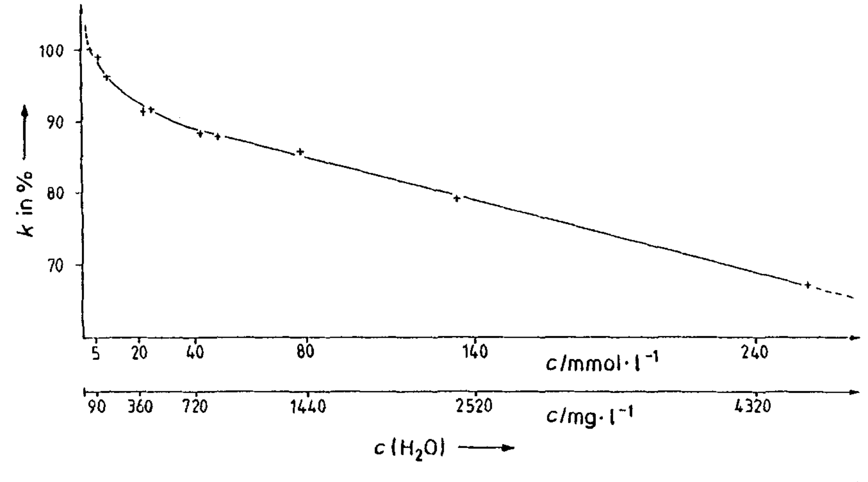


Figure 2. Influence of traces of water on the rate constant *k* of methylation of betaine **1a** with iodomethane in acetonitrile–water mixtures at 25°C

Table 1. Typical pseudo-first-order rate constants, 10^3k(l mol^{-1} s^{-1}), for reaction (1), determined in nine different solvents at temperatures (°C) given in parentheses by measuring the decrease in the long-wavelength UV–visible absorption band of **1a–g** at the given wavelength λ_{max}(nm)

Solvent	**1a**	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**
AC[a]	680 nm	677 nm	688 nm	700 nm	706 nm	716 nm	
	(5·1) 38·9						
	(10·2) 53·1	(10·2) 45·2	(10·1) 50·0	(10·0) 46·2	(10·1) 43·0	(10·1) 37·1	
	(15·4) 71·7						
	(20·3) 91·9	(20·6) 89·6	(20·4) 90·3	(20·4) 86·9	(20·5) 78·1	(20·5) 68·6	
	(25·2)124·1	(25·8)118·6	(25·4)120·8	(25·4)115·8	(25·5)102·3	(25·5) 89·7	
	(30·0)165·2	(30·1)150·8	(30·2)163·6	(30·6)157·0	(30·2)133·1	(30·4)116·5	
	(35·5)228·9	(35·2)213·7	(35·1)217·3	(35·4)214·6	(35·3)186·2	(35·4)161·8	
EtOAc[a]	750 nm	745 nm	754 nm	768 nm	774 nm	784 nm	
	(10·1) 33·3	(10·3) 36·5	(10·3) 33·9	(10·1) 29·1	(10·4) 28·7	(10·5) 24·7	
					(15·4) 38·5	(15·4) 33·6	
	(20·2) 58·9	(20·1) 65·9	(20·1) 60·9	(20·0) 57·2	(21·1) 52·9	(20·4) 46·1	
	(25·1) 75·5	(25·0) 84·9	(25·2) 81·6	(25·2) 71·5	(25·6) 67·7	(25·5) 59·7	
	(29·9)100·8	(30·0)109·0	(30·4)107·5	(30·1) 95·1	(30·6) 89·5	(30·3) 79·9	
	(35·1)127·8	(35·1)142·3	(35·3)147·8	(35·3)125·7	(35·6)116·1	(35·5)100·4	
An[a]	624 nm	618 nm	626 nm	638 nm	648 nm	659 nm	
	(10·1) 11·9	(10·3) 12·2	(10·6) 11·2	(10·6) 11·0	(10·2) 10·4	(10·2) 9·3	
	(15·2) 16·1	(15·6) 17·3	(15·5) 16·1	(15·5) 15·4	(15·3) 14·8	(15·3) 13·4	
	(20·1) 23·2	(20·4) 23·2	(20·8) 22·8	(20·6) 21·4	(20·8) 21·6	(20·7) 19·0	
	(25·4) 29·8	(25·6) 32·3	(25·7) 32·8	(25·8) 30·3	(25·8) 30·3	(25·6) 26·6	
	(30·1) 42·0	(30·5) 43·8	(30·6) 44·3	(30·7) 42·2	(30·8) 42·2	(30·6) 36·8	
	(35·5) 56·2	(35·9) 59·4	(35·6) 58·2	(35·4) 55·3	(35·5) 54·4	(35·5) 51·2	
CHCl$_3$[a]	720 nm	720 nm	733 nm	752 nm	761 nm	—	798 nm
	(16·2) 2·83	(13·9) 4·12	(13·8) 3·35	(13·9) 2·73	(13·8) 3·16		(13·8)2·63
	(21·1) 3·68	(20·0) 5·35	(20·0) 4·54	(20·0) 4·08	(20·0) 4·08		(20·0)3·06
	(25·8) 5·69	(25·1) 8·21	(25·0) 6·54	(25·1) 5·15	(25·1) 5·47		(25·0)3·93
	(29·5) 7·86	(29·9) 10·4	(29·9) 8·72	(30·0) 7·62	(30·0) 7·32		(29·9)5·40
		(35·0) 14·6	(35·0) 12·9	(35·0) 9·98	(35·1) 10·3		(35·3)7·57
NM	620 nm	616 nm	623 nm	632 nm	639 nm	654 nm	
	(25·0) 13·3	(25·0) 12·3	(25·0) 11·8	(25·0) 11·2	(25·0) 11·2	(25·0) 10·0	
PDC	619 nm	619 nm	623 nm	623 nm	640 nm	651 nm	
	(25·0) 16·2	(25·0) 16·7	(25·0) 16·4	(25·0) 15·5	(25·0) 14·7	(25·0) 13·8	
TMP[b]	657 nm	656 nm	660 nm	670 nm	677 nm	694 nm	
	(25·0) 76·8	(25·0) 79·5	(25·0) 78·6	(25·0) 73·3	(25·0) 67·1	(25·0) 58·4	
THF[a]	764 nm						
	(15·7) 45·4						
	(21·2) 60·6						
	(25·4) 80·9						
	(29·5)102·1						
	(34·0)135·4						
	(39·0)193·7						
DCE	682 nm						
	(16·3) 3·98						
	(25·7) 6·64						
	(34·0) 12·2						
	(38·9) 19·3						

[a] The λ_{max} values in this table are in good agreement with those given in Ref. 18.

[b] Solutions of the betaine dyes **1a–f** are unstable in TMP (>50% decomposition within 24 h) and the semi-logarithmic first-order plots indicate three half-lives. Despite this, the rate constants could be obtained from the linear part of the kinetic curves.

mixtures,[1,9] traces of water in solutions of **1a** in less polar solvents have a tremendous effect on the position of its solvatochromic UV–visible absorption band. For example, for **1a** a hypsochromic shift of 46 nm is observed on going from pure acetonitrile to a 98:2 (v/v) acetonitrile–water mixture! This can be used as a rapid procedure for determination of water in organic solvents.[9,10] For the same reason, the rate of methylation of **1a** should also depend strongly on the water content. This is indeed the case, as shown by Figure 2.

With increasing water content, the methylation rate of **1a** in acetonitrile–water mixtures decreases, owing first exponentially [up to $c(H_2O \approx 700\ \text{mg}\ l^{-1}]$ and then linearly, owing to preferential solvation of **1a** by the HBD solvent water. Hydrogen bonding to the phenoxide oxygen atom of **1a** reduces its nucleophilicity.

Substituent variation

The substituent-dependent shifts of the solvatochromic UV–visible absorption bands of **1a–g**, measured in a given solvent as the change in molar transition energy E_T, can be quantitatively described by means of a modified Hammett equation:

$$(E_{T,R} - E_{T,0})/(2\cdot303RT) = \rho_A\sigma \qquad (2)$$

first introduced by Kosower *et al.*[19] $E_{T,R}$ and $E_{T,0}$ refer to the absorption of the substituted and unsubstituted betaine dyes, respectively; σ is the common Hammett substituent constant[17] and ρ_A is called absorption constant because it refers to the susceptibility of the absorption behaviour of an absorbing species to a substituent change [= slope of the line given by equation (2)]. The ρ_A values given in Table 2 are in good agreement with those determined by Reichardt and Müller.[18]

These susceptibility parameters are solvent dependent and they exhibit a statistically significant, but nevertheless weak, linear correlation with the acceptor numbers, as shown in Figure 3, if one excludes HBD solvents such as alcohols. Increasing electron-accepting power of the non-HBD solvents correspond to a decrease in ρ_A. A linear correlation of similar weak quality is obtained with the $E_T(30)$ values (cf. inset in Figure 3) if HBD solvents (alcohols), haloalkanes (chloroform), and 1,4-dioxane are excluded (open squares in Figure 3). These solvents are known for their very specific interactions with solutes such as the betaines **1a–g**, and they have also been excluded in the correlation between *AN* and $E_T(30)$.[6]

Normal Hammett plots of the substituent-dependent rate constants of reaction (1), using ln *k* at different temperatures calculated from the Arrhenius equation, are found to be linear, as shown in figure 4, which also includes the respective temperature dependence of ln *k*. The corresponding Hammett reaction parameters, ρ_K, are given in Table 2. The linearity of the Hammett plot shown in Figure 4 is improved by correlating the ln *k* values, determined in a given solvent, instead of with σ, with ln *k* values measured in propane-1,2-diol carbonate (PDC), according to equation (3) ($k_0 = k_{1a}$):

$$\ln(k/k_0)_{\text{solv}} = \ln(k/k_0)_{\text{PDC}}\rho_{K'} \qquad (3)$$

In addition, the ρ_K and $\rho_{K'}$-values (cf. Table 2) correlate linearly with each other ($r = -0\cdot996$). This implies that the influence of substituents on the rate of reaction (1) is governed mainly, but not exclusively, by the same electronic factors which are described by the Hammett σ values. The solvent-dependent slopes of the Hammett relation (3), indicated by $\rho_{K'}$ (cf. Table 2), decrease with increasing *AN* or $E_T(30)$. This indicates a competition between the entering iodomethane molecule and the solvent molecules surrounding the nucleophilic phenoxide centre of **1a–g**: the easier the solvent molecules are replaced (i.e. the weaker their acceptor properties are), the more is the methylation rate governed

Table 2. Hammett absorption parameters ρ_A[a,b] and Hammett reaction parameters ρ_K[a,c] and $\rho_{K'}$[a,d], predetermined by UV–visible spectrophotometry from the substituent-dependent absorption of **1a–g**, and kinetically from the substituent-dependent alkylation reaction (1), respectively, and the regression coefficients *r* of the corresponding LFE relationships

Solvent	$-\rho_A$[b]	$-r$	$-\rho_K$[c]	$-r$	$-\rho_{K'}$[d]	$-r$
AC	2·28[e]	0·985	0·39	0·82	0·66	0·92
An	2·91[e]	0·974	0·30	0·95	0·93	0·98
$CHCl_3$	3·29[e]	0·991	0·74	0·97	0·37	0·84
EtOAc	1·52	0·994	0·51	0·94	0·53	0·99
NM	2·63	0·979	0·33	0·88	0·89	0·87
PDC	2·38	0·970	0·27	0·95	1·00	1·00
TMP	2·06	0·926	0·43	0·92	0·63	0·99

[a] Defined as the slope of the respective LFER plots.
[b] As defined by equation (2).
[c] As defined by the Hammett equation $\ln(k/k_0) = \rho_K\sigma$.
[d] As defined by equation (3).
[e] Taken from Ref. 18.

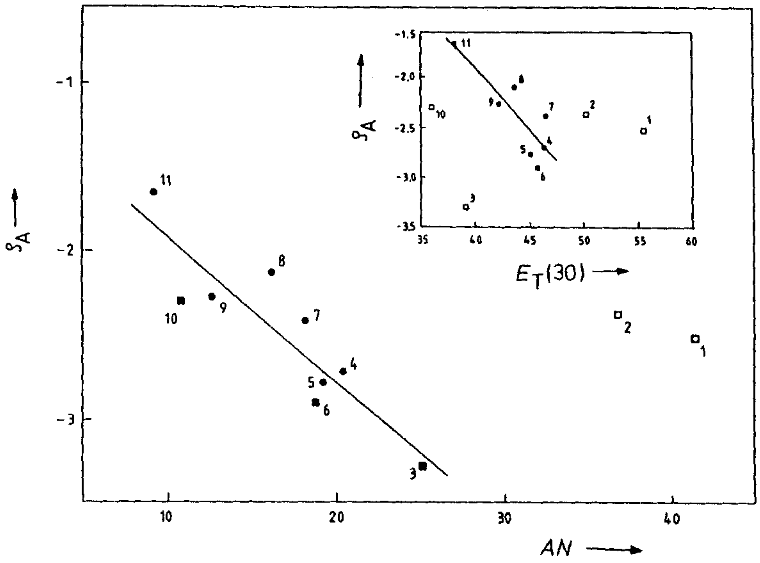


Figure 3. Linear correlation between absorption constants ρ_A, i.e. Hammett susceptibility parameters derived from UV–visible spectrophotometric measurements,[19] and the acceptor number *AN* (correlation coefficient $r = -0{\cdot}984$). Inset: correlation between ρ_A and $E_T(30)$. Squares refer to data from Ref. 18 and circles to data given in this paper. Solvent numbering: 1, MeOH; 2, *n*-BuOH; 3, $CHCl_3$; 4, NM; 5, DMSO; 6, An; 7, PDC; 8, TMP; 9, AC; 10, 1,4-dioxane; 11, EtOAc (abbreviations as given under Experimental)

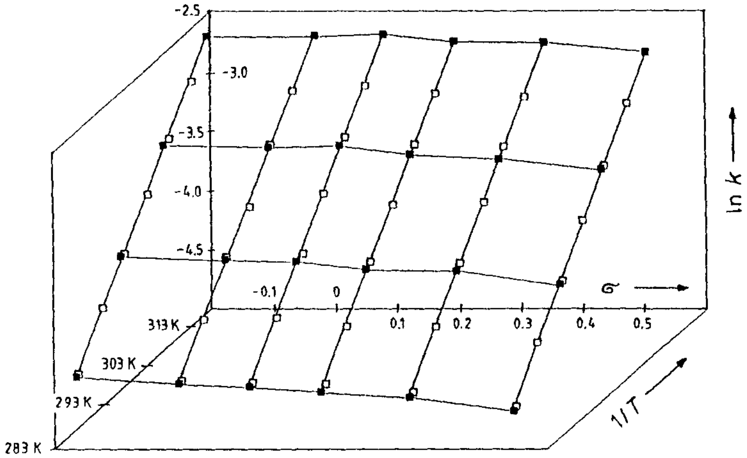


Figure 4. Three-dimensional plot showing the influence of reaction temperature (1/*T*) and substituent variation (σ) on the rate (ln *k*) of methylation of betaines **1a–g** with iodomethane in acetonitrile. ■, values calculated from the Arrhenius law; □, experimental values

by the substituent-regulated nucleophilicity of the betaine molecules.

Solvent variation

The solvent-dependent rate constants of reactions (1) (cf. Table 1) exhibit not simple correlation with *AN* and $E_T(30)$,[18] as shown in Figure 5 for betaine **1a**. For example, the largest rate constant is found in acetone, a solvent with only medium *AN* and $E_T(30)$ values. Two correlation lines are observed if one divides the solvents investigated into two groups, one including solvents with considerable EPD properties (high donor numbers[5]) and the other including mainly haloalkanes. Ethyl acetate and tetrahydrofuran, however, seem to belong to neither the first nor the second group. Poss-

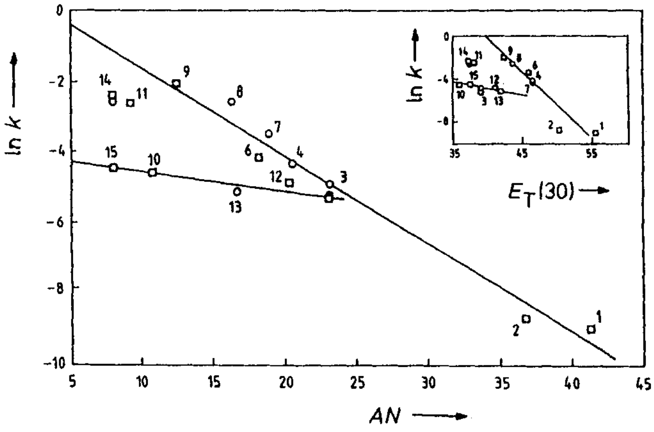


Figure 5. Correlation between the rates of methylation (ln *k*) of betaine **1a** at 25°C and the acceptor numbers *AN* of the reaction media [correlation coefficients $r = -0{\cdot}988$ (upper line) and $r = -0{\cdot}890$ (lower line)]. Inset: correlation between ln *k* and $E_T(30)$. Symbols and solvent numbering as in Figure 3, with the following additional solvents: 12, CH_2CL_2; 13, DCE; 14, THF; 15, C_6H_5Cl

ibly, in these solvents a change in the reaction mechanism occurs, as found for the closely related solvent methyl acetate (and mentioned before).

Table 3. Arrhenius activation parameters of reaction (1) in six solvents

Solvent	Betaine	$10^{-6}A$[a]	E_a[b]	$-r$[c]
$CHCl_3$	**1a**	1·31	47·1	0·992
	1b	8·60	45·9	0·997
	1c	8·36	46·2	0·997
	1d	7·15	46·3	0·998
	1e	0·141	42·2	0·995
	1g	0·0456	40·1	0·990
An	**1a**	5·10	46·9	0·999
	1b	2·88	45·4	0·999
	1c	8·82	48·2	0·999
	1d	6·24	47·5	0·999
	1e	8·12	48·2	0·999
	1f	9·15	48·8	0·999
AC	**1a**	4·16	42·9	0·998
	1b	5·20	43·7	0·997
	1c	4·48	43·2	0·999
	1d	4·40	43·3	0·999
	1e	2·59	42·2	0·998
	1f	2·63	42·6	0·997
EtOAc	**1a**	0·601	39·3	0·999
	1b	1·02	40·4	0·999
	1c	2·43	42·6	0·999
	1d	1·33	41·5	0·999
	1e	1·03	41·0	0·999
	1f	0·912	41·1	0·999
THF	**1a**	11·25	46·5	0·997
DCE	**1a**	8·75	51·9	0·991

[a] Pre-exponential factor in $l\,mol^{-1}\,s^{-1}$; standard error $\pm 0{\cdot}51\,mol^{-1}\,s^{-1}$.
[b] Activation energy in $kJ\,mol^{-1}$; standard error $\pm 1\,kJ\,mol^{-1}$.
[c] Regression coefficient of the linear correlation between ln *k* and $1/T$.

Temperature variation

Arrhenius plots (i.e. ln *k* versus $1/T$) are found to be linear in all cases, as shown in Figure 4. The corresponding activation parameters for reaction (1) in six solvents are given in Table 3.

For substituent variation in **1a–g**, an isoenthalpic behaviour is found in all solvents, i.e. the Arrhenius correlation lines are parallel to each other and no common point of intersection occurs.[20–24] This is in agreement with the observation that a point of intersection is also not found in the corresponding LFE relationship (i.e. ln *k* versus σ; cf. Figure 4). This means that the variation of substituents influences only the entropic contribution to the rate constants (i.e. the pre-exponential factor or $\Delta S^{\neq}$), and hardly the activation energy of reaction (1). This can explain the weak dependence of the rates on the Hammett substituent parameters, the latter reflecting the substituent-governed variation of the charge distribution around the reaction site, which, in turn, should manifest itself, at least in part, in the activation barrier of reaction (1). The improved LFE relationship according to equation (3), with propane-1,2-diol carbonate as a reference solvent, does not include the normal Hammett characteristics; it seems to be mainly governed by reaction entropy changes.

In contrast to the isoenthalpic behaviour of reaction (1), an isosolvent relationship (ISR) has been found for this reaction. That is, in the Arrhenius plots for one

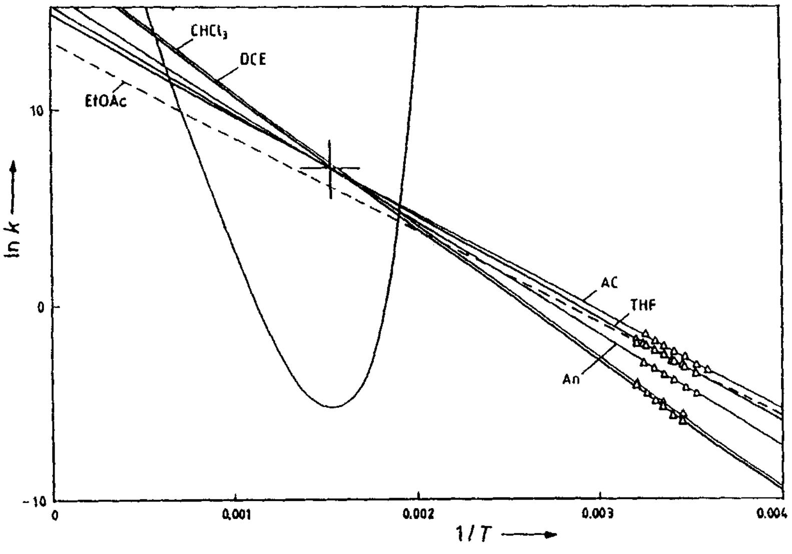


Figure 6. Arrhenius plot for the methylation of betaine **1a** with iodomethane in six solvents: acetonitrile (An), acetone (AC), tetrahydrofuran (THF), chloroform ($CHCl_3$), 1,2-dichloroethane (DCE) and ethyl acetate (EtOAc). The broken line is for EtOAc, which is not included in the isosolvent relationship. The curved line represents the *F* parameter

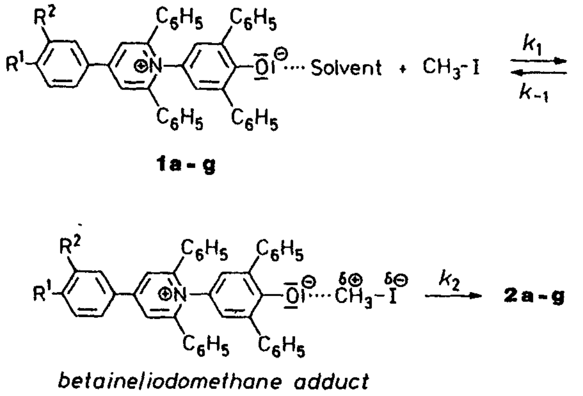
reaction carried out in different solvents, a point of intersection occurs as shown in Figure 6 for betaine **1a**, for which the temperature dependence of ln *k* has been measured in all solvents.

Ethyl acetate has to be excluded from this ISR, which again can be taken as a strong hint that reaction (1) follows another mechanism in this solvent.

DISCUSSION

In view of the described relationships, the observed kinetic results can be interpreted in terms of Scheme 2.

Owing to the differential shifts of the UV–visible absorption maxima observed in different solvents, we know that the coloured species followed spectroscopically is a betaine–solvent adduct. Actually, this corresponds to the negative solvatochromism of the betaine dyes **1a**–**g**, showing an increasing influence of the solvent acceptor properties on the sensitivity of the E_T values to substituent variation, as shown in Figure 3. The betaine–solvent adduct formation can be associated with a more or less localized interaction, which then explains the occurrence of two groups of solvents, as seen in Figure 5. The interaction with solvents such as MeOH, *n*-BuOH, $CHCl_3$ and CH_3CN (i.e. upper line in Figure 5) appears to be more specific and localized at the negatively charged phenoxide moiety, as depicted in Scheme 2. This interaction can be described as a pronounced donor–acceptor interaction. With solvents such as CH_2Cl_2, $ClCH_2CH_2Cl$ and C_6H_5Cl (i.e. lower line in Figure 5), the interaction seems to be less localized with respect to the phenoxide part, and is mainly due to van der Waals forces with the lipophilic aromatic phenyl rings of the betaine molecule.



Scheme 2

The actual nature of the intermediate betaine–iodomethane adduct (e.g. whether it is a more or less stable dipole–dipole or an outer-sphere complex) is not accessible by kinetic measurements.

From Scheme 2, the rate law given in equation (4) can be derived under pseudo-first-order and Bodenstein conditions for the intermediate betaine–iodomethane adduct. The rate law obtained in this way is first order in *c*(betaine) and $c_0(CH_3I)$, as required by the experimental results.

$$-\mathrm{d}c(\text{betaine})/\mathrm{d}t = [(k_1k_2)/(k_{-1}+k_2)]\,c_0(\mathrm{CH_3I})\,c(\text{betaine}) \quad (4)$$

Two extreme cases are possible: (i) $k_{-1} \gg k_2$, in which case the observed rate constant, k_{obs}, equals $Kk_2c_0(\mathrm{CH_3I})$, which means that the reaction of the betaine–iodomethane adduct is rate determining and governed by the (presumably very low) equilibrium concentration of this adduct; or (ii) $k_{-1} \ll k_2$; in this case k_{obs} corresponds to $k_1c_0(\mathrm{CH_3I})$ and the rate-determining step is the formation of the betaine–iodomethane adduct. It is important to note that the influence of the acceptor properties of less localized solvents on the reaction rate is far less pronounced than the influence of the more localized solvents. This follows from the greater slope of the correlation line in Figure 5 associated with the latter group of solvents. This supports case (1), that is, $k_{-1} \gg k_2$ is valid, because such a differentiation in two groups of solvents cannot be expected in case (ii) with $k_{-1} \ll k_2$. The observed rate is lower for solvents in which the phenoxide site is 'naked'. This can be explained by stabilization of the betaine–iodomethane intermediate by solvent molecules still present at the aromatic phenyl rings. In other words, the differentiation into two solvent groups occurs because an increase in K (which is certainly present) is overcompensated by a decrease in k_2.

The influence of the betain substituents on the alkylation rate is in agreement with these findings: the value of ρ_K, given in Table 2, decrease with increasing AN. This indicates a diminishing role of the substituents on the alkylation rate owing to the greater influence of the solvent replacement equilibrium.

Figure 6 shows the occurrence of an isokinetic relationship. From theoretical investigations of isokinetic (IKR) and isosolvent relationships (ISR),[20,23] it can be concluded that the isokinetic temperature, T_{iso},[16] corresponds to an active heat-bath frequency $\tilde{\nu}$ according to equation (5), if one neglects a minor contribution by the activation energy:

$$\tilde{\nu} = kT_{\mathrm{iso}}/(hc \times 100) \approx 0{\cdot}694T_{\mathrm{iso}} \quad (5)$$

For condensed phases, the theory assumes that energy is stored in a heat-bath (i.e. a necessary source of energy allowing the reaction site to overcome the energy barrier, which is not specified in detail) in the form of vibrational modes of the molecules surrounding of the reaction site. In the case of small reacting molecules this surrounding is the solvent or a heterogeneous catalyst, and indeed the respective vibrational modes can be found in their far-IR spectra. Interestingly, in contradiction to other ISRs, the solvents in which reaction (1) has been studied exhibit no far-IR or Raman absorption corresponding to a value of T_{iso} of 670 K (i.e. about 450 cm^{-1}), except for chloroform and 1,2-dichloroethane. Obviously, the large betaine molecules can act as the required heat-bath, providing the energy required to overcome the reaction barrier for the alkylation of the phenoxide moiety, i.e. the reaction site of the betaine molecule. Such behaviour has already been found for large molecules reacting in the gas phase.[24] Indeed, a vibrational absorption band at 450 cm^{-1}, found in the far-IR spectrum of betaine dye **1a** (cf. Figure 7), confirms this assumption.

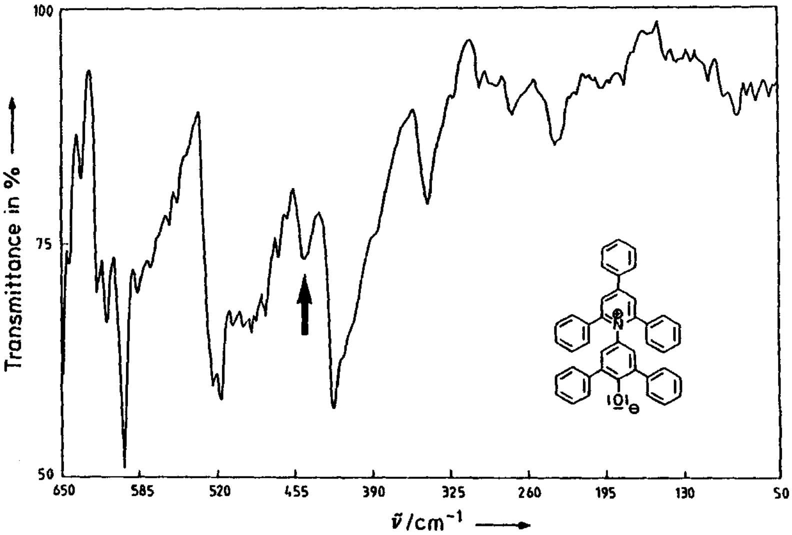


Figure 7. Fear-infrared spectrum of the solid, crystalline betaine dye **1a**. The far-IR absorption band which presumably corresponds to the isokinetic vibration is marked by an arrow

Further investigations by means of the thermochromism of the betaine dyes described in this paper and a penta-*tert*-butyl-substituted, more lipophilic betaine dye[6] strongly support these findings (unpublished results). The fact that the betain molecule is large enough to act as its own heat-bath explains why the observed ISR includes 'localized' in addition to 'less localized' solvent molecules. This in turn supports our view that the rate-determining step of the betaine alkylation is the reaction of the betaine–iodomethane adduct (cf. Scheme 2).

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