A rationalization of the solvent effect on the Diels–Alder reaction in ionic liquids using multiparameter linear solvation energy relationships†

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The Diels–Alder reaction between cyclopentadiene and three dienophiles (acrolein, methyl acrylate and acrylonitrile) having different hydrogen bond acceptor abilities has been carried out in several ionic liquids and molecular solvents in order to obtain information about the factors affecting reactivity and selectivity. The solvent effects on these reactions are examined using multiparameter linear solvation energy relationships. The collected data provide evidence that the solvent effects are a function of *both* the solvent and the solute. For a solvent effect to be seen, the solute must have a complimentary character; selectivities and rates are determined by the solvent hydrogen bond donation ability (α) in the reactions of acrolein and methyl acrylate, but not of acrylonitrile.

Introduction

The Diels–Alder reaction is one of the most important carbon–carbon bond-forming reactions used to prepare cyclic structures. This makes it a key step in the synthesis of many natural products and pharmaceutical compounds. Consequently, it has been very widely studied. One of the most interesting aspects of this reaction is its pronounced solvent dependence, which has been the subject of several studies in recent years, in order to enhance reactivity and, therefore, reduce waste created by by-products.

The Diels–Alder reaction between methyl acrylate and cyclopentadiene is perhaps the most intensively studied and can be considered as a model Diels–Alder reaction. It has been investigated in organic solvents by means of the Linear Solvation Energy Relationship (LSER), indicating that hydrogen bonding and dipolarity are important parameters explaining selectivity.[1]

However, the remarkable increase in reactivity and selectivity observed in aqueous solutions was discussed in the pioneering work of Breslow *et al.*[2,3] in terms of hydrophobic effects.[4] This property is governed by the limited ability of water to dissolve non-polar molecules; as a consequence hydrophobic organic molecules are forced together in water, which interact better with themselves than with the solute, and therefore the reaction rate increases. Studies by a large number of authors subsequently demonstrated that the reactivity in water is primarily determined by two solvent parameters: its hydrogen bond donating capacity and solvophobicity, the latter being the main factor.[5] This pattern strongly suggests that in water, a hydrogen bond donating solvent *par excellence*, the Diels–Alder reaction benefits not only from enforced hydrophobic interactions but also from hydrogen-bonding interactions. The role of viscosity on the kinetics of the Diels–Alder reaction has also been investigated and noted as a solvent effect. However, the dependence of the rate on the solvent viscosity is not clear and, therefore, has been both supported and criticised.[6–9]

Ionic liquids with similar properties to water, such as being highly ordered media and good hydrogen bond donors, have also been shown to have the potential to influence the outcome of Diels–Alder reactions. Therefore, ionic liquids have also been used as solvents to investigate solvent effects in Diels–Alder reactions. The first example of a Diels–Alder reaction involving an ionic liquid, ethylammonium nitrate, was published by Jaeger and Tucker in 1989.[10] They investigated the reaction between cyclopentadiene and methyl acrylate in $[EtNH_3][NO_3]$ and, surprisingly, the reaction gave a mixture of *endo* and *exo* products in a ratio of 6.7 : 1. Since then, a number of examples of Diels–Alder reactions in ionic liquids have been reported. Chloroaluminate ionic liquids were used for the first time as both solvents and catalysts for the synthetically important Diels–Alder reaction.[11] These studies showed *endo* selectivity and rate enhancement comparable to those with water for the reaction of cyclopentadiene with methyl acrylate in acidic room-temperature chloroaluminate ionic liquids, effects which were attributed to the Lewis acidity of the ionic liquid anion. Not many studies have been carried out in this type of ionic liquid, since they are extremely sensitive to water and are corrosive to many materials due to the presence of aluminium chloride.

Subsequently, Welton *et al.*[12] have investigated the influence of non-chloroaluminate ionic liquids on Diels–Alder reactions. In these papers it was proposed that the observed enhancement of selectivity and rate in the case of the reaction of cyclopentadiene and methyl acrylate were controlled by the ability of the ionic liquid to act as a hydrogen bond donor (cation effect), moderated by its hydrogen bond acceptor ability (anion effect). Based on these studies, they predicted that the highest selectivities will be observed in ionic liquids with the strongest hydrogen bond donor capacity, coupled with the weakest hydrogen bond acceptor ability. According to this reasoning, it is not surprising that good results have been reported for ionic liquids such as $[bmim][PF_6]$, $[bmim][BF_4]$ and [bmim][OTf], which comprise a

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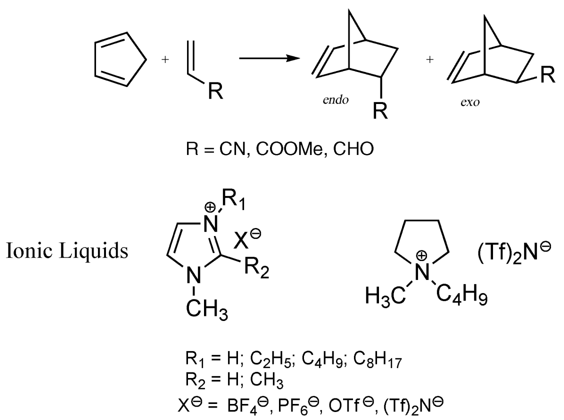
cation with an acidic proton, and non-polar and weakly basic anion.[13,14] Low yields have been reported for dialkylimidazolium bromide and trifluoroacetate ionic liquids, probably because of the Lewis basicity of the anions.[15] More recently, Dyson *et al.*[16] also investigated solvent effects in the Diels–Alder reaction between cyclopentadiene and methyl acrylate in a range of room-temperature ionic liquids. They concluded that properties of the ionic liquid, such as hydrogen bond donor capacity, steric bulk and overall polarity, are important in determining selectivity.

Finally, recent papers of Silvero *et al.*[17] and Kumar *et al.*[18] have investigated in detail the effect of metal triflates on *exo*/*endo* ratios and reaction rates, in typical Diels–Alder reactions performed in ionic liquids.

Although most of the factors affecting Diels–Alder reactions have been identified, their relative contributions are often not well known. Chemists have been trying to unravel the mystery of the influence of solvents in organic reactions for many years. As a consequence, much information has been collected in order to try to explain what the effects on the Diels–Alder reaction are. Notwithstanding the studies described above, an exhaustive study of solvent effects in Diels–Alder reactions for a variety of dienophiles in ionic liquids has not been reported, partly due to the lack of known properties such as the Hildebrand solubility parameter for these neoteric solvents.

It is the aim of this paper to investigate the use of ionic liquids as solvents for Diels–Alder reactions and to consider their solvent–solute interactions in order to obtain a better understanding of their solvent effects. Therefore, kinetic and product distribution studies using dienophiles with different hydrogen bond acceptor abilities (Scheme 1) have been carried out in order to compare reactivity and to obtain information about the hydrogen bond donor ability of ionic liquids.

It is hoped that greater understanding of solvent effects in ionic liquids will give us the information necessary to synthesise new ionic liquids with precisely tailored properties for particular chemical reactions.



Scheme 1

Results and discussion

The relationship between a solvent and solute is intimate and dependent upon the properties of both. Consequently, solvent effects on the selectivity of Diels–Alder reactions are dependent upon the nature of the dienophile. For this reason, we chose to study both carbonyl-containing and nitrile-containing dienophiles in order to get a more general insight into solvent effects in Diels–Alder reactions. The *endo*/*exo* selectivities of the cycloaddition reactions between cyclopentadiene and acrolein, methyl acrylate and acrylonitrile were measured in 9 ionic liquids and some conventional organic solvents at 25 °C. The *endo*/*exo* selectivities are reported in Table 1 and graphically represented in Fig. 1; some relevant solvent parameters are reported in Table 2.

It is clear from Fig. 1 that similar *endo*-selectivities are observed for acrolein and methyl acrylate, which are carbonyl-containing dienophiles, in contrast to acrylonitrile, which contains a nitrile group.

The selectivity [log(*endo*/*exo*)] of the Diels–Alder reaction between cyclopentadiene and methyl acrylate at 25 °C has long

Table 1 *Endo*/*exo* selectivities observed for the reaction between cyclopentadiene and three dienophiles at 25 °C

	Acrolein		Methyl acrylate		Acrylonitrile	
Solvent	*endo*/*exo*	log(*endo*/*exo*)	*endo*/*exo*	*log*(*endo*/*exo*)	*endo*/*exo*	log(*endo*/*exo*)
[Hbim][N(Tf)$_2$]	4.8	0.681	6.1	0.785	1.2	0.079
[bmim][BF$_4$]	4.2	0.623	4.6	0.663	1.9	0.279
[bmim][PF$_6$]	4.2	0.623	4.8	0.681	1.7	0.230
[emim][N(Tf)$_2$]	4.1	0.613	4.1	0.613	1.4	0.146
[bmim][OTf]	4.1	0.613	4.3	0.633	2.3	0.362
[bmim][N(Tf)$_2$]	3.9	0.591	4.3	0.633	1.3	0.114
[omim][N(Tf)$_2$]	3.8	0.580	4.1	0.613	1.3	0.114
[bmpy][N(Tf)$_2$]	3.7	0.568	4.2	0.623	1.6	0.204
[bm$_2$im][N(Tf)$_2$]	3.6	0.556	4.1	0.613	1.2	0.079
Acetonitrile	3.6	0.556	4.1	0.613	1.9	0.279
Acetone	3.6	0.556	3.4	0.531	1.7	0.230
Propylene carbonate	—	—	—	—	1.9	0.278
DMSO	—	—	3.9	0.591	2.0	0.301
Dichloromethane	3.2	0.505	—	—	1.4	0.146
Ethyl acetate	2.9	0.462	3.1	0.491	1.5	0.176
Toluene	2.4	0.380	2.7	0.431	1.1	0.041
1,4-Dioxane	—	—	3.2	0.505	—	—
Diethyl ether	—	—	2.8	0.447	—	—
Hexane	2.8	0.447	2.5	0.398	1.0	0.000
Methanol	—	—	5.5	0.740	—	—

Table 2 Solvent parameters

	Reichardt electrophilicity	Hydrogen bond donor acidity	Hydrogen bond acceptor basicity	Dipolarity/ polarisability index	Molar volume	Internal energy	Cohesive pressure
Solvent	E_T^N [b]	α [b]	β [b]	π^* [b]	V_M/cm^3 mol^{-1} [c]	ΔU/kJ mol^{-1} [c]	δ^2/J cm^{-3} [c]
[Hbim][N(Tf)$_2$]	0.840[a]	0.940[a]	0.230	1.090[a]	262	118[a]	450[a]
[bmim][BF$_4$]	0.670	0.627	0.376	1.047	202	201[a]	929[a]
[bmim][PF$_6$]	0.669	0.634	0.207	1.032	206	189	718[a]
[emim][N(Tf)$_2$]	0.658[a]	0.627[a]	0.225	0.998[a]	258	196	585
[bmim][OTf]	0.656	0.625	0.464	1.006	217	149[a]	645[a]
[bmim][N(Tf)$_2$]	0.645	0.617	0.243	0.984	292	191	554
[omim][N(Tf)$_2$]	0.630[a]	0.595[a]	0.291	0.961[a]	361	226	523
[bmpy][N(Tf)$_2$]	0.544	0.427	0.252	0.954	305	154	506
[bm$_2$im][N(Tf)$_2$]	0.541	0.381	0.239	1.010	309	179	625
Propylene carbonate	0.511	0.309	0.394	0.930	85	63	740
Dimethyl sulfoxide	0.471	0.160	0.725	1.027	71	43	600
Acetonitrile	0.460	0.350	0.370	0.799	53	31	590
Acetone	0.350	0.202	0.539	0.704	74	27	398
Dichloromethane	0.309	0.042	−0.014	0.791	64	26	410
Ethyl acetate	0.228	0.040	0.482	0.559	99	29	347
Toluene	0.100	−0.213	0.077	0.532	107	30	337
Hexane	0.009	0.070	0.040	−0.120	132	26	225

[a] Solvent parameters determined in this work. [b] Solvent parameters for ionic liquids from ref. 19. Solvent parameters for molecular solvents recalculated from ref. 20. [c] Data for ionic liquids obtained from ref. 21. Data for molecular organic solvents obtained from ref. 22.

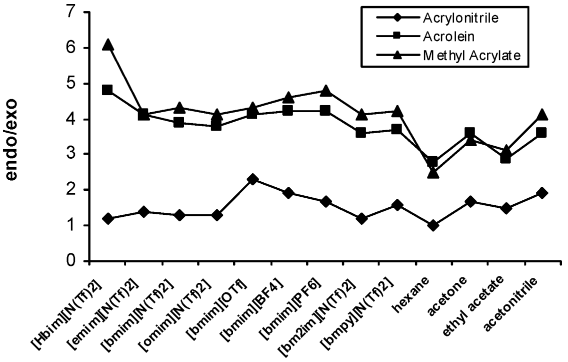


Fig. 1 Comparison of the *endo*-selectivities of the Diels–Alder reaction of cyclopentadiene with different dienophiles.

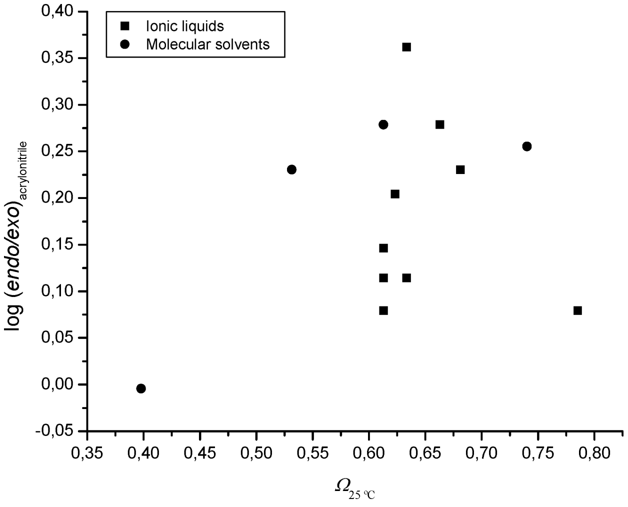


Fig. 2 The relationship between the log(*endo*/*exo*) of the reaction between cyclopentadiene and acrylonitrile and Berson's empirical solvent parameter at 25 °C ($\Omega_{25\,°C}$). Applying eqn (1): $a = -0.048$; $b = 0.367$; $R^2 = 0.332$.

been used as a solvent polarity scale (Ω, the Berson's empirical solvent parameter), reported in Table 1.[23]

$$\log(endo/exo)_{25\,°C} = a + b\Omega_{25\,°C} \quad (1)$$

The different sensitivity of acrylonitrile, methyl acrylate and acrolein to solvent effects on the selectivity can be used to comment on the generality of this scale. Plots of the correspondences to the equation are given in Fig. 2 and 3 for the data of acrylonitrile and acrolein respectively.

Whilst the linear relationship characterizing the data reported in Fig. 3 ($R^2 = 0.942$) confirms that the stereoselectivity of methyl acrylate and acrolein is affected by the solvent in a similar way, in contrast it can be understood from Fig. 2 ($R^2 = 0.332$) that the response of the stereoselectivity to a change of solvent for the methyl acrylate and acrylonitrile system is different: no correlation has been found between log(*endo*/*exo*) and $\Omega_{25\,°C}$. It is clear that, even when the reaction is similar to another Diels–Alder reaction, but with a non-carbonyl-containing dienophile, $\Omega_{25\,°C}$ fails to offer a prediction for the experimental outcome.

Since attempts to correlate the *endo*/*exo* selectivities to the solvent properties using single parameters relationships gave (with few exceptions) fairly poor correlations for all investigated dienophiles (see ESI, Fig. 1S–3S†), we have used multiparameter relationships (LSER), in order to gain a better understanding of the solvent effects on the selectivity of these reactions. As introduced by Kamlet, Abboud and Taft[24] and subsequently developed by Abraham *et al.*,[25] the LSER approach characterizes solvation effects in terms of nonspecific and specific interactions. Thus, a solvation property of interest (selectivity or reaction rate)

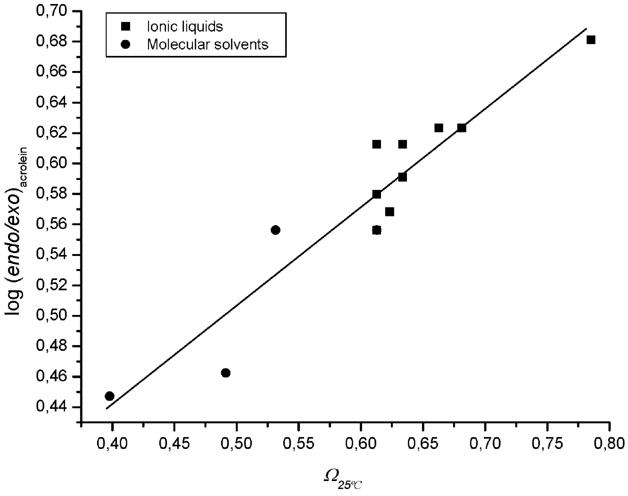


Fig. 3 The relationship between the log(*endo*/*exo*) of the reaction between cyclopentadiene and acrolein against Berson's empirical solvent parameter at 25 °C ($\Omega_{25\,°C}$). Applying eqn (1): $a = 0.183$; $b = 0.645$; $R^2 = 0.942$.

is modelled by a linear free energy relationship of the form of eqn (2) and eqn (3). In this case, the solvent-dependent property is the natural logarithm of the *endo*/*exo* ratio at 25 °C, α is a measure of the solvent hydrogen bond donor acidity, β is a measure of the hydrogen bond acceptor basicity, π^* is an index of solvent dipolarity/polarizability, ΔU is the internal energy of the solvent, V_M the molar volume and η viscosity. In eqn (3), E_T^N is the Reichardt electrophilicity, which can be written as linear function of both α and π^*.[26]

Both eqn (2) and eqn (3) were applied to selectivity data from reactions of each of the dienophiles in all the investigated ionic and molecular solvents (Table 3).

$$\ln(endo/exo) = const + a\alpha + b\beta + c\pi^* + d\Delta U + eV_M + f\eta \qquad (2)$$

$$\ln(endo/exo) = const + aE_T^N + b\beta + d\Delta U + eV_M + f\eta \qquad (3)$$

It is clear from Table 3 that the most significant factor in determining selectivity in the reaction of acrolein is the hydrogen bond donor ability of the solvent, α. The good fit observed considering only the α parameter further supports the strong hydrogen bond dependence on the *endo* selectivity for this reaction. This is consistent with the good hydrogen bond acceptor ability of this dienophile ($\beta \approx 0.8$), characterized by the presence of a carbonyl group. Moreover, the insignificant coefficients of π^* and V_M seem to indicate that these only have a slight effect on influencing the selectivity of the reaction between acrolein and cyclopentadiene. When the experimental selectivities were fitted against the predicted selectivities using the equation in Table 3, the correlation coefficient was 0.983 and the standard deviation 0.034 ($N = 14$) showing that predictions of selectivity for the Diels–Alder reaction between cyclopentadiene and acrolein in any conventional organic solvent or ionic liquid are possible with only small errors (Fig. 4).

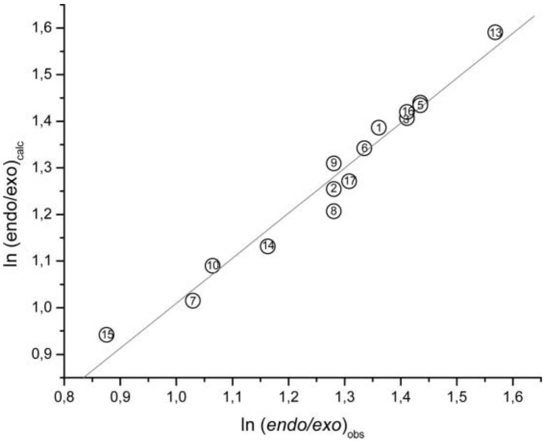


Fig. 4 Calculated *versus* observed selectivities of the Diels–Alder between acrolein and cyclopentadiene for several solvents. 1: [bmim][N(Tf)$_2$]; 2: [bm$_2$im][N(Tf)$_2$]; 3: [emim][N(Tf)$_2$]; 4: [bmim][BF$_4$]; 5: [bmim][PF$_6$]; 6: [omim][N(Tf)$_2$]; 7: hexane; 8: acetone; 9: acetonitrile; 10: ethyl acetate; 13: [Hbim][N(Tf)$_2$]; 14: dichloromethane; 15: toluene; 16: [bmim][OTf]; 17: [bmpy][N(Tf)$_2$].

The relatively high importance of the hydrogen bond donor and dipolarity/polarizability properties of the solvent, in contrast to the small contribution of the internal energy term, can also be clearly seen in the case of methyl acrylate (Table 3, Fig. 4S†). It is noteworthy that the exclusion of the internal energy term results in a decrease of R^2 only from 0.964 to 0.933, while the exclusion of π^* gives an R^2 of 0.833 and more importantly, the exclusion of α gives an R^2 of 0.614.

Finally, although only a very low *endo*-selectivity was observed in the case of acrylonitrile, attempts to correlate the observed values with solvent parameters have been performed. In this case, polarity described by Reichardt's dye, hydrogen bond basicity, molar volume and solute internal energy are the most appropriate solvent parameters to describe solvent effects on the selectivity of the reaction between cyclopentadiene and this dienophile (ESI, Fig. 5S†). Nevertheless, it being known that E_T^N is related to the hydrogen bond donor and the dipolarity/polarizability, we decided to also analyse our results using these parameters, so

Table 3 LSERs describing solvent effects on the selectivity of Diels–Alder reactions of cyclopentadiene

Dienophile	ln(*endo*/*exo*)	R^2_{adj} [b]	*F*[b]
Acrolein	$1.042 + 0.560\alpha + 0.116\pi^* - (3.929 \times 10^{-4})V_M$	0.960	105.4
Methyl acrylate	$0.936 + 0.515\alpha + 0.375\pi^* - (7.421 \times 10^{-4})\Delta U$	0.964	150.95
Acrylonitrile[a]	$0.335 + 0.328E_T^N + 0.493\beta + (2.818 \times 10^{-3})\Delta U - (3.168 \times 10^{-3})V_M$	0.949	66
	$0.318 + 0.112\alpha + 0.486\beta + 0.157\pi^* + (2.754 \times 10^{-3})\Delta U - (3.100 \times 10^{-3})V_M$	0.944	48.6

[a] The LSER expressed in terms of α and π^* gave a slightly poorer fit than that in which these two factors were combined into one, E_T^N. However, this LSER is given, so that comparison with those for acrolein and methyl acrylate can be more readily made. [b] *F* is the Fisher's test parameter for statistical treatment; R^2_{adj} is the correlation parameter for multiparameter fitting.

Table 4 Kamlet–Taft descriptors that characterize the dienophiles studied in this work

	Acrylonitrile	Acrolein	Methyl acrylate
α	0.315	0.345	0.130
β	0.369	~0.8[a]	0.452
π^*	0.824	0.873	0.642

[a] The UV cut-off of acrolein prevented the measurement of this value, which was therefore approximated.

Table 5 Second-order rate constants of the Diels–Alder reaction between cyclopentadiene and three dienophiles at 25 °C

	Acrolein	Methyl acrylate	Acrylonitrile
Solvent	$k_2 \times 10^4/\mathrm{M}^{-1}\ \mathrm{s}^{-1}$	$k_2 \times 10^5/\mathrm{M}^{-1}\ \mathrm{s}^{-1}$	$k_2 \times 10^5/\mathrm{M}^{-1}\ \mathrm{s}^{-1}$
[Hbim][N(Tf)$_2$]	163 ± 6	9.12 ± 0.01	4.53 ± 0.21
[bmim][BF$_4$]	1.76 ± 0.03	4.69 ± 0.04	4.48 ± 0.32
[bmim][PF$_6$]	1.40 ± 0.03	4.31 ± 0.11	2.63 ± 0.13
[emim][N(Tf)$_2$]	2.60 ± 0.05	4.19 ± 0.17	2.53 ± 0.84
[bmim][OTf]	2.16 ± 0.06	4.30 ± 0.07	1.06 ± 0.22
[bmim][N(Tf)$_2$]	2.30 ± 0.06	3.23 ± 0.01	3.64 ± 0.40
[omim][N(Tf)$_2$]	1.46 ± 0.04	3.31 ± 0.08	6.85 ± 0.93
[bmpy][N(Tf)$_2$]	1.93 ± 0.06	3.88 ± 0.03	5.04 ± 0.77
[bm$_2$im][N(Tf)$_2$]	1.40 ± 0.03	3.42 ± 0.20	4.00 ± 0.61
Acetonitrile	1.01 ± 0.02	2.21 ± 0.13	1.72 ± 0.27
Acetone	0.67 ± 0.01	1.12 ± 0.03	1.35 ± 0.25
Dichloromethane	1.50 ± 0.02	—	2.81 ± 0.93
Ethyl acetate	0.10 ± 0.00	—	1.01 ± 0.17
Toluene	1.00 ± 0.02	1.77 ± 0.18	—
Hexane	0.45 ± 0.01	1.23 ± 0.04	0.11 ± 0.05

that a quantification of the hydrogen bond donor and dipolarity/polarizability effect separately and a direct comparison with the LSERs of acrylonitrile and methyl acrylate could be made. The LSER expressed in terms of α and π^* gave, however, a slightly poorer fit than that in which these two factors were combined into one, $E_{\mathrm{T}}^{\mathrm{N}}$. Furthermore, it is noteworthy that the LSER for acrylonitrile involves more parameters than those of the other dienophile. This suggests that the situation is more complex. It can be seen that solvent effects on the selectivity in the case of carbonyl-containing dienophiles depend mainly upon the hydrogen bond donor ability of the solvent (α), while the changes in selectivity for acrylonitrile are mainly regulated by the hydrogen bond acceptor ability of the solvent (β) and other factors. The different significance of the solvent parameters in the suggested regression models can be explained by the different solvent properties of the dienophiles (Table 4).

Firstly, it can be noticed that the significance of α (hydrogen bond donor ability) in the LSER equations is consistent with the nucleophilic nature of the dienophiles. Acrolein presents a stronger hydrogen bond basicity, and it is therefore expected that hydrogen bond interactions with the solvent will be a greater factor in determining selectivity. The case of methyl acrylate, which is a better hydrogen bond acceptor than a donor, is similar. On the other hand, acrylonitrile is a poor hydrogen bond acceptor, with similar hydrogen bond donor ability, and large dipolarity/polarizability contributions. Thus, solvent effects on the selectivity for this dienophile are controlled by many factors, as seen in the LSER equation.

Solvent effect on rate

The second-order rate constants of the reaction between cyclopentadiene and the three selected dienophiles were determined at 25 °C in several organic solvents and ionic liquids (Table 5).

Generally, an enhancement of the second-order rate constant is observed for the reaction between cyclopentadiene and acrolein when performed in ionic liquids compared with traditional organic solvents. In particular, the chemical rate constant increases by more than 2 orders of magnitude when the solvent is changed from non-polar (*e.g.* hexane) to polar (*e.g.* [Hbim][N(Tf)$_2$]).

Clear evidence of the hydrogen bond effect in ionic liquids can be found in the results presented in Table 5. The rate of reaction decreases to almost half on going from [bmim][N(Tf)$_2$] to [bm$_2$im][N(Tf)$_2$]. This decrease is a consequence of the replacement of the slightly acidic hydrogen at position C-2 with a methyl group in the imidazolium cation. As a result, [bm$_2$im][N(Tf)$_2$] loses the ability to hydrogen bond to the carbonyl of acrolein by this proton, and even though hydrogen bonding can still occur from other protons, its α value is the lowest of all of the ionic liquids used, and these are expected to be much weaker. Moreover, the very large acceleration observed in [Hbim][N(Tf)$_2$] could be thought to be due to a stronger hydrogen bond interaction occurring between the highly polarised N–H bond of the cation of this ionic liquid with the carbonyl of acrolein.

In contrast, in the case of methyl acrylate the small observed decrease in acceleration when the reaction is performed in [bm$_2$im][N(Tf)$_2$], in comparison to its analogue [bmim][N(Tf)$_2$], argues against the fact that hydrogen bonding is the main factor in determining its reactivity.

Finally, the observed second-order rate constants, k_2, of the reaction between cyclopentadiene and acrylonitrile show that changes in the reaction rate occur in a random way. For example, it appears from the results that the polarity of the solvent is not strongly related to the differences in the rate constants. So, ionic liquids such as [bmim][PF$_6$], [emim][N(Tf)$_2$] and [bmim][OTf], which are highly polar solvents and have similar polarites to the other ionic liquids, have rate constants with magnitudes similar to those of relatively polar molecular solvents.

In addition, the changes in the reaction rates are not related to the hydrogen bond donor ability of the solvent, which is largely expected because of the poor hydrogen bond acceptor ability of the acrylonitrile in comparison to acrolein and methyl acrylate. Finally, a direct relationship with the solvophobicity of the solvent is also not seen.

To obtain a reasonable correlation of the kinetic constants with solvent parameters, the multiparameter correlations (eqn (2) and eqn (3)) previously employed for the selectivity data were used to fit the kinetic constants (single relationships of k_2 *vs.* some solvent parameters are reported in Fig. 6S–8S†).

The first point of note is that the R^2 values for these correlations are much poorer than those found for the selectivities of the same reactions. This suggests that the combination of factors leading to the changes in the rates of the reactions are more complex than those leading to changes in selectivity and are more sensitive to effects not covered in the analysis, such as subtle fluctuations in reaction conditions.

This partly arises from the selectivities being the result of the ratio of the reaction rates for the *endo* and *exo* products whereas the overall rate of the reaction is the sum of the rates for the two

Table 6 Correlations describing solvent effects on the rates of Diels–Alder reactions of cyclopentadiene

	$\ln k_2$	R^2	F
Acrolein	$-9.86 + 0.99\alpha - 1.53\beta + 1.34\pi^* - 0.002\eta$	0.852	14
	$-9.77 + 2.94E_T^N - 1.53\beta - 0.002\eta$	0.837	14
Methyl acrylate	$-11.36 + 1.81E_T^N$	0.691	17
	$-11.46 + 0.61\alpha + 0.91\pi^*$	0.684	17
Acrylonitrile	$-13.26 + 3.00\pi^*$	0.790	15

products. The consequence of this is that some effects are cancelled out in the selectivities of the reactions. For instance, the viscosity is present in the correlation for $\ln k_2$ for acrolein, whereas it is absent in the explanation of its selectivities.

Analysis of the equations in Table 6 leads to the conclusion that an increase in the second-order rate of the Diels–Alder reaction between cyclopentadiene and acrolein is favoured by good hydrogen bond donors and solvents interacting through dipole/polarizability effects (positive coefficients for α and π^*) while it decreases with viscosity and hydrogen bond acceptor solvents (negative coefficients for β and η) (Fig. 9S†). The positive influence of the ability of the medium to interact through dipoles/polarizability can be understood in terms of the stabilization of the transition state relative to the reactants, due to a more dipolar activated complex.[27] The accelerating effect of α is also quite understandable due to the presence of a carbonyl group in acrolein that can be subjected to electrophilic solvation, especially with good hydrogen bond donor solvents such as ionic liquids. At the same time, it is understandable that hydrogen bond acceptor solvents will not favour the reaction rate. Acrolein can interact with hydrogen bond acceptor solvents directly through its proton. As a consequence, a deactivation of acrolein will occur. The minus sign corresponding to viscosity indicates that a highly viscous environment can be considered to play an inhibitory role.

Both eqn (2) and eqn (3) can be considered good descriptors of the solvent effects responsible for the changes in the rate of the Diels–Alder reaction between cyclopentadiene and methyl acrylate. However, according to the dual-parameter model, which takes account of the importance of specific interactions such as hydrogen bond donation (α) and dipolarity (π^*) separately, both α and π^* are significant, but π^* plays a more important role in determining the reaction rates. Nevertheless, it is important to notice that the weak correlation obtained in Table 6 may be due to a lack of predictors in the equation or the inaccurate estimation of the predictors of second-order rate constants. In the first case, the predictors α and π^* or E_T^N are important factors in the understanding of solvent effects of this reaction; however, they are not enough on their own to fully understand solvent effects in the rate of the Diels–Alder reaction between cyclopentadiene and methyl acrylate. In the second case, an obvious scatter will appear in the representation of the relationship. In fact, some scatter appeared to be responsible for the weak correlation when the experimental values of $\ln k_2$ were plotted against its calculated values from Table 6 for the 17 solvents in order to show the efficiency of the suggested regression equations.

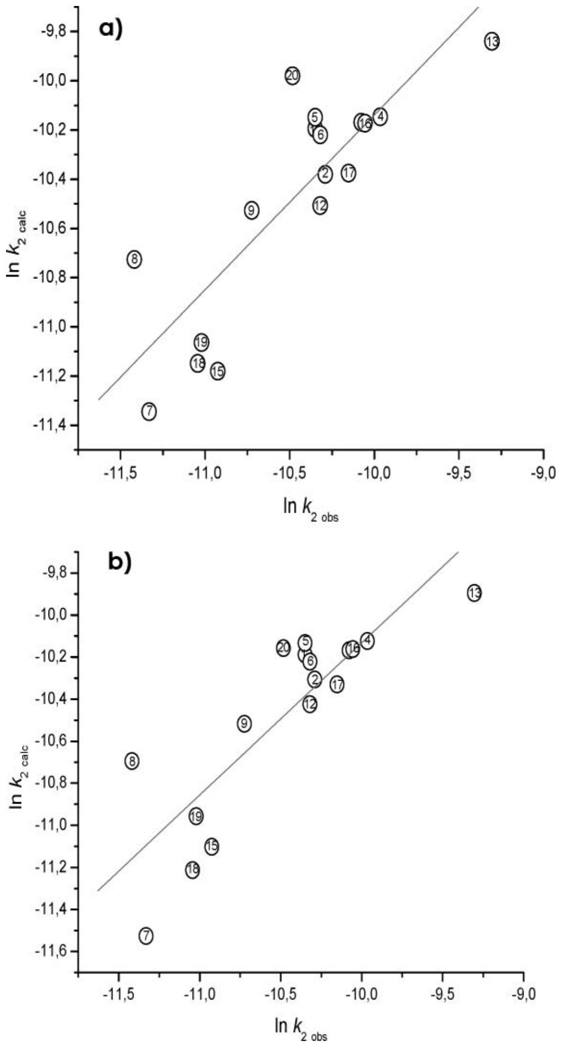


Fig. 5 Plot of the calculated values *versus* the observed values of $\ln k_2$ of the Diels–Alder reaction of methyl acrylate and cyclopentadiene for the 17 solvents. a) Model using E_T^N. b) Model using α and π^*. 1: [bmim][N(Tf)$_2$]; 2: [bm$_2$im][N(Tf)$_2$]; 3: [emim][N(Tf)$_2$]; 4: [bmim][BF$_4$]; 5: [bmim][PF$_6$]; 6: [omim][N(Tf)$_2$]; 7: hexane; 8: acetone; 9: acetonitrile; 12: dimethyl sulfoxide, 13: [Hbim][N(Tf)$_2$]; 15: toluene; 16: [bmim][OTf]; 17: [bmpy][N(Tf)$_2$]; 18: ether; 19: 1,4-dioxane; 20: methanol.

As can be seen in Fig. 5, the experimental and calculated values of $\ln k_2$ are in fair agreement ($R = 0.843$ and 0.850 respectively). This indicates that solvent effects on the rate of the Diels–Alder reaction between cyclopentadiene and methyl acrylate can be mainly explained in terms of hydrogen bond donor and dipolar/polarizability properties of the solvent, the latter being more significant.

Finally, for acrylonitrile the experimental and calculated values of $\ln k_2$ from Table 6 are found to be in good agreement ($R = 0.954$), showing that dipolarity/polarizability is the main factor responsible for the observed changes in the second-order rate constants of this Diels–Alder reaction (Fig. 10S†).

Conclusions

The response of Diels–Alder reactions to their solvent environment is complex, and different dependencies are found when measuring selectivity or kinetics and when different dienophiles are used. However, where studies of the same quantity for the same, or similar, dienophiles to those studied here are available in the literature, there is good agreement with our results, even though different approaches have been taken to the analysis.[10–16]

In conclusion, we can state on the basis of this study that the solvent effects that are seen in these Diels–Alder reactions are a function of *both* the solvent and the solute. For a solvent effect to be seen, the solute must have a complimentary character. For instance, when investigating both the selectivities and rates of these reactions, it was found that the solvent hydrogen bond donation ability (α) was important in the reactions of acrolein and methyl acrylate, but not of acrylonitrile.

Experimental

Dicyclopentadiene (90%), acrolein (90%), acrylonitrile (90%), mesitylene (≥99.8%) and bromobenzene (≥99.5%) were purchased from Fluka, methyl acrylate (99%) from Lancaster and anhydrous methanol (99.8%) from Aldrich. Methanol, mesitylene, acrylonitrile and bromobenzene were used without further purification; the ionic liquids were synthesized as reported in the ESI† and dried by heating *in vacuo* to 65 °C for 3 hours prior to use; the rest of solvents were dried by heating under reflux and distilled following standard drying procedures. Dicyclopentadiene was cracked before use; during the cracking process the collecting flask was kept in liquid nitrogen to avoid dimerization. Methyl acrylate was purified by several washings with an aqueous solution containing 5% sodium hydroxide and 20% sodium chloride and dried afterwards with anhydrous calcium chloride. The dried solution was distilled and stored over calcium hydride in a refrigerator. Before using, the monomer was distilled on a vacuum line. Acrolein was distilled from $CuSO_4$ at low pressure, placing the receiver flask in liquid nitrogen to avoid polymerization. All liquids were manipulated under a nitrogen atmosphere and syringe techniques were employed in their transfer.

GC measurements for the reaction of methyl acrylate and acrolein with cyclopentadiene were performed using a RH-WAX GC column (30 m × 0.25 mm ID × 50 μm). The conditions used for all runs were: injector temperature 250 °C; detector temperature 250 °C; oven temperature 120 °C and 100 °C respectively; total run time 15 min. GC measurements for the reaction of acrylonitrile were carried using a HP-Wax crosslinked polyethylene glycol column (30 m × 0.25 mm ID × 0.25 μm). The conditions used for all runs were: injector temperature 250 °C; detector temperature 250 °C; oven 70 °C for 15 min, then 10 °C min^{-1} up to 120 °C.

Equation coefficients and statistical parameters of LSER correlations were obtained by multilinear correlation analysis using Minitab 14 or SPSS statistical software.

Determination of the kinetic constants in ionic liquids and molecular solvents

The Diels–Alder reactions between cyclopentadiene and methyl acrylate or acrolein and were carried out under second-order conditions using UV-vis or GC techniques. In contrast, the kinetics of acrylonitrile were studied by UV under pseudo-first-order conditions, using an excess of the dienophile (20–100-fold), and by GC under second-order conditions with equal concentrations of reagents. All reactions were contained within 1 or 0.1 cm path length cuvettes, using a Perkin Elmer Lambda 2 or a Cary 2200 UV-vis spectrophotometer. Quartz cuvettes were sealed and filled with nitrogen before adding the reactants. The second-order kinetic constants are reported in Table 5.

Reaction of cyclopentadiene with methyl acrylate. In a typical experiment, methyl acrylate (172 μl, 1.9 mmol) was added to 2.1 ml ionic liquid in a capped vial under a nitrogen atmosphere and the mixture was stirred for 15 min before adding a standard, bromobenzene (0.1 ml, 9.4 mmol). Then, the reaction was initiated by injection of freshly cracked cyclopentadiene (150 μl, 1.9 mmol). The solution was magnetically stirred for 6 h 30 min under a nitrogen atmosphere. Aliquots (50 μl) were removed from the reaction mixture at various times, products and reagents were extracted using diethyl ether or other solvents (0.5 ml), and the extracts analyzed by GC. The kinetic constants were determined following the disappearance of the dienophile over time.

Reaction of cyclopentadiene with acrolein. In a typical experiment, the cell containing 2 ml of the solvent was thermostatted at the appropriate temperature (±0.1 °C) for 10 min. Acrolein (20 μl, 299 μmol) was then added, and the solution was mixed manually until homogeneous. Then, cyclopentadiene (24.8 μl, 299 μmol) was added. The second-order rate constants were determined by monitoring the decrease of absorbance of acrolein at appropriate wavelengths (normally 250–450 nm) in a 1 cm quartz UV cell. For all the reactions, the cuvettes were sealed with a septum to prevent evaporation of the reactants; evaporation of cyclopentadiene or/and acrolein could seriously hamper the kinetic measurements and lead to large errors in the determination of the rate constants.

Reaction of cyclopentadiene with acrylonitrile. The second-order rate constants for the reaction of acrolein with cyclopentadiene were determined by monitoring the decrease of absorbance of acrylonitrile at 240 nm using a 0.1 cm quartz UV cell. Typically, the initial concentration of cyclopentadiene was $\sim 10^{-2}$ M and that of acrylonitrile 20–100 times higher. In some cases the cut-off wavelength of the solvent did not allow the monitoring of the reaction by UV-vis spectroscopy, and therefore gas chromatography was used. When gas chromatography was used, the kinetic experiments were performed under second-order conditions (7.60×10^{-1} M), following the disappearance of the dienophile, using mesitylene as an internal standard.

Determination of the *endo*/*exo* ratio in the reaction of cyclopentadiene with methyl acrylate, acrolein and acrylonitrile in ionic liquids and molecular solvents

In a typical procedure to measure the *endo*/*exo* ratio, the dienophile (175 μl, 1.9 mmol) and freshly cracked cyclopentadiene (150 μl, 1.9 mmol) were added to 2.1 ml ionic liquid or molecular solvent in a sealed vial. The single solution was stirred at 25 °C for 24 h under nitrogen atmosphere. A sample of 50 μl was taken from the reaction and the product mixture and reagents were extracted from the ionic liquid, preferentially with diethyl ether (0.5 ml), but sometimes another molecular solvent (0.5 ml). Extracts were analyzed by GC to obtain the *endo*/*exo* ratios reported in Table 1.

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