Rationalisation of Solvent Effects in the Diels–Alder Reaction Between Cyclopentadiene and Methyl Acrylate in Room Temperature Ionic Liquids

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Abstract: The Diels–Alder reaction between cyclopentadiene and methyl acrylate in ionic liquids has been studied in detail. The effect of contamination of the ionic liquids by common impurities, *viz.* sodium and chloride ions, and water, on the selectivity has been investigated. The presence of high concentrations of chloride was found to decrease the selectivity. Anion and, in particular, cation effects have been investigated using an extensive series of air-stable room temperature ionic liquids, and kinetic parameters have been determined. It has been found that strongly interacting groups, particularly electrophilic moieties on the cation, accelerate the formation of the *endo* products. Substrate solubility intimately connected to the selectivity was found to be mainly anion dependent. An NMR-based solvent parameter scale and semi-empirical models are used to analyse the results and provide a tool for the prediction of selectivities in ionic liquids.

Keywords: cycloaddition; Diels–Alder reaction; ionic liquids; solvent effects

Introduction

The Diels–Alder reaction is one of the most important carbon-carbon bond forming reactions used to prepare cyclic structures.[1] It usually affords a mixture of isomers and the selectivity (and reaction rate) is highly solvent dependent. A number of factors, including the polarity of the solvent,[2] hydrogen bonding interactions,[3] and solvophobicity, are all important.[4] In addition, the presence of Lewis acid catalysts can substantially affect the reaction and lead to very high selectivities.[5]

The Diels–Alder reaction has been extensively studied in organic solvents and in water and, in general, higher reaction rates and selectivities are obtained in polar solvents rather than non-polar solvents.[6] Often, the reaction rates and *endo*:*exo* product selectivities are higher in aqueous solution.[7] These effects have been attributed to enhanced hydrogen bonding between the solvent and the transition state, as well as to enforced hydrophobic interactions, essentially creating a hydrophobic pocket, which facilitates alignment of the substrates.[8] The role of "internal pressure" has also been investigated, in particular for aqueous solutions of simple inorganic salts, such as LiCl, NaCl and $LiClO_4$.[9] β-Cyclodextrins (cycloheptaamyloses) are also used as hydrophobic accelerating agents as they provide a large non-polar cavity where the reaction may take place.[10]

Ionic liquids represent an interesting class of solvent in which to conduct the Diels–Alder reaction since they are polar and have no vapour pressure, potentially leading to high selectivities and facile product separation. The first example of a Diels–Alder reaction involving an ionic liquid, $[EtNH_3][NO_3]$, was published by Jaeger and Tucker in 1989.[11] The cycloaddition of cyclopentadiene to methyl acrylate was reported to yield selectivities comparable with those obtained when the same reaction was carried out in water, although reaction rates were somewhat lower. A number of examples of Diels–Alder reactions in a range of ionic liquids has since been reported. Notably, [bmim][L-lactate] (where $bmim^+$ is 1-butyl-3-methylimidazolium) was found to accelerate the reaction of cyclopentadiene and ethyl acrylate, but no chiral induction was observed and the *endo*:*exo* product ratio was relatively low.[12] In contrast, when the reaction was carried out in $[bmim][PF_6]$ an *endo*:*exo* ratio of 8:1 was obtained, higher than the selectivity for the corresponding reaction in water. The cyclo-

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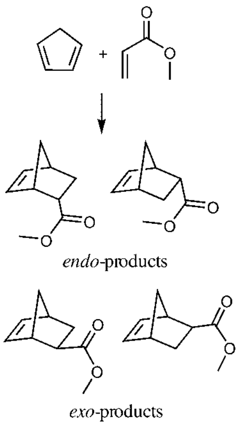
addition of cyclopentadiene to methyl acrylate in chloroaluminate ionic liquids takes place with very high rates and selectivities (*endo*:*exo* ratio = 15), although the ionic liquids cannot be reused.[13] Chloroaluminate ionic liquids have also been shown to promote selectivities towards different products depending on the mol fraction of aluminium(III) chloride employed.[14] It has also been reported that the addition of a Lewis acids, such as $Sc(CF_3SO_3)_3$, to the ionic liquid can dramatically increase the selectivity and the rate of the Diels–Alder reaction.[15] Choline-zinc chloride-type ionic liquids also show promise, but the high viscosities, typically greater than 1000 cP, necessitate the use of either a co-solvent or mechanical stirring.[16] The addition of dialkylimidazolium salts to dichloromethane has been found to catalyse the reaction between cyclopentadiene and crotonaldehyde or methacrolein; the reaction does not take place in the absence of the salt additives, and the imidazolium salt has thus been suggested to act as a Lewis acid catalyst in the reaction.[17]

The influence of ionic liquids on the Diels–Alder reaction has been investigated by Welton and co-workers, who proposed that the improved *endo*:*exo* product ratios, and associated acceleration of formation, in the case of cyclopentadiene and methyl acrylate, are 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 such a hypothesis, 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.[18] According to this reasoning it is not surprising that good results have been reported for ionic liquids like [bmim][PF_6], which comprises a cation with an acidic proton, and a non-polar and weakly coordinating anion.

Ionic liquids have considerable potential for Diels–Alder reactions due to the variety of cation-anion combinations that are available, and in this paper we provide a detailed investigation of the reaction between cyclopentadiene and methyl acrylate in the absence of catalyst and identify the key parameters for optimising the reaction.

Results and Discussion

The cycloaddition of cyclopentadiene to methyl acrylate (Scheme 1) is perhaps the most intensively studied Diels–Alder reaction, and has been conducted in organic solvents,[2,6,19,20] water[7,8] and in a series of room temperature ionic liquids.[11,13,14,16,18,21] As such, the reaction was chosen for the study described herein.



Scheme 1. The Diels–Alder cycloaddition of cyclopentadiene to methyl acrylate.

We initially conducted the reaction between cyclopentadiene and methyl acrylate in a series of ionic liquids with the same cation, *viz*. [bmim]$^+$, and different anions, i.e., tetrafluoroborate [BF_4]$^-$, hexafluorophosphate [PF_6]$^-$, hexafluoroantimonate [SbF_6]$^-$ and bis(trifluoromethylsulfonyl)imide [Tf_2N]$^-$. In the typical experiment, the reaction was performed at room temperature for 24 hours and the products were extracted into diethyl ether and analysed by GC. The results from these studies are listed in Table 1.

The *endo*:*exo* ratio obtained in [bmim][BF_4] is considerably lower than that reported previously (3.5 *versus* 4.6) whereas the *endo*:*exo* ratio obtained in [bmim] [Tf_2N] is comparable to the literature value.[17] It was noted from these experiments that [bmim][Tf_2N] forms a single phase with the substrates (as do [bmim] [SbF_6] and [bmim][CF_3COO]), whereas the other systems were biphasic. Consequently, the effect of the concentration of the reactants in the ionic liquid was investigated. Cyclopentadiene and methyl acrylate in a 1.5:1 mol · mol^{-1} ratio were added to between 1 and 8 mol equivalents of [bmim][BF_4]. With mol ratios of [bmim][BF_4]: methyl acrylate below 6 the system was biphasic and at 6 and above the reaction system was homogeneous. The results from these experiments are depicted in Figure 1 and it is clear that there is a significant increase in the *endo*:*exo* ratio when the reaction becomes homogeneous. Similar findings were observed for [bmim][PF_6].

Table 1. Selectivities in the reaction between cyclopentadiene and methyl acrylate in [bmim]$^+$-based ionic liquids.[a]

Anion	*endo*:*exo* ratio	Yield[b] [%]
[BF_4]$^-$	3.5	97
[PF_6]$^-$	3.8	97
[SbF_6]$^-$	4.2	94
[Tf_2N]$^-$	4.2	99
[CF_3COO]$^-$	4.4	96

[a] Cyclopentadiene (0.16 mL, 2.1 mmol) and methyl acrylate (0.12 mL, 1.4 mmol) were mixed in ionic liquid (0.30 mL) at room temperature. Reaction time 24 hours.

[b] Yields calculated from GC.

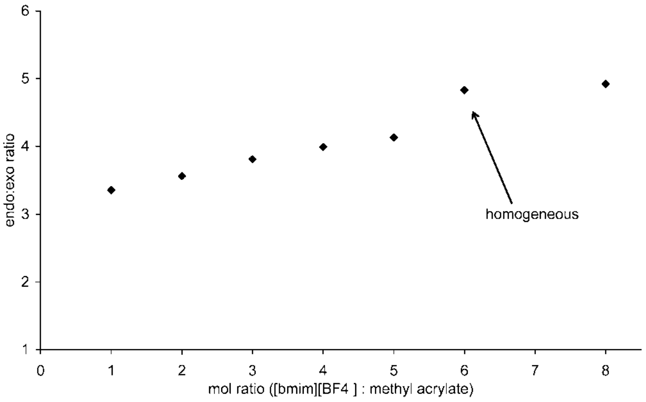


Figure 1. Selectivities at different concentrations of starting material (cyclopentadiene:methyl acrylate = 1.5 : 1 mol · mol^{-1}) in [bmim][BF$_4$].

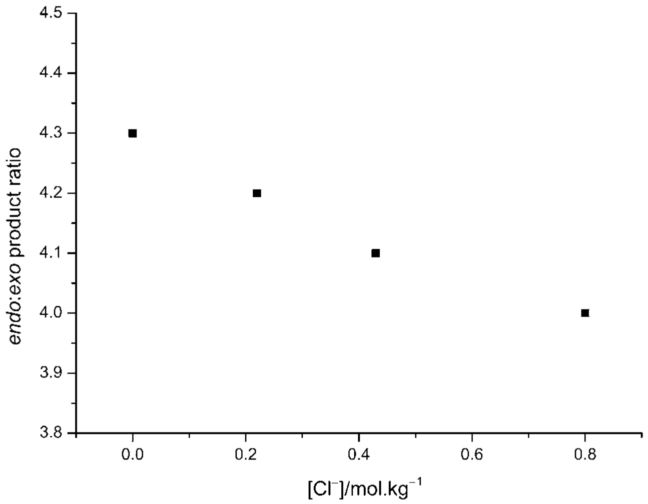


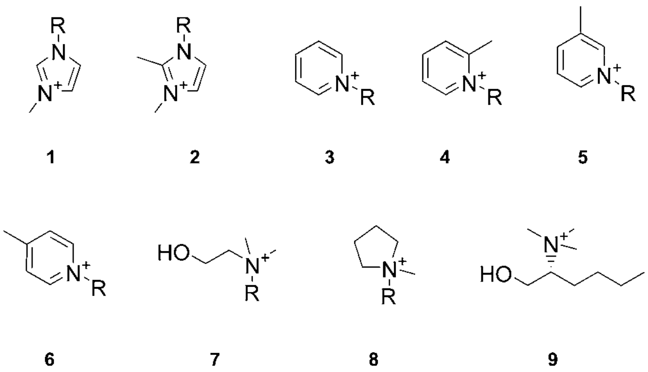
Figure 2. The effect of chloride contamination in [bmim][Tf$_2$N] on the *endo*:*exo* ratio.

In two ionic liquids which formed homogeneous systems throughout the substrate concentration range investigated, [bmim][Tf$_2$N] and [bmim][CF$_3$COO], the selectivity appeared to be independent of the solvent volume.

Before undertaking a detailed investigation based on a large series of different ionic liquids the effect of impurities, that are commonly encountered in ionic liquids, on the Diels–Alder was established. It has been suggested that impurities in ionic liquids, such as halide ions, may disrupt hydrogen bonding interactions.[18] Since hydrogen bonding interactions lead to improved *endo*:*exo* selectivities in Diels–Alder reactions, the presence of halide ions could be detrimental. In catalysed reactions, for example, chloride and water impurities have been shown to have a tremendous influence and can lead to reproducibility problems.[22] Known quantities of sodium ions, chloride ions and water were added to [bmim][BF$_4$] prepared *via* the methylation of 1-butylimidazole with [Me$_3$O][BF$_4$], a halide-free route.[22] Molar ratios of cyclopentadiene:methyl acrylate : ionic liquid of 1.5 : 1 : 1 were employed and yields and product ratios were determined by GC after 24 hours. Under these conditions the system was biphasic, and only a small decrease in the selectivity was observed on the addition of chloride contaminants, *ca.* 10% following addition of 4 mol · kg^{-1} of [bmim][Cl] to the [bmim][BF$_4$] ionic liquid. It is likely that in the biphasic system the reaction does not take place in the ionic liquid phase. Thus, in order to discern the influence of residual chloride, a homogeneous system was studied. Using the same method, but with chloride-free [bmim][Tf$_2$N] in place of [bmim][BF$_4$], the selectivity decreased by about 8% when going from the pure ionic liquid to ionic liquid containing 0.8 mol · kg^{-1} of [bmim][Cl] (see Figure 2). The latter concentration is, however, very high, and also affects the physical properties of the ionic liquids, and it is unlikely that such concentrations would be present in ionic liquids as contaminants. Addition of small quantities of salts to molecular solvents can have a tremendous influence on the *endo*:*exo* selectivities in Diels–Alder reactions,[23] however, it would appear that if the solvent is ionic itself, then the effect of salt impurities is negligible.

As the substrates were miscible with [Tf$_2$N]$^-$ ionic liquids, the reaction between cyclopentadiene and methyl acrylate was monitored in a range of [Tf$_2$N]$^-$ ionic liquids in order to evaluate the cation effect in more detail. The cations used are depicted in Figure 3 and the *endo*:*exo* ratios and yields are summarised in Table 2.

From Table 2 a number of trends can be appreciated. In general, selectivities decrease as the length of the alkyl chain attached to the cation increases. For example, the selectivity decreases from 5.1 in 1,3-dimethylimidazolium [Tf$_2$N]$^-$ (entry 2) to 3.9 in the 1-octyl-3-methylimidazolium salt (entry 6). Similar trends were observed for other series of alkyl-substituted cations and are summarised in Figure 4. In addition, the presence of func-



a R = CH$_3$ **e** R = C$_8$H$_{17}$
b R = C$_2$H$_5$ **f** R = C$_3$H$_6$CO$_2$H
c R = C$_4$H$_9$ **g** R = C$_3$H$_6$CN
d R = C$_6$H$_{13}$ **h** R = CH$_2$C$_6$H$_5$

Figure 3. Ionic liquid cation structures.

Table 2. Cation effect on *endo*:*exo* selectivities in the cycloaddition of cyclopentadiene to methyl acrylate in $[Tf_2N]^-$-based ionic liquids.[a]

Entry	Cation	*endo*:*exo* ratio	Yield[b] [%]
1[c]	–	3.3	97
2	**1a**	5.1	98
3	**1b**	4.3	98
4	**1c**	4.2	97
5	**1d**	4.1	96
6	**1e**	3.9	95
7	**1f**	5.4	95
8	**1g**	4.4	95
9	**1h**	5.1	99
10	**2b**	4.6	98
11	**2c**	4.4	97
12	**3b**	4.6	97
13	**3c**	4.1	96
14	**3d**	4.1	96
15	**3e**	4.0	95
16	**3h**	4.6	97
17	**4b**	4.2	98
18	**4c**	3.9	95
19	**4h**	4.3	98
20	**5c**	3.9	97
21	**5e**	3.8	96
22	**6b**	4.7	99
23	**6c**	4.2	97
24	**6h**	4.8	98
25	**7b**	5.5	98
26	**7c**	5.1	98
27	**7d**	4.7	98
28	**7h**	5.2	98
29	**8c**	4.8	97
30	**8h**	4.8	95
31	**9**	5.6	98

[a] Cyclopentadiene (0.16 mL, 2.1 mmol) and methyl acrylate (0.12 mL, 1.4 mmol) ionic liquid (0.30 mL) at room temperature. Reaction time 24 hours.

[b] Yields calculated from GC.

[c] Neat.

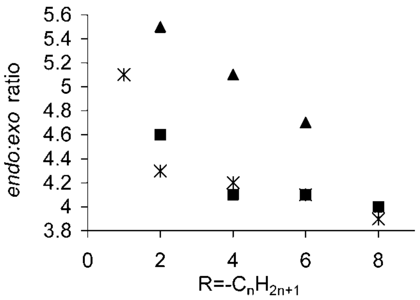


Figure 4. *Endo*:*exo* product selectivities as a function of alkyl chain length for cations; ∗ 1-alkyl-3-methylimidazolium; ■ *N*-alkylpyridinium; ▲ *N*-alkyl-(2-hydroxyethyl)-*N*,*N*-dimethylammonium. In all cases the anion is $[Tf_2N]^-$.

tional groups such as hydroxy, carboxyl, nitrile or benzyl groups increase the selectivity compared to an alkyl chain. Surprisingly, higher selectivities are observed in 1-alkyl-2,3-dimethylimidazolium ionic liquids than in their 1-alkyl-3-methylimidazolium analogues. This observation, in conjunction with the relatively high selectivities in the *N*-alkylpyridinium salts, indicates that the hydrogen bond donor properties of the cation do not satisfactorily account for selectivities. However, as shown by the high *endo:exo* ratios obtained in the *N*-alkyl-*N*-(2-hydroxyethyl)-*N*,*N*-dimethylammonium liquids, hydrogen bond donor moieties which are separated somewhat from the centre of charge on the cation, do appear to improve the selectivity.

The reaction between cyclopentadiene and methyl acrylate in several ionic liquids was followed *in situ* by ^1H and ^{13}C NMR spectroscopy in order to establish the influence of the ionic liquids on the reaction rate (Table 3). Reaction profiles were evaluated by solving the relevant second-order rate law differential analytically. [Equation (1): A denotes methyl acrylate and B cyclopentadiene, k_{exo} = rate constant for *exo* products, k_{endo} = rate constant for *endo* products. Further details are provided in the supporting information.]

$$-\frac{d[A]}{dt} = [A](t)\cdot[B](t)\cdot(k_{exo} + k_{endo}) \qquad (1)$$

It was found that the rate of formation of the *exo* product remained unaffected by the presence of the ionic liquid, whereas higher overall selectivities were accompanied by more rapid formation of the *endo* products. As the reaction is irreversible, this should stem from a lowering of the relative energy of the transition states leading to the *endo* products, while the transition states yielding the *exo* products are not significantly influenced by the choice of cation, at least in the cases studied. Consequently, designing ionic liquids that give rise to reverse selectivities in this particular reaction will be a major challenge.

An important aspect of the application of ionic liquids is their potential as recyclable solvents, and this is also the case for their use in the Diels–Alder reaction. The ionic liquids could be re-used after extraction of the products with diethyl ether, although a slight decrease in selectivity was observed in subsequent reactions (see Table 4). The effect was found to be rather small and is possibly a consequence of the presence of residual dicyclopentadiene in the ionic liquid.

Prediction of the *Endo*:*Exo* Ratio

An NMR spectroscopy-based empirical solvent parameter scale, the Δ scale, has previously been used to analyse the solubility of carbon monoxide in ionic liquids.[24] We have found that this scale can be applied to the anal-

Table 3. Rate constants for the reaction of cyclopentadiene and methyl acrylate at 26 °C in different $[Tf_2N]^-$-based ionic liquids.

Cation	*endo*:*exo* ratio	$10^6\, k_{endo}$ [M^{-1} sec^{-1}]	σ_{endo} [M^{-1} sec^{-1}][a]	$10^6\, k_{exo}$ [M^{-1} sec^{-1}]	σ_{exo} [M^{-1} sec^{-1}][a]
7b	5.5	37	1.2	3.4	0.1
2c	4.4	32	0.6	3.3	0.1
1c	4.2	28	0.9	3.5	0.2
3c	4.1	21	0.4	3.7	0.3

[a] Standard deviation at the 95% confidence level.

Table 4. Selectivities after recovery and reuse of the ionic liquid.[a]

Ionic Liquid Cation	Run		
	1	2	3
1c	4.2	4.2	4.0
1a	5.1	4.9	4.9
1h	5.1	5.0	4.9
2c	4.4	4.4	4.3
7h	5.2	5.0	4.9
8c	4.8	4.8	4.5

[a] Results are shown as selectivities (*endo*: *exo* product ratios); all ionic liquids incorporate the $[Tf_2N]^-$ anion. Reaction time 24 hours.

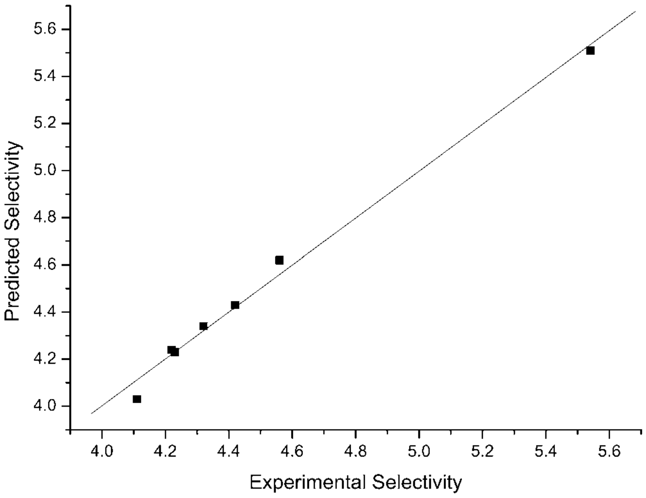


Figure 5. Calculated *versus* observed selectivities (*cf.* Table 2) for seven different ionic liquids: entries 13, 4, [bmim][SbF_6], 1, 16, 11 and 25 according to increasing selectivities (further details are provided in the Supporting Information).

ysis of observed selectivities in the Diels–Alder reaction between cyclopentadiene and methyl acrylate with good results (see Figure 5). The Δ scale was used in preference to the Kamlet–Taft solvent polarity scale,[25–29] which is only available for a few ionic liquids,[30,31] and where values differ significantly owing to the use of different solvatochromic probes. The equation providing the best fit has the form:

$$endo{:}exo \text{ product ratio} = 1.97\cdot\Delta_a^N + 3.03\cdot\Delta_b^N - 4.39\cdot\Delta_c^N + 1.87\cdot\Delta_d^N + 1.33,$$

where the ^{13}C NMR chemical shifts of chloroform and 1,2-dichloroethane dissolved in the ionic liquid, referenced against cyclohexane, are used to obtain Δ_b and Δ_c, respectively. The ^{13}C shift difference between the nitrile carbon of benzonitrile and the methyl carbon of toluene is used to determine Δ_d, whereas the shifts of the ^{19}F signals of 2-fluoropyridine and fluoropyridine are compared to obtain Δ_a. The Δ values were normalised to Δ^N values by setting the corresponding parameter value for cyclohexane as zero, and that of DMSO as 1. The good fit ($R = 0.996$, $\sigma = 0.05$, $n = 7$; for details see Supporting Information) suggests that the lowering of the transition state energies is related to overall interactions between the transition state and the solvent, rather than highly specific, structure dependent interactions. This hypothesis is based on the fact that the probes used in this particular solvent scale bear little resemblance to the reactants used in the study.

While this empirical solvent scale would allow one to predict *endo*:*exo* ratios based on secondary data for any ionic liquid, it is still necessary to determine the parameters experimentally. A semi-empirical solvent scale, such as the TLSER scale (theoretical linear solvent free-energy relationship),[28,32] circumvents this limitation by using semi-empirical computational methods, such as the MNDO algorithm, to describe solvents and evaluate their properties. The electrostatic acities and basities (q^+ and q^-, respectively),[28,32] covalent acities and basities (ε_a and ε_b)[28,32] and molar refractivities (n_m)[33] were determined with MOPAC 6 for a selection of the cations used in the study, using the MNDO algorithm. The AM1 and PM3 algorithms were also investigated, but yielded inferior results.[28,32] The coefficient of correlation was 0.93 and the standard deviation 1.7×10^{-3} ($n = 26$) when experimental selectivities in $[Tf_2N]^-$ ionic liquids were fitted using the equation (see Figure 6):

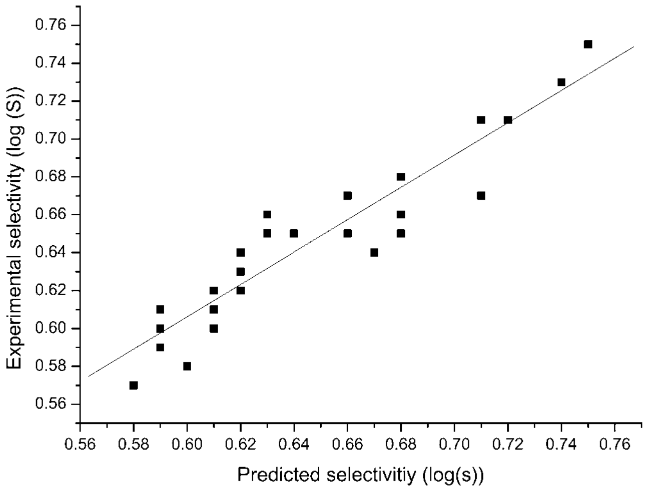


Figure 6. Observed *versus* calculated *endo*:*exo* product ratios for different cations.

$$\log(S) = -3.2\times10^{-3}\varepsilon_a + 9.7\times10^{-3}\times\varepsilon_b - 1.3\times q^{+} + 1.3\times q^{-} - 2.7\times10^{-3}\times n_m + 8.5\times10^{-1},$$

where S denotes the *endo*:*exo* product ratio for the reaction under standard conditions (For further details see Supporting information).

Although the coefficient of determination is rather low, 0.85, the relationship is of sufficient significance to allow for the prediction of selectivities in ionic liquids comprising new cations. It is worth noting that the method can be calibrated for other anions and potentially other substrates.

Both methods point towards the presence of basic groups, or acidic protons, leading to improved *endo*:*exo* selectivities. Cativiela and co-workers correlated the selectivity in the cycloaddition of cyclopentadiene to (−)-menthyl acrylate with the Kamlet–Taft parameters for organic solvents.[6] They concluded that all types of interaction (π^* – non-specific, mainly coulombic, α – hydrogen bond donor acity – as well as β – hydrogen bond acceptor basity) contributed to the overall selectivity, although the relative contribution of α was about twice that of β.

The product selectivity in the Diels–Alder reaction in $[\text{bmim}]^+$-based ionic liquids has previously been analysed primarily in terms of hydrogen bonding interactions between the transition state and the cation. It was proposed that ionic liquids with strong hydrogen bonding interactions between the cation and anion will be poor solvents for the Diels–Alder reaction, due to competition between the anion and the transition state for hydrogen bonding with the cation. The analysis of ^{1}H NMR shift data for several ionic liquids indicates that the shift of the proton in the 2-position of the imidazolium ring is influenced by π-stacking of the cations as well as hydrogen bonding interactions between the cation and the anion.[34] In the case of imidazolium ionic liquids, hydrogen bonding between the ionic liquid cation and the anion is also manifested in the occurrence of a $C_{im}-H\cdots A^-$ stretch of around 3126 cm^{-1} for [bmim][PF$_6$] and 3060 cm^{-1} for 1-ethyl-3-methylimidazolium chloride, respectively.[35] The change in wavenumber and intensity is correlated to the degree of hydrogen bonding between the anion and the cation, but is unlikely to be influenced by π-stacking to the same extent as the ^{1}H NMR shift data. Thus, if there is a strong hydrogen-bonding interaction between the cation and the anion, and the selectivity is dependent on the degree to which the transition state can compete with the anion for hydrogen bonding, the selectivity should follow roughly the same trend as the shift of the $C_{im}-H\cdots A^-$ stretch. This is indeed what is observed (see Table 5), although the correlation is qualitative.

Hydrogen-bonding interactions are relatively weak (4–5 kcal·mol^{-1}), whereas the energy needed to separate ions is much stronger (calculated at the B3LYP/6–31G* level to be 95 kcal·mol^{-1} in vacuum).[36] Thus, even when ionic liquids are diluted in substantial volumes of molecular solvents, cation-anion interactions remain, and the IR spectra of the ionic liquids change relatively little when going from neat to very dilute solutions in neutral solvents.

Progressing from [bmim][PF$_6$] to [bmim][Tf$_2$N], there is a change in ν_{CH} of 5 cm^{-1} and the selectivity decreases from 5.0 to 4.3, whereas changing from [bmim][Tf$_2$N] to [bmim][TFA] results in a change in frequency of 34 cm^{-1} and only in a negligible change in selectivity. A similar trend is seen for the ^{1}H NMR shift of the C(2) proton. Thus, there does not appear to be a strong correlation between hydrogen bonding and selectivity for 1-butyl-3-

Table 5. Spectroscopic data, ^{1}H NMR shifts and selectivities in $[\text{bmim}]^+$ ionic liquids.

Anion	ν_{CH} [cm^{-1}][a]	^{1}H NMR[b]	*endo*:*exo* ratio	*endo*:*exo* ratio[c]
$[PF_6]^-$	3126	8.7	5.0	4.8
$[BF_4]^-$	3123	8.8	4.9	4.6
$[Tf_2N]^-$	3121	8.7	4.3	4.3
$[CF_3COO]^-$	3087	9.8	4.4	4.2

[a] Wavenumber of the absorption maximum of the $C_{im}-H\cdots A^-$ stretch.

[b] Shift of the C(2) proton in the neat ionic liquid.

[c] Data from ref.[17]

methylimidazolium ionic liquids, although the highest selectivity, when investigating the anion effect, is seen in the ionic liquid with the least strong hydrogen bonding interaction between the cation and the anion. For the $[\mathrm{Tf_2N}]^-$ series, higher *endo*:*exo* ratios are obtained in ionic liquids where the cation is functionalised with hydrogen bond donor moieties separated in space from the centre of charge.

Conclusions

Based on the experimental evidence currently available, the selectivity of Diels–Alder reactions in ionic liquids appears to be dependent on the following factors:

1. Hydrogen bond donor capacity of the ionic liquid – the “solvent” ions can stabilise the transition state (TS) of the Diels–Alder reaction by bonding, e.g., to the carbonyl oxygen in methyl acrylate, as stated before.
2. Steric bulk – long substituents on the cation lead to lower selectivities, presumably due to steric interaction between the TS and the cation.
3. “Hardness” of the ionic liquids ions – strong electrostatic association between the ionic liquid ions leads to less interaction between the ionic liquid and the TS. This can be overcome by using functionalised ionic liquids with hydrogen bond donor moieties removed from the immediate proximity of the centre of charge of the cation or anion. Ionic liquid ions with highly delocalised or shielded centres of charge associate less closely with one-another.
4. HOMO and LUMO π orbital interactions – the presence of a LUMO low energy promotes interaction between the TS and the ionic liquid, whereas a low-energy HOMO has the opposite effect.
5. Overall “polarity” of the ionic liquid – several empirical polarity scales, most notably the Kamlet–Taft scale, have already been used to describe the selectivity in the Diels–Alder reaction, indicating that all types of interactions contribute to yield higher selectivities, the *endo* TS has a higher dipole moment than the *exo* one. Thus, polarisable solvents can lower the energy of *endo* TS more than that of the *exo* TS.
6. Salt impurities in the ionic liquids appear to have only a minor effect on the selectivity of the reaction.

From the large dataset provided herein it is clear that multiple factors influence the product selectivity in the Diels–Alder reaction. The *semi*-empirical theoretical method described (*vide supra*), suggests that π-orbital overlap, as promoted by a low energy LUMO and decreases in the presence of a low energy HOMO on the ionic liquid cation, may well be of importance. Most likely, the product ratio is dependent on several factors, of which hydrogen bonding interactions is important.

Experimental Section

Starting Materials

Methyl acrylate was distilled prior to use and cyclopentadiene was obtained by cracking dicyclopentadiene, distilled under reduced pressure, and stored at $-70\,^\circ\mathrm{C}$.

Diels–Alder Reactions

In the typical Diels–Alder reaction cyclopentadiene (0.17 mL, 2.00 mmol) and methyl acrylate (0.12 mL, 1.35 mmol) were added to ionic liquid (0.30 mL) and stirred with a magnetic stirrer on a water bath equipped with a thermostat. The reaction was carried out at room temperature for 24 h. The syntheses were performed under an inert atmosphere of dry nitrogen. After 24 hours the products were extracted three times with diethyl ether and analysed by GC.

Preparation of Ionic Liquids

1-Butyl-3-methylimidazolium **1c** salts of $[\mathrm{BF_4}]^-$,[37] $[\mathrm{PF_6}]^-$,[38] and $[\mathrm{SbF_6}]^-$,[39] were obtained according to literature procedures. The ionic liquids listed in Table 2 identified as: **1a** $[\mathrm{Tf_2N}]$,[34] **1b**$[\mathrm{Tf_2N}]$,[34] **1c**$[\mathrm{Tf_2N}]$,[34] **1d**$[\mathrm{Tf_2N}]$,[38] **1e**$[\mathrm{Tf_2N}]$,[40] **1f**$[\mathrm{Tf_2N}$,[41] **1 g**$[\mathrm{Tf_2N}]$,[42] **1 h**$[\mathrm{Tf_2N}]$,[43] **2b**$[\mathrm{Tf_2N}]$,[34] **2c**$[\mathrm{Tf_2N}]$,[39] **3c**$[\mathrm{Tf_2N}]$,[44] **3d**$[\mathrm{Tf_2N}]$,[45] **3e**$[\mathrm{Tf_2N}]$,[45] **8c**$[\mathrm{Tf_2N}$,[46] and **9** $[\mathrm{Tf_2N}]$,[47] were prepared according to literature procedures, as were *N*-ethylpyridinium bromide 3bBr,[48] *N*-benzylpyridinium bromide **3 h**Br,[49] *N*-ethyl-2-methylpyridinium bromide **4b**Br,[50] *N*-butyl-2-methylpyridinium chloride **4c**Cl,[50] *N*-benzyl-2-methylpyridinium bromide **4 h**Br,[51] *N*-ethyl-4-methylpyridinium bromide **6b**Br,[52] *N*-butyl-4-methylpyridinium chloride **6c**Cl, *N*-benzyl-4-methylpyridinium bromide **6 h**Br,[53] *N*-ethyl-*N*,*N*-dimethyl-*N*-(2-hydroxyethyl)ammonium bromide **7b**Br,[52] *N*-butyl-*N*,*N*-dimethyl-*N*-(2-hydroxyethyl)ammonium chloride **7c**Cl,[54] *N*-hexyl-*N*,*N*-dimethyl-*N*-(2-hydroxyethyl)ammonium chloride **7d**Cl,[54] *N*-benzyl-*N*,*N*-dimethyl-*N*-(2-hydroxyethyl)ammonium bromide **7 h**Br,[54] and *N*-benzyl-*N*-methylpyrrolidinium bromide **8 h**Br.[54] *N*-Butyl-3-methylpyridinium **5c** dicyanimide and *N*-octyl-3-methylpyridinium tetrafluoroborate **5e**$[\mathrm{BF_4}]$ were provided by Lonza. Chloride-free1-butyl-3-methylimidazolium tetrafluoroborate **1c**$[\mathrm{BF_4}]$ was obtained according to literature.[22]

The synthesis and characterisation of the new ionic liquids *N*-benzyl-*N*-methylpyrrolidinium bis(trifluoromethylsulfonyl)imide **8 h**, *N*-ethylpyridinium bis(trifluoromethylsulfonyl)imide **3b**, *N*-benzylpyridinium bis(trifluoromethylsulfonyl)imide **3 h**, *N*-ethyl-2-methylpyridinium bis(trifluoromethylsulfonyl)imide **4b**, *N*-butyl-2-methylpyridinium bis(trifluoromethylsulfonyl)imide **4c**, *N*-benzyl-2-methylpyridinium bis(trifluoromethylsulfonyl)imide **4 h**, *N*-butyl-3-methylpyridinium bis(trifluoromethylsulfonyl)imide **5c**, *N*-octyl-3-methylpyridinium bis(trifluoromethylsulfonyl)imide **5e**, *N*-ethyl-4-methylpyridinium bis(trifluoromethylsulfonyl)imide **6b**, *N*-butyl-4-methylpyridinium bis(trifluoromethylsulfonyl)imide **6c**, *N*-benzyl-4-methylpyridinium bis(trifluoromethylsulfonyl)imide **6 h**, *N*-ethyl-*N*,*N*-dimethyl-*N*-(2-hydroxyethyl)ammonium bis(trifluoromethylsulfonyl)imide **7b**, *N*-butyl-*N*,*N*-dimethyl-*N*-(2-hydroxyethyl)ammonium bis(trifluoromethylsulfonyl)-

imide **7c**, *N*-hexyl-*N*,*N*-dimethyl-*N*-(2-hydroxyethyl)ammonium bis(trifluoromethylsulfonyl)imide **7d**, *N*-benzyl-*N*,*N*-dimethyl-*N*-(2-hydroxyethyl)ammonium bis(trifluoromethylsulfonyl)imide **7 h** is provided in the Supporting Information.

Analytical Procedures

GC analyses were carried out on a Varian Chrompack CP-3380 equipped with a capillary column (25 m × 0.25 mm, using He as carrier gas). Spectroscopic data were analysed using WinNMR 6.1 (Bruker), gNMR 4.0 (Cherwell Scientific) and Spectrum 3.02 (Perkin Elmer). Numerical analyses were carried out with Scientist 2.0 (Micromath).

IR spectra were recorded on a Perkin-Elmer FT-IR 2000 system. NMR spectra were measured on Bruker DRX 400 and AC 200 MHz spectrometers in sweep-off mode, with chemical shifts given in ppm and coupling constants (*J*) in Hz. TMS was used as external standard. Electrospray ionisation mass spectra (ESI-MS) were recorded on a ThermoFinnigan LCQ^{TM} Deca XP Plus quadrupole ion trap instrument on samples diluted in acetonitrile. Samples were infused directly into the source at a rate of 5 $\mu L \cdot min^{-1}$ using a syringe pump, and the spray voltage was set at 5 kV and the capillary temperature at 50 °C as described previously.[55] Elemental analyses were carried out at the Institute of Chemical Sciences and Engineering (EPFL). Differential scanning calorimetry was performed using a SETARAM DSC 131. Semi-empirical calculations were performed using MOPAC 6.0.[56] Δ parameter values were determined according to published procedures.[24]

Supporting Information

Preparation of the novel ionic liquids, Δ^N parameters, kinetic data and *semi*-empirically calculated parameters are available as supporting information.

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