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Diels-Alder Reactions in Room-Temperature Ionic Liquids.

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Abstract. The Diels-Alder cycloaddition reaction between methyl acrylate and cyclopentadiene has been investigated in a number of air and moisture stable ionic liquids. The *endo*/*exo* ratio of the reaction has been used as an initial probe of the nature of the solvents.

Room-temperature ionic liquids are a new class of liquids that are constituted entirely of ions. Hence, they provide a solvent environment that is quite unlike any other available at room temperature. Although they have now been known for some time,[1] relatively little synthetic chemistry has been reported in them. Notable exceptions are the use of chloroaluminate(III) ionic liquids as a combination of catalyst and solvent for a number of organic Friedel-Crafts reactions,[2] and related organometallic reactions.[3,4]

With their unique character, the ionic liquids may induce solvent effects on a wide range of processes. As part of our wider study on the effect of the ionic environment on reaction processes we have been investigating a number of Diels-Alder reactions in these systems. The Diels-Alder reaction remains one of the most useful carbon-carbon bond-forming reactions in organic chemistry. Of particular interest here is the reaction of cyclopentadiene with methyl acrylate, which leads to a mixture of *exo* and *endo* products. This reaction has been widely investigated in a range of molecular solvents and solvent influences on the *endo*/*exo* selectivity of the reaction are well understood. They may be viewed as being due to the "polarity" of the solvent leading to the stabilisation of the more polar (*endo*) activated complex.[5] More recently the effect has been attributed to solvophobic interactions that generate an "internal pressure" and promote the association of the reagents in a "solvent cavity" during the activation process. As highly ordered hydrogen-bonded solvents, ionic liquids have the potential to have dramatic effects on Diels-Alder reactions.

Dialkylimidazolium bromides and trifluoroacetates have been used as catalysts, in dichloromethane solution, for the addition of cyclopentadiene and either crotonaldehyde or methacrolein.[6] Here the effect was attributed to the Lewis acidity of the salts. The only instance of a pure ionic liquid being used as a solvent for Diels-Alder reactions was the demonstration of the strong *endo* selectivity of the addition of cyclopentadiene and methyl acrylate (Scheme 1) in $[EtNH_3][NO_3]$ which was also associated with considerable acceleration of the process.[7] In this paper, we use the ionic liquids $[bmim][BF_4]$, $[bmim][ClO_4]$, $[emim][CF_3SO_3]$, $[emim][NO_3]$ and $[emim][PF_6]$ {where $[emim]^+$ is the 1-ethyl-3-methylimidazolium cation and $[bmim]^+$ is the 1-butyl-3-methylimidazolium cation} as solvents for the same reaction. These ionic liquids are air-stable and although they will absorb moisture from the air, this can be easily removed by gentle heating (60 °C) over night.

In a typical reaction, the diene and dienophile are added to the ionic liquid directly. Two phases are formed and the mixture is stirred at 25 °C for 72 hours. The organic layer is separated and any residual organic material can be extracted from the ionic liquid with either diethyl ether or petrol (60-80 °C) to leave the pure ionic liquid, which may be reused.

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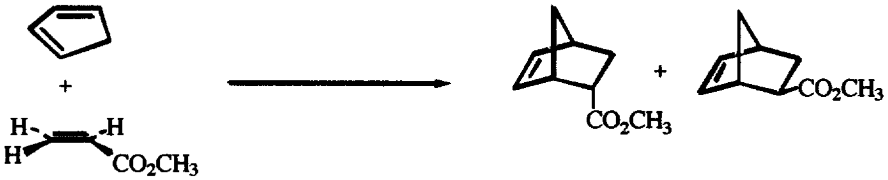

Scheme 1. The reaction of cyclopentadiene and methyl acrylate

Table 1 shows the results of a number of Diels-Alder additions of methyl acrylate and cyclopentadiene (Scheme 1) in a [emim][BF_4] ionic liquid. It can be seen that at room temperature the yield of the reaction increases with time up to 72 hours. Also the selectivity of the reaction for the *endo* product slightly decreases with time and the amount of dicyclopentadiene formed in the competing Diels-Alder dimerisation of cyclopentadiene increases. Further increases in reaction time were found to have no significant effect on either the yield or the selectivity of the reaction. When the reaction is conducted at a higher temperature (60 °C) extending the reaction time beyond 2 hrs has little effect on yield and again decreases the selectivity of the reaction.

Table 1. Results of the Diels-Alder addition of methyl acrylate and cyclopentadiene in a [emim][BF_4] ionic liquid.

Conc. / M	Time / hrs	Temp / °C	Yield / %	Ratio *endo*/*exo*	Ratio product:dicyclopentadiene
0.30	2	20	50	85:15 (5.7:1)	100:0
0.30	20	20	77	82:18 (4.6:1)	97:3
0.30	72	20	91	81:19 (4.3:1)	98:2
0.30	72	45	79	79:21 (3.8:1)	99:1
0.30	2	60	71	81:19 (4.3:1)	99:1
0.30	20	60	76	78:22 (3.6:1)	98:2
0.30	72	60	77	77:23 (3.4:1)	97:3
0.30	72	70	78	75:25 (3.0:1)	94:6
0.15	2	20	41	86:14 (6.1:1)	88:12
0.15	72	20	81	84:16 (5.3:1)	98:2

Since the maximum yield in the [bmim][BF_4] ionic liquid was obtained at by reaction for 72 hours at 25 °C with the starting materials in a concentration of 0.3 M, when using the other ionic liquids (Table 2) as far as possible the conditions for the reactions were kept the same. However, [emim][NO_3] has a melting point between 38-41 °C and [emim][PF_6] has a melting point between 58-62 °C requiring higher reaction temperatures, 45 °C and 70 °C respectively. So that direct comparisons could be made the reaction was repeated in the [bmim][BF_4] ionic liquid at these temperatures.

At 25 °C, the [bmim][BF_4] ionic liquid shows strong *endo* selectivity with an*endo*/*exo* ratio up to 6.1:1 (86:14). This compares to 6.7:1 (87:12) for methanol, 5.2:1 (84:16) for ethanol, 4.2:1 (81:19) for acetone and 2.9:1 (74:26) for diethyl ether, under similar conditions.[5] The *endo* selectivity decreases as both the concentration of the reagents and the temperatures of the reactions are increased. This is in accord with observations in conventional organic solvents. Selectivities in the other ionic liquids (Table 2) show similar results and the lower selectivities in

[emim][NO_3] and [emim][PF_6] may simply reflect the higher temperatures of these reactions. The ionic liquids show selectivities that are characteristic of hydrogen-bonded, polar organic solvents.

Table 2. Results of the Diels-Alder addition of methyl acrylate and cyclopentadiene in a variety of ionic liquids.

Ionic Liquid	Conditions	Yield (%)	Ratio *endo*:*exo*	Ratio product:dicyclopentadiene
[bmim][ClO_4]	72 hrs/25 °C	75	84:16 (5.3:1)	97:3
[emim][CF_3SO_3]	72 hrs/25 °C	56	83:17 (4.9:1)	93:7
[bmim][BF_4]	72 hrs/25 °C	91	81:19 (4.3:1)	98:2
[emim][NO_3]	72 hrs/45 °C	57	77:23 (3.3:1)	89:11
[emim][PF_6]	72 hrs/70 °C	34	76:24 (3.2:1)	88:12
[$EtNH_3$][NO_3][7]	72 hrs/25 °C	98	87:13 (6.7:1)	?

In recent years two solvent systems have shown particular promise as solvents for Diels Alder reactions, water and 5M $LiClO_4$ in ether.[8,9] In water the *endo*/*exo* ratio under conditions similar to ours are reported as 9.2:1 (90:10)[8] or 7.4:1 (88:12).[10] This increased selectivity for the *endo* adduct is associated with an increased rate of reaction that has lead to the use of water for a number of Diels-Alder reactions. However, the use of moisture sensitive reagents is obviously precluded.

Adding $LiClO_4$ to ether also increases the preference for the *endo* product.[9] The efficacy of $LiClO_4$ in ether as a medium for the Diels-Alder reaction has been attributed to the Lewis acidity of the lithium cation, although it has also been shown to accelerate reactions that proceed via polarised intermediates.[9] The imidazolium cations of the ionic liquids may exhibit some Lewis acidity, but it is unlikely that if this were the only effect of importance, that such similar results would be seen for the reaction in both media. We are continuing to investigate this behaviour.

Finally, when our results are compared to those in ethylammonium nitrate it can be seen that we achieve lower *endo*/*exo* ratios.[7] It is possible that this is a consequence of a more highly ordered structure for the ethylammonium salt, which is held together by N-H hydrogen bonds rather than the weaker C-H hydrogen bonds that dominate in our imidazolium salts.

The room-temperature ionic liquids give substantial *endo* selectivity enhancements in the reaction of cyclopentadiene with ethyl acrylate when compared to non-polar solvents. Hence, they offer the potential to be useful solvents for Diels-Alder cycloadditions, and related reactions, particularly for moisture and oxygen sensitive reagents. Unlike the $LiClO_4$ in ether solvent system, the reactions are biphasic and products can be isolated simply by decanting the organic layer. They are also preferred to the use of water since they allow the use of moisture sensitive reagents and traces of organic materials are easily removed *in vacuo*. We are continuing to investigate these reactions in a number of ionic liquids.

References

1 J. S. Wilkes, J. A. Levisky, R. A. Wilson and C. L. Hussey, *Inorg. Chem.*, 1982, **21**, 1263.

2 J. Boon, J. Levisky, J. Pflug and J. Wilkes, *J. Org. Chem.*, 1986, **51**, 480.

3 J.K.D. Surette, L. Green and R.D. Singer, *J. Chem. Soc. Chem. Commun.*, 1996, 2753.

4 Paul J. Dyson, Martin C. Grossel, N. Srinivasan, T. Vine, T. Welton, D. J. Williams, A. J. P. White, and T. Zigras, *J. Chem. Soc., Dalton Trans.*, 1997, 3465.

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5 J. A. Berson, Z. Hamlet and W. A. Mueller, *J. Am. Chem. Soc.*, 1962, **84**, 297.

6 J. Howarth, K. Hanlon, D. Fayne and P. McCormac, *Tet. Lett.*, 1997, **38**, 3097.

7 D. A. Jaeger and C. E. Tucker, *Tet. Lett.*, 1989, **30**, 1785.

8 R. Breslow, U. Maitra and C. Ridout, *Tet. Lett.*, 1983, **24**, 1901.

9 H. Waldmann, *Angew. Che. Int. Ed. Engl.*, 1991, **30**, 1306.

10 A. A.-Z. Samii, A. de Savignac, I. Rico and A. Lattes, *Tetrahedron*, 1985, **41**, 3683.