Diels-Alder Reaction in Air- and Moisture-stable Zinc-containing Ionic Liquids

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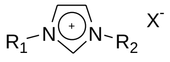
Diels-Alder reactions in a number of air- and moisture-stable dialkylimidazolium halide-$ZnCl_2$ ionic liquids are reported. High yields and high endo selectivities have been observed. The ionic liquids could then be recyclable without loss of reactivity.

Keywords: Ionic liquid; Diels-Alder reaction; Dialkylimidazolium chloride; Zinc chloride.

Ionic liquids are attractive clean dipolar aprotic solvents[1] that provide an excellent medium for performing Diels-Alder reaction, Friedel-Crafts reaction, Heck reaction, alkylation, and hydrogenation.[2] They exhibit many obvious advantages including the ease of product isolation, the absence of measurable solvent vapor pressure, and the potential for recycling.

The well known room temperature chloroaluminate (III) ionic liquid exhibits good catalytic behavior as well as polar solvent media, but its extreme moisture sensitivity is a major disadvantage.[3] Unlike the aluminate ionic system, the air- and moisture-stable 1,3-dialkylimidazolium halide and zinc halide ionic liquids, such as 1-ethyl-3-methylimidazolium chloride-zinc chloride (EMIC-$ZnCl_2$), 1-methyl-3-*n*-octylimidazolium bromide-zinc bromide (C_8MIB-$ZnBr_2$), and 1,3-di-*n*-octylimidazolium bromide-zinc bromide (C_8C_8IB-$ZnBr_2$), were synthesized by our group and showed low melting temperatures.



	R_1	R_2	X
EMIC:	CH_3	C_2H_5	Cl
C_5MIB:	CH_3	$CH_2CH(CH_3)CH_2CH_3$	Br
C_8MIB:	CH_3	n-C_8H_{17}	Br
C_8C_8IB:	n-C_8H_{17}	n-C_8H_{17}	Br

The melting points of imidazolium halide-zinc halide mixtures depended on their composition. For example, a 1:1 molar ratio of EMIC-$ZnCl_2$ mixture was liquid at 30 °C. A higher or lower content of $ZnCl_2$ rendered the melting point higher. The viscosity of these ionic liquids was much lower than that of choline-$ZnCl_2$.[4] From the negative FAB mass spectrum of EMIC-$ZnCl_2$ ionic liquid with 3:1, 1:1, 1:2, and 1:3 molar ratios, we observed the Lewis acidic $ZnCl_3^-$ (*m/z* 169), $Zn_2Cl_5^-$ (*m/z* 303), $Zn_3Cl_7^-$ (*m/z* 437), and $Zn_4Cl_9^-$ (*m/z* 571, a trace amount) species whose amount increased as the $ZnCl_2$ content increased in the ionic liquid.[5] The same species has been observed in quaternary choline chloride-$ZnCl_2$ ionic liquid.[6] Therefore, the Lewis acidity and the catalytic activity of Zn-containing ionic liquid depended on the content of $ZnCl_2$. We utilized the imidazolium halide-zinc halide ionic liquid not only as catalyst but also as solvent to investigate whether the Diels-Alder reaction was affected by Zn-containing ionic liquids, although it has been reported that $ZnCl_2$ presented no catalytic activity for the reaction between butadiene and methyl acrylate in benzene.[7]

A number of dienes **1** and dienophiles **2** were attempted to proceed in Zn-containing ionic liquids which were generated by heating a suitable ratio of ZnX_2 and dialkylimidazolium halide. To carry out the reaction, a dienophile was mixed with ionic liquid by stirring to form a complex and the diene was then added. Owing to the viscosity of ionic liquid, the mixture of *endo*- and *exo*- (or *para*- and *meta*) products **3** was extracted with diethyl ether followed by chloroform to ensure that the product did not remain in the ionic liquid. The ionic liquid was almost quantitatively recovered and could be reused. Other single solvents such as ethyl acetate, diethyl ether, acetone, and hexane gave poor yields. The reaction products were purified by column chromatography and the proportion of *endo*/*exo* or *para*/*meta* was analyzed from the ratio of peak areas by gas chromatography. The results are summarized in Table 1.

A model Diels-Alder reaction of cyclopentadiene (**1a**)

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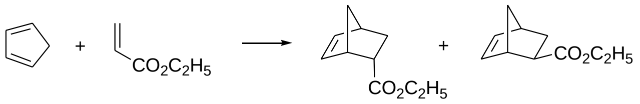
Table 1. The Results of Diels-Alder Reaction between Dienes and Dienophiles in Ionic Liquid[a]

Entry	Diene	Dienophile	Ionic liquid (ratio)	Reaction temp	Reaction time	Product	Yield (%)[b]	*Endo*/*exo* ratio[c]
1	**1a**	**2a**	EMIC-$ZnCl_2$ (1:1)	rt	1 h	**3aa**	37	4:1
2	**1a**	**2a**	EMIC-$ZnCl_2$ (1:1)	rt	12 h	**3aa**	94	5:1
3	**1a**	**2a**	EMIC-$ZnCl_2$ (1:2)	rt	10 min	**3aa**	73	13:1
4	**1a**	**2a**	EMIC-$ZnCl_2$ (1:2)	rt	1 h	**3aa**	92	12:1
5	**1a**	**2a**	EMIC-$ZnCl_2$ (1:2)	rt	2 h	**3aa**	95	12:1
6	**1a**	**2a**	C_8MIB-$ZnBr_2$ (1:2)	rt	10 min	**3aa**	97	10:1
7	**1a**	**2a**	C_8C_8IB-$ZnBr_2$ (1:2)	rt	10 min	**3aa**	87	10:1
8	**1a**	**2b**	EMIC-$ZnCl_2$ (1:2)	rt	10 min	**3ab**	88	> 99:1
9	**1a**	**2c**	EMIC-$ZnCl_2$ (1:2)	rt	10 min	**3ac**	89	20:1
10	**1a**	**2d**	EMIC-$ZnCl_2$ (1:2)	rt	10 min	**3ad**	74	11:1
11	**1a**	**2e**	EMIC-$ZnCl_2$ (1:2)	rt	12 h	**3ae**	85	2:1
12	**1b**	**2a**	EMIC-$ZnCl_2$ (1:2)	rt	12 h	**3ba**	24	–
13	**1b**	**2a**	EMIC-$ZnCl_2$ (1:2)	50 °C	8 h	**3ba**	92	–
14	**1b**	**2b**	EMIC-$ZnCl_2$ (1:2)	rt	2 h	**3bb**	90	–
15	**1c**	**2a**	EMIC-$ZnCl_2$ (1:2)	rt	12 h	**3ca**	27	–[d]
16	**1c**	**2a**	EMIC-$ZnCl_2$ (1:2)	50 °C	8 h	**3ca**	90	–[d]
17	**1c**	**2b**	EMIC-$ZnCl_2$ (1:2)	rt	2 h	**3cb**	83	–[d]
18	**1c**	**2c**	EMIC-$ZnCl_2$ (1:2)	rt	1 h	**3cc**	88	–[d]
19	**1a**	**2a**	Benzene + 5%$ZnCl_2$	rt	2 h	**3aa**	46	7:1
20	**1a**	**2a**	Benzene + 5%$ZnCl_2$	rt	5 h	**3aa**	59	7:1
21	**1a**	**2a**	EMIC-$ZnCl_2$ (1:2) Used five times	rt	2	**3aa**	90	12:1

[a] Reaction conditions: 7.5 mmol of diene and 5 mmol of dienophile, 2.5 mmol of ionic liquid. [b] Isolated yield after chromatography.
[c] The ratios estimated by GC. [c] Determined by GC analysis. [d] Only one product detected by GC and ^1H NMR spectrum.

and ethyl acrylate (**2a**) was first studied in a 1:1 or 1:2 molar ratio of EMIC-$ZnCl_2$ ionic liquid at room temperature (entry 1-5). In each ratio, the product yield increased as a function of time, while the stereochemistry selectivity remained essentially constant. The optimum condition to give both high yield and high *endo*/*exo* value of the products **3aa-*endo*** and **3aa-*exo*** was found under 1:2 molar ratio of EMIC-$ZnCl_2$ for 2 hours (entry 5). The high *endo* selectivity was attributed to solvophobic interaction and solvent polarity.[8] No significant dimerization and polymerization of cyclopentadiene were observed, presumably because the ester **2a**-$ZnCl_2$ complex was not capable of activating the reaction among dienes.

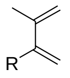


1a **2a** **3aa-*endo*** **3aa-*exo***

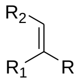
Compared with the same reaction in benzene consisting of a catalytic amount of $ZnCl_2$, the much reactive **1a**, instead of butadiene, reacted with **2a** for 2 hours to give the adduct in 47% yield with 7:1 of *endo*/*exo* ratio. Under a longer reaction time, the yield only increased to 59% (entries 19 and 20). The reaction rate and *endo* selectivity of Diels-Alder reactions conducted in ionic liquids proved to be far superior to that observed in traditional Diels-Alder reaction media. The recovered Zn-containing ionic liquid was reused at least five times with almost no drop in activity or yield (entry 21).

For different dialkylimidazolium ionic liquids, C_8MIB-$ZnBr_2$ and C_8C_8IB-$ZnBr_2$ at 1:2 molar ratio, the result was even better for C_8MIC-$ZnBr_2$, yielding 97% in 10 minutes (entries 6 and 7). A slightly low yield was obtained in the case of using C_8C_8IB-$ZnBr_2$ as solvent and catalyst. However, it should be noted that some of the ionic liquid would be taken off into the organic solvent during extraction owing to the organic property of the longer carbon chain. The composition of recovered ionic liquid was changed. They were not suitable for reuse.

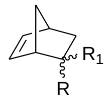
The reaction between cyclopentadiene (**1a**) and acrolein (**2b**), methyl vinyl ketone (**2c**), trans-crotonaldehyde (**2d**), and acrylonitrile (**2e**) in EMIC-$ZnCl_2$ (1:2) proceeded cleanly and smoothly at room temperature to give corresponding products **3aa**-**3ae**, respectively, in high yield (entries 8-11).



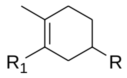
	R
1b:	CH_3
1c:	H



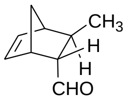
	R	R_1	R_2
2b:	CHO	H	H
2c:	$COCH_3$	H	H
2d:	CHO	H	CH_3
2e:	CN	H	H



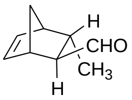
	R	R_1
3ab:	CHO	H
3ac:	$COCH_3$	H
3ae:	CN	H



	R	R_1
3ba:	$CO_2C_2H_5$	CH_3
3bb:	CHO	CH_3
3ca:	$CO_2C_2H_5$	H
3cb:	CHO	H
3cc:	$COCH_3$	H



3ad-endo



3ad-exo

The high *endo* selectivity was also observed except for the reaction of **1a** with **2e** which only gave a 2:1 ratio of *endo*/*exo*. The reaction with more reactive aldehyde or ketone dienophiles was completed in 10 minutes. On the other hand, the reaction with less reactive acrylonitrile needed 12 hours for completion. Interestingly, even the less reactive dienes, 2,3-dimethylbutadiene (**1b**) and isoprene (**1c**), reacted with active vinyl aldehyde **2b** or ketone **2c** and gave a good yield at room temperature (entries 12-18). The formation of an adduct of **1b** or **1c** with **2a** took place at a considerably lower rate under the same condition (entries 12 and 15). The yield increased substantially when the temperature rose to 50 °C and the reaction time to 8 hours. Surprisingly, the reaction of isoprene (**1c**) with **2a**-**2c** supplied exclusively the corresponding *para*-adduct, 1-methyl-4-substituted-cyclohexenes **3ca**-**3cc**, as single product without contamination with the other *meta* regioisomer, 1-methyl-5-substituted-cyclohexenes. In all cases, both the yield and the *endo*/*exo* ratio decreased with extending the reaction time.

In summary, we have shown that the 1:2 molar ratio of air- and moisture-stable EMIC-$ZnCl_2$ ionic liquid provided an excellent media and catalyst for performing clean Diels-Alder reactions. This ionic liquid, indeed, dramatically enhanced the Diels-Alder reaction rate and the *endo* stereoselectivity. The activity of recycled ionic liquid remained intact after the fifth use.

EXPERIMENTAL SECTION

Unless otherwise stated, reagents were obtained from commercial suppliers and used as received. NMR spectra were obtained using a Bruker-200 NMR spectrometer.

Preparation of ionic liquids

The 1:1 or 1:2 molar ratio of dialkylimidazolium halides (EMIC,[9] C_8MIB,[10] and C_8C_8IB[11]) to ZnX_2 (X = Cl or Br) were mixed in a flask and heated to 90 °C for 2 days to afford a colorless liquid.[9] The resulting ionic liquids (EMIC-$ZnCl_2$, C_8MIB-$ZnBr_2$ and C_8C_8IB-$ZnBr_2$) were cooled to room temperature and kept in a N_2-filled glove box.

Procedure for the Diels-Alder reaction

Dienophile **2** (5 mmol) was added to 2.5 mmol of ionic liquid and stirred for 10 minutes at room temperature. Diene **1** (7.5 mmol) was added successively. The resulting mixture was stirred at room temperature or 50 °C. The reaction times are given in Table 1. After reaction was complete, the adduct was extracted with diethyl ether (2 mL × 5) followed by chloroform (2 mL × 2). This crude product was subjected to GC analysis and purified by column chromatography over silica gel eluting with hexane/ethyl acetate (10:1) to yield pure Diels-Alder products **3aa**, **3ab**, **3ac**, **3ad**, **3ae**, **3ba**, **3bb**, **3ca**, **3cb**, and **3cc**. The ^1H NMR spectral data were in agreement with their structures.

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REFERENCES

1. Aki, S. N. V. K.; Brennecke, J. F.; Samanta, A. *Chem. Commun.* **2001**, 413.
2. (a) Sheldon, R. *Chem. Commun.* **2001**, 2399. (b) Wasserscheid, P.; Keim, W. *Angew. Chem. Int. Ed.* **2000**, *39*, 3772. (c) Welton, T. *Chem. Rev.* **1999**, *99*, 2071. (d) Earle, M. J.; Seddon, K. R. *Pure Appl. Chem.* **2000**, *72*, 1391. (e) Kumar, A. *Chem. Rev.* **2001**, *101*, 1.
3. Lee, C. W. *Tetrahedron Lett.* **1999**, *40*, 2461.
4. Abbott, A. P.; Capper, G.; Davies, D. L.; Rasheed, R. K.; Tambyrajah, V. *Green Chem.* **2002**, *4*, 24.

5. Hsiu, S. I.; Huang, J. F.; Sun, I. W. *Electrochim. Acta* **2002**, *47*, 4367.
6. Abbott, A. P.; Capper, G.; Davies, D. L.; Munro, H. L.; Rasheed, R. K.; Tambyrajah, V. *Chem. Commun.* **2001**, 2010.
7. Inukai, T.; Kasai, M. *J. Org. Chem.* **1965**, *30*, 3567.
8. Fischer, T.; Sethi, A.; Welton, T.; Woolf, J. *Tetrahedron Lett.* **1999**, *40*, 793.
9. Lin, Y. F.; Sun, I. W. *Electrochim. Acta* **1999**, *44*, 2771.
10. Dzyuba, S. V.; Bartsch, R. A. *J. Heterocycl. Chem.* **2001**, *38*, 265.
11. Dzyuba, S. V.; Bartsch, R. A. *Chem. Commun.* **2001**, 1466.