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DOI: 10.1039/C5RA09710J

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Cite this: DOI: 10.1039/x0xx00000x

Synthesis of MacMillan catalyst tailored with ionic liquid as a recoverable catalyst for asymmetric Diels-Alder reaction

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Received ooth January 2012,
Accepted ooth January 2012

DOI: 10.1039/x0xx00000x

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MacMillan catalyst was tailored with imidazolium ionic liquid by ester linkage that acts as recoverable and reusable catalyst for asymmetric Diels-Alder reaction. Diels-Alder reaction between cyclopentadiene and crotonaldehyde was carried out using MacMillan catalyst modified with ionic liquid (5 mol%) and trifluoroacetic acid (5 mol%) as co-catalyst in acetonitrile/water (95/5) at room temperature, gave 94% conversion of Diels-Alder adduct with *exo/endo* (1:1.1) and 90% *ee* of *endo* product. The catalyst was recovered and reused up to 5 cycles with slight decrease in *ee* and conversions of product.

Introduction

Diels-Alder reaction is an important tool for the synthesis of enantiomerically enriched cyclohexene moiety and also for carbon-carbon bond formation reaction. It is a key step for the synthesis of many natural products and pharmaceutical compounds.[1–4] Enantioselective Diels-Alder reaction was used for the synthesis of (-)-oseltamivir by Fukuyama and co-workers.[5,6] The first enantioselective Diels-Alder reaction was reported by MacMillan and co-workers, involving an organocatalyst, which proceeds by a LUMO-lowering activation mechanism.[7–9] Several organocatalysts employed for the enantioselective Diels-Alder reaction are chiral diamines,[10–12] hydrazides,[13–19] and diarylprolinol ether.[20–21]

Organocatalysts used in this reaction have some limitations like required high catalyst loading, long reaction time and also these catalysts are not easily separated from the reaction mixture therefore difficult to recover and recycle. Several research groups have made successful attempts to overcome these problems by immobilizing or attaching the catalytic unit on a recyclable supports. Tyrosine-derived imidazolidin-4-one was immobilized on supports through covalent bond on modified polyethylene glycol,[22] poly(methylhydrosiloxane) (PHMS),[23] siliceous and polymer-coated mesocellular foam (MCF),[24] mesoporous organosilica sphere,[25] and chiral organosilica polymer.[26] Liang et al reported, use of internal functionalities of the dendrimer to attach imidazolidinone as guests to the interior of the dendrimer using olefin metathesis.[27] Pecinovsky et al developed a nanoporous heterogeneous chiral catalyst via acid-induced liquid crystal self-assembly and subsequent photopolymersiation of monomer of imidazolidinone unit.[28] Selkälä et al immobilized MacMillan catalyst on JandaJel^{TM} through amide bond using JandaJel-NH_2 and N-Fmoc-protected (S)-phenylalanine.[29] Haraguchi et al used polymer supported sulphonic acid for immobilization of MacMillan catalyst by ionic interaction via ion exchange between sulfonated polymer and quaternary ammonium salt.[30] They also developed main chain polymer by the reaction of chiral imidazolidinone dimer with disulfonic acid.[31] Mitsudone et al also supported MacMillan catalyst on montmorillonite clay using cation exchange method.[32] Fluorous tag and tetraarylphosphonium with Macmillan catalyst can act as a recoverable catalyst.[33,34] Room temperature ionic liquids were also used for recovery of MacMillan catalyst.[35] Imidazolium based ionic liquids connected with MacMillan catalyst through covalent bond and supported on silica were also used for this reaction.[36,37] In our ongoing research project on the development of recoverable catalyst, recently we have developed a α,α-diphenyl-(L)-prolinol modified with imidazolium ionic liquid as recoverable catalyst for asymmetric reduction of ketones.[39] Herein, we wish to report the synthesis of MacMillan catalyst tailored with imidazolium ionic liquid as a recoverable catalyst for the enantioselective Diels-Alder reaction.

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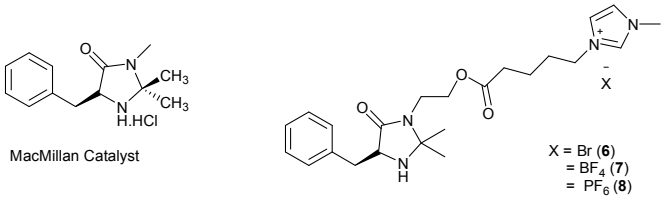
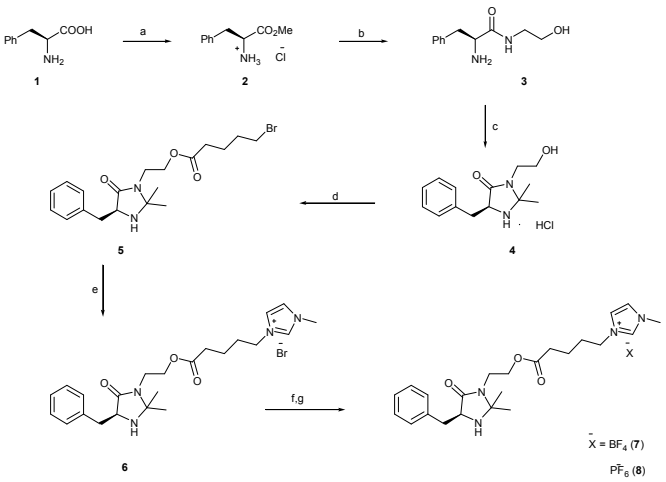


Figure 1. MacMillan's catalyst and modified MacMillan catalyst with ionic liquid

Results and discussion

Preparation of modified McMillan catalyst tailored with ionic liquid

MacMillan catalyst tailored with imidazolium cation and bromide, tetrafluoroborate and hexafluorophosphate anion (**6–8**) shown in figure 1. Precursors **1–4** were synthesized according to procedures reported by Kristense et al.[38] Bromoester **5** was synthesized by using a 5-bromopentanoyl chloride and compound **4** in the presence of methanesulfonic acid at rt, afforded in 70% yield. The bromoester **5** was treated with 1-methylimidazole at 100℃ for 20 min, gave MacMillan catalyst @ imidazolium bromide (**6**) in 91% yield. The counter anion bromide of ionic liquid (**6**) was exchanged KBF_4 and KPF_6 in acetone and water solvent, which afforded tetrafluoroborate (BF_4) and hexafluoroborate (PF_6) anion containing ionic liquids with 75% and 81% yields, respectively.

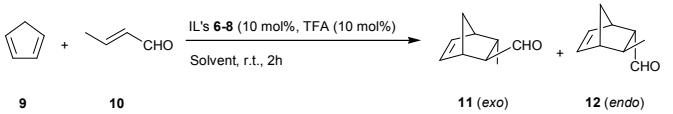


Scheme 1. (a) $SOCl_2$, methanol, r.t., 28 h, 97% (b) Ethanolamine, r.t., 26 h, 84% (c) Acetone, i-PrOH, p-TSA, reflux, 5 h, 81% (d) CH_3SO_3H, 5-bromovalleric acyl chloride, 0-5 °C, 3.5 h, 70% (e) 1-Methylimidazole, 100 °C, 10 min, 91% (f) KBF_4, H_2O/Acetone, r.t., overnight, 75% (g) KPF_6, Acetone/H_2O, r.t., overnight, 82%.

Optimization of reaction conditions for Diel-Alder reaction

Ionic liquid supported MacMillan catalysts (**6–8**) were used for Diels-Alder reaction by choosing crotonaldehyde (**9**) and cyclopentadiene (**10**) as model substrates. Initially, we screened different solvents for Diels-Alder reaction using IL **6** (10 mol%) and trifluoroacetic acid (10 mol%) as co-catalyst (Table 1). Acetonitrile as a solvent was found to be better than other solvents (water and methanol), gave 74% conversion of Diels-Alder adduct with *exo/endo* (1/1) and 75% *ee* of *endo* product (**12**). In a methanol we have obtained 12% desired product (**11** and **12**) and 88% of its dimethyl acetal was formed as a by-product (Table 1, entry 5). Non-polar solvent like dichloromethane also gave comparable *ee* of *endo* product, but conversion of product was poor compared to acetonitrile (Table 1, entry 6). We have also screened the IL **7** and **8** in acetonitrile, IL **8** gave better *ee* of *endo* product (**12**) compared to other IL's (Table 1, entries 7, 8). The effect of water was studied for the reaction and found that 5% water in acetonitrile improved the *ee* and ratio of *endo* product (Table 1, entry 9). Catalyst loading 2 mol% was sufficient to convert product, but better *ee* (90%) was obtained with 5 mol% (Table 1, entries 10 and 11). We have also isolated the product by column chromatography in 84% isolated yield. We further increased the amounts of water up to 10% in acetonitrile and *ee* was retained but conversion dropped to 80% (Table 1, entry 12).

Table 1 Screening of different solvents and ionic liquids as a catalysts for Diels-Alder reaction. [a]



Entry	Catalyst	Solvents	Conversions (%)[b]	(*exo/endo*)[c]	*ee* (*endo*)[d]
1	**6**	Acetonitrile	73	1.0/1.0	75
2	**6**	THF	-	-	-
4	**6**	Water	44	1.0/1.4	45
5	**6**	MeOH	12[e]	1.3/0.7	53
6	**6**	CH_2Cl_2	42	1.1/1.0	70
7	**7**	Acetonitrile	81	1.1/0.9	83
8	**8**	Acetonitrile	76	1.0/1.0	85
9	**8**	Acetonitrile/ water (95/5)	88	1.0/1.2	88
10	**8**	Acetonitrile/ Water (95/5)	82	1.0/1.2	85[f]
11	**8**	Acetonitrile/Water (95/5)	94	1.0/1.1	90[g,h]
12	**8**	Acetonitrile / Water (90:10)	80	1.0/1.1	90[g]

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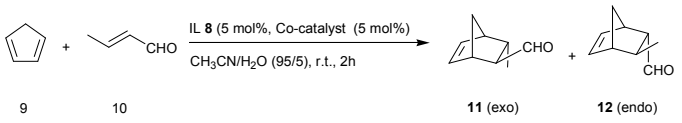
[a]IL **6-8** (2-10 mol%) was dissolved in solvent (1 mL), trifluoroacetic acid (2-10 mol%), crotonaldehyde (0.5 mmol, 42 µL) and cyclopentadiene (0.5 mmol, 41 µL) was added and stirred at room temperature. [b]Conversion of product was determined by Gas Chromatography. [c]*Exo/endo* ratio was determined by Gas Chromatography. [d]Ee was determined by Gas Chromatography using β-Dex chiral column. [e]88% Dimethyl acetal of desired product was formed as a by-product. [f]Catalyst **8** (2 mol%) was used. [g]Catalyst **8** (5 mol%) was used. [h]84% isolated yield was obtained after purification by column chromatography.

Effect of different co-catalyst on Diels-Alder reaction

The effects of different acids as co-catalysts were investigated for the Diels-Alder reaction between crotonaldehyde and cyclopentadiene using IL **8** as a catalyst (Table 2). Trifluoroacetic acid (TFA) was found to be a better choice of co-catalyst in terms of conversion and *ee* of *endo* product compared to the other co-catalysts like HCl, H_2SO_4, acetic acid, $HClO_4$ and p-TSA. In case of $HClO_4$ and acetic acid ratio of *endo* product (**12**) was improved, but conversion and *ee* of *endo* product (**12**) were poor compared to TFA.

Table 2 Screening of different Co-catalysts for Diels-Alder reaction catalysed by IL **8**.[a]



9 10 **11** (exo) **12** (endo)

Entry	Co-catalyst	Conversion [b] (%)	(*exo/endo*)[c]	*Ee*[d] (%)
1	HCl	30	1/1.1	76
2	H_2SO_4	26	1/1.1	40
3	CH_3COOH	11	1/1.4	70
4	Trifluoroacetic acid	94	1/1.1	90
5	$HClO_4$	26	1/1.4	55
6	p-TSA	61	1/1.2	82
7	-	2	1/1.3	44

[a]IL **8** (5 mol%) was dissolved in CH_3CN/water (95/5, 1 mL), Co-catalyst (5 mol%), Crotonaldehyde (0.5 mmol, 42 µL) and cyclopentadiene (0.5 mmol, 41 µL) was added and stirred at room temperature. [b]Conversion was determined by Gas Chromatography. [c]*Exo/endo* ratio was determined by Gas Chromatography. [d]*Ee* was determined by Gas Chromatography using β-Dex chiral column

Comparisons of recoverable MacMillan catalysts

We have compared the results of **IL 8** with other reported recoverable MacMillan catalysts for enantioselective Diels-Alder reaction between crotonaldehyde and cyclopentadiene. (Table 3). Results show that **IL 8** found to be better than other reported catalysts in terms of less catalyst loading (5 mol%), less reaction time and comparable *ee* of *endo* Diels-Alder product (**12**).

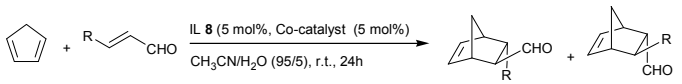
Substrate scope for Diels-Alder reaction

After optimization of reaction conditions for the Diels-Alder reaction, we wish to generalize the substrate scope. We carried out the Diels-Alder reaction between cyclopentadiene and cinamaldehyde derivatives (**13a-d**) using IL **8** (5 mol%) and TFA (5 mol%) in acetonitrile/water (95/5) at room temperature for 24 h. Cinnamaldehyde gave 92% yield of corresponding Diels-Alder adduct with *exo/endo* (1.2:1) and *ee* for **14a**/**15a** (82/78) (Table 3, entry 1). Electron withdrawing group (nitro) at *p*-position on cinnamaldehyde (**13b**) gave comparable yield and *ee* of *exo* product (**14a**) was dropped (entry 2). Electron donating group (methoxy) on *p*-position of cinnamaldehyde (**13d**) found to be less reactive compared to cinnamaldehyde and *p*-nitro-cinnamaldehyde (entry 3). *p*-Chloro-cinnamaldehyde (**13c**) did not show significant difference in reactivity and enantioselectivity compared to cinnamaldehyde (entries 1 and 3).

Table 3 Comparisons of recoverable reported MacMillan catalysts with **IL 8** for enantioselective Diels-Alder reaction between crotonaldehyde and cyclopentadiene.

Entry	Recoverable MacMillan Catalyst	Catalyst loading (mol%), reaction time (h)	Yield (%) (*exo/endo*)	*ee* (*endo*) (%)	Ref.
1	Immobilized on JandaJel™	10, 24	91 (1/1.2)	91	29
2	Nanoporous heterogeneous	10, 24	71 (1/1.3)	90	28
3	Fluorous organocatalyst	10, 40	80 (1/0.9)	92	33
4	Montmorillonite clay	0.1g, 48	85 (1/1.7)	89	32
5	Polymer supported via ion exchange	10, 24	99 (1/0.8)	83	30
6	Supported ionic liquid catalyst	10, 22	61 (1/1)	83	36,37
7	Tetraarylphosphonium Supported	10, 12	95 (1/1.4)	92	34
8	IL-**8**	5, 2	94 (1/1.1)	90	This paper

Table 4 Substrates scope for Diels-Alder reaction using IL **8**.[a]



9 **13a**; R = Ph
13b; R = 4-NO2-Ph
13c; R = 4-Cl-Ph
13d; R = 4-OMe-Ph

14a-d (exo) **15a-d** (endo)

Entry	Substrate	*exo/endo*[b]	Yield (%)[c]	*ee*[d] (%) (*exo/endo*)
1	**13a**	1.2:1	92	82/78
2	**13b**	1.2:1	84	75/76
3	**13c**	1.1:1	87	80/82
4	**13d**	1.1:1	61	75/nd

[a] IL **8** (5 mol%) was dissolved in CH_3CN/water (95/5, 1 mL), trifluoroacetic acid (5 mol%), Cinnamaldehyde or its derivatives (0.5 mmol) and cyclopentadiene (0.5 mmol) was added and stirred at room temperature. [b]Calculated by ^{1}H-NMR. [c]Isolated yield after purification by column chromatography. [d]*Ee* was determined by HPLC using Chiralcel OD-H column after reduction to alcohol.

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Recovery and reusability of the IL 8

The recycling of MacMillan catalyst tailored with imidazolium ionic liquid **8** was successfully achieved for the enantioselective Diels-Alder reaction between cyclopentadiene (**9**) and crotonaldehyde (**10**) (Table 5). The IL **8** was recovered and reused up to 5 cycles with minor loss of conversions of Diels-Alder adducts and 90–86**%** *ee's* of *endo* product (**12**) but *exo/endo* ratios were retained. After the fresh catalytic cycle, the reaction mixture was passed through a pad of anhydous sodiumsulfate to remove the water from the reaction. The solvent was removed under vacuum and hexane:diethyl ether (5 mL, 1:1) was added, IL **8** was becaming a viscous liquid and the product was in the solvent, which was decanted off. The ^{1}H-NMR and ^{19}F-NMR and HRMS data of recovered catalyst and fresh catalyst in agreement (SI, Figure 4, 6). We have treated IL **8** with 1 equivalent of trifluoroacetic acid in acetonitrile/water (95/5), recorded the ^{1}H-NMR and peak at 2.3 ppm of OCH_2CO of the ester linker indicate that ester is not hydrolising during the reaction (SI, Figure 5).

Table 5 Recycling performance of IL **8** for Diels-Alder reaction between crotonaldehyde and cyclopentadiene. [a]

Entry	Cycle	Leaching of catalyst (mg)[b]	Conversion[c] (%)	*exo/endo*[d]	*ee*[e] (%) *Endo*
1	0	0.12	94	1 : 1.1	90
2	1	0.10	90	1 : 1.1	89
3	2	0.00	88	1 : 1.1	88
4	3	0.01	87	1 : 1.1	88
5	4	0.02	81	1 : 1.1	88
6	5	0.02	81	1 : 1.1	87

[a]IL **8** (5 mol%, 14 mg) was dissolved in CH_3CN/water (95/5, 1mL), trifluoroacetic acid (5 mol%), crotonaldehyde (0.5 mmol, 42 µL) and cyclopentadiene (0.5 mmol, 41 µL) was added and stirred at room temperature for 24 h. [b]Leaching of the catalyst was determined by HPLC and details are given in ESI. [b]Conversion checked by Gas Chromatography. [c]Diestereomaric ratio was calculated by Gas Chromatography. [d]E*e* was determined by Gas Chromatography using β-Dex chiral column.

Experimental

Materials and methods

Cyclopentadiene was prepared from its dimer. Crotonaldehyde was freshly disttiled and used. Proton and carbon nuclear magnetic resonance spectra (^{1}H and ^{13}C NMR, respectively) were recorded on 400 MHz (operating frequencies: ^{1}H, 400.13 MHz; ^{13}C, 100.61 MHz) Jeol-FT-NMR spectrometer at ambient temperature. The chemical shifts (δ) for all compounds are listed in parts per million downfield from tetramethylsilane using the NMR solvent as an internal reference. The reference values used for deuterated chloroform ($CDCl_3$) and were 7.26 and 77.00 ppm for ^{1}H and ^{13}C NMR spectra, respectively. HRMS analysis was carried out using Agilent G6530AA LC Q-TOF mass spectrometer. Thin layer chromatography was carried out using Merck Kieselgel 60 F254 silica gel plates. Column chromatography separations were performed using silica gel 230-400 mesh. All the new synthesized compounds were characterized by ^{1}H, ^{13}C NMR and HRMS and known compounds were characterised by ^{1}H and ^{13}C NMR. The experimental procedure for the known compounds were followed according to literature reports and given in supporting information (SI). The enantiomeric excess of Diels-Alder products was determined on Shimadzu LC-2010HT using OD-H and AD-H chiral columns and Shimadzu GC-2010 plus using β-dex chiral column. The optical rotation was taken using Rudolph digipol polarimeter.

Synthetic procedures

2-((5R)-5-benzyl-2,2-dimethyl-4-oxopyrrolidin-3-yl)ethyl-5-bromopentanoate (5)

In a 100 mL round bottom flask, anhydrous CH_3SO_3H (12 mL) was cooled in an ice/water bath and compound **4** (2.83 g, 10 mmol) was added in 20 min followed by the addition of 5-bromopentanoyl chloride and the reaction mixture was stirred at 0-5 °C for 3.5 h. The clear solution was diluted with diethyl ether and transferred to a separatory funnel and more diethyl ether was added to give phase separation. The bottom yellow layer of the product was allowed to drip directly into a mixture of dichloromethane (60 mL) and aq. solution of K_2CO_3 (12.0 g dissolved in 70 mL). After complete addition, the organic phase was separated. The aq. phase was extracted with dichloromethane (2 x 30 mL) and the combined solvent was dried over anhydrous Na_2SO_4 and concentrated in vacuum. The product **5** was further purified by column chromatography using a mixture of hexane/ethyl acetate (70:30) to afford yellow liquid (2.86 g, 70%). $[\alpha]_D^{25}$ = - 36.6 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.25–7.15 (m, 5H), 4.13–4.07 (m, 2H), 3.74 (t, 1H, *J* = 5.49 Hz), 3.51–3.46 (m, 1H), 3.36 (t, 2H, *J* = 6.59 Hz), 3.37–3.33 (m, 1H), 3.16–3.11 (m, 1H), 3.03 (d, 1H, *J* = 5.86 Hz), 2.24 (t, 2H, *J* = 7.69 Hz), 1.86–1.79 (m, 2H), 1.74–1.68 (m, 2H), 1.22 (s, 3H), 1.11 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.1, 173.2, 136.4, 129.3(2C), 128.3(2C), 126.5, 75.7, 61.1, 58.4, 38.9, 36.6, 33.8, 31.1, 28.5, 27.6, 26.2, 24.4 ppm.

(R)-3-(5-(2-(4-benzyl-2,2-dimethyl-5-oxoimidazolidin-1-yl)ethoxy)-5-oxopentyl)-1-methyl-1H-imidazol-3-ium bromide (6)

Compound **5** (5 mmol, 2.04 g) and 1-methylimidazole (6 mmol, 0.492 g) were heated at 100° C for 10 min and cooled to room temperature. The reaction mixture was washed with diethyl ether to remove an excess of 1-methylimidazole. The residue was dried under reduced pressure to afford compound **6** (2.21 g, 90%) as a light yellow hygroscopic liquid. $[\alpha]_D^{25}$ = - 16.3 (c 1.2, MeOH); ^{1}H NMR ($CDCl_3$, 400MHz) δ 10.13 (s, 1H), 7.52 (s, 1H), 7.45 (s, 1H), 7.24–7.13 (m, 5H), 4.32 (t, 2H, *J* = 7.63 Hz), 4.01 (s, 3H), 4.05–4.01 (m, 2H), 3.7–3.64 (m, 1H), 3.49–3.36 (m, 1H), 3.15–3.12 (m, 1H), 3.00–2.95 (m, 2H), 2.29 (t, 2H, *J* = 8.01 Hz), 1.94–1.89 (m, 2H), 1.61–1.57 (m, 2H), 1.20 (s, 3H),

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1.11 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.5, 172.5, 137.1, 136.7, 129.3 (2C), 128.4 (2C), 126.7, 123.3, 122.1, 75.9, 61.6, 58.6, 49.4 38.9, 36.9, 36.5, 32.7, 29.2, 27.8, 26.3, 20.9 ppm. HRMS (ESI) calcd for $C_{23}H_{33}N_4O_3^+$ $[M]^+$: 413.2547; found 413.2531.

(R)-3-(5-(2-(4-benzyl-2,2-dimethyl-5-oxoimidazolidin-1-yl)ethoxy)-5-oxopentyl)-1-methyl-1H-imidazol-3-ium tetrafluoroborate (7)

The ionic liquid **6** (1 mmol, 0.491 g) was dissolved in a mixture of water/acetone (1:1, 10 mL) and potassium tetrafluoroborate (1.2 mmol, 0.152 g) was added and stirred at room temperature for overnight. After reaction, acetone was removed and the aqueous layer was extracted with CH_2Cl_2 (10 mL x 3). The combined organic layer was washed with water (5 mL x 3), dried with anhydrous Na_2SO_4, filtered and concentrated under vacuum to give ionic liquid **7** (0.373 g, 75%). $[\alpha]_D^{25}$ = - 14.9 (c 1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400MHz) δ 8.91 (s, 1H), 7.38 (s, 1H), 7.33 (s, 1H), 7.25–7.15 (m, 5H), 4.17 (t, 2H, *J* = 6.87 Hz), 4.12–4.04 (m, 2H), 3.88 (s, 3H), 3.72 (t, 1H, *J* = 6.10 Hz), 3.51–3.40 (m, 1H), 3.18–3.14 (m, 1H), 3.06–2.93 (m, 2H), 2.29 (t, 2H, *J* = 6.87 Hz), 1.90–1.85 (m, 2H), 1.60–1.56 (m, 2H), 1.22 (s, 3H), 1.14 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.5, 172.6, 136.8, 136.4, 129.3(2C), 128.5(2C), 126.7, 123.5, 122.2, 76.0, 61.7, 58.7, 49.3, 38.9, 37.0, 36.1, 32.7, 29.0, 27.8, 26.3, 20.9 ppm. ^{19}F NMR ($CDCl_3$, 304 MHz) δ -150.9 (s). HRMS (ESI) calcd for $C_{23}H_{33}N_4O_3^+$ $[M]^+$: 413.2547; found 413.2564.

(R)-3-(5-(2-(4-benzyl-2,2-dimethyl-5-oxoimidazolidin-1-yl)ethoxy)-5-oxopentyl)-1-methyl-1H-imidazol-3-ium hexafluorophosphate (8)

The ionic liquid **6** (3 mmol, 1.47 g) was dissolved in a mixture of water/acetone (1:1, 30 mL) and potassium hexafluorophosphate (3.6 mmol, 0.66 g) was added and stirred at room temperature for overnight. After reaction, acetone was removed and the aqueous layer was extracted with CH_2Cl_2 (30 mL x 3), the combined organic layer was washed with water (15 mL x 3), dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum to give ionic liquid **8** (1.35 g, 81%). $[\alpha]_D^{25}$ = - 19.7 (c 1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400MHz) δ 8.52 (s, 1H), 7.31–7.16 (m, 7H), 4.14–4.05 (m, 4H), 3.84 (s, 3H), 3.74–3.67 (m, 1H), 3.42–3.53 (m, 1H), 3.19–3.16 (m, 1H), 3.07–3.03 (m, 1H), 2.98–2.93 (m, 1H), 2.29 (t, 2H, *J* = 6.48, Hz), 1.91–1.85 (m, 2H), 1.62–1.55 (m, 2H), 1.23 (s, 3H), 1.15 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) 174.6, 172.7, 136.9, 136.0, 129.4 (2C), 128.5 (2C), 126.8, 123.5, 122.1, 76.1, 61.7, 58.7, 49.4, 39.0, 37.0, 36.1, 32.7, 28.9, 27.8, 26.3, 20.9 ppm. ^{19}F NMR ($CDCl_3$, 304 MHz) δ -71.9 (d, *J* = 563.74 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz) δ -144.0 (septet, *J* = 758.75 Hz). HRMS (ESI) calcd for $C_{23}H_{33}N_4O_3^+$ $[M]^+$: 413.2547; found 413.2530.

General procedure of enantioselective Diels-Alder reduction

IL **8** (5 mol%, 14 mg) was taken in acetonitrile/water (95/5) (1 mL) and TFA (5 mol%) was added and stirred for 5 min, then α,β-unsaturated aldehyde (0.5 mmol) was added and reaction mixture was stirred for 10 min at rt. Finally, cyclopentadiene (0.5 mmol) was added and reaction was stirred at rt for specified time. Conversion was monitored by GC in case of crotonaldehyde and rest was checked by TLC using Hexane/EtOAc (80/20). The solvent was evaporated by rotavapor and products were purified by column chromatography.

Procedure for recycling of catalyst

After the fresh catalytic cycle of the reaction, the solvent was passed through a pad of anhydrous sodiumsulfate to remove the water from the reaction. Solvent of the reaction mixture was removed under vaccum and hexane:diethyl ether (5 mL, 1:1) was added, IL **8** was precipited out as viscous liquid and the product was in the solvent which was decanted off. The residue IL **8** was dissolved in acetonitrile/water (95/5) and TFA (5 mol%) was added and resulting mixture was stirred at rt for 10 min then crotonaldehyde (2.0 mmol) and cyclopentadiene (2.0 mmol) was added. The reaction was monitored on GC. Solvent was evaporated by rotavapor. Similar procedure was also followed for next catalytic run.

Conclusions

In conclusion, we have developed an efficient method for the enantioselective Diels-Alder reaction catalyzed by recoverable MacMillan catalyst tailored with imidazolium ionic liquid at room temperature. IL **8** (5 mol%) acts as catalyst in presence co-catalyst trifluoroacetic acid (5 mol%) for the Diels-Alder reaction between cyclopentadiene and crotonaldehyde, gave 94% conversion of product with *exo/endo* (1/1.1) and 90% *ee* of *endo* product which is comparable to MacMillan catalyst and better than other reported reusable catalysts. Ionic liquid supported MacMillan catalyst **8** can be recovered and reused up to 5 cycles with minor decrease in conversions Diels-Alder but *ee's* was in range of 90–87%.

Acknowledgements

SS acknowledges the financial assistance from Science and Engineering Research Board (SERB), Department of Science and technology (DST), India, under scheme Fast Track Young Scientist (SB/FT/CS-020/2012) and University Science Instrumentation Center (USIC), University of Delhi, India for analytical data. Authors are thankful to DU-DST mass facility at USIC. MSC is thankful to University Grant Commission (UGC), New Delhi for providing SRF.

Notes and references

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† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

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View Article Online
DOI: 10.1039/C5RA09710J

Graphical Abstract

Synthesis of MacMillan catalyst tailored with ionic liquids as a recoverable catalyst for asymmetric Diels-Alder reaction

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