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PAPER

Recyclable copper catalysts based on imidazolium-tagged C_2-symmetric bis(oxazoline) and their application in D–A reactions in ionic liquids†

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Functional imidazolium ionic liquids have been developed as a new class of versatile catalysts. C_2-symmetric and unsymmetric imidazolium-tagged bis(oxazoline) ligands were prepared, and the anions of the ligands were altered by ion-exchange reactions. The catalysts based on the new ligands and $Cu(OTf)_2$ were applied in asymmetric Diels–Alder reactions between *N*-acryloyl/*N*-crotonoyloxazolidinones **15** and 1,3-cyclohexandiene/cyclopentadiene **16** in different ionic liquids and in dichloromethane (DCM). The catalysts achieved a high level of activity and enantioselectivity, as well as good recyclability: cycloadduct (*S*)-**17ab** was attained at 98% conversion and 97% *ee* in $[Bmim]NTf_2$. Moreover, the catalyst could be recycled 20 times without an obvious loss of activity or enantioselectivity. By comparison, we deduced that the C_2 symmetry of the new ligands was crucial for obtaining high *ee* values. Toxicity studies of the ligands were performed for the first time.

Introduction

During the past several decades, chiral bis(oxazolines) (box), such as **1**, have proven to be very effective ligands that afford high levels of activity and enantioselectivity in many reactions.[1–8] Because most catalysts are expensive and because the metal as well as the ligands are highly toxic to the environment and humans, the recycling of catalysts now assumes an even greater importance. A number of approaches for preventing the expensive chiral metal complex from running off during the recovery and/or recycling process have been investigated.[9] Among them, the use of ionic liquids as a biphasic system is a very promising approach.[10] The properties of ionic liquids, such as low volatility, immiscibility with non-polar organic solvents and stability, make them excellent candidates for solvents in green processes.[11–14] In addition, ionic liquids can improve catalyst stability, and some unexpected transformations that would be impossible under ordinary reaction conditions have been observed in ionic liquids.[15,16] However, even if the catalyst dissolves well in an ionic liquid, the activity of the catalyst often dramatically decreases after several runs. Such decreases are usually caused by the catalysts leaching during product extraction from the reaction system or by the catalysts abating during the purification of the ionic phase before recycling.[17] The limitations of a catalyst or ligand in ionic liquids may be minimised by the presence of an ion tag on the frame of the ligand. The ionic nature could ideally render the catalyst or ligand insoluble in non-polar solvents so that the product could be extracted to leave a recyclable phase that contains the catalyst.[17,18] The ion-tagging strategy has attracted more attention in recent years.

The asymmetric Diels–Alder (D–A) reaction is one of the representative reactions that are catalysed by chiral box–metal complexes, and several previous attempts have been made to immobilise catalysts with ionic liquids in this reaction. Meracz and Oh[19] have reported that ionic liquids can enhance the enantioselectivity and the *endo*:*exo* ratio of the D–A reaction between *N*-crotonoyloxazolidinone and cyclopentadiene. Compared to the *ee* obtained in dichloromethane (DCM), the *ee* obtained in 1,3-dibutylimidazolium tetrafluoroborate $[DiBuIm]BF_4$ increased from 52% to 92%, and the *endo*:*exo* ratio increased from 79:21 to 97:3. Chang-Eun Yeom and Hye Won Kim[16] have reported that the reactivity and selectivity were highly dependent upon the properties of the ionic liquids. Because of the increased activity of their catalyst; the amount of ligand–metal complex could be reduced to 0.6 mol% without a significant compromise in the selectivity and recycled 18 times, with a decrease of *ee* in the 6th run. Imidazolium-tagged bis(oxazoline) **2** was prepared and used as a chiral ligand in the

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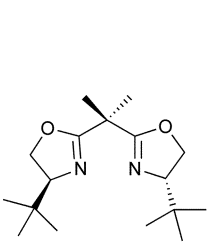
copper-catalysed D–A reaction between *N*-acryloyl/*N*-crotonoyloxazolidinones and 1,3-cyclohexandiene in the ionic liquid 1-ethyl-3-methylimidazolium bis[(trifluoromethyl)-sulfonyl]-imide [Emim]NTf_2.[20] Complete conversion and enatioselectivities of up to 86% *ee* were obtained for the reaction between *N*-acryloyloxazolidinone and 1,3-cyclohexandiene in [Emim]NTf_2. In this case, the catalyst could be recycled 10 times without loss of activity or enantioselectivity. An *ee* of up to 95% was obtained for the reaction between *N*-acryloyloxazolidinone and cyclopentadiene, although the recyclability of the catalyst in this case was not discussed. This report revealed that the introduction of an imidazolium tag into bis(oxazoline) significantly improved the capability to recover and reuse the catalyst for reactions performed in ionic liquids.



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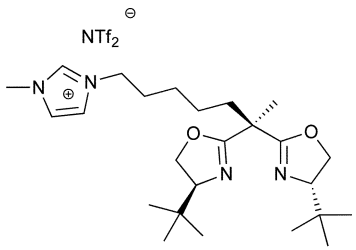

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Among the different immobilisation approaches, the preservation of the C_2 symmetry of the ligand has been regarded as a desirable feature, which was thought to be crucial for high *ee* values.[21–24] However, Cozzi[25] and Mandoli's work[26] clearly demonstrated that boxes with C_2 symmetry are not necessary for high enantioselectivity in the cyclopropanation of different olefin substrates and other copper-catalysed asymmetric transformations with insoluble polymer-bound-approach box ligands. The enantioselectivity actually matches the variations in the steric hindrance at the bridge position but not those in ligand symmetry. Whether C_2-symmetric features affect the ionic-tagged box ligands has not been investigated until now.

Our team has synthesized a series of novel quarternary ammonium salt-modified chiral ferrocenylphosphine-imine ligands, and their applicability in asymmetric C–C and C–N bond formation was demonstrated. High enantioselectivity was obtained in the Pd-catalyzed asymmetric substitution of 1,3-diphenyl-2-propenyl acetate, with dimethyl malonate (up to 94.6% *ee*) and benzylamine (up to 92.6% *ee*).[27] Herein, we designed and prepared the imidazolium-tagged bis(oxazoline); for comparison, both C_2-symmetric and C_2-unsymmetric ligands were included. Their performance in the copper-catalysed asymmetric D–A reaction between *N*-acryloyl/*N*-crotonoyloxazolidinones and 1,3-cyclohexandiene/cyclopentadiene in different solvents were evaluated and compared. When C_2-symmetric **10b** was used as a ligand, the D–A reaction between *N*-acryloyloxazolidinones and 1,3-cyclohexandiene in the ionic liquid 1-butyl-3-methylimidazolium bis[(trifluoromethyl)sulfonyl]-imide [Bmim]NTf_2 yielded a 98% conversion with a 90 : 10 *endo*:*exo* ratio and 97% *ee*. More importantly, the catalyst in the reaction system could be recycled as many as 20 times without obvious loss of activity and enantioselectivity.

Results and Discussion

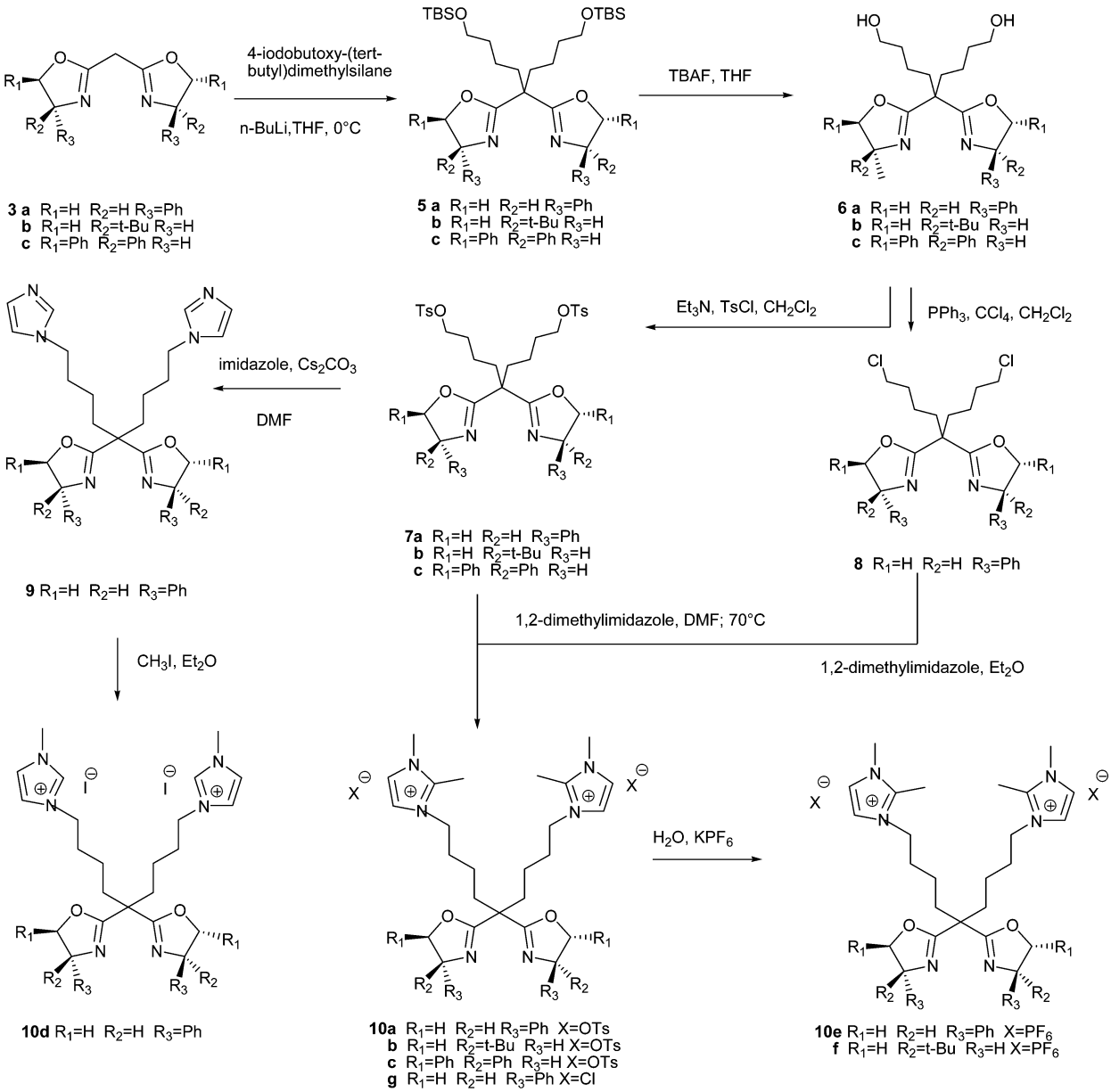
Preparation of C_2-symmetric/unsymmetric imidazolium-tagged bis(oxazoline)

Deprotonation of **3** in THF with 1.2 eq of BuLi was performed at 0 °C. The addition of the resultant solution to an excess of 4-iodobutoxy-(*tert*-butyl)dimethylsilane **4** in THF afforded the desired (*tert*-butyl)dimethylsilane-butyl-substituted bis(oxazoline) **5**. Hydrolysis of **5** with TBAF in THF gave the hydroxyl-substituted box **6**, which was converted to tosyl-substituted box **7** by TsCl in CH_2Cl_2. The imidazolium tag was introduced in the final step by the reaction of **7** with 1,2-dimethylimidazole in DMF at 70 °C, which afforded the tosyl salts **10**. C_2-symmetric box **9** was obtained when **7a** was reacted with imidazole in DMF catalysed by Cs_2CO_3. Box **9** reacted with methyl iodide in Et_2O to give iodide salt **10d**. The hydroxyl-substituted box **6a** was chloridised using PPh_3 in CCl_4 as the reagent. Chloride salt **10g** was obtained by treating the product **8** with 1,2-dimethylimidazole in Et_2O. The hexafluorophosphoric salts **10e** and **f** were synthesised from the tosyl salts through ion exchange of **10a** and **b** (see Scheme 1). The preparation of C_2-unsymmetric imidazolium-tagged chiral bis(oxazoline) ligand **14** was similar to that of the C_2-symmetric box, except the amount of BuLi and (4-iodobutoxy)(*tert*-butyl)dimethylsilane **4** in the deprotonation step was changed to 0.5 eq, and the temperature was maintained at −78 °C (see Scheme 2). **3b** was converted to **18** by $(CH_2O)_n$ and Et_3N. **19** was afforded once **18** reacted with Tf_2O in the presence of 1,2-dimethylimidazole as a base at −78 °C, after that the imidazolium tag was introduced by the reaction of **19** with 1,2-dimethylimidazole in CH_3CN. **20b** was synthesised through ion exchange of **20a** (see Scheme 3).

Asymmetric Diels–Alder reactions

We began our study by evaluating the newly synthesised ligands in an asymmetric D–A reaction between *N*-acryloyloxazolidinone **15a** and cyclohexa-1,3-diene **16b**. The catalysts were typically prepared in MeOH by stirring $Cu(OTf)_2$ (10 mol%) and the appropriate bis(oxazoline) (11 mol%) at room temperature for 1 h. After the metal–ligand complex formed, MeOH was removed under vacuum. The solvents (ionic liquids or dried DCM) were added to the system, followed by the addition of the substrates. The resultant mixture was stirred for the required time at room temperature.

Table 1 summarises the results of a comparative study of imidazolium-tagged bis(oxazoline) **10a–g**, **20a–b** with different anions, C_2-unsymmetric imidazolium-tagged chiral bis(oxazoline) ligand **14** and unfunctionalised (*S*,*S*)-*t*-Bu-box **3b**, **7b** as ligands for the Diels–Alder reaction between **15a** and **16b** in [Bmim]NTf_2. The *tert*-butyl-substituted bis(oxazoline) was the optimum ligand and yielded significantly higher *ee*s than its phenyl-substituted and diphenyl-substituted counterparts in most cases (Table 1, entries 1 and 2, entries 4, 7 and 10). The catalyst derived from **10b** yielded cycloadduct (2*S*)-**17ab** at 98% conversion and 97% *ee* in [Bmim]NTf_2 (Table 1, entry 4), whereas the catalyst derived from **10a** yielded only 80% *ee* (Table 1, entry 4). The same reaction catalysed by the complex based on **2** could achieve 77% *ee* in [Emim]NTf_2.[20] The ideal performance of the catalyst based on **10b** was also expected because of the longer



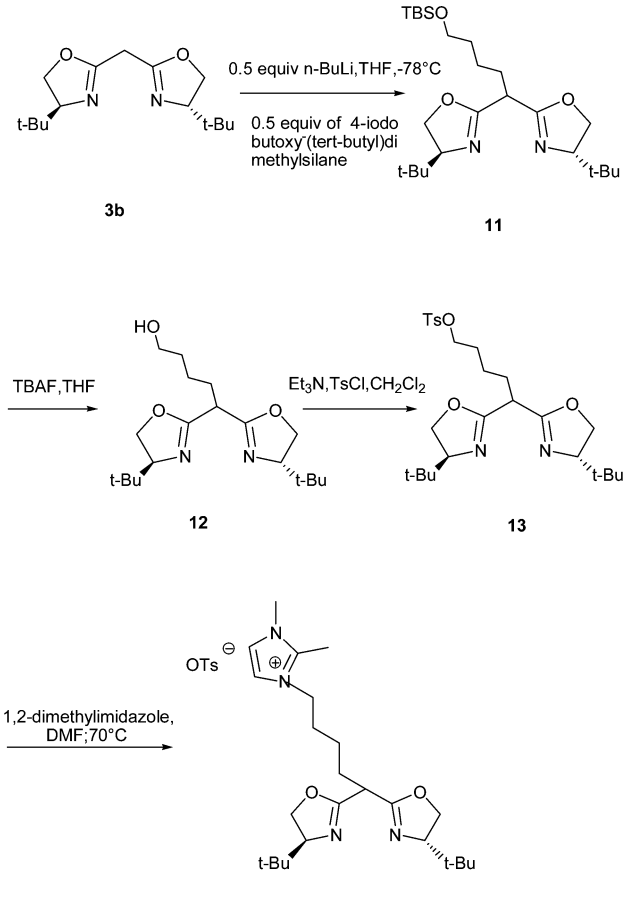
Scheme 1 The synthesis of C_2 symmetric imidazolium-tagged bis(oxazoline).

alkyl chains on the carbon bridge between the two oxazoline moieties. For ligands with shorter alkyl chains, the results of the D–A reaction were decreased (Table 1, entries 4 and 8, entries 11 and 12).

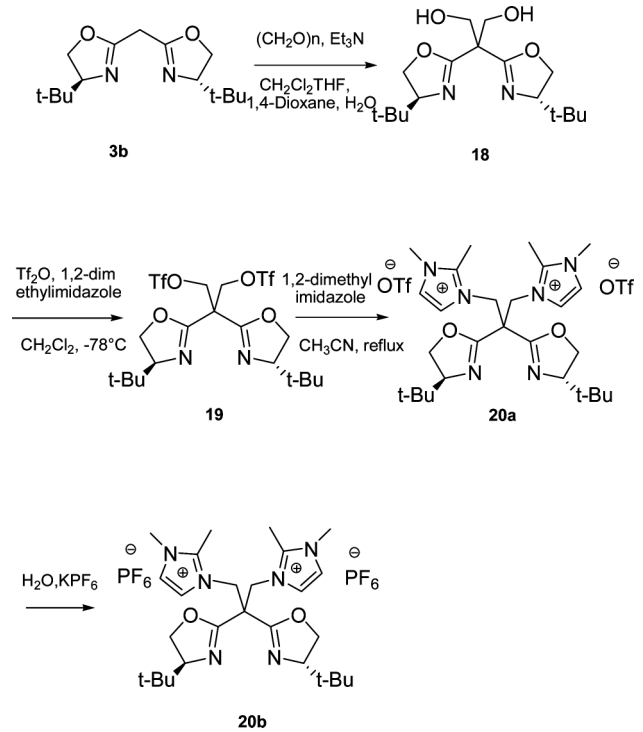
The anions of the ligands affect the enantioselectivity and activity. Tosyl-anion ligands **10a** and **10b** yielded better enantioselectivities and activities than hexafluorophosphoric, bromo, chloride, or iodide salts (Table 1, entry 3–9). The C_2-symmetric copper complex of bis(oxazoline) **10b** yielded better enantioselectivity and activity (entry 4, 98% conversion and 97% *ee*) than the C_2-unsymmetric catalyst based on **14** (entry 10, 82% conversion and 83% *ee*). The *endo* : *exo* ratio did not vary significantly (Table 1, entry 3–9). Qian[31] has reported a chiral anion modified ionic liquid derived from L-proline as an asymmetric organocatalyst for direct asymmetric aldol reactions in $[BMIm]BF_4$ and $[BMIm]PF_6$, results in these two ionic liquids obviously contrast, this was proposed to be caused by differences in the electronic properties of the anion parts. We presume the anion parts of the ligand affect the results through steric bulk and the guess could be demonstrated below in a theoretical mechanistic study.

A reaction without catalyst in $[Bmim]SbF_6$ has been carried out by Yeom and Kim,[16] the reaction yielded a 91 : 9 *endo* : *exo* mixture of the racemic adduct in 15% yield. We presume that the high *ee* values were caused by the preservation of the C_2-symmetry feature of the ligands, which was consistent with Burguete's report.[21]

The performance of the copper complexes based on the $[OTs]^-$ salt **10b** and unfunctionalised (*S*,*S*)-*t*-Bu-box **3b** as Lewis-acid catalysts for the Diels–Alder reaction between



Scheme 2 The synthesis of C_2-unsymmetric imidazolium-tagged bis(oxazoline).

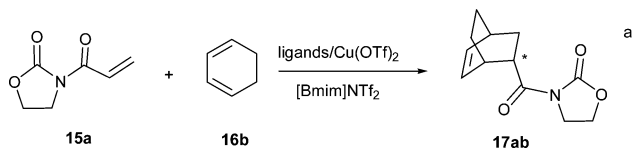


Scheme 3 The synthesis of C_2-symmetric imidazolium-tagged bis(oxazoline) (short line).

N-acryloyloxazolidinone **15a** and cyclohexa-1,3-diene **16b** in [Bmim]NTf_2 or DCM were studied; the results are shown in Table 2. The ionic-tagged ligand showed almost no reactivity in DCM. The reaction only occurred in hydrophobic ionic liquids, such as [Bmim]PF_6 and [Bmim]NTf_2, whereas no reaction was observed in hydrophilic ionic liquids, such as [Bmim]BF_4, and polar solvents, such as MeOH. This result was consistent with previous reports in the literature.[20] An enhancement in both the rate and enantioselectivity was also obtained with a catalyst based on (*S,S*)-*t*-Bu-box in [Bmim]NTf_2 compared with the same catalyst in DCM. The enhancement in both the rate and the enantioselectivity may result from an improvement of the stability of the catalyst by ionic liquids as well as from unexpected transformations that occur in the ionic liquid–catalyst system that would be impossible in DCM.

Various substrates were subsequently tested using the C_2-symmetric imidazolium-tagged chiral bis(oxazoline) **10b** as the ligand. The results are summarised in Table 3. The oxazolidin-2-one substitutes were more active than those based on pyrrolidin-2-one (Table 3, entry 1–5, entry 6–10). Cyclopentadiene was the most reactive diene: 94% conversion and 90% *ee* were obtained within 5 min of the addition of *N*-acryloyloxazolidinone and cyclopentadiene, whereas the same result after the addition of *N*-acryloyloxazolidinone and cyclohexa-1,3-diene required 48 h (Table 3, entry 2). Almost no reaction occurred after the addition of *N*-acryloyloxazolidinone and isoprene.

Table 1 Screening of the ligands in an asymmetric Diels–Alder reaction[a]



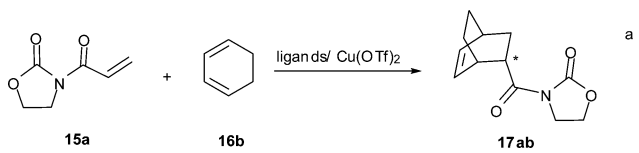
Entry	Ligand	Conversion [%]	*endo*:*exo*[b]	*ee* [%][b]
1	**3b**	82	82 : 18	84
2	**7b**	74	88 : 12	91
3	**10a**	97	85 : 15	80
4	**10b**	98	90 : 10	97
5	**10c**	62	80 : 20	32
6	**10d**	54	85 : 15	40
7	**10e**	96	85 : 15	47
8	**10f**	98	90 : 10	59
9	**10g**	63	85 : 15	43
10	**14**	82	83 : 17	83
11	**20a**	74	88 : 12	43
12	**20b**	61	90 : 10	18

[a] The ratio of **15a**/**16b**/ligand/Cu(OTf)$_2$ is 1.0/3.0/0.11/0.1, and the reactions were carried out for 48 h. [b] Enantiomeric excess and the *endo* : *exo* ratio were determined by HPLC (chiralpak AD-H column, hexane/*i*PrOH: 98 : 2, 1.0 mL min^{-1}).

Recyclability of the catalysts

To evaluate the recyclability of the catalysts generated from our new ligand **10b**, we performed the asymmetric D–A reaction between *N*-acryloyloxazolidinone **15a** and cyclohexa-1,3-diene

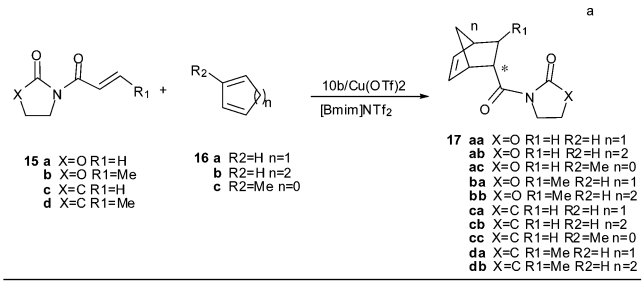
Table 2 Screening of solvents in the asymmetric D–A reaction of *N*-acryloyzl-l,3-oxazolidine-2-one **15a** and cyclohexa-1,3-diene **16b**[a]



Entry	Ligand	Solvent	Conversion [%]	*endo* : *exo*[b]	*ee* [%][b]
1	**10b**	CH_2Cl_2	0	—	—
2	**10b**	[Bmim]PF_6	95	88 : 12	80
3	**10b**	[Bmim]BF_4	0	—	—
4	**10b**	[Bmim]BF_4	0	—	—
5	**10b**	[Bmim]NTf_2	98	90 : 10	97
6	**10b**	MeOH	0	—	—
7	**3b**	CH_2Cl_2	70	79 : 21	80
8	**3b**	[Bmim]NTf_2	82	82 : 18	84

[a] The ratio of **15a**/**16b**/ligand/Cu(OTf)$_2$ is 1.0/3.0/0.11/0.1. [b] Enantiomeric excess and the *endo* : *exo* ratio were determined by HPLC (chiralpak AD-H column, hexane/*i*PrOH: 98 : 2, 1.0 mL min^{-1}).

Table 3 Asymmetric D–A reaction of various substrates using the catalyst derived from ligand **10b**[a]



Entry	Product	Time	Conversion [%]	*endo* : *exo*[b]	*ee* [%][b]
1	**17aa**	5 min	94	88 : 12	90
2	**17ab**	48 h	98	90 : 10	97
3	**17ac**	24 h	0	—	—
4	**17ba**	60 min	99	93 : 7	96
5	**17bb**	48 h	73	93 : 7	77
6	**17ca**	48 h	23	89 : 11	17
7	**17cb**	48 h	9	89 : 11	10
8	**17cc**	48 h	8	89 : 11	9
9	**17da**	48 h	0	—	—
10	**17db**	48 h	0	—	—

[a] The ratio of **15a**/**16b**/ligand/Cu(OTf)$_2$ is 1.0/3.0/0.11/0.1. [b] Enantiomeric excess and *endo* : *exo* ratio were determined by HPLC (chiralpak AD-H, Chiralcel OD-H, Chiralcel OJ-H, hexane/*i*PrOH).

16b in [Bmim]NTf_2. After extraction with diethyl ether, the ionic-liquid-containing catalyst was subjected to vacuum to remove traces of diethyl ether, then flushed with inert gas and charged with further portions of **15a** and **16b** at room temperature. The activity and enantioselectivity were maintained even after the catalyst was reused 20 times (Fig. 1, conversion 83%, *ee* 93% on the 20th cycle).

The recyclability of the catalyst based on the C_2-symmetric imidazolium-tagged box **10b**, C_2-unsymmetric box **14** and traditional ligand **3b** were studied and compared; the results are summarised in Fig. 2. The imidazolium-tagged catalyst derived from C_2-symmetric imidazolium-tagged box **10b** could be used at least 20 times without a significant decrease in

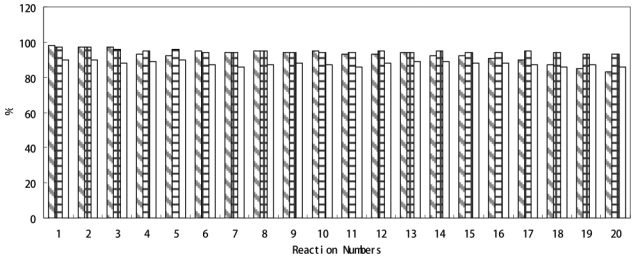


Fig. 1 Variation in percentage conversion (hatched), percentage *ee* (reticle) and percentage *endo* (blank) upon recycling the Diels–Alder reactions between **15a** and cyclohexa-1,3-diene **16b** in [Bmim]NTf_2 using catalysts generated from **10b** and Cu(OTf)$_2$.

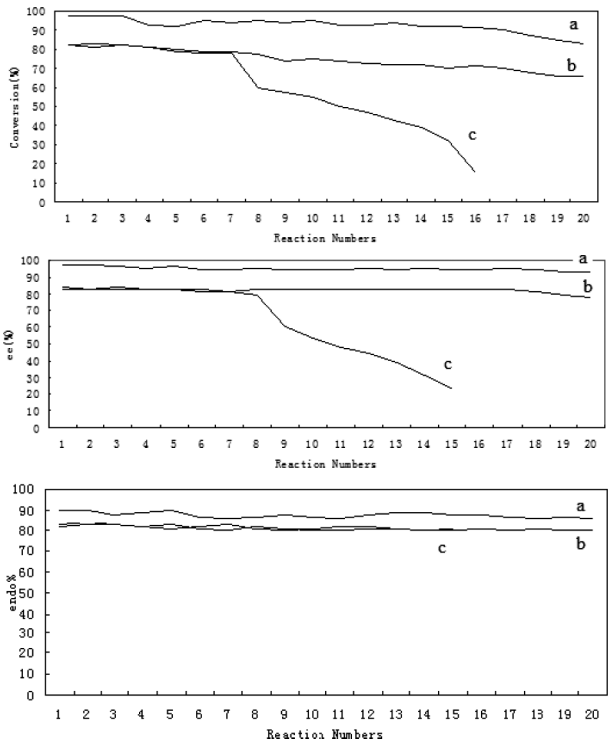


Fig. 2 Variation in percentage conversion (1), percentage *ee* (2) and percentage *endo* (3) upon recycling the Diels–Alder reactions between **15a** and cyclohexa-1,3-diene **16b** or cyclopentadiene **16a** in [Bmim]NTf_2 using catalysts generated from Cu(OTf)$_2$ and **10b** (a), **14** (b), and **3b** (c), respectively.

the enantioselectivity or conversion. The catalyst based on the C_2-unsymmetric imidazolium tagged box **14** could also be subjected to 20 cycles with little loss of reaction activity and enantioselectivity, although the catalyst produced a relatively lower *ee* value (from 83% to 78%) and conversion (82% to 66%). In contrast, the catalyst generated from the neutral ligand **3b** could be reused only 7 times; the reaction activity and enantioselectivity decreased sharply during the 8th reaction using the ionic liquid. This result was consistent with the results of Chang-Eun Yeom.[16] it seems that the *endo* : *exo* ratio could not be significantly affected by the cycle time. The loss of activity and enantioselectivity during recycling with the catalyst based on **3b** and the maintenance activity and enantioselectivity for catalysts derived from **10b** and **14** demonstrated that the introduction of an ionic tag to the ligand assures that the catalyst is insoluble in non-polar solvents. Consequently, the product

could be extracted, which left the catalyst in the recyclable phase. To prove that the catalyst containing imidazolium-tagged box could maintain better activity in [Bmim]NTf_2, we decreased the amount of catalyst to 5% and even to 1 mol%. The conversion of the Diels–Alder reactions between **15a** and cyclopentadiene **16a** exhibited a slight decrease (91% and 82%, respectively) after 48 h. Thus, the C_2-symmetric imidazolium-tagged box could be well maintained and reused efficiently in the ionic liquid [Bmim]NTf_2. More importantly, the recyclability of the catalyst based on ligand **10b** was the best catalyst in asymmetric D–A reactions reported thus far; both the activity and the enantioselectivity were well maintained even after being recycled 20 times.

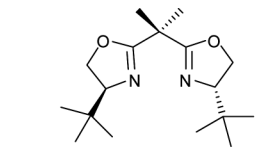
Toxicity studies of the ligands

The luminescent-bacteria toxicity test (LBT) was developed as an alternative to animal testing[28] and has become a basic test for ecotoxicological testing of chemicals, waste water and eluates from soil and sediment.[29] Herein, we employed this method to test the toxicity of ligands. The LC_{50} of the ligands was studied, and the results are compared in Table 4. We presume that the variation in the toxicity is caused mainly by variations of the ligands' anion component. The ligands were more toxic than traditional organic ligand **1** when the anion was $[OTs]^-$ (Table 4, entries 1,7,9 and 10), whereas they were less toxic than (or comparable with) **1** when the anion was $[PF_6]^-$ or $[I]^-$ (Table 4, entries 1,7,11–13). However, considering the good recyclability of the catalyst based on **10b**, our ligands were more environmentally friendly.

Theoretical mechanistic study

A theoretical mechanistic study was conducted to explain the origin of the enantioselectivity at a molecular level. The enantioselectivity-determining step of the Diels–Alder reaction catalysed by bis(oxazoline)–Cu(II) **10b**–Cu–**15a** was calculated using the B3LYP/6-31G(d) scheme in the Gaussian03 software package (Fig. 3). The calculation of the presumed catalyst–substrate complex suggested a degree of distortion for the bound dienophile, which was similar to the result calculated by Evans.[30] A more marked difference in the steric environment about the two prochiral faces, as compared to the stereochemical model calculated by Johnson and Evans,[30] was noted. The results are consistent with the high level of observed enantioselection. Because of the imidazolium salt tagged to the long alkyl chains on the carbon bridge between the two oxazoline moieties and especially because of the bulky $[OTs]^-$ anion section, the steric environment was enhanced once the diene attacked from the α-*Si* face. (Since one of the long alkyl chains on the carbon bridge was more curved than the other one, the imidazolium salt tagged to it and the bulky $[OTs]^-$ anion section were close to the Cu(II), which increased the steric block and made it more difficult for the diene to attack from the α-*Si* face.) This result provided additional evidence for the square-planar model. In addition, we conjectured that after the number of alkyl-chain carbon atoms on the carbon bridge changed from 4 to 2, the imidazolium salt and the $[OTf]^-$ anion would not enhance the steric environment in the transition state because the cation/anion section could not approach the Cu(II) but would hinder the diene attacking from the α-*Re* face and result in a decrease in the *ee* value.

Table 4 Toxicity studies of the ligands



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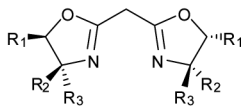
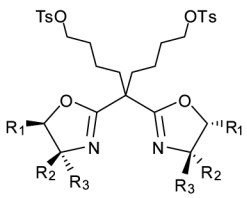
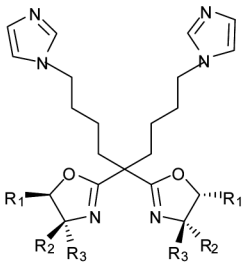


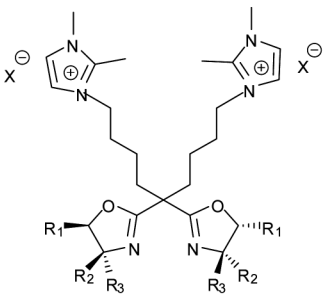
3a R_1=H R_2=H R_3=Ph
b R_1=H R_2=t-Bu R_3=H
c R_1=Ph R_2=Ph R_3=H



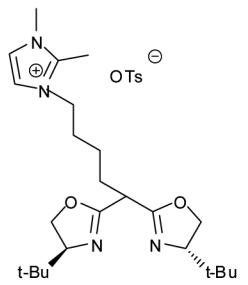
7a R_1=H R_2=H R_3=Ph
b R_1=H R_2=t-Bu R_3=H
c R_1=Ph R_2=Ph R_3=H



9 R_1=H R_2=H R_3=Ph



10a R_1=H R_2=H R_3=Ph X=OTs
b R_1=H R_2=t-Bu R_3=H X=OTs
c R_1=Ph R_2=Ph R_3=H X=OTs
g R_1=H R_2=H R_3=Ph X=Cl
e R_1=H R_2=H R_3=Ph X=PF_6
f R_1=H R_2=t-Bu R_3=H X=PF_6



14

Entry	Ligand	LC_{50} [μg mL^{-1}]
1	**1**	45
2	**3a**	68
3	**3b**	76
4	**3c**	—[a]
5	**7b**	55
6	**7c**	—
7	**9**	33
8	**10a**	—
9	**10b**	11
10	**10c**	11.1
11	**10d**	75
12	**10e**	100
13	**10f**	70
14	**14**	—

[a] the LC50 could not be detected.

Conclusions

In conclusion, C_2-symmetric and unsymmetric imidazolium-tagged bis(oxazoline) ligands were successfully and conveniently prepared, and the anions of the ligands could be altered by ion exchange. The catalysts based on the new ligands and $Cu(OTf)_2$ were applied to asymmetric Diels–Alder reactions

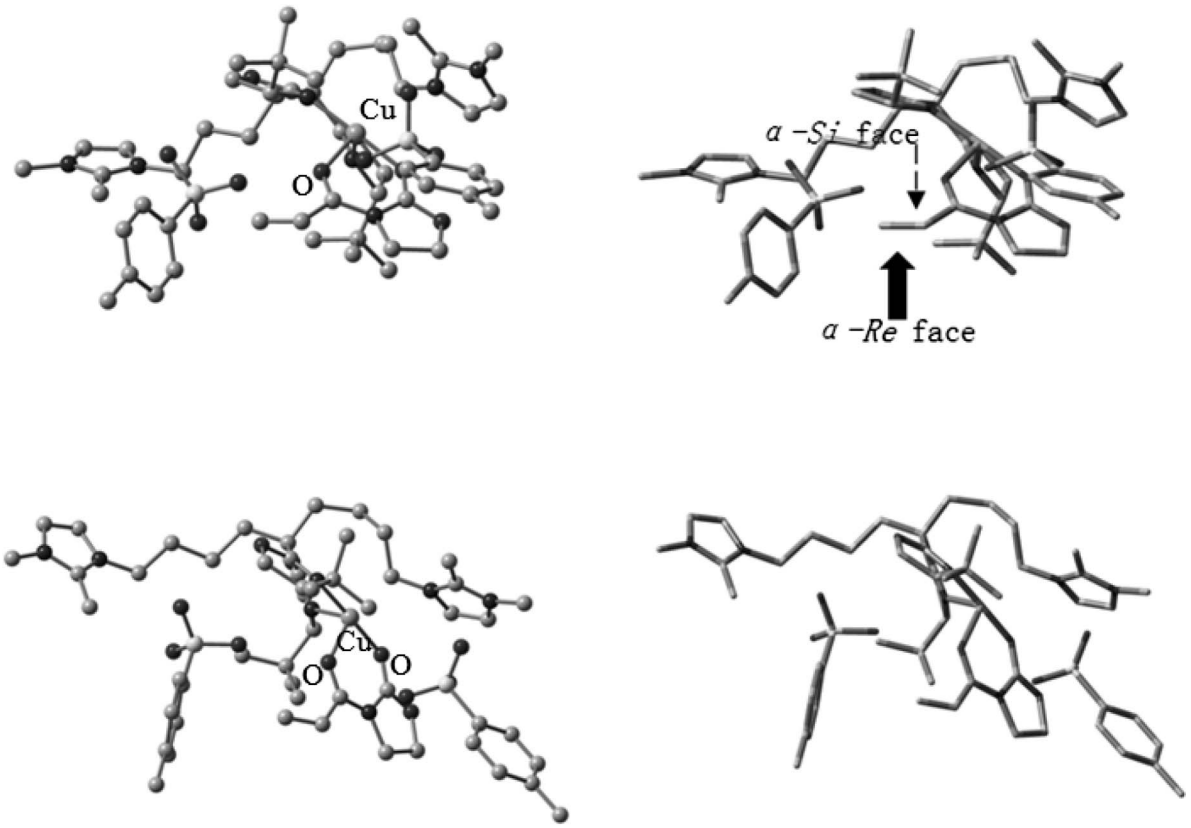


Fig. 3 B3LYP/6-31G(d) optimised geometry of the **10b**–Cu–**15a** complex model for enantioselective cycloadditions. Hydrogen atoms were omitted for clarity.

between *N*-acryloyl/*N*-crotonoyloxazolidinones **15** and 1,3-cyclohexandiene/cyclopentadiene **16** in different ionic liquids and DCM. The catalyst derived from **10b** yielded cycloadduct (*S*)-**17ab** at 98% conversion and 97% *ee* in [Bmim]NTf_2. Furthermore, the catalyst based on **10b** could be recycled at least 20 times without an obvious loss of activity or enantioselectivity. Compared to previously reported reaction systems, the performance of the new catalyst in hydrophobic ionic liquids, especially in [Bmim]NTf_2, achieved our initial design goal: both a high level of enantioselectivity and good recyclability were attained. At the same time, our study showed that the C_2-symmetry of the new ligands was crucial for achieving high *ee* values. Our process, which was simple and easy to operate, possesses vast potential for environmentally friendly processes in the chemical industry. Further research on C_2-symmetric imidazolium-tagged bis(oxazoline) ligands and their performance in asymmetric reactions is ongoing in our laboratory.

Experimental section

General Procedures

All manipulations involving air-sensitive materials were performed using standard Schlenk-line techniques under an atmosphere of nitrogen or argon in oven-dried glassware. DCM was distilled from calcium hydride, and methanol was distilled from Mg. Copper(II) triflate and the ionic liquid were purchased from commercial suppliers and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 300 instrument. Analytical high-performance liquid chromatography (HPLC) was performed on an Knauer Smartline series HPLC equipped with a variable wavelength detector and Daicel Chiralpak AD-H, Chiralcel OD-H and Chiralcel OJ-H columns. Enantiomeric excess was calculated from the HPLC profile.

Synthesis of 5,5-bis[(*R*)-4,5-dihydro-4-phenyloxazol-2-yl]nonane-1,9-di(*tert*-butyl)dimethylsilane 5a

A solution of **3a** (1.000 g, 3.25 mmol) in 20 mL of dry THF was cooled to 0 °C under a N_2 atmosphere. A solution of *n*-BuLi (4.48 mL, 2.9 M in hexane, 6.50 mmol) was added to the solution dropwise, the resulting mixture was stirred at 0 °C for 1 h, and then **4** (3.680 g, 11.70 mmol) was added slowly to the mixture. After the addition was complete, the ice bath was removed, and the solution was left to warm to room temperature and stirred for an additional 12 h. After this time, the reaction mixture was quenched by the addition of water (15 mL) and extracted with DCM (3 × 15 mL). The organic fractions were combined, washed with brine (1 × 40 mL) and H_2O (1 × 40 mL), and dried over Na_2SO_4. The solvent was removed under vacuum to afford a thick, dark, oily residue, which was purified by column chromatography (SiO_2, PE/EtOAc, 10/1) to afford **5a** as a pale yellow oil; yield: 1.130 g (70%). $[\alpha]_D^{20}$ = +90.5 (*c* = 0.50, CH_2Cl_2). ^{1}H NMR(400 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 10H, oxazoline-*ph*), 5.25–5.20 (dd, *J* = 8.4 Hz and 1.6 Hz, 2H, oxazoline-C$H_a$$H_b$O), 4.67–4.62 (dd, *J* = 8.4 Hz and

1.6 Hz, 2H, oxazoline-CH_aH_bO), 4.12–4.08 (t, J = 8.4 Hz, 2H, oxazoline-CHN), 3.63–3.60 (m, 4H, CH_2CH_2O), 2.13–2.11 (m, 4H, CCH_2CH_2), 1.58–1.54 (m, 4H, $CH_2CH_2CH_2$), 1.39–1.35 (m, 4H, $CH_2CH_2CH_2$), 0.89 (s, 18H, OSiC(CH_3)$_3$), 0.02 (s,12H, OSiCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.3, 142.5, 128.9, 127.7, 126.9, 75.3, 69.8, 63.1, 46.5, 33.3, 32.8, 26.2, 20.6, −5.0. MS (ESI): $m:z$ = 679.5 M+1$^+$. Anal. calc. for $C_{39}H_{62}N_2O_4Si_2$: C, 68.98; H, 9.20; N, 4.13; found: C, 69.26; H, 8.58; N, 4.61.

Synthesis of 5,5-bis[(*R*)-4,5-dihydro-4-phenyloxazol-2-yl]nonane-1,9-diol 6a

A solution of **5a** (0.966 g, 1.40 mmol) in 32 mL of dry THF was cooled to 0 °C under a N_2 atmosphere. TBAF (2.100 g) in 9 mL of THF was added to the solution dropwise, and the resulting mixture was warmed to room temperature and stirred for 8 h. The reaction mixture was subsequently quenched by the addition of water (30 mL), washed with EtOAc (30 mL) and then with brine (30 mL), and extracted with EtOAc (2 × 30 mL). The organic fractions were dried over Na_2SO_4, and the solvent was removed under vacuum to afford the crude product, which was purified by column chromatography (SiO_2, EtOAc) to afford **6a** as a yellow oil; yield: 0.434 g (69%). $[\alpha]_D^{20}$ = +113.6 (c = 0.50, CH_2Cl_2), ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.20 (m, 10H, oxazoline-ph-CH), 5.22–5.18 (dd, J = 8.0 Hz and 2.0 Hz, 2H, oxazoline-CH_aH_bO), 4.65–4.61 (dd, J = 8.0 Hz and 2.0 Hz, 2H, oxazoline-CH_aH_bO), 4.12–4.08 (t, J = 8.0 Hz, 2H, oxazoline-CHN), 3.53–3.49 (m, 4H, CH_2CH_2O), 2.07–2.00 (m, 4H, CCH_2CH_2), 1.41–1.38 (m, 4H, $CH_2CH_2CH_2$),1.24–1.22 (m, 4H, $CH_2CH_2CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4, 142.3, 128.9, 127.9, 126.9, 75.3, 69.5, 61.7, 46.7, 32.5, 20.5. MS (ESI): $m:z$ = 451.3 M+1$^+$. Anal. calc. for $C_{27}H_{34}N_2O_4$: C, 71.97; H, 7.61; N, 6.22; found: C, 71.53; H, 7.08; N, 5.79.

Synthesis of 5,5-bis[(*R*)-4,5-dihydro-4-phenyloxazol-2-yl]nonane-1,9-ditosylate 7a

To a solution of **6a** (0.434 g, 0.96 mmol) in 20 mL of DCM, TsCl (0.736 g, 3.86 mmol) and Et_3N (0.390 g, 3.86 mmol) were added under a N_2 atmosphere, and the mixture was stirred for 8 h. The reaction mixture was subsequently quenched by the addition of brine (20 mL). The organic layer was washed with water (3 × 20 mL) and dried over Na_2SO_4, and the solvent was removed under vacuum to afford the crude product, which was purified by column chromatography (SiO_2, EtOAc/PE60-90 1/1) to afford **7a**; yield: 0.540 g (70%). mp: 116–118 °C $[\alpha]_D^{20}$ = +162.5 (c = 2.00, CH_2Cl_2), ^{1}H NMR ($CDCl_3$): δ = 7.76 (m, 4H, OTs-ph-CH), 7.35–7.23 (m, 10H, OTs-ph-CH + oxazoline-ph-CH), 5.23–5.19 (dd, J = 8.0 Hz and 2.0 Hz, 2H, oxazoline-CH_aH_bO), 4.66 (dd, J = 8.0 Hz and 2.0 Hz, 2H, oxazoline-CH_aH_bO), 4.11 (t, J = 8.0 Hz, 2H, oxazoline-CHN), 4.02 (t, J = 8.0 Hz, 4H, CH_2CH_2O), 2.42 (s, 6H, OTs-CH_3), 2.04–1.95 (m, 4H, CCH_2CH_2), 1.70–1.65 (m, 4H, $CH_2CH_2CH_2$), 1.33–1.36 (m, 4H, $CH_2CH_2CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 144.8, 142.2, 129.9, 128.9, 127.9, 126.8, 75.2, 70.3, 69.7, 46.1, 32.3, 29.1, 21.7, 20.1. MS (ESI): $m:z$ = 759.4 M+1$^+$, Anal. calc. for $C_{41}H_{42}N_2O_8S_2$: C, 64.88; H, 6.11; N, 3.69; found: C, 64.54; H, 6.53; N, 3.48.

Synthesis of 1,1′-{5,5-bis[(*R*)-4,5-dihydro-4-phenyloxazol-2-yl]nonane-1,9} bis-(1,2-dimethyl-1*H*-imidazole) diOTs 10a

7a (0.270 g, 0.36 mmol) and 1,2-dimethyl-1H-imidazole were dissolved in 2 mL of DMF, and the solution was heated to 70 °C for 24 h under N_2 atmosphere. DMF was removed under high vacuum. The residue was washed with Et_2O (3 × 10 mL) until it changed to a light-yellow solid; yield: 0.290 g (85%). mp: 82–84 °C $[\alpha]_D^{20}$= +55.4 (c = 0.08, CH_3OH), ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.66 (m, 6H, imidazole-CH + OTs-ph-CH), 7.49–7.18 (m, 10H, OTs-ph-CH +oxazoline-ph-CH), 7.10–7.08 (m, 6H, OTs-ph-CH +oxazoline-ph-CH), 5.23–5.21 (dd, 2H, J = 8.0 Hz and 2.0 Hz, 2H, oxazoline-CH_aH_bO), 4.68–4.64 (dd, 2H, J = 8.0 Hz and 2.0 Hz, 2H, oxazoline-CH_aH_bO), 4.17–4.07 (m, 4H, oxazoline-CHN + CH_2CH_2mim), 3.82 (s, 6H, imidazole-CH_3), 3.48–3.45 (m, 4H, CCH_2CH_2), 2.65(s, 6H, imidazole-CH_3), 2.31(s, 6H, OTs-CH_3), 1.84–1.18(m, 8H, $CH_2CH_2CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 144.3, 144.1, 129.3, 128.9, 128.8, 127.8, 127.4, 126.9, 126.1, 122.9, 121.6, 76.9, 75.3, 69.6, 48.4, 35.5, 32.5, 29.8, 29.5, 21.5, 21.0. MS (ESI): $m:z$ = 304.4 M^{2+}, $m:z$ = 171.0 M$^-$. HRMS (ESI): calc. for $C_{37}H_{48}N_6O_2^{2+}$: 304.1919, found: 304.1914

Synthesis of 1,1′-{5,5-bis[(*R*)-4,5-dihydro-4-phenyloxazol-2-yl]nonane-1,9} bis-(1,2-dimethyl-1*H*-imidazole) dihexafluorophosphate 10e

10a (0.290 g, 0.30 mmol) was dissolved in 2 mL of H_2O, and KPF_6 (0.220 g, 1.10 mmol) was added to the solution and stirred for 6 h at room temperature. The resultant white solid was filtered and dried under vacuum to afford the product; yield: 0.250 g (86%). mp: 108–111 °C $[\alpha]_D^{20}$ = +49.3 (c = 0.08, MeOH), ^{1}HNMR (400 MHz, DMSO): δ = 7.64–7.58 (m, 4H, imidazole-CH), 7.57–7.26 (m, 10H, oxazoline-ph-CH), 5.21–5.20 (dd, 2H, J = 8.0 Hz and 2.0 Hz, 2H, oxazoline-CH_aH_bO), 4.67–4.66 (dd, 2H, J = 8.0 Hz and 2.0 Hz, 2H, oxazoline-CH_aH_bO), 4.11–4.07 (m, 6H, oxazoline-CHN + CH_2CH_2mim), 3.74 (m, 6H, imidazole-CH_3), 2.57(s, 6H, imidazole-CH_3), 1.98–1.24(m, 12H, $CH_2CH_2CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4, 142.3, 139.3, 128.9, 128.6, 127.8, 127.4, 126.9, 126.1, 122.8, 121.6, 69.6, 48.4, 35.5, 32.5, 29.8, 29.5, 21.0, 10.2. MS (ESI): m:z = 304.6 M^{2+}, m:z = 144.9 M$^-$. HRMS (ESI): calc. for $C_{37}H_{48}N_6O_2^{2+}$: 304.1919, found: 304.1914, calc. for PF_6^-: 144.9807, found: 144.9809.

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