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Journal of Organometallic Chemistry 690 (2005) 5237–5254
Journal of Organometallic Chemistry
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Design and synthesis of new bidentate alkoxy-NHC ligands for enantioselective copper-catalyzed conjugate addition

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Received 27 January 2005; received in revised form 5 April 2005; accepted 8 April 2005
Available online 6 June 2005

Abstract

A new family of chiral alkoxy-*N*-heterocyclic carbene (NHC) ligands has been designed for the enantioselective copper-catalyzed conjugate addition of dialkylzincs to enones. These new bidentate NHC ligands were synthesized in high overall yields using a five-step procedure starting from commercially available β-aminoalcohols. Influence of the temperature, base, solvent and copper source were studied in order to optimize the stereoselectivity of the addition. High reactivity and excellent enantioselectivity were obtained at ambient temperature with a range of cyclic enones and dialkylzinc. Addition to acyclic enones has also been studied.

Keywords: Chiral *N*-heterocyclic carbene; Alkoxy-imidazolinium salts; Asymmetric catalysis

1. Introduction

During the last decade, the chemistry of carbene has gained importance in the catalysis area through the use of carbene species as spectator ligands for transition-metal centers. The spectacular advance in this area is due to the remarkable efforts and strategies developed by chemists to build stable and isolable carbene species [1]. *N*-Heterocyclic carbenes (NHC) are the most well known example of this phenomenon [2]. Indeed, since the first isolation and characterization of stable NHC **1** by Arduengo et al. [3] in 1991 (see Fig. 1), many complexes containing NHC have been synthesized and used in important organometallic transformations including many C–C and C–N cross-coupling [4] and the popular metathesis reactions [5]. These new NHC complexes showing an exceptional catalytic activity associate to a better thermal stability than complexes containing phosphine units, allow many synthetic transformations requiring harsher conditions. Use of NHCs in enantioselective catalysis is a natural extension in this field and many complexes containing chiral NHC unit have been synthesized and used in stereoselective catalysis with moderate to high enantiomeric excess [6] (see Fig. 2).

In the copper-catalyzed area, Arduengo has developed a few NHC–copper complexes in 1993 but the catalytic properties of these complexes were not investigated [7]. It was not until 1999 that Woodward et al. could demonstrated that a copper complex containing an Arduengo-type carbene **1** accelerates considerably the copper-catalyzed addition of diethylzinc to cyclohexenone [8]. In light of these results, Alexakis and Mangeney [9] have reported the use of chiral NHCs in the copper-catalyzed conjugate addition [10] in 2001. Designed a C_2-symmetry strategy, the chiral NHC precursors **2** (Fig. 2) gave low to good enantioselectivities in the alkylation of diethylzinc to cyclic enones (up to

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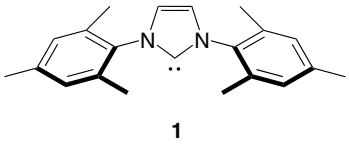
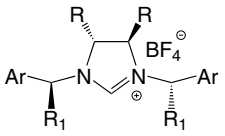
doi:10.1016/j.jorganchem.2005.04.027

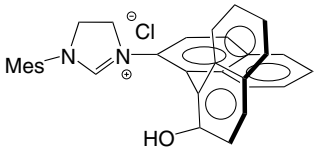


1

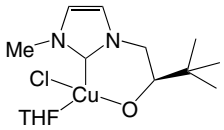
Fig. 1.



2
Alexakis/Mangeney (2001)



3
Hoveyda (2002/2004)



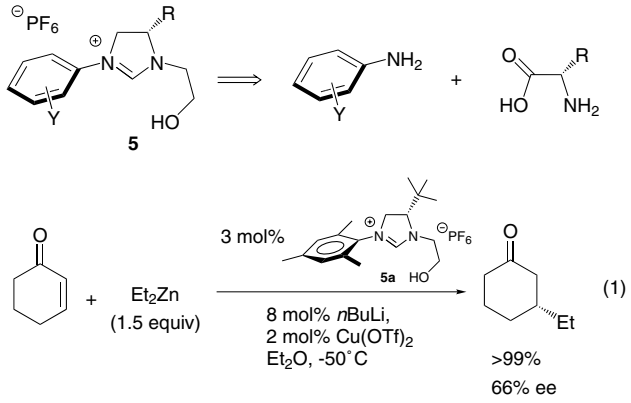
4
Arnold (2004)

Fig. 2.

93% ee). Recently, Okamoto et al. [11] have used the same ligands **2** in copper-catalyzed allylic alkylations, but moderate enantioselectivities were obtained (up to 70% ee).

In 2002, Hoveyda et al. [12] described a very efficient chiral bidentate NHC precursor **3** based on an axial symmetric aminohydroxybinaphtalene, which was first used to form a chiral Ru-complex for asymmetric olefin metathesis (up to 96% ee). Hoveyda has recently studied its use in copper-catalyzed allylic alkylations and obtained high enantioselectivities (up to 98% ee) showing the power of this new class of chelating NHCs. At the same time, Arnold et al. [13] isolated the first chiral chelating alkoxy-NHC–copper (II) complex **4** and use it in the copper conjugate addition of diethylzinc on cyclohexenone. However, moderate enantioselectivity was obtained (up to 51% ee).

Recently, we have reported the first synthesis of chiral alkoxy-imidazolinium salts **5** [14] (Scheme 1) derived from amino acid in a six-step procedure. These salts have been first used as chiral derivatizing agents for ee determination of chiral carboxylate. Based on the work of Woodward and Alexakis and Mangeney, we decided to evaluate their potential as new chelating alkoxy-NHC



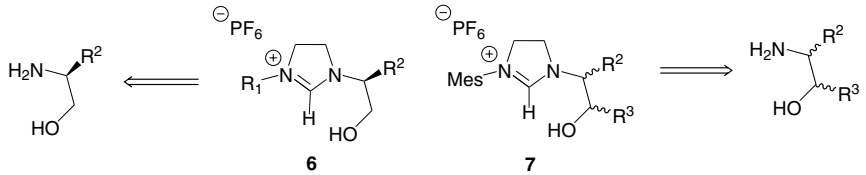
5

Scheme 1. Use of chiral alkoxy-imidazolinium salts **5** in enantioselective 1,4-addition.

ligands in the enantioselective copper-conjugate addition of diethylzinc to cyclohexenone (Eq. (1)). The desired copper (II)-alkoxy-NHC catalyst is formed in situ by adding two equivalents of *n*-butyllithium to the alkoxy-imidazolinium salt **5** in the presence of the copper salt $Cu(OTf)_2$ at −50 °C in diethylether. Under these conditions, the conjugate addition of diethylzinc to 2-cyclohexenone is finished within 4 h. However, low to moderate enantioselectivities were obtained, reaching 66% ee with imidazolinium salt **5a** derived from *tert*-leucine [15].

The high reactivity but modest enantioselectivity obtained with these salts **5** led us to place the chiral center on the alkoxy side chain near the imidazolinium ring. As reported in a preliminary study [16], the alkoxy-imidazolinium salts **6** (Fig. 3) lead to efficient copper (II)-alkoxy-NHC catalysts for the enantioselective copper-catalyzed conjugate addition to 2-cyclohexenone.

Herein, we report an extension of this new class of chiral chelating alkoxy-imidazolinium salts through the synthesis of several other salts **6** and **7** (Fig. 3) easily accessible from commercially available β-aminoalcohols and various substituted anilines or alkylamines. A complete study of these new ligands in the enantioselective conjugate addition to various cyclic enones and also other Michael acceptors involving acyclic enones and nitroalkenes was performed. Influence of the aryl and alkyl groups of the ligand in the stereoselective induction and the reaction conditions (effect of the temperature, the base, the solvent and the copper source) were fully studied for optimization of the enantioselective addition.



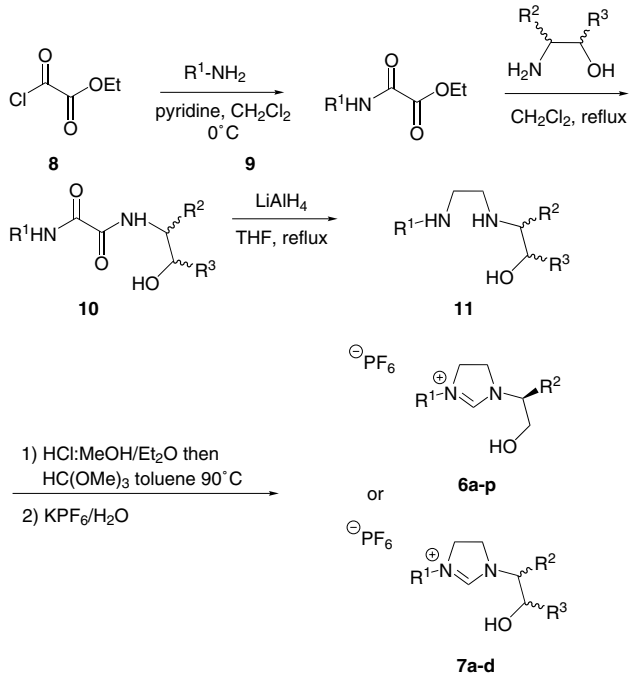
6 **7**

Fig. 3.

2. Preparation of chiral alkoxy-imidazolinium salts 6 and 7

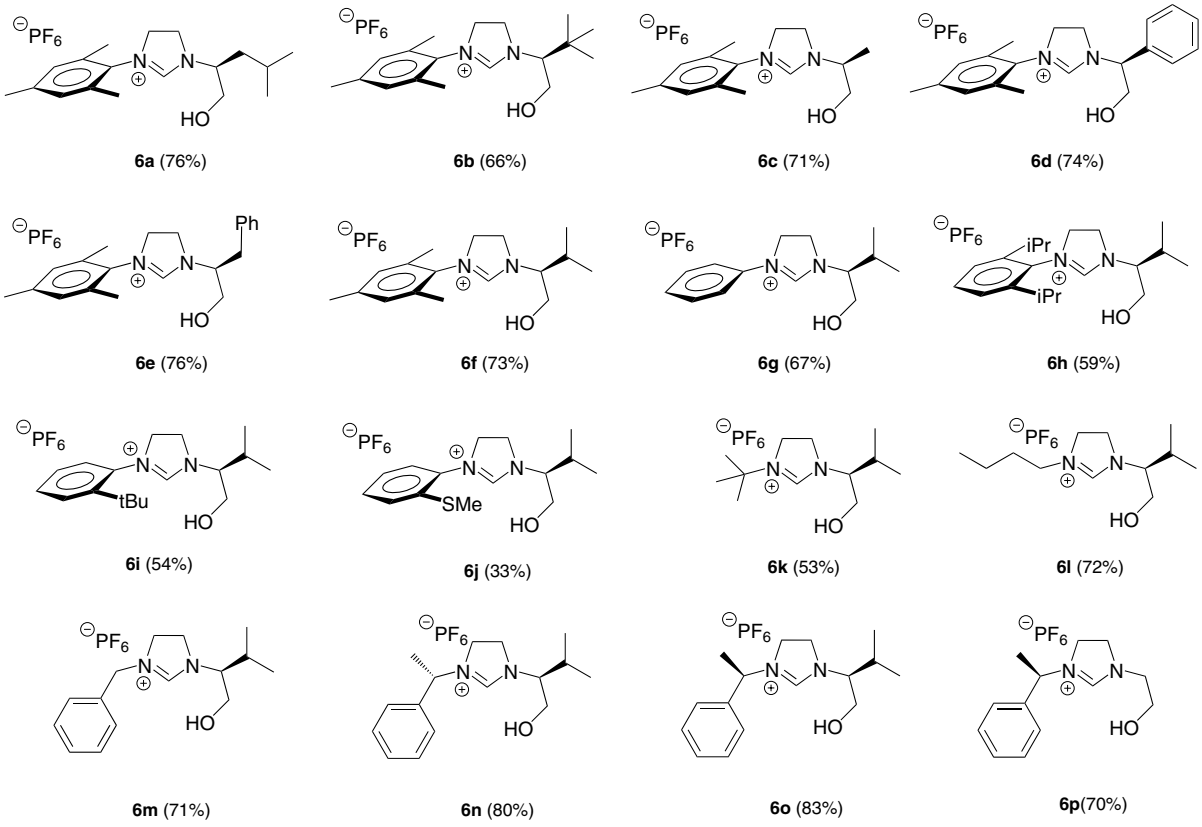
The simple procedure for synthesizing alkoxy-imidazolinium salts **6** and **7** from enantiopure amino-alcohols is described in Scheme 2 [17]. Ethyloxalylchloride **8** is condensed onto primary amine (aniline or alkylamine) to give the corresponding oxanilic ethylester **9**. Treatment with the chiral aminoalcohol in refluxed dichloromethane provides the oxalamide **10** in pure form without purification. After $LiAlH_4$ reduction, the resulting diamine **11** was treated with anhydrous HCl followed by condensation with trimethylorthoformate to provide the desired imidazolinium chloride.

Finally, the chloride salt was easily purified by a simple anion exchange with KPF_6 to give the corresponding potassium hexaflurophosphate alkoxy-imidazolinium salts **6** or **7** in pure form. This short and modular synthesis of chiral alkoxy-NHCs provides an efficient route to the development of new class of chiral catalysts. Two different families of chelating NHC ligands have been developed for the copper-catalyzed conjugate addition: one derived from 2-substituted β-amino alcohols (imidazolinium salts **6a**–**p**, Scheme 3) and the other one derived from several 1,2-disubstituted β-amino alcohols (imidazolinium salts **7a**–**d**, Scheme 4).

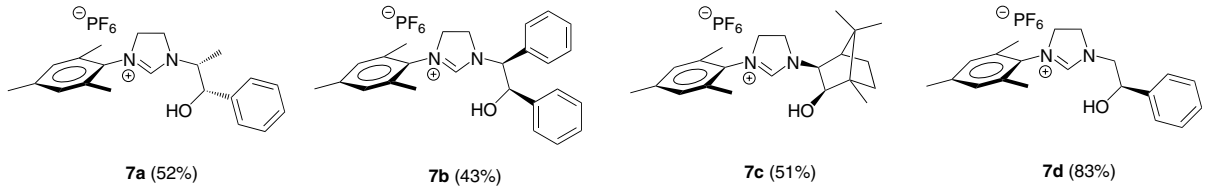


Scheme 2. Synthesis of alkoxy-imidazolinium salts **6** and **7**.

Two X-ray analyses were performed on salts **6a** and **7b** to confirm the structure and absolute configuration of this new type of NHC ligands (Fig. 4). Importantly, all imidazolinium salts were isolated in pure form with modest to good overall yields (33–76%). They are air



Scheme 3. Alkoxy-imidazolinium salts **6a**–**p** derived from 2-substituted β-amino alcohols.



Scheme 4. Alkoxy-imidazolinium salts **7a**–**d** derived from 1,2-disubstituted β-amino alcohols.

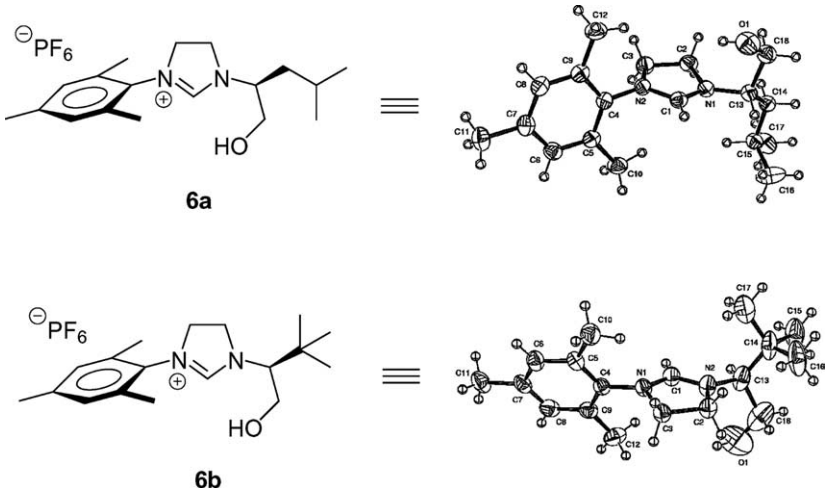


Fig. 4. X-ray structures of alkoxy-imidazolinium salts **6a** and **6b** (PF_6 counter anions were omitted for clarity).

stable and can be synthesized in multigram scale without further purification.

3. Enantioselective 1,4-addition of diethylzinc to cyclohexen-2-one: optimization of reaction conditions

The potential of this new class of chiral alkoxy-NHCs in the enantioselective copper-conjugate addition was then evaluated. We chose the alkylation of cyclohexen-2-one with diethylzinc as the reference reaction. To optimize the reactivity and the enantiocontrol of the conjugate addition, the effect of temperature, of copper source, of ligand:precatalyst ratio, of base and finally of solvent were examined. This study has been achieved with the imidazolinium salt **6a**.

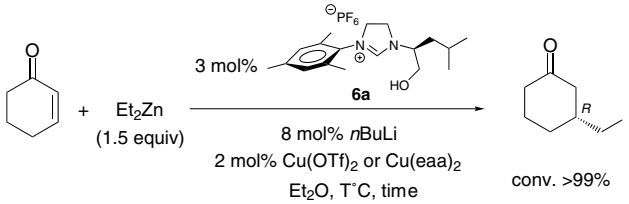
3.1. Influence of the temperature

Results of the study of the effect of temperature on the reactivity and enantioselectivity of the conjugate addition are summarized in Table 1.

Complete conversion was obtained in diethylether after 8 h at −50 °C with 75% ee using 3 mol% of imidazolinium salt **6a** and 8 mol% of *n*BuLi in the presence of 2 mol% of copper (II) triflate ($Cu(OTf)_2$) as precatalyst (entry 1). Replacement of precatalyst by a more soluble copper complex such as copper (II) ethylacetoacetate ($Cu(eaa)_2$) accelerates the reaction allowing the addition to be carried out in only 1 h without loss of enantioselectivity (entry 2).

Lowering the reaction temperature (−78 °C) led to a slight decrease of enantioselectivity to 70% ee with $Cu(eaa)_2$ (entry 2). The phenomenon was dramatically accentuated with $Cu(OTf)_2$ where the stereoselectivity reached only 15% ee. We are unable to bring an adequate explanation for this important difference of

Table 1
Optimization of reaction conditions: importance of the temperature



Entry	T (°C)	$Cu(OTf)_2$		$Cu(eaa)_2$	
		Time (h)	ee (%)[a]	Time (h)	ee (%)[a]
1	−50	4	75	1	76
2	−78	10	15[b]	4	70
3	−25	1	78	1	68
4	0	0.5	83	0.5	56
5	20	0.5	86	0.5	48
6	45	0.5	84	0.5	45

[a] Determined by chiral GC analysis (Lipodex E).
[b] Conv. = 42%.

stereoselectivity between these two pre-catalysts. We then decided to perform the reaction at higher temperature. In the case of $Cu(eaa)_2$, significant decrease of the enantioselectivity was observed with 48% ee at ambient temperature. However, in the case of $Cu(OTf)_2$, as clearly shown in the graphic (Fig. 5), the effect was curiously inverted to obtain higher enantioselectivities at higher temperature. Thus, the best result (86% ee, entry 5) was obtained by performing the reaction at room temperature.

Hoveyda [18] and Leighton [19] have recently observed similar unusual relationship between temperature and enantioselectivity in the copper-catalyzed enantioselective conjugate addition using chiral phosphine ligands. To explain this surprising phenomenon, we postulated that the catalytic copper species formed at lower temperature are different than species formed at ambient temperature, and performed two experiments with $Cu(OTf)_2$ to test this (Table 2). First, we preformed the alkoxy-NHC copper (II) catalyst at 0 °C and performed the addition at −50 °C (entry 1). In this case, a very poor enantioselectivity was observed (49%). Inversely, when we preformed the copper catalyst at −50 °C and added the 2-cyclohexenone and the diethylzinc at ambient temperature, good enantioselectivity up to 85% was obtained. In the first case, the copper clusters formed at ambient temperature conserve their form at lower temperature and are inactive. In the second case, we suspect that the copper cluster formed at −50 °C is immediately transformed to the active cluster when the reaction takes place at 20 °C.

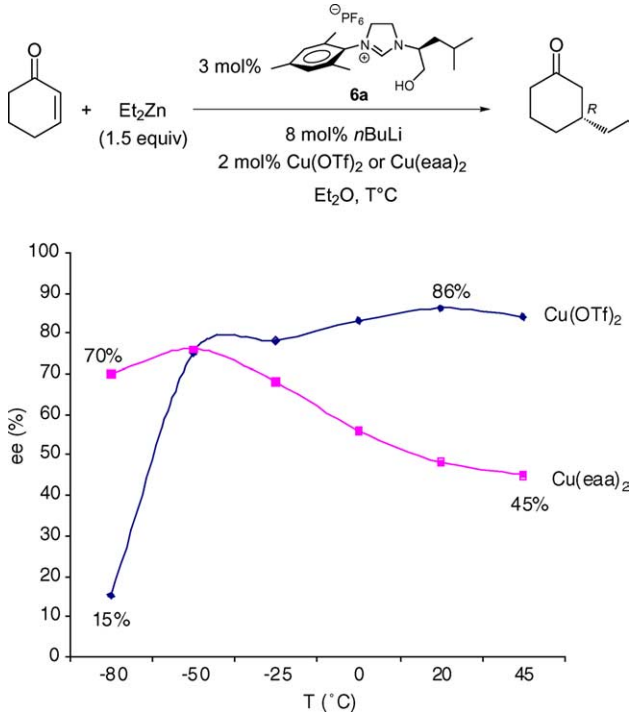
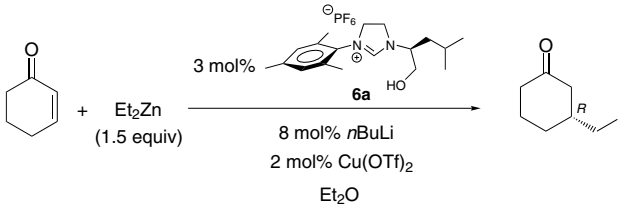


Fig. 5. Unusual relationship between the copper source, the temperature and the enantioselectivity.

Table 2
Evidence of temperature effect in the formation of the alkoxy-NHC copper (II) catalyst species

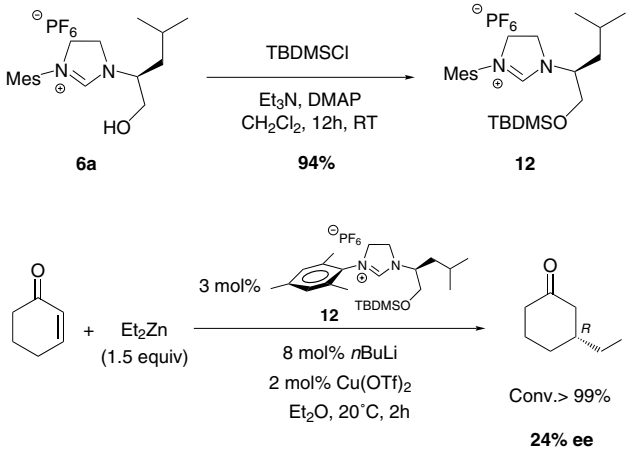


Entry	Conditions	Time (h)	Conv. (%)[a]	ee (%)[b]
1	*n*BuLi was added at O °C Et_2Zn and 2-cyclohexenone were added at −50 °C	2	20	49
2	*n*BuLi was added at −50 °C Et_2Zn and 2-cyclohexenone were added at 20 °C	1	>99	85

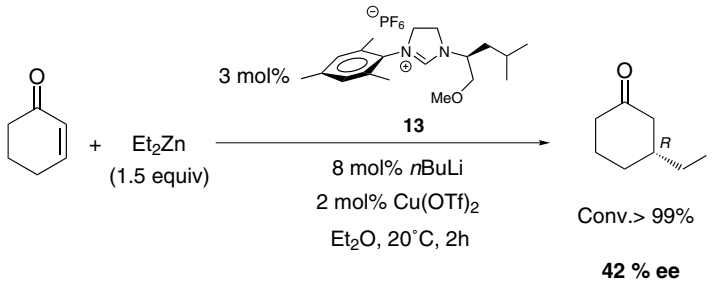
[a] Determined by GC analysis.
[b] Determined by chiral GC analysis (Lipodex E).

3.2. Importance of the hydroxymethylene side chain in the enantiocontrol of the conjugate addition

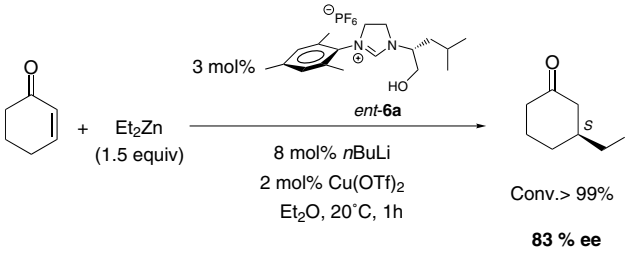
The hydroxymethylene side chain in the NHC ligand is probably crucial for the enantiocontrol of the conjugate addition. To prove this, the hydroxyl function was protected by a *tert*-butyldimethylsilyl group to avoid the covalent O–metal bond. Fortunately, it was possible to realize several synthetic transformations directly onto the imidazolinium salts by using a weak base. Thus, the protected imidazolinium **12** was isolated in excellent yield from imidazolinium salt **6a** using a small excess of Et_3N as proton sponge (Scheme 5). Its use in conjugate addition of diethylzinc to cyclohexenone at room temperature led to a significant decrease in stereoselectivity (24% ee).



Scheme 5.



Scheme 6.



Scheme 7.

Moreover, we tested the methyl ether imidazolium salt **13** to observe if the dative MeO–metal bond allowed to conserve similar enantioselectivity in the conjugate addition. However, 42% ee has been obtained indicating that covalent O–metal bond is critical for the enantiocontrol of the reaction (Scheme 6). The requirement of the hydroxyl function for high enantioselectivity strongly suggests that these alkoxy-NHC ligands act as a LX bidentate ligand.

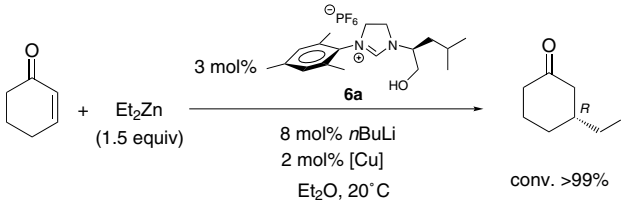
At this stage of the study, it was necessary to verify whether the absolute configuration of the stereogenic center in the alkoxy-NHC ligand showed a significant influence on the enantiocontrol of the conjugate addition. Thus, using the β-amino alcohol derived from unnatural D-leucine, the enantiomer of imidazolinium salt **6a** was synthesized. A slight variation of enantioselectivity (83% ee instead of 86% ee) was observed with the (*ent*)-**6a** salt in the alkylation of Et_2Zn on 2-cyclohexenone (Scheme 7).

3.3. Influence of the copper pre-catalyst source and the ligand/copper salt ratio

As we can see above, the copper salt presents an important effect of the enantioselectivity. Thus, we tested several other copper pre-catalysts including copper (I) salts in the enantioselective addition at ambient temperature. Compared to the initial copper triflate salt, the benzene–Cu(OTf) complex or the hydrated copper acetate complex gave lower ee (Table 3, entries 2 and 3). Like $Cu(eaa)_2$, the LX type copper complex $Cu(acac)_2 \cdot H_2O$ gave poor results at ambient temperature.

We then tested the less expensive copper (II) chloride. In this case, the enantioselectivity reached only 60% ee.

Table 3
Study of the copper source in the enantioselective addition



Entry	Copper precatalyst	Time (h)	ee (%)[a]
1	$Cu(OTf)_2$	0.5	86
2	$CuOTf \cdot C_6H_6$	1	80
3	$Cu(OAc)_2 \cdot H_2O$	1	80
4	Cu(eaa)2	1	48
5	$Cu(acac)_2 \cdot H_2O$	1	54
6	$CuCl_2$	1	60
7	CuCl	2	59
8	CuTC	1	65

[a] Determined by chiral GC analysis (Lipodex E).

At last, we tested the copper (I) salts such as CuCl or the well-known Cu–TC developed by Alexakis [10], to finally reach 59–65% ee. In conclusion, the X_2 type copper salts are the most efficient pre-catalysts for the conjugate addition using the alkoxy-NHC ligands.

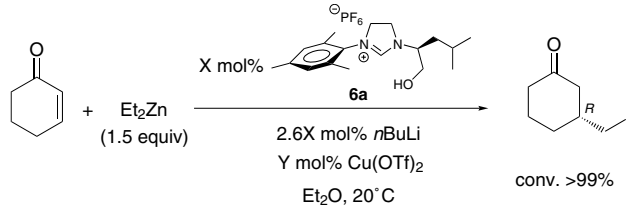
Because the alkoxy-NHC copper catalyst is formed in situ, we then evaluated the ratio between the chiral ligand and the copper salt. As shown in Table 4, the best enantioselectivity is reached with a small excess of alkoxy-NHC ligand (ratio 3/2, entry 2). A large excess of chiral ligand (entries 3 and 4) leads to a dramatic effect on the enantioselectivity, which fell to 29% ee.

Moreover, we optimized the catalytic process where the $Cu(OTf)_2$ loading could be decreased to 0.10 mol% and the alkoxy-NHC ligand **6a** loading to 0.15 mol%. Under these conditions, complete conversion was observed after 1 h without significant loss of enantioselectivity (83% ee, Scheme 8).

3.4. Influence of the base and the solvent

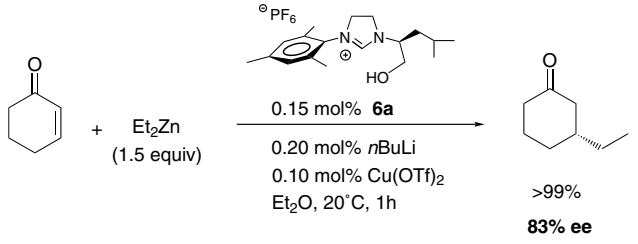
We then studied the effect of the base used for the formation of the alkoxy-NHC copper cluster on the enantiocontrol of the conjugate addition. Three different

Table 4
Importance of the ligand/copper precatalyst ratio



Entry	**6a**/$Cu(OTf)_2$	Time (h)	ee (%)[a]
1	2/2	1	82
2	3/2	0.5	86
3	5/2	1	52
4	10/2	1	29

[a] Determined by chiral GC analysis (Lipodex E).



Scheme 8. Optimization of catalytic process.

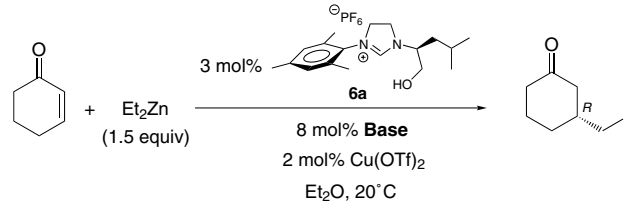
bases were successively evaluated: metallic base, carbonate base and organic base. In a first time, we performed the reaction without base and were surprised to obtain 28% ee (Table 5, entry 2). We presume that diethylzinc is basic enough to generate the *N*-heterocyclic carbene but not the alkoxide.

In the case of metallic base such as *n*-butyllithium, potassium or sodium *tert*-butoxide, the enantioselectivity was very similar, around 86% ee (entries 1, 3 and 4). However, when carbonate bases were used, the enantioselectivity was strongly affected and reached 56% ee in the best case (obtained with $BaCO_3$, entry 8). These results could be explained by the lower basicity of these inorganic bases. Indeed, the carbonates were able to form the carbene but were not basic enough to generate the alkoxylate and form the effective covalent O–metal bond. More interestingly, the use of organic base, which are often less expensive and easier to handle than metallic bases, gave similarly high enantioselectivity (87% ee, entry 9). However, this was only observed with strong organic base, such as DBU.

We have therefore studied the effect of the solvent and the results are summarized in Table 6. By performing the addition in toluene or THF in the presence of DBU instead of *n*BuLi, the best enantiocontrol was obtained and reached 89% ee (entries 4 and 6). One other advantage in the use of organic base is the possibility to perform the conjugate addition in organic solvents such as dichloromethane, acetonitrile or ethylacetate, which are known to be incompatible with metallic bases. However, the enantioselectivity was not really improved in these solvents (around 84%, entries 7–9).

To conclude this section, copper (II) triflate is the most efficient complex to perform the conjugate addition of diethylzinc to cyclohexen-2-one at room temperature in quantitative yield and high enantioselectivity with these new bidentate alkoxy-NHC ligands. A small excess of chiral ligand (ratio 3:2) gives the best ees.

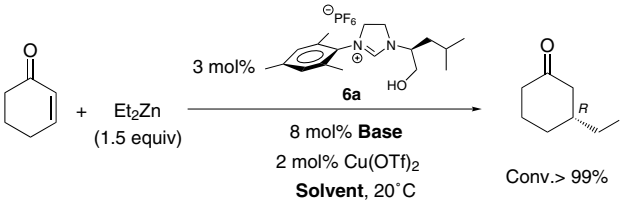
Table 5
Variation of the base



Entry	Base	Time (h)	Conv. (%)[a]	ee (%)[b]
1	*n*BuLi	0.5	>99	86
2	Neat	1	>99	28
3	*t*BuOK	1	>99	87
4	NaOtBu	2	>99	85
5	Cs_2CO_3	1	>99	43
6	Ag_2CO_3	4	15	45
7	K_2CO_3	1	>99	35
8	$BaCO_3$	1	>99	56
9	DBU	1	>99	87
10	Pyridine	1	>99	72
11	Et_3N	1	>99	25

[a] Determined by GC analysis.
[b] Determined by chiral GC analysis (Lipodex E).

Table 6
Variation of the solvent



Entry	Solvent	Base	Time (h)	ee (%)[a]
1	Et_2O	*n*BuLi	0.5	86
2	Et_2O	DBU	1	87
3	THF	*n*BuLi	1	85
4	THF	DBU	1	89
5	Toluene	*n*BuLi	1	75
6	Toluene	DBU	1	89
7	CH_2Cl_2	DBU	1	82
8	AcOEt	DBU	1	85
9	CH_3CN	DBU	1	84

[a] Determined by chiral GC analysis (Lipodex E).

The alkoxymethylene side chain is necessary in order to obtain good enantiocontrol of the reaction. Thus, to form the alkoxylate-NHC bidentate ligand, the use of metallic bases is not really necessary and can be replaced by a strong organic base. At last, any common organic solvent can be used without significant variation of the enantioselectivity.

4. Enantioselective 1,4-addition of diethylzinc to cyclohexen-2-one: design of the structure ligand

Having established the optimal conditions for the use of these new chelating NHCs in the conjugate addition, we have then studied the relationships between the chiral backbone of the imidazolinium salts and the stereoselectivity. We initially examined the influence of the alkyl group of the stereogenic center in the alkoxy-side chain derived from the β-amino alcohols (Fig. 6). Except for the methyl group which gave lower ee (imidazolinium salt **6c**, 79% ee), we have observed a slight difference in the enantioselectivity between the more hindered *tert*-butyl group (imidazolinium salt **6b**, 87% ee) and the other alkyl groups such as phenyl (86% ee, **6d**), benzyl (83% ee, **6e**) and isopropyl (85% ee, **6f**).

Most important in the structural relationship, the aromatic unit derived from the anilines leads to a significant variation of the enantioselectivity. Replacement of the mesityl unit by a less hindered aromatic group such as phenyl (imidazolinium **6g**) resulted in a dramatic effect on the enantioselectivity reaching 54% ee. This effect becomes more pronounced when the mesityl is replaced by a more hindered aromatic moiety such as 2,6-(*i*Pr)-C_6H_3 group (imidazolinium **6h**), where the ee decreases to 29%. Hoveyda has recently observed this phenomenon during the enantioselective allylic substitution with the bidentate NHC ligand **3** [12]. Gade and Bellemin-Laponaz [6i] have also reported the effect of the NHC aromatic substituents size in the enantioselectivity during the asymmetric hydrosilylation reaction catalyzed by an oxazoline–NHC rhodium complex. On the other hand, desymmetrization of the aromatic unit with a bulky substituent such as *tert*-butyl group (imidazolinium **6i**) or a chelating thioalkyl ether group (imidazolinium **6j**) in *ortho* position do not improve the ee (77% and 75% ee, respectively).

The aromatic unit in the alkoxy-NHC ligand appears to be crucial in order to obtain higher enantioselectivity in the copper conjugate addition. We therefore investigated the potential of the other alkoxy-NHC ligands **6k**–**p** bearing an alkyl group instead of the aromatic unit (Table 7). Moderate to poor enantioselectivities were observed with these salts despite the presence of the bulky *tert*-butyl group (imidazolinium **6k**, entry 1).

Similarly moderate enantioselectivities were obtained with the imidazolinium **6m**–**p** bearing a benzylic group

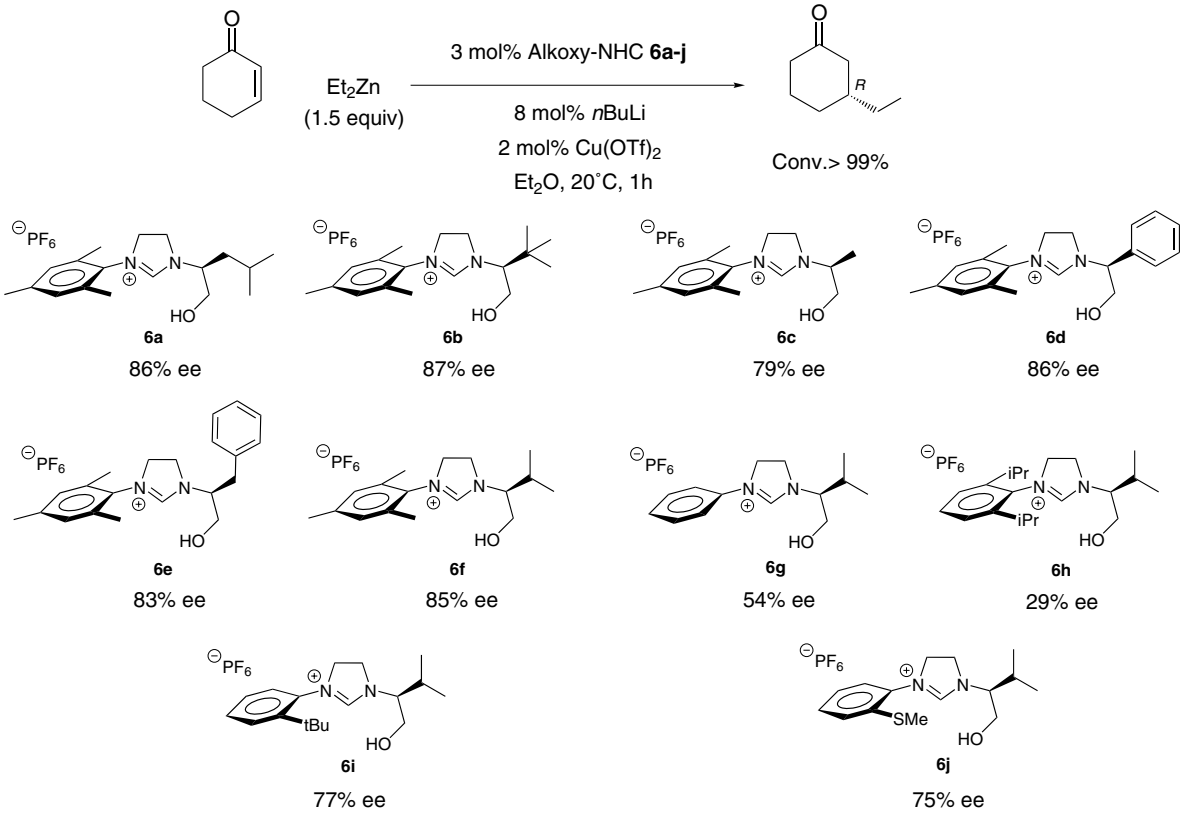
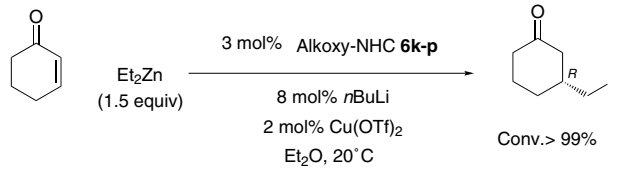


Fig. 6. Evaluation of the alkoxy-NHC ligands **6a**–**j**.

Table 7
Evaluation of the alkoxy-NHC ligands **6k–p**



Entry	Alkoxy-NHC	Time (h)	ee (%)[a]
1	**6k**	2	73
2	**6l**	1	71
3	**6m**	1	63
4	**6n**	1	75
5	**6o**	1	80
6	**6p**	4	2

[a] Determined by chiral GC analysis (Lipodex E).

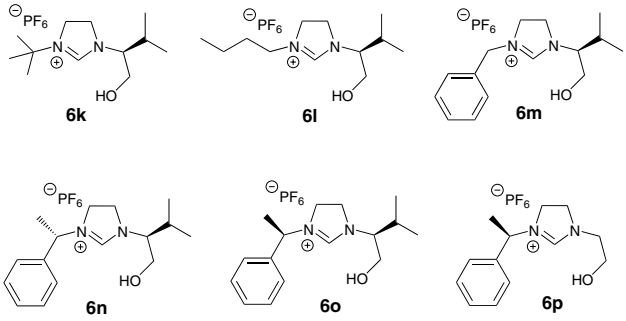
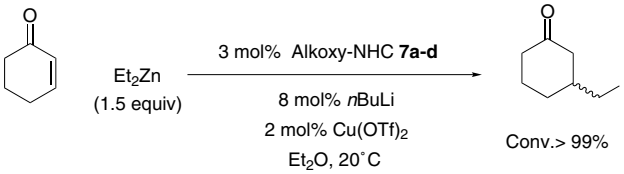
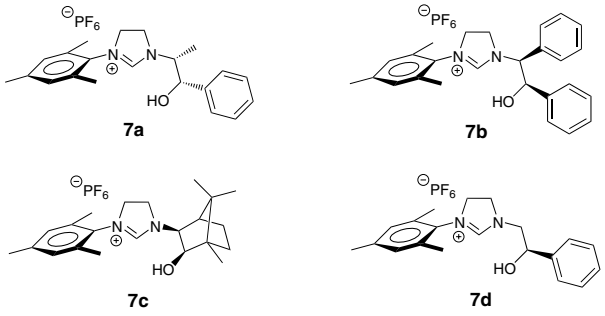


Table 8
Evaluation of the 1,2-disubstituted alkoxy-NHCs **7a–d**



Entry	Alkoxy-NHC	Time (h)	ee (%)[a]
1	**7a**	1	42 (*R*)
2	**7b**	0.5	42 (*S*)
3	**7c**	1	7 (*S*)
4	**7d**	1	17 (*R*)

[a] Determined by chiral GC analysis (Lipodex E).



(Table 7, entries 3–6). Moreover, the presence of a supplementary stereogenic center in the benzyl unit (salts **6n** and **6o**, derived from D or L enantiopure α-methyl benzylamine) does not allow an increase of the enantioselectivity. To verify if the match/mismatch effect was responsible for this, we performed the conjugate addition with the alkoxy-NHC **6p**, which possess only one stereogenic center derived from the benzyl unit. In this case, no enantioselectivity was observed.

To complete the study on the backbone imidazolinium salt, we tested the alkoxy-NHC ligands **7** bearing a second stereogenic center on the alkoxy side chain (Table 8). The significantly lower enantioselectivity of the NHCs **7a–c** (entries 1–3) derived respectively, from norephedrine, 1,2-diphenylethanol and amino-isoborneol, indicates that the presence of a substituent near the chelating function induces a dramatic steric hindrance for the enantiocontrol of the addition. To improve this, we synthesized the mono-alkyl substituted 1-phenyl-1-hydroxylmethylene imidazolinium salt **7d** and obtained a lower enantioselectivity (17% ee, entry 4) than with salts **7a** and **7b**. This last result is completely in accordance with the one reported by Arnold et al. [13] with the alkoxy-NHC copper (II) complex **7** (Fig. 2) bearing a 1-*tert*-butyl substituent in alkoxy side chain (51% ee have been observed at −20 °C).

In summary, in the area design of the alkoxy-NHCs, the nature of the chiral center is not truly significant for the enantioselectivity of the copper-catalyzed conjugate addition. Nevertheless, two points are crucial that lead to high stereoselectivities: firstly, because the design of these ligands is not based on C_2-symmetry, a mesityl unit is recommended, hindering one side of the ligand and thereby disfavoring approach of the substrate from

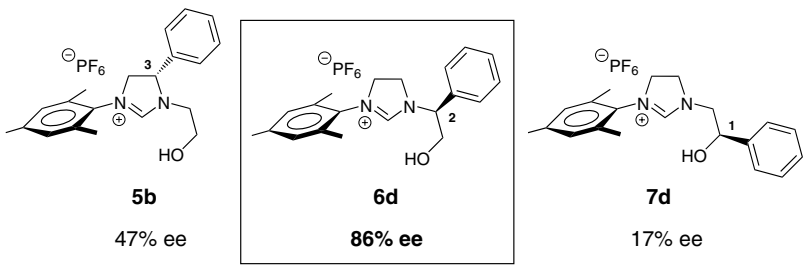


Fig. 7.

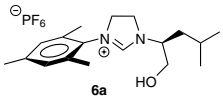
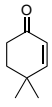
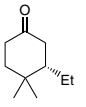
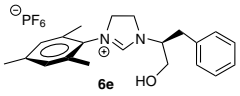
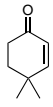
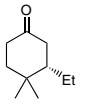
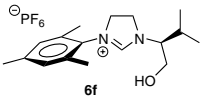
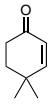
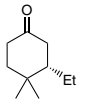
this direction. Secondly, as shown in Fig. 7, the stereogenic center in the alkoxymethylene side chain must be placed absolutely in the C2 position, near the NHC backbone.

5. Enantioselective Cu-catalyzed conjugate addition of dialkylzinc to cyclic enones at ambient temperature

With the imidazolinium salts **6a**, **6f** and **6e** identified as the most efficient alkoxy-NHCs ligands for the enantioselective copper conjugate addition, we undertook a survey of the reaction scope involving several cyclic enones and dialkylzinc (Table 9). Remarkably, alkylation with the dimethylzinc, which proved to give poor reactive performance in conjugate addition, lead to the desired 3-methylcyclohexanone in quantitative yield after 3 h and 88% ee (entry 1). 2-Cyclohexenone may be alkylated with the more steric bulky diisopropylzinc with complete conversion after 1 h and lower stereoselectivity up to 79% ee (entry 2). With the more hindered cyclic enone, such as 4,4-dimethylcyclohexenone (entry 3), 12 h of reaction are necessary to obtain a total conversion with diethylzinc at room temperature. However, the best enantioselectivity is thus observed in this case, reaching 93% ee.

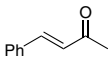
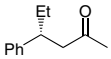
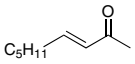
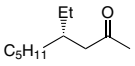
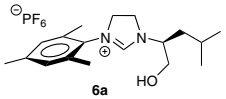
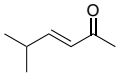
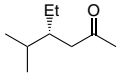
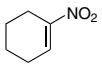
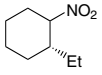
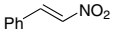
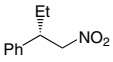
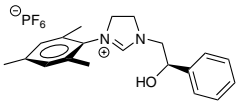
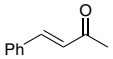
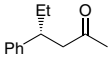
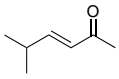
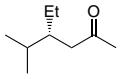
The use of $Cu(eaa)_2$ allowed to perform the addition within 4 h, but the stereoselectivity was truly affected (55% ee, entry 3). Curiously, the reaction time can be diminished to 2 h with ligand **6e** using similar conditions without loss of enantioselectivity (94%, entry 7). Moreover, when ligand **6f** is used, the reactivity is preserved but the enantioselectivity decreased to 85% ee (entry 8). An adequate explanation for this ambiguous relationship between reactivity and enantioselectivity is not obvious. As recently emphasized by Hoveyda [18], it is impossible to generate a general catalyst for all

Table 9
Enantioselective Copper-catalyzed conjugate addition of dialkylzinc to a series of cyclic enones

Entry	Alkoxy-NHC	Substrat	Alkylzinc	Product	Copper salt	Time(h)	Conv.(%)[a]	ee (%)[b]
1			Me_2Zn		$Cu(OTf)_2$	3	>99	88[c]
2			iPr_2Zn		$Cu(OTf)_2$	1	>99	79
3	 **6a**		Et_2Zn		$Cu(OTf)_2$ $Cu(eaa)_2$	12 4	>99 >99	93 55
4			Et_2Zn		$Cu(OTf)_2$	0.5	>99	90
5			Et_2Zn		$Cu(OTf)_2$	1	>99	72
6			iPr_2Zn		$Cu(OTf)_2$	1	>99	53
7	 **6e**		Et_2Zn		$Cu(OTf)_2$	2	>99	94
8	 **6f**		Et_2Zn		$Cu(OTf)_2$	2	>99	85
9			Et_2Zn		$Cu(OTf)_2$	2	>99	86

[a] Determined by GC analysis. [b] Determined by chiral GC analysis (Lipodex E). [c] Determined by chiral GC analysis (Chiraldex BTA).

Table 10
Enantioselective Cu-catalyzed conjugate addition of various Michael acceptors with alkoxy-NHC **6a** and **7d** (copper salt: $Cu(OTf)_2$)

Entry	Alkoxy-NHC	Substrat	Product	Time(h)	Conv.(%)[a]	ee (%)[b]
1				1	>99	34
2				1	>99	11
3	 **6a**			1	>99	5
4				1	>99	21
5				1	>99	37
6	 **7d**			1	>99	27
7				1	>99	16

[a] Determined by GC analysis. [b] Determined by chiral GC analysis (Lipodex E).

conjugate addition and more difficult to anticipate the reactivity or the stereoselectivity.

Addition of Et_2Zn on 2-cycloheptenone with alkoxy-NHC **6a** is achieved in 1 h at room temperature with 90% ee (entry 4). Under similar conditions, 86% ee is observed with ligand **6f** (entry 9). We have then tried to alkylate the α,β-unsaturated lactone with Et_2Zn (entry 5) and obtained total conversion after 1 h. However, moderate enantioselectivity was observed (72% ee). Finally, in the case of 2-cyclopentenone, alkylation with the diisopropylzinc gave a low stereoselectivity up to 53%.

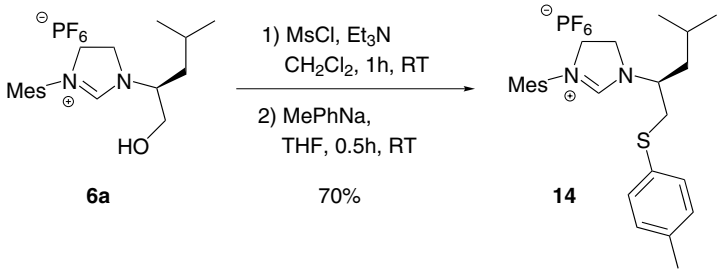
6. Enantioselective Cu-catalyzed conjugate addition of diethylzinc to other Michael acceptors

In order to generalize the use of our alkoxy-NHC **6a** in the enantioselective conjugate addition, we next screened several other Michael acceptors with acyclic enones [20] and nitroalkenes [21,22]. These substrates, which are known to be problematic, were tested under identical conditions at ambient temperature. The results are summarized in Table 10.

Whereas the high reactivity of the catalytic system is conserved for all substrates (complete conversion within 1 h), we have been disappointed in the stereoselectivity of the addition. 34% ee is observed in the best case with acyclic enones (entry 1). Similarly enantioselectivities were observed for the nitroalkene family, with which no value over 37% ee obtained (entry 5). We have also verified if the 1-substituted alkoxy-NHC **7d** bearing the stereogenic center directly on the hydroxyl group allowed to give higher ees. However, poor stereoselectivities were also observed in this case. These last results show clearly the scope of use of the alkoxy-NHC family in the copper-catalyzed conjugate addition. Nevertheless, at this time, no chiral NHC, including these recently developed, has been reported as efficient ligands for this class of enones. As enantioselectivities of over 95% were obtained with the most efficient Cu-phosphine-based systems reported by Hoveyda [21] or Leighton [19], development of new efficient chiral NHCs for acyclic substrates continues to be a challenge.

7. Conclusion

We have reported the development of a new class of chiral alkoxy-NHC ligands readily accessible in a five-step procedure from β-aminoalcohols. A small library of these chelating NHCs has been achieved by a modular synthesis allowing the design of the structure backbone. High reactivity and enantioselectivity were obtained at



6a 70% **14**

Scheme 9.

room temperature in the copper-conjugate addition of dialkylzinc to cyclic enones with low loading of catalyst (up to 0.10 mol%). Future works will focus on the development of new bidentate NHCs bearing other chelating groups (such as S-Ar or PPh_2), which could be synthesized directly from the alkoxy-imidazolinium salts in two steps (Scheme 9). These new ligands are currently being examined in other asymmetric catalytic transformations, particularly in the allylic alkylation and the Heck coupling reaction. These results will be reported in due course.

8. Experimental

8.1. General

^1H (400 MHz), ^{13}C (100 MHz), ^{31}P (162 MHz) and ^{19}F (376.5 MHz) NMR spectra were recorded on a Bruker ARX400 spectrometer with complete proton decoupling for nucleus other than ^1H. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, ^1H: δ 7.27 ppm, ^{13}C: δ 77.0 ppm and $(CD_3)_2CO$: ^1H: δ 2.05 ppm, ^{13}C: δ 205.1 ppm). Data are reported as follows: chemical shift δ in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quadruplet, sept = septuplet, m = multiplet), coupling constants (Hz), integration and attribution. High-resolution mass spectra (HRMS) were recorded at the Centre Régional de Mesures Physiques de l'Ouest (CRMPO), Université de Rennes 1 on a Micromass ZABSpecTOF instrument. Melting points were measured on a heating microscope Reichert and were uncorrected. Optical rotations were recorded using a polarimeter Perkin–Elmer 341. Elemental analysis was performed at Service de microanalyse I.C.S.N. - C.N.R.S. 91198 Gif sur Yvette, France. The conversions of conjugate additions were measured using gas chromatography (capillary column – HP-1, 0.25 μm, 30 m, 0.32 mm) with cyclododecane as internal standard and enantiomeric excesses were calculated using chiral gas chromatography (capillary column – Lipodex E, 0.2 μm, 25 m, 0.25 mm). The products of conjugate additions were identified according to the literature.

8.2. Materials

All non-aqueous reactions were performed under an argon atmosphere using oven-dried glassware. Toluene and trimethylorthoformate were distilled from sodium metal under nitrogen. Tetrahydrofuran and diethyl ether were distilled from sodium metal/benzophenone ketyl under nitrogen. Dichloromethane, methanol, triethylamine and pyridine were distilled from calcium hydride under nitrogen. The 2 N anhydrous HCl/solution was prepared by addition, at 0 °C, of acetyl chloride to dry methanol. All others chemical reagents and solvents were obtained from commercial sources and used without further purification. Analytical TLC were performed on Merck silica gel $60F_{254}$ plates, and visualized under UV-light. Chromatographic purifications were performed on a column with 230–400 mesh silica gel (Merck 9385) using the indicated solvent system.

8.3. Typical procedure for the synthesis of oxalamic acid ethyl ester (*9*)

To a solution of aniline or amine (10 mmol) and pyridine (970 μL, 12 mmol, 1.2 equiv.) in dry DCM (10 mL) was added dropwise ethyl oxalyl chloride **8** (1.33 mL, 12 mmol, 1.2 equiv.) at 0 °C. The resulting solution was stirred at room temperature overnight. The mixture was diluted with ethyl acetate, washed successively with 1 N HCl (two times), saturated $NaHCO_3$ solution and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo to afford the desired product **9**.

8.4. Typical procedure for the synthesis of oxalamides (*10*)

A solution of **9** (2 mmol) and aminoalcohol (2.5 mmol, 1.25 equiv.) in dry DCM (5 mL) was refluxed overnight. The mixture was diluted with ethyl acetate, washed with 1 N HCl and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo to afford the oxalamide **10**.

8.5. Typical procedure for the synthesis of diamines (**11**)

The oxalamide **10** (2 mmol) was added to a suspension of $LiAlH_4$ (300 mg, 8 mmol, 4 equiv.) in dry THF (10 mL) at 0 °C. The reaction mixture was refluxed overnight. After cooling to 0 °C, water and 15% NaOH solution were added dropwise and the resulting solid material was removed by filtration under a celite bed. The filtrate was concentrated in vacuo to afford the diamine **11**.

8.6. Typical procedure for the synthesis of imidazolinium salts (**6**, **7** and **13**)

To a solution of diamine **11** (2 mmol) in dry diethyl ether (10 mL) was added dropwise, at 0 °C, a 2 N anhydrous HCl/methanol solution (1 mL, 2 mmol, 1 equiv.). A white precipitate was immediately formed. After 10 min. stirring, the solvent was evaporated to afford the corresponding chlorhydrate of diamine in quantitative yield. The salt was dissolved in dry toluene (6 mL), trimethylorthoformate (1.1 mL, 10 mmol, 5 equiv.) was added and the mixture was heated to 90 °C for 12 h. After cooling to room temperature, the solvents were evaporated in vacuo, the imidazolinium chloride was dissolved in distilled water (20 mL). The aqueous layer was washed with ethyl acetate before adding KPF_6 (740 mg, 4 mmol, 2 equiv.) at room temperature. A white precipitate was rapidly formed. After 2 h stirring, the imidazolinium salt was extracted with dichloromethane (20 mL). The organic layer was washed with brine, dried over $MgSO_4$ and concentrated in vacuo to afford the desired product.

8.6.1. 1-((1S)-1-Hydroxymethyl-3-methyl-butyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6a**)

White solid (3.3 g, 76%). (reaction realized on 10 mmol); m.p. = 173 °C (AcOEt/pentane). $[\alpha]_D^{20} = +5.0$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 8.68$ (s, 1H, 1CH), 7.05 (s, 2H, $2CH_{ar}$), 4.54 (s, 1H, OH), 4.43 (m, 4H, $2CH_2$), 4.11 (m, 1H, CH), 3.83 (m, 1H, $1CH_2$), 3.79 (m, 1H, $1CH_2$), 2.32 (s, 6H, $2CH_3$), 2.29 (s, 3H, $1CH_3$), 1.81 (m, 2H, $1CH_2$), 1.52 (m, 1H, 1CH), 1.01 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 0.98 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): $\delta = 160.9$, 141.6, 137.3, 132.8 (2C), 131.2 (2C), 62.0, 61.0, 52.0, 47.4, 38.0, 26.0, 23.8, 22.7, 21.6, 18.2 (2C). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C^+: $C_{18}H_{29}N_2O$: 289.2280, found: 289.2283. Elemental Analysis: calc. for $C_{18}H_{29}F_6N_2OP$: C, 49.77; H, 6.73; N, 6.45; found: C, 49.81; H, 6.97; N, 6.31. Structure analysis: $C_{18}H_{29}N_2O$, PF_6, $M_r = 434.40$, orthorhombic, $P2_12_12_1$, $a = 8.2453(4)$, $b = 13.6604(5)$, $c = 18.5642(5)$ Å, $V = 2090.96(14)$ Å^3, $Z = 4$, $D_x = 1.380$ Mg m^{-3}, λ(Mo Kα) = 0.71073 Å, $\mu = 1.94$ cm^{-1}, $F(000) = 912$, $T = 120$ K. The sample (0.42 * 0.32 * 0.30 mm) is studied on a NONIUS Kappa CCD with graphite monochromatized Mo Kα radiation. The cell parameters are obtained with Denzo and Scalepack [23] with 10 frames (psi rotation: 1° per frame). The data collection [24] ($2\theta_{max} = 54°$, 97 frames via 2.0° omega rotation and 20 s per frame, range HKL: H, −10,10; K, −17,17; L −23,24) gives 15,689 reflections. The data reduction with Denzo and Scalepack [23] leads to 4787 independent reflections from which 3877 with $I > 2.0\sigma(I)$. The structure was solved with SIR-97 [25] which reveals the non hydrogen atoms of the molecule. After anisotropic refinement, many hydrogen atoms may be found with a Fourier Difference. The whole structure was refined with SHELXL-97 [26] by the full-matrix least-square techniques (use of F^2 magnitude; x, y, z, β_{ij} for P, F, N, O and C atoms, x, y, z in riding mode for H atoms; 245 variables and 3877 observations with $I > 2.0\sigma(I)$; calc. $w = 1/[\sigma^2(F_o^2) + (0.105P)^2 + 0.73P]$ where $P = (F_o^2 + 2F_c^2)/3$ with the resulting $R = 0.057$, $R_w = 0.149$ and $S_w = 1.010$, $\Delta\rho < 0.35$ e Å^{-3}).

8.6.2. 1-((1S)-1-Hydroxymethyl-2,2-dimethyl-propyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6b**)

White solid (573 mg, 66%); m.p. = 155 °C (AcOEt/pentane). $[\alpha]_D^{20} = +27.0$ ($c = 1$ in chloroform). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 8.69$ (s, 1H, CH), 7.05 (s, 2H, $2CH_{ar}$), 4.71 (s, 1H, OH), 4.47 (m, 4H, $2CH_2$), 4.02 (m, 1H, $1CH_2$), 3.95 (m, 1H, $1CH_2$), 3.81 (dd, J(H,H) = 4 and 10 Hz, 1H, 1CH), 2.33 (s, 6H, $2CH_3$), 2.30 (s, 3H, $1CH_3$), 1.13 (s, 9H, $3CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): $\delta = 160.1$, 139.7, 135.3(2C), 130.8, 129.3 (2C), 70.1, 56.5, 50.3, 48.5, 33.0, 26.3 (3C), 19.7, 16.4 (2C). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C^+: $C_{18}H_{29}N_2O$: 289.2280, found: 289.2273. Structure analysis $C_{18}H_{29}N_2O$, PF_6, $M_r = 434.40$, orthorhombic, $P2_12_12_1$, $a = 8.3706(3)$, $b = 15.6046(6)$, $c = 16.1125(6)$ Å, $V = 2104.6(1)$ Å^3, $Z = 4$, $D_x = 1.371$ Mg m^{-3}, λ(Mo Kα) = 0.71073 Å, $\mu = 1.93$ cm^{-1}, $F(000) = 912$, $T = 120$ K. The sample (0.45 * 0.40 * 0.40 mm) is studied on a NONIUS Kappa CCD with graphite monochromatized Mo Kα radiation. The cell parameters are obtained with Denzo and Scalepack [23] with 10 frames (psi rotation: 1° per frame). The data collection [24] ($2\theta_{max} = 54°$, 148 frames via 2.0° omega rotation and 20 s per frame, range HKL: H, −10,10; K, −20,20; L −20,20) gives 24,755 reflections. The data reduction with Denzo and Scalepack [23] leads to 4827 independent reflections from which 4191 with $I > 2.0\sigma(I)$. The structure was solved with SIR-97 [25]

which reveals the non hydrogen atoms of the molecule. After anisotropic refinement, many hydrogen atoms may be found with a Fourier Difference. The whole structure was refined with SHELXL-97 [26] by the full-matrix least-square techniques (use of F^2 magnitude; x, y, z, β_{ij} for P, F, N, O and C atoms, x, y, z in riding mode for H atoms; 254 variables and 4191 observations with $I > 2.0\sigma(I)$; calc $w = 1/[\sigma^2(F_o^2) + (0.12P)^2 + 1.2P]$ where $P = (F_o^2 + 2F_c^2)/3$ with the resulting $R = 0.068$, $R_w = 0.185$ and $S_w = 1.046$, $\Delta\rho < 0.57$ e Å^{-3}).

8.6.3. 1-((1S)-2-Hydroxy-1-methyl-ethyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6c**)

White solid (554 mg, 71%); m.p. = 169 °C (AcOEt/pentane). $[\alpha]_D^{20} = +18.2$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 8.45$ (s, 1H, 1CH), 6.91 (s, 2H, 2CH$_{ar}$), 4.43 (t, J(H,H) = 5 Hz, 1H, OH), 4.28 (m, 4H, 2CH$_2$), 4.01 (m, 1H, 1CH), 3.71 (m, 1H, 1CH$_2$), 3.61 (m, 1H, 1CH$_2$), 2.19 (s, 3H, 1CH$_3$), 2.16 (s, 6H, 2CH$_3$), 1.31 (d, J(H,H) = 7 Hz, 3H, 1CH$_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): $\delta = 158.3$, 139.6, 135.5, 130.9 (2C), 129.2 (2C), 61.3, 56.3, 50.1, 45.8, 38.0, 19.7, 16.3 (2C). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 707.7 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 707.7 Hz). HRMS (FAB), calc. for C$^+$: $C_{15}H_{23}N_2O$: 247.1810, found: 247.1808.

8.6.4. 1-((1S)-2-Hydroxy-1-phenyl-ethyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6d**)

White solid (670 mg, 74%); m.p. = 143 °C (AcOEt/pentane). $[\alpha]_D^{20} = +22.5$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 8.83$ (s, 1H, 1CH), 7.51 (m, 5H, 5CH$_{ar}$), 7.01 (s, 2H, 2CH$_{ar}$), 5.14 (dd, J(H,H) = 4 and 9 Hz, 1H, 1CH$_2$), 4.82 (t, J(H,H) = 5 Hz, 1H, OH), 4.44 (m, 2H, 1CH$_2$), 4.32 (m, 2H, 1CH$_2$), 4.24 (m, 1H, 1CH$_2$), 4.18 (m, 1H, 1CH$_2$), 2.35 (s, 6H, 2CH$_3$), 2.30 (s, 3H, 1CH$_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): $\delta = 158.7$, 139.8, 135.5, 134.0 (2C), 131.0, 129.4 (2C), 128.9 (2C), 128.8, 127.5 (2C), 64.1, 60.7, 50.3, 47.4, 19.8, 16.5 (2C). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C$^+$: $C_{20}H_{25}N_2O$: 309.1967, found: 309.1971.

8.6.5. 1-((1S)-1-Hydroxymethyl-2-phenyl-ethyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6e**)

White solid (712 mg, 76%); m.p. = 51 °C (AcOEt/pentane). $[\alpha]_D^{20} = -66.3$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 8.42$ (s, 1H, CH), 7.40 (m, 3H, 3CH$_{ar}$), 7.23 (m, 2H, 2CH$_{ar}$), 7.00 (s, 2H, 2CH$_{ar}$), 4.59 (s, 1H, OH), 4.46 (m, 1H, CH), 4.44 (m, 4H, 2CH$_2$), 3.95 (m, 2H, 1CH$_2$), 3.17 (t, J(H,H) = 7 Hz, 2H, 1CH$_2$), 2.26 (s, 6H, 1CH$_3$), 2.23 (s, 3H, 1CH$_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): $\delta = 158.5$, 139.6, 136.5, 130.5, 129.1 (2C), 128.7 (2C), 128.4 (2C), 127.7, 126.6 (2C), 62.1, 59.9, 49.9, 45.9, 33.7, 19.6, 16.1 (2C). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.4 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.4 Hz). HRMS (FAB), calc. for C$^+$: $C_{21}H_{27}N_2O$: 323.2123, found: 323.2119.

8.6.6. 1-((1S)-1-Hydroxymethyl-2-methyl-propyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6f**)

White solid (3.07 g, 73%). (reaction realized on 10 mmol); m.p. = 205 °C (AcOEt/pentane). $[\alpha]_D^{20} = -1.2$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 8.64$ (s, 1H, 1CH), 7.06 (s, 2H, 2CH$_{ar}$), 4.53 (t, J(H,H) = 5 Hz, 1H, OH), 4.45 (m, 4H, 2CH$_2$), 4.00 (m, 1H, 1CH$_2$), 3.89 (m, 1H, 1CH$_2$), 3.67 (m, 1H, 1CH), 2.33 (s, 6H, 2CH$_3$), 2.30 (s, 3H, 1CH$_3$), 2.19 (m, 1H, 1CH), 1.13 (d, J(H,H) = 7 Hz, 3H, 1CH$_3$), 1.06 (d, J(H,H) = 7 Hz, 3H, 1CH$_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): $\delta = 159.3$, 139.9, 136.5, 131.0 (2C), 129.4 (2C), 67.1, 58.5, 50.3, 46.6, 26.9, 19.9, 19.1, 18.3, 16.5 (2C). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.1 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.1 Hz). HRMS (FAB), calc. for C$^+$: $C_{17}H_{27}N_2O$: 275.2123, found: 275.2120.

8.6.7. 1-((1S)-1-Hydroxymethyl-2-methyl-propyl)-3-phenyl-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6g**)

White solid (506 mg, 67%); m.p. = 109 °C (AcOEt/pentane). $[\alpha]_D^{20} = -18.7$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 9.26$ (s, 1H, 1CH), 7.47 (m, 4H, 4CH$_{ar}$), 7.36 (m, 1H, 1CH$_{ar}$), 4.68 (m, 2H, 1CH$_2$), 4.49 (t, J(H,H) = 5 Hz, 1H, OH), 4.42 (m, 2H, 1CH$_2$), 3.99 (m, 1H, 1CH$_2$), 3.92 (m, 1H, 1CH$_2$), 3.71 (m, 1H, 1CH), 2.22 (m, 1H, 1CH), 1.10 (d, J(H,H) = 7 Hz, 3H, 1CH$_3$), 1.07 (d, J(H,H) = 7 Hz, 3H, 1CH$_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): $\delta = 154.5$, 136.3, 129.6 (2C), 126.4, 117.5 (2C), 67.8, 58.9, 47.9, 46.7, 26.8, 19.1, 18.3. ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C$^+$: $C_{14}H_{21}N_2O$: 233.1654, found: 233.1654.

8.6.8. 3-(2,6-Diisopropyl-phenyl)-1-((1S)-1-hydroxymethyl-2-methyl-propyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6h**)

White solid (545 mg, 59%); m.p. = 141 °C (AcOEt/pentane). $[\alpha]_D^{20} = +15.8$ ($c = 1$ in acetone). ^{1}H NMR

(400 MHz, CD_3COCD_3): δ = 8.76 (s, 1H, 1CH), 7.52 (t, J(H,H) = 8 Hz, 1H, $1CH_{ar}$), 7.38 (d, J(H,H) = 8 Hz, 2H, $2CH_{ar}$), 4.58 (t, J(H,H) = 5 Hz, 1H, OH), 4.47 (m, 4H, $2CH_2$), 3.98 (m, 1H, $1CH_2$), 3.88 (m, 1H, $1CH_2$), 3.68 (m, 1H, 1CH), 3.15 (m, 2H, 2CH), 2.19 (m, 1H, 1CH), 1.31 (d, J(H,H) = 7 Hz, 6H, $2CH_3$), 1.22 (d, J(H,H) = 7 Hz, 6H, $2CH_3$), 1.12 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 1.08 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 159.1, 146.5 (2C), 130.6, 130.2, 124.4 (2C), 67.0, 58.0, 52.7, 46.4, 26.7, 25.0 (2C), 23.8 (2C), 22.8 (2C), 18.8, 18.1. ^{19}F NMR (376.5 MHz, CD_3COCD_3): δ = −73.0 (d, J(F,P) = 708.1 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): δ = −143.0 (sept, J(P,F) = 708.1 Hz). HRMS (FAB), calc. for C^+: $C_{20}H_{33}N_2O$: 317.2593, found: 317.2594.

*8.6.9. 3-(2-tert-Butyl-phenyl)-1-((1S)-1-hydroxymethyl-2-methyl-propyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6i**)*

White solid (469 mg, 54%); m.p. = 165 °C (AcOEt/pentane). $[\alpha]_D^{20}$ = −4.9 (c = 1 in acetone). ^1H NMR (400 MHz, CD_3COCD_3): δ = 8.71 (s, 1H, 1CH), 7.68 (dd, J(H,H) = 1 and 8 Hz, 1H, $1CH_{ar}$), 7.50 (m, 2H, $2CH_{ar}$), 7.41 (td, J(H,H) = 1 and 8 Hz, 1H, $1CH_{ar}$), 4.56 (m, 3H, OH and $1CH_2$), 4.37 (m, 2H, $1CH_2$), 3.99 (m, 1H, $1CH_2$), 3.89 (m, 1H, $1CH_2$), 3.70 (m, 1H, 1CH), 2.18 (m, 1H, 1CH), 1.46 (s, 9H, $3CH_3$), 1.13 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 1.05 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 159.7, 147.3, 134.6, 130.2, 129.6, 128.6, 127.6, 67.2, 58.2, 54.4, 46.4, 35.3, 31.0 (3C), 25.1, 19.0, 18.1. ^{19}F NMR (376.5 MHz, CD_3COCD_3): δ = −73.0 (d, J(F,P) = 708.6 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): δ = −143.0 (sept, J(P,F) = 708.6 Hz). HRMS (FAB), calc. for C^+: $C_{18}H_{29}N_2O$: 298.2280, found: 298.2283.

*8.6.10. 1-((1S)-1-Hydroxymethyl-2-methyl-propyl)-3-(2-methylsulfanyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6j**)*

Limpid oil (280 mg, 33%). $[\alpha]_D^{20}$ = +4.7 (c = 1 in acetone). ^1H NMR (400 MHz, CD_3COCD_3): δ = 8.84 (s, 1H, 1CH), 7.54 (m, 3H, $3CH_{ar}$), 7.35 (m, 1H, $1CH_{ar}$), 4.68 (m, 1H, OH), 4.57 (m, 2H, $1CH_2$), 4.41 (m, 2H, $1CH_2$), 4.14 (m, 1H, 1CH), 3.81 (m, 2H, $1CH_2$), 2.58 (s, 3H, $1CH_3$), 2.82 (m, 2H, $1CH_2$), 1.53 (m, 1H, 1CH), 1.02 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 0.99 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 158.6, 136.0, 133.9, 130.2, 127.6, 126.7, 126.2, 60.6, 59.6, 50.8, 46.1, 36.3, 24.1, 22.1, 20.9, 14.5. ^{19}F NMR (376.5 MHz, CD_3COCD_3): δ = −73.0 (d, J(F,P) = 708.0 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): δ = −143.0 (sept, J(P,F) = 708.0 Hz). HRMS (FAB), calc. for C^+: $C_{16}H_{25}N_2OS$: 293.1688, found: 293.1689.

*8.6.11. 3-tert-Butyl-1-((1S)-1-hydroxymethyl-2-methyl-propyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6k**)*

White solid (480 mg, 67%); m.p. = 93 °C (AcOEt/pentane). $[\alpha]_D^{20}$ = −6.8 (c = 1 in acetone). ^1H NMR (400 MHz, CD_3COCD_3): δ = 8.46 (s, 1H, 1CH), 4.35 (s, 1H, OH), 4.20 (m, 2H, $1CH_2$), 4.12 (m, 2H, $1CH_2$), 3.87 (m, 1H, $1CH_2$), 3.75 (m, 1H, $1CH_2$), 3.50 (m, 1H, 1CH), 2.04 (m, 1H, CH), 1.48 (s, 9H, $3CH_3$), 1.00 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 0.98 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 155.8, 66.6, 58.7, 56.0, 45.3, 44.8, 26.8 (3C), 26.6, 19.0, 18.2. ^{19}F NMR (376.5 MHz, CD_3COCD_3): δ = −73.0 (d, J(F,P) = 708.1 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): δ = −143.0 (sept, J(P,F) = 708.1 Hz). HRMS (FAB), calc. for C^+: $C_{12}H_{25}N_2O$: 213.1967, found: 213.1961.

*8.6.12. 3-Butyl-1-((1S)-1-hydroxymethyl-2-methyl-propyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6l**)*

Limpid oil (514 mg, 72%). $[\alpha]_D^{20}$ = −3.7 (c = 1 in acetone). ^1H NMR (400 MHz, CD_3COCD_3): δ = 8.42 (s, 1H, 1CH), 4.37 (t, J(H,H) = 5 Hz, 1H, OH), 4.13 (m, 4H, $2CH_2$), 3.87 (m, 1H, $1CH_2$), 3.78 (m, 1H, $1CH_2$), 3.63 (t, J(H,H) = 7 Hz, 2H, $1CH_2$), 3.46 (m, 1H, 1CH), 2.04 (m, 1H, CH), 1.71 (m, 2H, $1CH_2$), 1.37 (m, 2H, $1CH_2$), 1.01 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 0.99 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 0.93 (t, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 157.7, 66.4, 58.6, 47.5, 47.3, 45.9, 29.1, 28.5, 26.8, 18.8, 18.1, 12.5. ^{19}F NMR (376.5 MHz, CD_3COCD_3): δ = −73.0 (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): δ = −143.0 (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C^+: $C_{12}H_{25}N_2O$: 213.1967, found: 213.1964.

*8.6.13. 3-Benzyl-1-((1S)-1-hydroxymethyl-2-methyl-propyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6m**)*

White solid (555 mg, 71%); m.p. = 49 °C (AcOEt/pentane). $[\alpha]_D^{20}$ = −6.7 (c = 1 in acetone). ^1H NMR (400 MHz, CD_3COCD_3): δ = 8.62 (s, 1H, 1CH), 7.44 (m, 5H, $5CH_{ar}$), 4.84 (d, J(H,H) = 7 Hz, 2H, $1CH_2$), 4.44 (t, J(H,H) = 5 Hz, 1H, OH), 4.15 (m, 2H, $1CH_2$), 4.00 (m, 2H, $1CH_2$), 3.89 (m, 1H, $1CH_2$), 3.78 (m, 1H, $1CH_2$), 3.52 (m, 1H, 1CH), 2.05 (m, 1H, CH), 1.03 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 1.01 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 157.7, 66.4, 58.6, 47.5, 47.3, 45.9, 29.1, 28.5, 26.8, 26.6, 18.8, 18.1, 12.5. ^{19}F NMR (376.5 MHz, CD_3COCD_3): δ = −73.0 (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): δ = −143.0 (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C^+: $C_{15}H_{23}N_2O$: 247.1810, found: 247.1810.

*8.6.14. 1-((1S)-1-Hydroxymethyl-2-methyl-propyl)-3-((1S)-1-phenyl-ethyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6n**)*

White solid (650 mg, 80%); m.p. = 93 °C (AcOEt/pentane). $[\alpha]_D^{20} = -7.5$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): δ = 8.67 (s, 1H, 1CH), 7.42 (m, 5H, $5CH_{ar}$), 5.02 (q, J(H,H) = 7 Hz, 1H, 1CH), 4.57 (t, J(H,H) = 5 Hz, 1H, OH), 4.12 (m, 2H, $1CH_2$), 3.97 (m, 2H, $1CH_2$), 3.89 (m, 1H, $1CH_2$), 3.78 (m, 1H, $1CH_2$), 3.56 (m, 1H, 1CH), 2.07 (m, 1H, CH), 1.78 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 1.02 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 1.00 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 156.6, 138.2, 128.7 (2C), 128.2, 126.3 (2 C), 66.6, 58.4, 57.4, 46.4, 45.4, 26.6, 18.8, 18.6, 18.2. ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.1 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.1 Hz). HRMS (FAB), calc. for C^+: $C_{16}H_{25}N_2O$: 261.1967, found: 261.1966.

*8.6.15. 1-((1S)-1-Hydroxymethyl-2-methyl-propyl)-3-((1R)-1-phenyl-ethyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6o**)*

White solid (674 mg, 83%); m.p. = 81 °C (AcOEt/pentane). $[\alpha]_D^{20} = +0.6$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): δ = 8.64 (s, 1H, 1CH), 7.44 (m, 5H, $5CH_{ar}$), 5.06 (q, J(H,H) = 7 Hz, 1H, 1CH), 4.41 (t, J(H,H) = 5 Hz, 1H, OH), 4.12 (m, 2H, $1CH_2$), 3.98 (m, 2H, $1CH_2$), 3.89 (m, 1H, $1CH_2$), 3.78 (m, 1H, $1CH_2$), 3.54 (m, 1H, 1CH), 2.06 (m, 1H, CH), 1.78 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 1.02 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 0.99 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 156.6, 138.1, 128.8 (2C), 128.3, 126.4 (2C), 66.7, 58.6, 57.3, 46.3, 45.5, 26.6, 18.9, 18.6, 18.2. ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C^+: $C_{16}H_{25}N_2O$: 261.1967, found: 261.1970.

*8.6.16. 1-(2-Hydroxy-ethyl)-3-((1R)-1-phenyl-ethyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**6p**)*

White solid (517 mg, 71%); m.p. = 47 °C (AcOEt/pentane). $[\alpha]_D^{20} = +10.0$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): δ = 8.50 (s, 1H, 1CH), 7.43 (m, 5H, $5CH_{ar}$), 5.02 (q, J(H,H) = 7 Hz, 1H, 1CH), 4.25 (t, J(H,H) = 5 Hz, 1H, OH), 4.16 (t, J(H,H) = 10 Hz, 2H, $1CH_2$), 3.93 (t, J(H,H) = 10 Hz, 2H, $1CH_2$), 3.82 (q, J(H,H) = 5 Hz, 1H, $1CH_2$), 3.78 (t, J(H,H) = 5 Hz, 2H, $1CH_2$), 1.76 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 156.4, 138.1, 128.7 (2C), 128.2, 126.4 (2C), 57.5, 57.3, 50.0, 48.2, 46.8, 18.7. ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C^+: $C_{130}H_{19}N_2O$: 219.1497, found: 219.1492.

*8.6.17. 1-((1R,2S)-2-Hydroxy-1-methyl-2-phenyl-ethyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**7a**)*

White solid (487 mg, 52%); m.p. = 165 °C (AcOEt/pentane). $[\alpha]_D^{20} = -21.0$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): δ = 8.50 (s, 1H, 1CH), 7.55 (m, 2H, $2CH_{ar}$), 7.42 (m, 2H, $2CH_{ar}$), 7.34 (m, 1H, $1CH_{ar}$), 7.02 (s, 2H, $2CH_{ar}$), 5.25 (d, J(H,H) = 4 Hz, 1H, OH), 5.18 (t, J(H,H) = 4 Hz, 1H, 1CH), 4.60 (m, 1H, 1CH), 4.32 (m, 4H, $2CH_2$), 2.28 (s, 6H, $2CH_3$), 2.20 (s, 3H, $1CH_3$), 1.44 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 158.0, 140.6, 139.7, 135.4, 130.9 (2C), 129.3 (2C) 128.2 (2C), 127.7, 126.1 (2C), 73.1, 59.7, 50.2, 48.2, 19.8, 16.4 (2C), 12.4. ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.0 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.0 Hz). HRMS (FAB), calc. for C^+: $C_{21}H_{27}N_2O$: 321.2123, found: 321.2119.

*8.6.18. 1-((1S,2R)-2-Hydroxy-1,2-diphenyl-ethyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**7b**)*

White solid (487 mg, 52%); m.p. = 148 °C (AcOEt/pentane). $[\alpha]_D^{20} = -10.0$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): δ = 8.81 (s, 1H, 1CH), 7.46 (m, 10H, $10CH_{ar}$), 7.04 (s, 2H, $2CH_{ar}$), 5.78 (d, J(H,H) = 6 Hz, 1H, CH), 5.27 (d, J(H,H) = 6 Hz, 1H, 1CH), 4.99 (s, 1H, OH), 4.43 (m, 1H, $1CH_2$), 4.31 (m, 3H, $2CH_2$), 2.35 (s, 6H, $2CH_3$), 2.28 (s, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 158.3, 140.8, 139.8, 135.4, 133.2, 133.0 (2C), 130.8 (2C) 129.3 (2C), 129.2 128.9, 128.6 (2C), 128.2 (2C), 126.4 (2C), 72.2, 67.3, 50.1, 48.0, 19.7, 16.4 (2). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.0 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.0 Hz). HRMS (FAB), calc. for C^+: $C_{26}H_{29}N_2O$: 385.2280, found: 385.2282.

*8.6.19. 1-((2S,3R)-3-Hydroxy-4,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**7c**)*

White solid (496 mg, 51%); m.p. = 217 °C (AcOEt/pentane). $[\alpha]_D^{20} = +32.0$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): δ = 8.79 (s, 1H, 1CH), 7.04 (s, 2H, $2CH_{ar}$), 5.04 (d, J(H,H) = 6 Hz, 1H, 1CH), 4.66 (m, 1H, OH), 4.36 (m, 4H, $2CH_2$), 4.07 (dd, J(H,H) = 6 and 7 Hz, 1H, 1CH), 3.86 (d, J(H,H) = 7 Hz, 1H, 1CH), 2.32 (s, 6H, $2CH_3$), 2.29 (s, 3H, $1CH_3$), 1.85 (m, 1H, $1CH_2$), 1.25 (s, 3H, $1CH_3$), 1.19 (m, 2H, $1CH_2$), 0.97 (s, 3H, $1CH_3$), 0.88 (s, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 158.3, 139.6, 135.1, 131.1 (2C), 129.2 (2C), 79.2, 65.3, 51.1,

49.7, 49.4, 46.9, 46.7, 31.4, 26.3, 20.6, 20.1, 19.7, 16.4 (2C), 10.5. ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.2 Hz). calc. for C^+: $C_{22}H_{33}N_2O$: 341.2593, found: 341.2602.

*8.6.20. 1-((2R)-2-Hydroxy-2-phenyl-ethyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**7d**)*

White solid (754 mg, 83%); m.p. = 192 °C (AcOEt/pentane). $[\alpha]_D^{20} = +65.2$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 8.50$ (s, 1H, 1CH), 7.52 (d, 2H, J(H,H) = 7 Hz, $2CH_{ar}$), 7.42 (dt, 2H, J(H,H) = 2 and 7 Hz, $2CH_{ar}$), 7.34 (m, 1H, $1CH_{ar}$), 7.04 (s, 2H, $2CH_{ar}$), 5.29 (m, 2H, $1CH_2$ EtOH), 4.60 (m, 1H, $1CH_2$), 4.39 (m, 3H, $2CH_2$), 3.97 (t, J(H,H) = 4 Hz, 2H, $1CH_2$), 2.29 (s, 6H, $2CH_3$), 2.28 (s, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 159.4, 141.1, 139.8, 135.5, 131.2 (2C), 129.4 (2C) 128.4, 127.7 (2C), 125.7 (2C), 69.6, 54.8, 50.7, 49.9, 19.8, 16.4 (2C). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C^+: $C_{20}H_{25}N_2O$: 309.1967, found: 309.1963.

*8.6.21. 1-((1S)-1-Methoxymethyl-3-methyl-butyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (ent-**6a**)*

White solid (599 mg, 69%); m.p. = 171 °C (AcOEt/pentane). $[\alpha]_D^{20} = -5.4$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 8.67$ (s, 1H, 1CH), 7.05 (s, 2H, $2CH_{ar}$), 4.54 (s, 1H, OH), 4.42 (m, 4H, $2CH_2$), 4.11 (m, 1H, CH), 3.82 (m, 1H, $1CH_2$), 3.80 (m, 1H, $1CH_2$), 2.32 (s, 6H, $2CH_3$), 2.29 (s, 3H, $1CH_3$), 1.82 (m, 2H, $1CH_2$), 1.53 (m, 1H, 1CH), 1.00 (d, J(H,H) = 7 Hz, 3H, $1CH_3$), 0.97 (d, J(H,H) = 7 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 160.9, 141.6, 137.3, 132.8 (2C), 131.2 (2C), 62.0, 61.0, 52.0, 47.4, 38.0, 26.0, 23.8, 22.7, 21.6, 18.2 (2C). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C^+: $C_{18}H_{29}N_2O$: 289.2280, found: 289.2282.

*8.6.22. 1-((1R)-1-Hydroxymethyl-3-methyl-butyl)-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**13**)*

White solid (627 mg, 70%); m.p. = 139 °C (AcOEt/pentane). $[\alpha]_D^{20} = +4.7$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 8.70$ (s, 1H, 1CH), 7.08 (s, 2H, $2CH_{ar}$), 4.47 (m, 4H, $2CH_2$), 4.26 (m, 1H, CH), 3.69 (d, J(H,H) = 6 Hz, 2H, $1CH_2$), 3.45 (s, 3H, $1CH_3$), 2.34 (s, 6H, $2CH_3$), 2.32 (s, 3H, $1CH_3$), 1.85 (m, 2H, $1CH_2$), 1.57 (m, 1H, 1CH), 1.02 (d, J(H,H) = 6 Hz, 3H, $1CH_3$), 1.00 (d, J(H,H) = 6 Hz, 3H, $1CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 159.1, 139.8, 135.4, 130.9 (2C), 129.4 (2C), 70.3, 57.9, 56.9, 50.3, 45.7, 36.4, 24.2, 21.9, 20.9, 19.8, 16.3 (2C). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.0 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.0 Hz). HRMS (FAB), calc. for C^+: $C_{19}H_{31}N_2O$: 303.2436, found: 303.2432.

*8.6.23. 1-[(1S)-1-(tert-Butyl-dimethyl-silanyloxymethyl)-3-methyl-butyl]-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-3H-imidazol-1-ium hexafluorophosphate (**12**)*

To a solution of imidazolinium salt **6a** (217 mg, 0.5 mmol), triethylamine (85 μL, 0.6 mmol, 1.2 equiv.) and DMAP (3 mg, 0.025 mmol, 0.05 equiv.) in dry DCM (10 mL) was added *tert*-butyldimethylsilyl chloride (90 mg, 0.6 mmol, 1.2 equiv.). The reaction mixture was stirred overnight at room temperature. The reaction was then quenched with saturated $NaHCO_3$ solution. The organic layer was washed with distilled water (10 mL) then brine, dried over $MgSO_4$, filtered and concentrated. A purification by silica gel chromatography dichloromethane/acetone (9/1) as eluent afford the desired product as a white solid (254 mg, 0.47 mmol, 93%); m.p. = 119 °C (AcOEt/pentane). $[\alpha]_D^{20} = +18.8$ ($c = 1$ in acetone). ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 8.79$ (s, 1H, 1CH), 7.07 (s, 2H, $2CH_{ar}$), 4.46 (m, 4H, $2CH_2$), 4.17 (m, 1H, CH), 4.01 (m, 1H, $1CH_2$), 3.92 (m, 1H, $1CH_2$), 2.33 (s, 6H, $2CH_3$), 2.30 (s, 3H, $1CH_3$), 1.84 (m, 2H, $1CH_2$), 1.60 (m, 1H, 1CH), 1.02 (d, J(H,H) = 6 Hz, 3H, $1CH_3$), 1.00 (d, J(H,H) = 6 Hz, 3H, $1CH_3$), 0.92 (s, 9H, $3CH_3$), 0.14 (s, 6H, $2CH_3$). ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 158.8, 139.9, 135.4, 131.0 (2C), 129.5 (2C), 61.9, 59.1, 50.3, 46.2, 36.2, 25.1 (3C), 24.2, 22.0, 20.9, 19.8, 17.7 (2C), −4.3, −6.4 (2C). ^{19}F NMR (376.5 MHz, CD_3COCD_3): $\delta = -73.0$ (d, J(F,P) = 708.2 Hz). ^{31}P NMR (162 MHz, CD_3COCD_3): $\delta = -143.0$ (sept, J(P,F) = 708.2 Hz). HRMS (FAB), calc. for C^+: $C_{24}H_{43}N_2OSi$: 403.3145, found: 403.3151.

8.7. Typical procedure for conjugate addition to enones at room temperature

A dry Schlenk tube was charged with copper source (0.02 mmol, 0.02 equiv.), imidazolinium salt (0.03 mmol, 0.03 equiv.) and cyclododecane (internal standard) and dry solvent (3 mL) was added. The resulting solution was cooled to 0 °C, upon which *n*BuLi (50 μL, 0.08 mmol, 0.08 equiv. as 1.6 M solution in hexanes) was added. After stirring for 5 min, diethyl zinc (1.5 mL, 1.5 mmol, 1.5 equiv. as 1 M solution in hexanes) was added and the solution was warmed up to room temperature. The mixture was stirred for 5 min before adding the substrate (1 mmol). The advancement of the reaction was followed by gas chromatography or by TLC (hexane/diethyl ether 8/2). The

reaction was quenched by the addition of HCl (5 mL of a 1 M aqueous solution). The resulting mixture was stirred until clear and enantiomeric excess could be measured directly using chiral gas chromatography. The product could be extracted with diethyl ether, washed with brine, dried over $MgSO_4$ and the solvent concentrated in vacuo to yield the crude product, which could be purified by flash column chromatography (hexane/diethyl ether 8/2) to provide the pure product.

9. Supplementary materials

Crystallographic data for the structural have been deposited with the Cambridge Crystallographic Data Center, CCDC Nos. 250113 and 249960 for compounds **6a** and **6b**, respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

Acknowledgments

This work was supported by the CNRS and the Ministère de la Recherche et de la Technologie (Grant to H.C.). We thank Pr. A. Alexakis for helpful discussion, for the generous gift of CuTC complex and also for the CPG analysis of 3(*R*)-methylcyclohexanone.

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