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Design of Chiral Hydroxyalkyl- and Hydroxyarylazolinium Salts as New Chelating Diaminocarbene Ligand Precursors Devoted to Asymmetric Copper-Catalyzed Conjugate Addition

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The design and the synthesis of a set of new chiral hydroxyalkyl- and hydroxyaryl-chelating diaminocarbene ligands is reported. Comparative catalytic studies show the importance of the scaffold design around the NHC unit to obtain a high enantiocontrol in Cu-catalyzed asymmetric conjugate addition (ACA). Whereas low selectivities are observed when the stereogenic centre is placed within the N-heterocyclic ring, an interesting match effect can be observed when central chirality is located within both of the two side chains, which enables up to 92 % *ee* in the catalysis reaction.

Introduction

Discovered by Öfele[1] and Wanzlick[2] in 1968 and isolated in the free state by Arduengo[3] in 1991, N-heterocyclic carbene (NHC) ligands have been widely and successfully employed in organometallic catalysis.[4] Because of their exceptional capacity to establish strong bonds with metal centers, these ligands will likely supplant phosphorus-based ligands, which will allow a remarkable acceleration in a large number of chemical transformations[4] such as olefin metathesis, carbon–carbon and carbon–nitrogen cross-coupling reactions, as well as hydrogenation and hydrosilylation. Logically, the exploration of these valuable ligands for asymmetric catalysis has been reported.[5] Among the growing number of chiral NHC ligands based on a wide range of structures, a new promising class has recently emerged: the hydroxy-chelating diaminocarbenes (Figure 1).

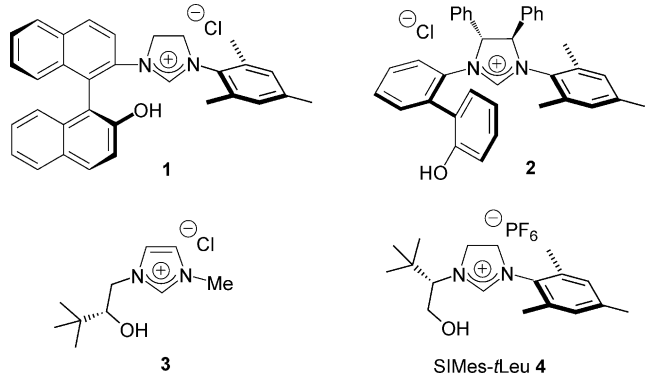

Figure 1. Hydroxyl-chelating azolium salts used in asymmetric transformations as diaminocarbene ligand precusors.

Pioneering in this field are Hoveyda and coworkers with the chiral binaphthol-NHC precursor **1**,[6] and more recently with the readily available biphenol-NHC precursor **2**[7] based on the 1,2-diphenylethylenediamine skeleton as a source of chirality.

These NHC precursor ligands were successfully used in asymmetric metathesis,[7,8] in enantioselective allylic substitution[9] and also in asymmetric conjugate addition (ACA).[10] Another class such as the alkyloxy-NHCs derived from the (*tert*-butyl-hydroxy-ethyl)azolium salts **3** and **4** have independently been reported by Arnold[11] and our group.[12] Whereas the Arnold's imidazolium salt **3** gives a moderate selectivity in the copper-catalyzed conjugate ad-

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dition of diethylzinc to 2-cyclohexenone (51%ee), our hydroxyalkyl salt **4**, containing the stereogenic centre in the α-position, afforded higher selectivities (89% *ee*). Moreover, **4** is extremely suitable for the formation of *all*-chiral quaternary centres using Grignard reagents toward various 3-substituted-2-cyclohexenones (up to 96% *ee*)[13] or 3-allyl-substituted 2-cyclohexenones where a remarkable regiodivergent addition (1,4 vs. 1,6) occurred (up to 98% *ee*).[14] To improve the potential of this promising class of chelating NHCs, we have kept on making efforts to improve the scaffold's design, and we have attempted to compare two different types of NHC precursors: on one hand, the imidazolinium salts **5** and **8** exhibit a stereogenic centre within the N-heterocycle, and on the other hand, the azolium salts **6**–**7** and **9** bear a stereogenic centre within the chelating side chain (Figure 2). The activity and the selectivity of these new ligands, which are readily available from chiral amino acids or α-methylarylamines, have been evaluated in the asymmetric copper-catalyzed conjugate addition of organometallic reagents to several cyclic enones.

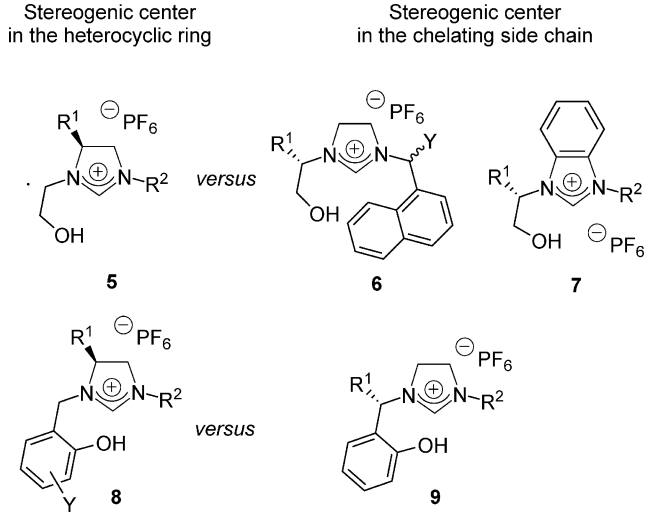


Figure 2. Proposed design study of chelating diaminocarbene ligands for asymmetric conjugate addition (ACA).

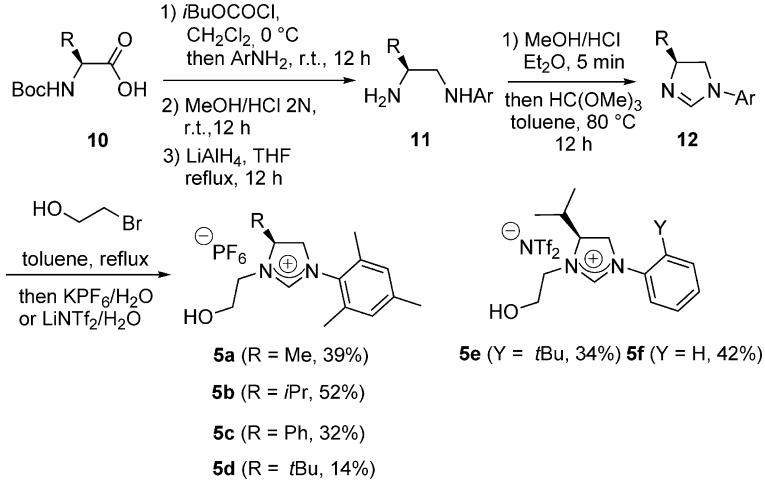
Results and Discussion

Synthesis of Hydroxyalkyl-Imidazolinium Salts 5

The synthetic routes to enantiopure imidazolinium salts **5** are shown in Scheme 1.[15] In the first approach, the mixed-anhydride-mediated coupling between commercially available Boc-protected amino acids **10** and substituted anilines led to the formation of the corresponding amides. After the removal of the carbamate by anhydrous hydrochloric acid in methanolic solution, the amide function was reduced with $LiAlH_4$ to afford, after chromatography, the diamines **11** in excellent yields. At this point, formation of the diamine chlorhydrate followed by condensation of trimethyl orthoformate in toluene resulted in the formation of enantiopure imidazolines **12**. Finally, the desired chiral hydroxyalkyl-imidazolinium salts **5** were obtained by an alkylation with 2-bromoethanol followed by an anion exchange with KPF_6 or $LiNTf_2$. Through this methodology, six optically pure hydroxyalkyl-imidazolinium salts, **5a**–**5f**, were isolated after purification on silica gel with moderate to good overall yields.

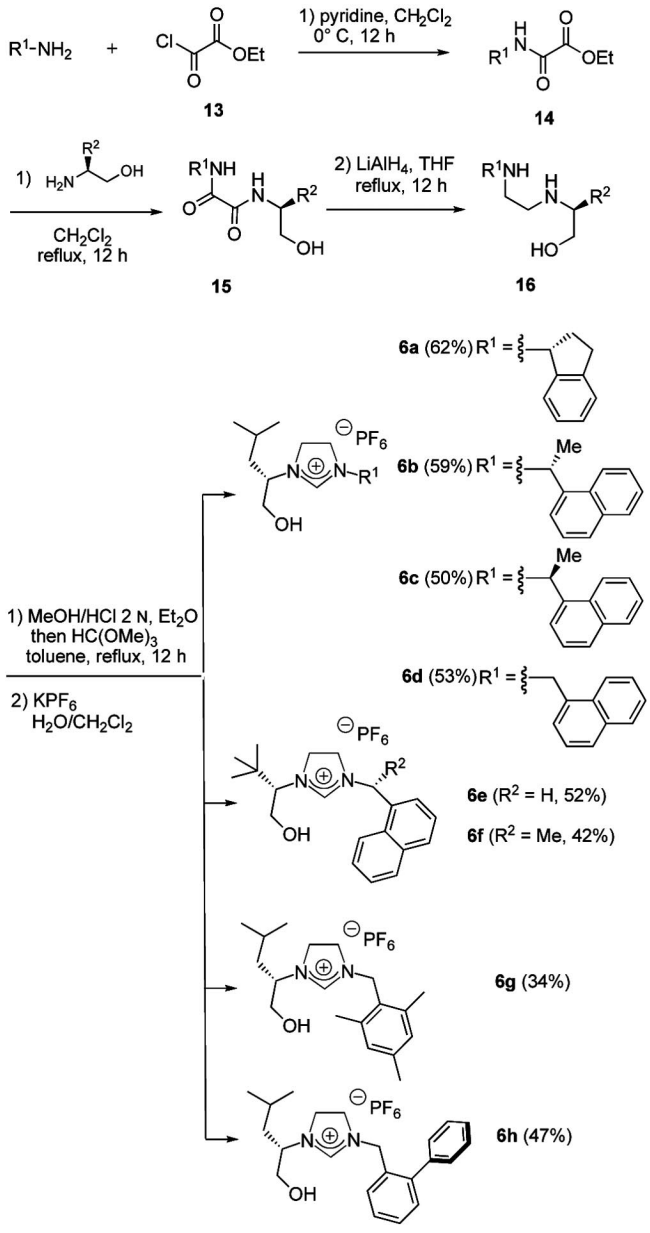
Synthesis of Hydroxyalkyl-Imidazolinium Salts 6

The five-step synthetic procedure for the family of hydroxyalkyl salts **6** is shown in Scheme 2.[12] Primary amines such as 1-naphthylmethylamine, (*R*)- or (*S*)-α-methyl-1-naphthylmethylamine or (*R*)-indolamine were condensed onto commercially available ethyloxalylchloride **13** to give the corresponding oxanilic diethylesters **14**. The reaction of enantiopure (*R*)-leucinol or (*R*)-*tert*-leucinol with **14** in refluxing dichloromethane provided the oxalamides **15** in pure form without any purification. After reduction of the diamide function by lithium and aluminium hydride, the resulting diamines **16** were successively treated with a 2 N anhydrous HCl solution in methanol and then with trimethyl orthoformate in refluxing toluene to provide the desired imidazolinium chloride salts. Finally, the chloride salts



Scheme 1. Synthesis of hydroxyalkyl-imidazolinium salts **5a**–**5f**.

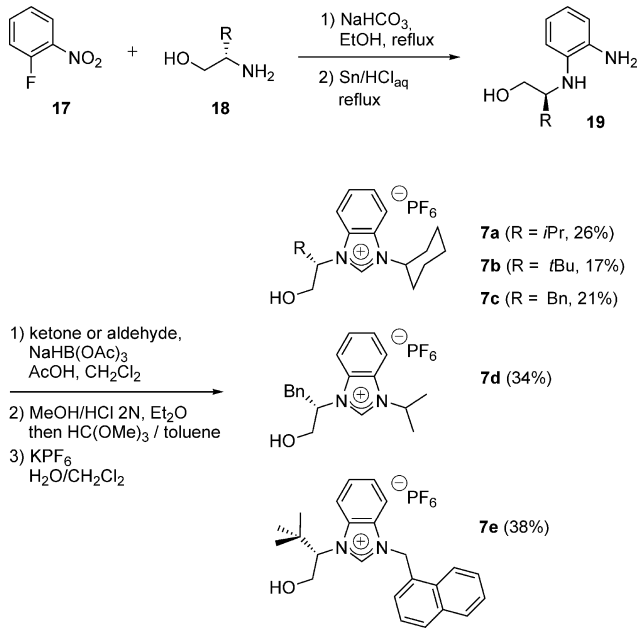
were treated with KPF_6 to give the corresponding hexafluorophosphate hydroxyalkyl-imidazolinium salts **6a**–**6h** in pure form and good overall yields ranging from 34 to 62%.



Scheme 2. Synthesis of hydroxyalkyl-imidazolinium salts **6a**–**6h**.

Synthetic Route to Hydroxyalkyl-Benzimidazolium Salts 7

As shown in Scheme 3, the synthesis of compounds **7** started by reacting enantiopure β-amino alcohols **18** with 2-fluoronitrobenzene **17** in dichloromethane at reflux. After the reduction of the nitro group with tin in refluxing 3 M hydrochloric aqueous solution, the expected monoalkylated diamines **19** were isolated in moderate to good yields. Alkylations of the free amine were performed by a reductive amination step using cyclohexanone, acetone or 1-naphthaldehyde. The resulting dialkylated diamines were then converted into their hydrochlorides before the cyclization step, which was performed in the presence of trimethyl orthoformate in refluxing toluene. Finally, anionic metathesis with potassium hexafluorophosphate led to the desired hexafluorophosphate benzimidazolium salts **7a**–**7e** in good overall yields ranging from 17 to 38% over five steps.

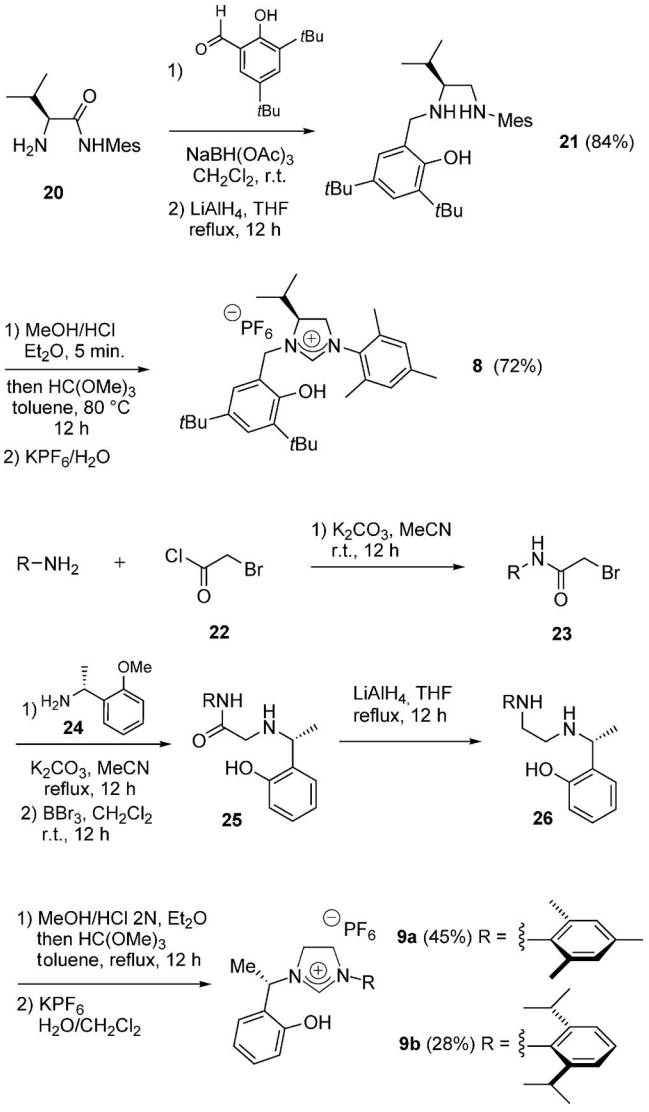


Scheme 3. Synthesis of hydroxyalkyl-benzimidazolium salts **7a**–**7e**.

Synthesis of Benzyloxy-Imidazolinium Salt 8 and (*R*)-α-Methylbenzyloxy-Imidazolinium Salts 9

In comparison with the hydroxyalkyl-imidazolinium salts **5**, the synthetic route to the benzyloxy-imidazolinium salts **8** was slightly adapted in order to accommodate the introduction of the chelating hydroxyaryl fragment (Scheme 4). Reductive amination performed on amine **20** in the presence of 2-hydroxy-3,5-*tert*-butyl-benzaldehyde followed by reduction of the amide function gave the corresponding diamines **21** in good yields (84%). The cyclization process followed by the aforementioned anionic metathesis step yielded the expected hexafluorophosphate salts **8** in 72% yield. For the synthesis of the (*R*)-α-methylbenzyloxy-chelating imidazolinium salts **9**, the synthetic route developed for hydroxyalkyl-imidazolinium salt **6** was not suitable (see Scheme 2). Indeed, the steps for both the reduction of oxalamide **15** and the methyl phenyl ether cleavage gave moderate yields. Consequently, the expected salts **9** were isolated in lower overall yields (20%). We therefore decided to develop a more suitable synthetic route, as shown in Scheme 4. The condensation of various substituted anilines or 1-naphthylmethylamine onto the commercial 2-bromoethanoyl chloride **22** afforded the 2-bromoacetamides **23**. Alkylation of the enantiopure α-methyl-2-methoxybenzylamine **24** by **23** in acetonitrile over 12 h at reflux, followed by methyl phenyl ether cleavage in the presence of BBr_3 in

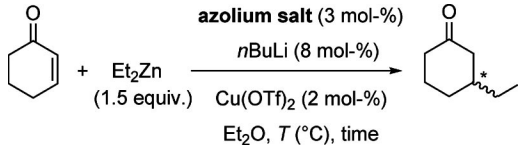
dichloromethane at room temperature, afforded the corresponding 2-aminoacetamides **25** in good isolated yields after column chromatography. Reduction of amides **25** to the corresponding diamines **26** was achieved by the use of lithium and aluminium hydride in refluxing tetrahydrofuran. Finally, the usual cyclization procedure led to the isolation of the expected hexafluorophosphate imidazolinium salts **9** in good overall yields ranging from 28 to 45% over six steps.



Scheme 4. Synthetic routes to benzyloxy-imidazolinium salts **8** and **9a**–**9b**.

Activity and Selectivity of Hydroxy-Chelating Azolium Salts 5–9 in Copper-Catalyzed Asymmetric Conjugate Addition (ACA)

With these different hydroxy-chelating azolium salts **5**–**9** in our hands, we then evaluated both their activity and selectivity in copper-catalyzed asymmetric conjugate addition (ACA). For this purpose, we chose the addition of diethylzinc to 2-cyclohexenone as the model reaction (Scheme 5). The hydroxyalkyl-NHC–copper catalytic species was prepared in situ by a double deprotonation of the hydroxyalkyl-azolium salt (3 mol-%) with *n*-BuLi in the presence of copper(II) triflate (2 mol-%) in anhydrous diethyl ether. The addition of the diethylzinc leads to the formation of the catalytic copper(I) species[16] that can react with the substrate.



Scheme 5. Model of asymmetric conjugate addition studied with azolium salt NHC precursors.

Evaluation of Azolium Salt NHC Precursors 5a–5f Bearing a Stereogenic Center on the NHC Ring

As shown in Table 1, a complete conversion occurred after 4 h at –50 °C in diethyl ether when the azolium salts **5a**–**5h** were used, which shows the efficiency of the NHC–Cu catalytic entities. As expected, a very low enantioselectivity was observed with the salt **5a** bearing a methyl substituent at the stereogenic center (entry 1, 29%), while the use of a more sterically hindered moiety such as isopropyl **5b** or phenyl **5c** resulted in an improvement of the enantiocontrol (entries 2 and 3, 50 and 45% *ee*, respectively). The best selectivity was obtained with the salt **5d** containing the more bulky *tert*-butyl group (entry 4, 60% *ee*). Interestingly, a higher *ee* (entry 5, 66%) could be reached when the reaction was performed at room temperature.

Table 1. Evaluation of the hydroxyalkyl-imidazolinium salts **5a**–**5f** bearing a stereogenic center within the N-heterocyclic ring for the conjugate addition of diethylzinc to 2-cyclohexenone.[a]

Entry	Ligand	Temp. [°C]	Time [h][b]	*ee* [%][c]
1	**5a**	–50	4	29 (*R*)
2	**5b**	–50	4	50 (*R*)
3	**5c**	–50	4	45 (*R*)
4	**5d**	–50	4	60 (*R*)
5	**5d**	+20	1	66 (*R*)
6	**5e**	–50	4	41 (*R*)
7	**5f**	–50	4	40 (*R*)

[a] Conditions: **5** (3 mol-%), *n*BuLi (8 mol-%), $Cu(OTf)_2$ (2 mol-%), 2-cyclohexenone (1 mmol), Et_2Zn (1.5 mmol), Et_2O. [b] Time necessary to reach complete conversion. [c] Determined by chiral GC analysis (Lipodex E).

To explain these moderate enantioselectivities, we supposed that the three-dimensional unit was too far from the metallic center and was therefore unable to correctly transfer the chiral information to the substrate during the addition. One alternative to improve the chiral induction within this class of NHC precursors may lie in the possibility of locking the N substituents in fixed conformations, as recently reported by Grubbs and coworkers[19] (Figure 3). Indeed, the stereogenic centers on the N heterocycle were

able to efficiently transfer the chiral information directly from the α-position of the nitrogen atom through steric repulsions with the *ortho* substituents in the aromatic unit. Under these constrained structural conditions, only one atropisomer could be formed as a result of *anti* relationships. We therefore investigated the synthesis of some chelating homologues of these NHC precursors, bearing only one chiral center at the β-position of the *N*-aryl substituent instead of the usual α-position (Figure 3). However, the crucial point was to prove that a similar transfer of chirality could be reached with the azolium salt **5e** bearing a 2-*tert*-butylphenyl group.

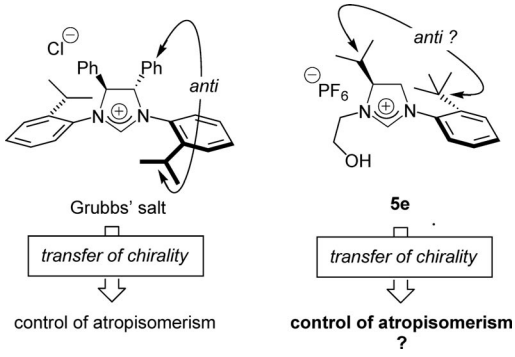


Figure 3. Proposed transfer of chirality for hydroxyalkyl-imidazolinium **5e**.

A preliminary study of the transfer of the chiral information from the stereogenic center at the β-position to the aryl substituent of the nitrogen was realized on the L-proline scaffold.[17] As shown in Figure 4, when a small aryl substituent such as a methyl was used, the steric hindrance was too small to generate a preferentially locked conformation.

Therefore, the cyclization of diamine **27** gave both conformers **28a** (*syn*) and **28b** (*anti*) as a result of the rapid internal rotation of the *o*-tolyl unit around the C–N axis. We were surprised to observe these two conformers in the same unit cell, as shown in a single-crystal diffraction study.[18] On the other hand, in the case of diamine **29**, bearing the more bulky *tert*-butyl group, the rate of the C–N internal rotation is significantly reduced by steric repulsions, which promotes the unique formation of *anti*-atropisomer **30**, as expected. Once this concept was validated, we then applied it through the formation of the hydroxyalkyl-chelating imidazolinium salt homologue **5e**. Regarding the structure and atom connectivity from a single-crystal diffraction study of the chiral imidazoline **12e**, the direct precursor of salt **5e**, we were enthusiastic to observe the expected *anti* relationship between the *ortho*-positioned *tert*-butyl group and the isopropyl stereogenic center (Figure 5). Therefore, we anticipated that the alkylation of imidazoline **12e** by bromoethanol (see Scheme 1) should give the locked conformer **5e** with the aforementioned *anti* relationship. Unfortunately, attempts to crystallize the isolated salt **5e** in order to confirm its solid-state structure failed.

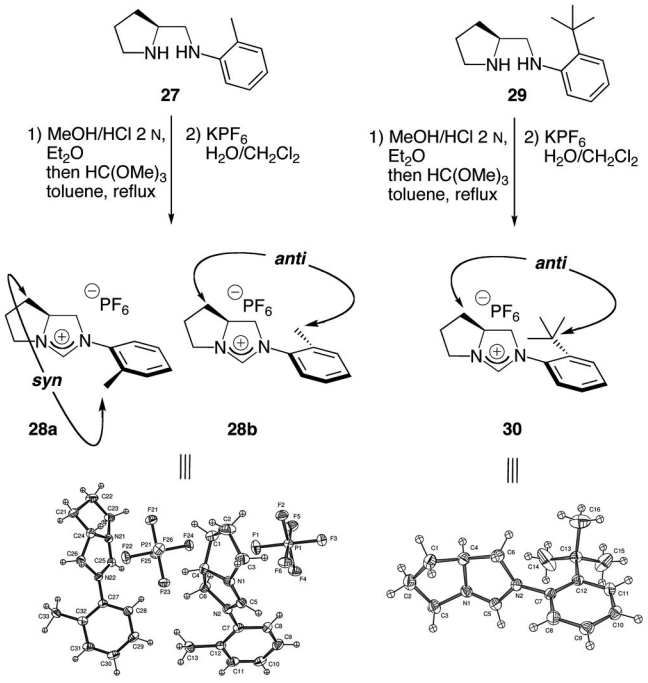


Figure 4. Preliminary studies of the transfer of chiral information from the β-position of the nitrogen through steric repulsions.

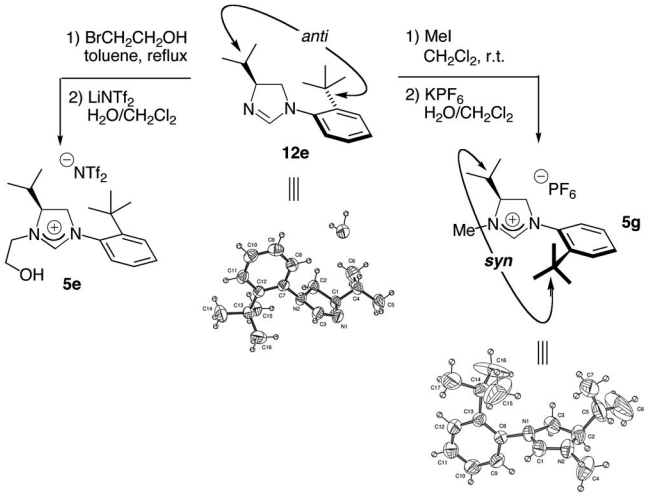
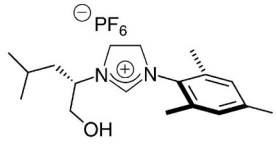


Figure 5. Solid-state structures of chiral imidazoline **12e** and chiral imidazolinium salt **5g** obtained by methylation of imidazoline **12e** (PF_6^- counter anions have been omitted for clarity).

With this postulated atropisomer salt in our hands, we then decided to evaluate it in ACA while hoping to observe an increase in the asymmetric induction. As shown in Table 1 (entries 6), salt **5e** gave lower enantioselectivity (41% *ee*) than the homologous mesityl-N-substituted salt **5b** (50% *ee*). Additionally, a similar selectivity (40% *ee*) was observed with the phenyl analog **5f** (entry 7). These low selectivities might have arisen from the inability of the stereogenic centre to transfer the chiral information from the β-position of the N atom through steric repulsion. As we were not able to obtain the crystal structure of **5e**, a structural elucidation of the structurally similar salt **5g** was at-

tempted. The latter was obtained in an excellent yield as white crystals through the alkylation of the imidazoline **12e** by methyl iodide and anionic metathesis exchange. This time, **5g** could be crystallized and its solid-state structure was then confirmed by a single-crystal diffraction study (Figure 5). We were astonished to observe in salt **5g** a *syn* relationship between the *tert*-butyl and the isopropyl groups although they exhibited an *anti* relation in the imidazoline precursor **12e** (Figure 5). This could arise from an inversion of conformation during the nitrogen quaternarisation process. An alternate explanation could be that both conformers (*anti* and *syn*) exist in solution but that only one (not the same for **5e** and **5g**) crystallizes. This last hypothesis might explain the low selectivities observed within this family of ligands. Several ab initio calculations are currently underway in order to find a clear-cut explanation.

After the failure to reach an efficient enantiocontrol in the ACA reaction using the hydroxyalkyl-chelating NHC **5** bearing the stereogenic center within the heterocyclic unit, we focused our attention on the azolium salts **6** and **7** bearing the stereogenic center within the chelating side chain. We anticipated that an increase in the steric hindrance around the metal–NHC environment would lead to an improvement in the enantioselectivity in relation to that previously obtained with SIMes-leucinol salts **4a** (86% *ee*).[12]



SIMes-Leu **4a**

Two approaches were attempted. Firstly, with hydroxyalkyl salts **6**, we envisioned that a better enantiodiscrimination could be reached by replacing the nonchelating mesityl N substituent group by a chiral bulky fragment. The salt **6a**, bearing an (*R*)-indane moiety, was first evaluated, but only a decrease of selectivity was observed (Table 2, entry 1, 80% *ee*), which was probably due to a less favorable steric hindrance. Salts **6b** and **6c**, bearing a chiral α-methylnaphthyl group, were therefore evaluated. A significant match/mismatch effect between the two chiral centers was observed (entries 2–3). Whereas the (*S*)-α-methylnaphthyl **6c** gave an *ee* value similar to the one obtained with the indane salt **6a** (entry 2, 82%), a doping of enantioselectivity was observed with the matched ligand **6b** (entry 3, 90%). With respect to ligand design, we clearly demonstrated that the orthogonally oriented mesityl group cannot be regarded as the ideal bulky unit for the application of NHC ligands in ACA of 2-cyclohexenone with Et_2Zn. In addition, we were astonished to obtain a similar doping effect in the case of salt **6d** in which the methyl stereogenic center is absent (entry 4, 92% *ee*). This important result suggests that an optimal conformation of the naphthyl unit should be reached in the case of the ligands bearing either no α-methyl or the (*R*)-α-methyl group so that the steric repulsions between the enone entity and the naphthyl fragment could be minimized. Consequently, the rate of transfer of the ethyl group to the enone would increase in comparison with the case of the initial ligand **4a** bearing a mesityl group, to lead to a better *ee* (Figure 6). Inversely, in the case of the ligand bearing the (*S*)-methylnaphthyl entity, a conformation is adopted which brings some unfavorable steric interactions, which leads to a significant decrease of the selectivity.

Table 2. Evaluation of the hydroxyalkyl-azolinium salts **6** and **7** bearing a stereogenic center within the chelating side chain for the conjugate addition of diethylzinc to 2-cyclohexenone.[a]

Entry	Ligand	Time [h][b]	*ee* [%][c]
1	**6a**	1	80 (*R*)
2	**6b**	1	90 (*R*)
3	**6c**	1	82 (*R*)
4	**6d**	1	92 (*R*)
5	**6e**	1	80 (*R*)
6	**6f**	1	68 (*R*)
7	**6g**	1	63 (*R*)
8	**6h**	1	89 (*R*)
9	**7a**	1	19 (*R*)
10	**7b**	6	26 (*S*)
11	**7c**	1	25 (*R*)
12	**7e**	2	0

[a] Conditions: **6** or **7** (3 mol-%), *n*BuLi (8 mol-%), $Cu(OTf)_2$ (2 mol-%), 2-cyclohexenone (1 mmol), Et_2Zn (1.5 mmol), Et_2O. [b] Time necessary to reach complete conversion. [c] Determined by chiral GC analysis (Lipodex E).

In addition to these successful ligands, the two other substituted benzyl-based ligands **6g** and **6h** were evaluated (entries 7–8). Whereas the mesitylenemethyl salt **6g** gave a significantly lower enantioselectivity (63%), a good *ee* value was reached with salt **6h**, bearing a phenyl substituent in the *ortho* position to the benzyl unit (89%, entry 7). This result is similar to the *ee* value obtained with the naphthylmethyl salt **6d**. Unexpectedly, when the isobutyl stereogenic group within the chelating hydroxyalkyl side chain of **6d** was replaced by the bulkier *tert*-butyl group (salts **6e** and **6f**), the selectivity was not increased, but on the contrary was diminished to 80% and 68% respectively (entries 5–6). It arises from these results that the presence of a bulky group at the stereogenic center of both the chelating *and* the nonchelating side chains is unfortunately incompatible with the goal of improving the selectivity.[19]

Secondly, we tested the bicyclic NHC-based ligands **7**, where the presence of a bicyclic NHC system in which the NHC ring is fused together with an aromatic group, was expected to freeze the conformation and also engender steric repulsions, which in turn were expected to improve the selectivity. Unfortunately, very poor *ee* values were obtained with ligands **7a**–**7e**, regardless of the nature of both the stereogenic center of the chelating arm and the nonchelating N substituent (entries 9–12). The absence of selectivity observed in the case of **7e** could arise from the formation of π-stacking interactions between the naphthyl and the phenyl groups, which would lead to a conformation where the naphthyl group is far from the reacting center.[20]

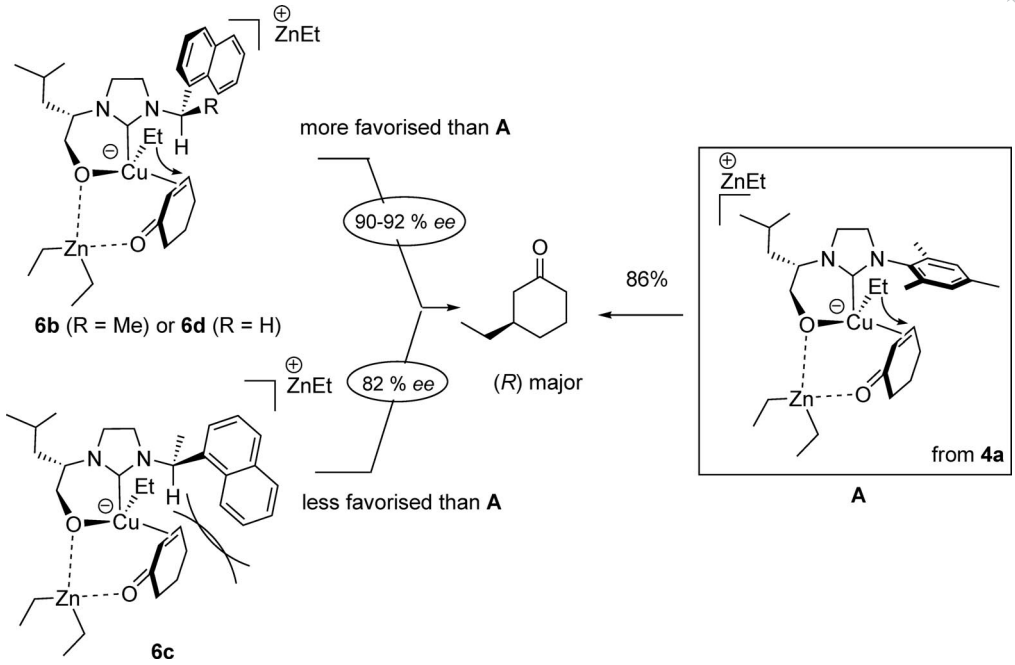


Figure 6. Proposed intermediates for the match/mismatch effect observed with NHCs derived from **6b** and **6c**.

In the concept of architectural design of NHCs dedicated to improving the selectivity of ACA, a different approach was then attempted with imidazolinium salts **8** and **9**, bearing a hydroxyphenyl-chelating function. Based on Hoveyda's results with salt **2**, where the effects of axial and atropisomeric chiralities were combined, we tried to check if the chirality transfer from the isopropyl group in **8** could also lead to interesting selectivities (Figure 7).

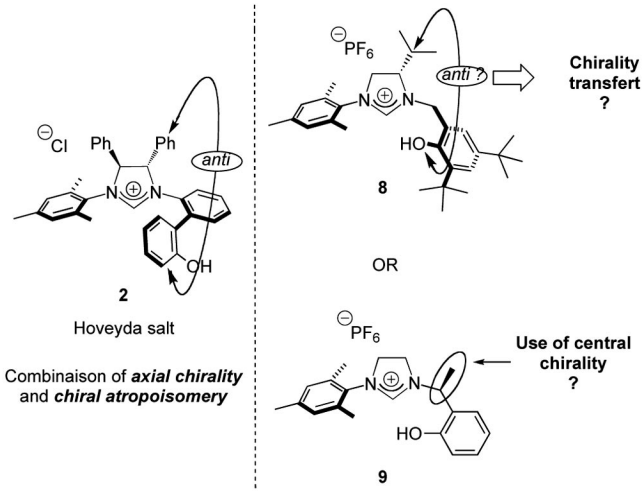


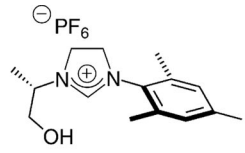
Figure 7. New architectural design related to the hydroxyphenyl-chelating function in the imidazolinium salts **8** and **9**.

Unfortunately, very low *ee* values could be reached, independent of the conditions used (Table 3 entries 1–2). Therefore, we tried to evaluate the efficiency of salts **9**, where the atropisomer is replaced by a central chiral center in the hydroxyaryl-chelating arm. Thus salts **9a** and **9b** were tested (entries 3–6), and an encouraging result (78% ee) was obtained when **9a** and *t*BuOK were employed. As a similar *ee* value (78%) was obtained with SIMes-Ala **4b** derived from alaninol,[12] which bears a methyl group on the chiral carbon, it can be anticipated that a high *ee* should be reached if an analog of **9** bearing a more bulky group (e.g. *i*Bu or *t*Bu) on the chiral carbon is used.[21]

Table 3. Evaluation of the benzyloxy-imidazolinium salts **8** and **9** in the conjugate addition of diethylzinc to 2-cyclohexenone.[a]

Entry	Ligand	Base	Time [h][b]	*ee* [%][c]
1	**8**	*n*BuLi	1	20 (*S*)
2	**8**	*t*BuOK	2	8 (*S*)
3	**9a**	*n*BuLi	1	64 (*S*)
4	**9a**	*t*BuOK	1	78 (*S*)
5	**9b**	*n*BuLi	1	11 (*S*)
6	**9b**	*t*BuOK	2	4 (*S*)

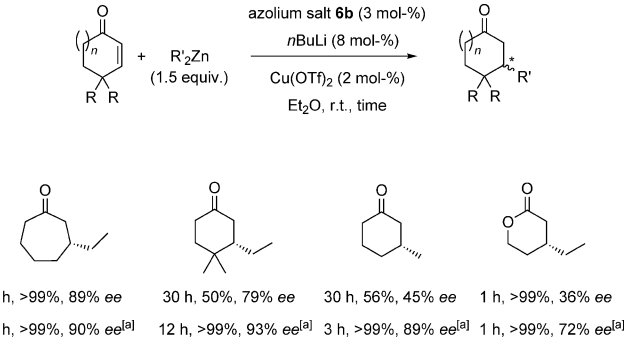
[a] Conditions: **8** or **9** (3 mol-%), base (8 mol-%), $Cu(OTf)_2$ (2 mol-%), 2-cyclohexenone (1 mmol), Et_2Zn (1.5 mmol), Et_2O. [b] Time necessary to reach complete conversion. [c] Determined by chiral GC analysis (Lipodex E).



SIMes-Ala **4b**

Finally, various enones were tested towards the addition, at room temperature, of Et_2Zn in the presence of the Cu–**6b** catalyst (Scheme 6). Although better *ee* values were obtained with ligands **6c** or **6d** in the reaction of cyclohexenone, **6b** was selected because it was more chemically stable than **6c** and **6d**, which thus led to more reproducible results. The results were compared with those obtained

using salt **4a**.[12] Except for the case of 2-cycloheptenone, where similar and good *ee* values were obtained (89%), it is worth noting that lower enantioselectivities and in some cases a lower reactivity were observed with salt **6b**.



Scheme 6. Scope of ACA substrates with the new hydroxyalkyl-NHC precursor **6b** derived from leucinol and (*S*)-α-methylnaphthylamine.[a] Results obtained with SIMes-leu **4a** (see ref.[12]).

Conclusions

In conclusion, we have reported the development of several classes of chiral hydroxyalkyl- and hydroxyphenyl-chelating NHC ligands using amino acids as a chiral pool. The employed modular syntheses allowed the isolation of a few small libraries of chiral hydroxyalkyl- or hydroxyaryl-azolium hexafluorophosphate salts. Structural parameters were also studied through the determination of structure–activity relationships in the enantioselective copper-catalyzed conjugate addition of diethylzinc to 2-cyclohexenone. Whereas all the NHC salt precursors bearing the stereogenic center within the N-heterocyclic ring gave disappointing results (salts **5** and **8**), good to high enantioselectivities (up to 92% *ee*) were obtained at room temperature with hydroxyalkyl- and hydroxyphenyl-imidazolinium salt **6** and **9** where the chiral centre is located on the chelating side chain. The presence of an additional phenyl unit, fused together with the N-heterocycle, led only to a decrease of the selectivity (benzymidazolium salts **7**). However, except for 2-cycloheptenone (89%ee), we were disappointed to observe lower enantioselectivities when different cyclic enones were screened as substrates with the best-identified hydroxyalkyl-NHC precursor **6b** (ranging from 36 to 79%). Further work is currently in progress in our laboratory aiming at the introduction of bulkier chiral groups into the hydroxyphenyl-chelating side chain in salt **9a**. We expect that a significant improvement of the enantiomeric excesses in ACA will be reached. Extending the use of this family of ligands to other enantioselective metal-catalyzed transformations dealing with palladium or copper will be intensively studied.

Experimental Section

General: ^{1}H (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 nuclei other than ^{1}H. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, ^{1}H: δ = 7.27 ppm, ^{13}C: δ = 77.0 ppm and $(CD_3)_2CO$: ^{1}H: 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 Reichert microscope and were uncorrected. Optical rotations were recorded using a Perkin–Elmer 341 polarimeter. 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 – H*P*$\bar{1}$, 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. All nonaqueous reactions were performed under an argon atmosphere using oven-dried glassware. Toluene and trimethyl orthoformate 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/MeOH 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 was performed on Merck silica gel $60F_{254}$ plates, and the plates were visualized under UV light. Chromatographic purifications were performed on a column with 230–400 mesh silica gel (Merck 9385) using the indicated solvent system.

General Procedure for the Synthesis of Hydroxyalkyl-Imidazolinium Salts 5: To a solution of imidazole **12** (1 mmol) in acetone (1 mL) was added 2-bromoethanol (5 mmol, 2 equiv.). The reaction mixture was stirred at reflux for 48 h. After being cooled to room temperature, $LiNTf_2$ (1.2 mmol, 1.2 equiv.) or KPF_6 (1.2 mmol, 1.2 equiv.) was added at room temperature. After 30 min of stirring, the solvent was removed under reduced pressure. The residue was dissolved in dichloromethane, and the organic layer was washed with brine, dried with $MgSO_4$ and concentrated in vacuo. Purification by flash chromatography (CH_2Cl_2/acetone, 3:1) afforded the corresponding imidazolium salt **5**.

General Procedure for the Synthesis of Hydroxyalkyl-Imidazolinium 6 and -Benzimidazolium Salts 7: To a solution of diamine (1 equiv.) in dry diethyl ether (5 mL/mmol) was added dropwise at 0 °C a 2 N HCl/MeOH solution (1 equiv.). A white precipitate was rapidly formed. After 10 min of stirring, the solvent was removed in vacuo to afford the corresponding chlorhydrate of diamine. This salt was dissolved in dry toluene (3 mL/mmol), and trimethyl orthoformate (10 equiv.) was added. The reaction mixture was stirred at 100 °C overnight. After being cooling to room temperature, the solvents were evaporated in vacuo, and the imidazolinium chloride was dissolved in distilled water. The aqueous layer was washed with ethyl acetate before the addition of potassium hexafluorophosphate (1.3 equiv.). After 20 min of stirring at room temperature, the imidazolinium or benzimidazolium salt was extracted with dichloromethane. The organic layer was washed with brine, dried with magnesium sulfate and concentrated under reduced pressure. The resulting crude product was purified by flash chromatography on sil-

ica gel (dichloromethane/acetone, 9:1) to afford the expected azolium salt.

General Procedure for the Synthesis of Hydroxyaryl-Imidazolinium Salts 8, 9: To a solution of diamine (1 equiv.) in dry diethyl ether (5 mL/mmol) was added dropwise, at 0 °C, a 2 N anhydrous HCl/MeOH solution (2 equiv.). A white precipitate was rapidly formed. After 10 min of strirring, the solvent was evaporated to afford the corresponding chlorhydrate of diamine. This salt was dissolved in dry toluene (3 mL/mmol), and trimethyl orthoformate (10 equiv.) was added. The reaction mixture was stirred for 90 min at 100 °C. After being cooling to room temperature, the solvents were evaporated in vacuo, and the imidazolinium chloride was dissolved in distilled water. The aqueous layer was washed with ethyl acetate before with the addition of potassium hexafluorophosphate (1.3 equiv.). After 20 min of stirring at room temperature, the imidazolinium salt was extracted with dichloromethane. The organic layer was washed with brine, dried with magnesium sulfate and concentrated under reduced pressure. The resulting crude product was purified by flash chromatography on silica gel (dichloromethane/acetone, 9:1) to afford the expected azolium salt.

Selected Salts

(4*S*)-1-(2-*tert*-Butylphenyl)-4,5-dihydro-3-(2-hydroxyethyl)-4-isopropyl-1*H*-imidazol-3-ium Bis(trifluoromethylsulfonyl)azanide (5e): Slightly yellow oil (352 mg, 62%). $[\alpha]_D^{20}$ = +16.8 (*c* = 1, chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (s, 1 H, H-13), 7.55 (d, ^3J = 7.4 Hz, 1 H, H-9), 7.43 (t, ^3J = 7.4 Hz, 1 H, H-7), 7.32 (t, ^3J = 7.4 Hz, 1 H, H-8), 7.18 (d, ^3J = 7.4 Hz, 1 H, H-6), 4.62 (dt, ^3J = 4.8, 11.8 Hz, 1 H, H-2), 4.30 (t, ^3J = 11.8 Hz, 1 H, H-1), 3.95 (t, ^3J = 11.8 Hz, 1 H, H-1′), 3.85 (m, 3 H, H-14, H-15), 3.64 (m, 1 H, H-14′), 2.39 (m, 1 H, H-3), 1.39 (s, 9 H, H-12), 1.07 (d, ^3J = 7.0 Hz, 3 H, H-4), 1.01 (d, ^3J = 7.0 Hz, 3 H, H-4′) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2 (1 C, C-13), 147.4 (1 C, C-5), 134.1 (1 C, C-10), 130.7 (1 C, C-9), 129.5 (1 C, C-7), 128.8 (1 C, C-8), 128.1 (1 C, C-6), 119.1 (q, $^1J_{C,F}$ = 321.2 Hz, 1 C), 65.0 (1 C, C-2), 57.3 (1 C, C-1), 54.8 (1 C, C-15), 47.7 (1 C, C-14), 35.6 (1 C, C-11), 31.7 (3 C, C-12), 26.7 (1 C, C-3), 17.7 (1 C, C-4), 14.4 (1 C, C-4′) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –73.0 (d, $^1J_{F,C}$ = 321.2 Hz, 6 F) ppm. HRMS calcd. for $C_{18}H_{29}N_2O$ $[M]^+$ 289.2280; found 289.2280.

3,4-Dihydro-5-[(1*S*)-1-(hydroxymethyl)-3-methylbutyl]-2-[(1*R*)-1-(naphth-1-yl)ethyl]-1*H*-imidazolin-1-ium Hexafluorophosphate (6b): White solid (160 mg, 65% yield). $[\alpha]_D^{20}$ = –44.0 (*c* = 1, acetone); m.p. 101 °C. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.99 (m, 4 H, H-20, H_{ar}), 7.68 (td, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1 H, H_{ar}), 7.61 (m, 2 H, H_{ar}), 7.53 (m, 1 H, H_{ar}), 5.63 (q, ^3J = 6.8 Hz, 1 H, H-1), 3.89 (m, 4 H, H-13, H-14), 3.75 (dd, ^2J = 12.0 Hz, ^3J = 3.6 Hz, 1 H, H-16), 3.56 (dd, ^2J = 12.0, ^3J = 8.8 Hz, 1 H, H-16), 1.93 (d, ^3J = 6.8 Hz, 3 H, H-12), 1.53 (m, 3 H, H-15, H-17), 1.36 (m, 1 H, H-18), 0.98 (d, ^3J = 6.8 Hz, 3 H, H-19), 0.92 (d, ^3J = 6.4 Hz, 3 H, H-19) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 156.7 (1 CH, C-20), 134.6 (1 C, C_{ar}), 132.6 (1 C, C_{ar}), 130.8 (1 C, C_{ar}), 130.4 (1 CH, C_{ar}), 129.8 (1 CH, C_{ar}), 127.9 (1 CH, C_{ar}), 126.8 (1 CH, C_{ar}), 125.9 (1 CH, C_{ar}), 124.6 (1 CH, C_{ar}), 122.1 (1 CH, C_{ar}), 61.4 (1 CH_2, C-16), 59.8 (1 CH, C-15), 54.8 (1 CH, C-1), 47.4 (1 CH_2, C-13), 45.1 (1 CH_2, C-14), 36.9 (1 CH_2, C-17), 25.1 (1 CH, C-18), 22.7 (1 CH_3, C-19), 21.9 (1 CH_3, C-19), 19.4 (1 CH_3, C-12) ppm. ^{31}P NMR (162 MHz, CD_2Cl_2): δ = –143.1 (sept, 1 P, ^1J = 711.5 Hz) ppm. ^{19}F NMR (376 MHz, CD_2Cl_2): δ = –73.1 (d, 6 F, ^1J = 711.5 Hz) ppm. HRMS (Maldi/TOF): calcd. for $C_{21}H_{29}N_2O$ $[M]^+$ 325.2280; found 325.2287. $C_{21}H_{29}F_6N_2OP$ (470.43): calcd. C 53.62, H 6.21, N 5.95; found C 53.15, H 6.15, N 6.17.

3,4-Dihydro-5-[(1*S*)-1-(hydroxymethyl)-3-methylbutyl]-2-(naphth-1-ylmethyl)-1*H*-imidazolin-1-ium Hexafluorophosphate (6d): White solid (270 mg, 55% yield). $[\alpha]_D^{20}$ = 2 (*c* = 0.1, acetone); m.p. 62 °C. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.86 (m, 3 H, H_{ar}), 7.81 (s, 1 H, H-19), 7.56 (ddd, ^3J = 6.9 Hz, ^3J = 8.4 Hz, ^4J = 1.5 Hz, 1 H, H_{ar}), 7.50 (ddd, ^3J = 6.9 Hz, ^3J = 8.0 Hz, ^4J = 1.2 Hz, 1 H, H_{ar}), 7.45 (m, 2 H, H_{ar}), 4.98 (s, 2 H, H-1), 3.82 (m, 2 H, H-12), 3.76 (m, 2 H, H-13), 3.67 (m, 1 H, H-14), 3.59 (dd, ^2J = 12.0 Hz, ^3J = 3.5 Hz, 1 H, H-15), 3.44 (dd, ^2J = 12.0 Hz, ^3J = 8.7 Hz, 1 H, H-15), 2.68 (s broad, 1 H, OH), 1.40 (m, 2 H, H-16), 1.21 (m, 1 H, H-17), 0.83 (d, ^3J = 6.5 Hz, 3 H, H-18), 0.80 (d, ^3J = 6.5 Hz, 3 H, H-18) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 157.9 (1 CH, C-19), 134.8 (1 C, C_{ar}), 131.8 (1 C, C_{ar}), 131.2 (1 C, C_{ar}), 130.0 (1 CH, C_{ar}), 129.5 (1 CH, C_{ar}), 128.3 (1 CH, C_{ar}), 128.1 (1 CH, C_{ar}), 127.4 (1 CH, C_{ar}), 126.3 (1 CH, C_{ar}), 123.1 (1 CH, C_{ar}), 61.8 (1 CH_2, C-15), 60.0 (1 CH, C-14), 50.8 (1 CH_2, C-1), 48.9 (1 CH_2, C-12), 46.0 (1 CH_2, C-13), 37.7 (1 CH_2, C-16), 25.4 (1 CH, C-17), 23.1 (1 CH_3, C-18), 22.3 (1 CH_3, C-18) ppm. ^{31}P NMR (162 MHz, CD_2Cl_2): δ = –144.3 (sept, ^1J = 712.4 Hz, 1 P) ppm. ^{19}F NMR (376 MHz, CD_2Cl_2): δ = –71.4 (d, ^1J = 712.4 Hz, 6 F) ppm.

3,4-Dihydro-5-[(1*S*)-1-(hydroxymethyl)-2-dimethylpropyl]-2-[(1*R*)-1-(naphth-1-yl)ethyl]-1*H*-imidazolin-1-ium Hexafluorophosphate (6f): White solid (667 mg, 42% yield). $[\alpha]_D^{20}$ = –41.0 (*c* = 1, acetone); m.p. 65 °C. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.87 (m, 4 H, H-20, H_{ar}), 7.52 (m, 3 H, H_{ar}), 7.40 (d, *J* = 6.4 Hz, 1 H, H_{ar}), 5.55 (q, ^3J = 6.8 Hz, 1 H, H-1), 3.82 (m, 6 H, H-13, H-14, H-15, H-16), 3.44 (dd, ^2J = 10.4 Hz, ^3J = 3.6 Hz, 1 H, H-16), 2.45 (s broad, 1 H, OH), 1.82 (d, ^3J = 6.8 Hz, 3 H, H-12), 0.90 (s, 9 H, H-18) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 157.87 (CH, C-20), 134.56 (C, C_{ar}), 132.51 (C, C_{ar}), 130.75 (C, C_{ar}), 130.41 (CH, C_{ar}), 129.78 (CH, C_{ar}), 127.91 (CH, C_{ar}), 126.86 (CH, C_{ar}), 125.85 (CH, C_{ar}), 124.50 (CH, C_{ar}), 122.05 (CH, C_{ar}), 70.75 (CH, C-15), 57.91 (CH_2, C-16), 54.82 (CH, C-1), 48.13 (CH_2, C-13), 47.56 (CH_2, C-14), 33.82 (C, C-17), 27.44 (CH_3, C-18), 19.36 (CH_3, C-12) ppm. ^{31}P NMR (162 MHz, CD_2Cl_2): δ = –144 (sept, ^1J = 710.3 Hz, 1 P) ppm. ^{19}F NMR (376 MHz, CD_2Cl_2): δ = –72.5 (d, ^1J = 710.3 Hz, 6 F) ppm. HRMS (Maldi/TOF): calcd. for $C_{21}H_{29}N_2O$ $[M]^+$ 325.2280; found 325.228. $C_{21}H_{29}F_6N_2OP$ (470.43): calcd. C 53.62, H 6.21, N 5.95; found C 53.06, H 6.24, N 5.67.

2-Cyclohexyl-5-[(1*S*)-1-(hydroxymethyl)-3-methylpropyl]-1*H*-benzimidazol-1-ium Hexafluorophosphate (7a): White solid (500 mg, 39% yield). $[\alpha]_D^{20}$ = –7.0 (*c* = 1, acetone); m.p. 132 °C. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.94 (s, 1 H, H-17), 7.76 (m, 2 H, H_{ar}), 7.64 (m, 2 H, H_{ar}), 4.47 (tt, ^3J = 3.7 Hz, ^3J = 12.0 Hz, 1 H, H-1), 4.34 (ddd, ^2J = 6.3 Hz, ^3J = 9.7 Hz, ^3J = 3.2 Hz, 1 H, H-14), 4.16 (ddd, ^2J = 6.3 Hz, ^3J = 11.6 Hz, ^3J = 4.9 Hz, 1 H, H-14), 3.99 (ddd, ^3J = 12.4 Hz, ^3J = 4.9 Hz, ^3J = 3.2 Hz, 1 H, H-13), 2.77 (m, 1 H, OH), 2.45 (m, 1 H, H-15), 2.23 (d, ^3J = 12.2 Hz, 2 H, H_{cy}), 1.88 (m, 4 H, H_{cy}), 1.73 (d, ^3J = 12.8 Hz, 1 H, H_{cy}), 1.56 (m, 2 H, H_{cy}), 1.34 (dt, ^2J = 13.2 Hz, ^3J = 3.6 Hz, 1 H, H_{cy}), 1.27 (dt, ^2J = 13.2 Hz, ^3J = 3.6 Hz, 1 H, H_{cy}), 1.10 (d, ^3J = 6.6 Hz, 3 H, H-16), 0.74 (d, ^3J = 6.7 Hz, 3 H, H-16) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 137.0 (1 CH, C-17), 131.4 (1 C, C_{ar}), 130.0 (1 C, C_{ar}), 126.7 (1 CH, C_{ar}), 126.5 (1 CH, C_{ar}), 113.1 (1 CH, C_{ar}), 112.8 (1 CH, C_{ar}), 66.5 (1 CH, C-13), 60.1 (1 CH_2, C-14), 58.2 (1 CH, C-1), 31.7 (1 CH_2, C_{cy}), 31.6 (1 CH_2, C_{cy}), 28.9 (1 CH, C-15), 24.6 (1CH_2, C_{cy}), 24.5 (1 CH_2, C_{cy}), 24.0, (1 CH_2, C_{cy}), 18.6 (1 CH_3, C-16), 18.5 (1 CH_3, C-16) ppm. ^{31}P NMR (162 MHz, CD_2Cl_2): δ = –144.4 (sept, ^1J = 710.6 Hz, 1 P) ppm. ^{19}F NMR (376 MHz, CD_2Cl_2): δ = –72.5 (d, 6 F, ^1J = 710.6 Hz). HRMS (Maldi/TOF): calcd. for $C_{18}H_{27}N_2O$ $[M]^+$ 287.2123, found 287.2122. $C_{18}H_{27}F_6N_2OP$ (432.38): calcd. C 50.00, H 6.29, N 6.48; found C 49.72, H 6.11, N 6.43.

5-[(1*S*)-1-(Hydroxymethyl)-3-dimethylpropyl]-2-(naphth-1-yl)-1*H*-benzimidazol-1-ium Hexafluorophosphate (7e): White solid (55 mg, 81% yield). $[\alpha]_D^{20}$ = +1.2 (*c* = 1, acetone); m.p. 123 °C. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.83 (s, 1 H, H-22), 7.91 (m, 2 H, H_{ar}), 7.75 (m, 2 H, H_{ar}), 7.60 (m, 3 H, H_{ar}), 7.49 (m, 2 H, H_{ar}), 7.44 (d, ^3J = 8.2 Hz, 1 H, H_{ar}), 7.38 (dd, ^3J = 7.0 Hz, ^4J = 1.0 Hz, 1 H, H_{ar}), 6.07 (s, 2 H, H-1), 4.50 (dd, ^3J = 8.4 Hz, ^3J = 4.2 Hz, 1 H, H-18), 4.15 (m, 2 H, H-19), 2.48 (s broad, 1 H, OH), 0.86 (s, 9 H, H-21) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 140.5 (1 CH, C-22), 138.4 (1 C, C_{ar}), 134.4 (1 C, C_{ar}), 132.8 (1 C, C_{ar}), 132.2 (1 C, C_{ar}), 131.3 (1 C, C_{ar}), 131.0 (1 CH, C_{ar}), 130.8 (1 CH, C_{ar}), 129.8 (1 CH, C_{ar}), 128.2 (1 CH, C_{ar}), 128.1 (1 CH, C_{ar}), 128.0 (1 CH, C_{ar}), 127.6 (1 CH, C_{ar}), 127.1 (1 CH, C_{ar}), 125.9 (1 CH, C_{ar}), 122.1 (1 CH, C_{ar}), 113.8 (1 CH, C_{ar}), 60.5 (1 CH_2, C-19), 50.1 (1 CH_2, C-1), 35.3 (1 CH, C-18), 30.3 (1 C, C-20), 27.3 (3 CH_3, C-21) ppm. ^{31}P NMR (162 MHz, CD_2Cl_2): δ = –144.6 (sept, ^1J = 710.6 Hz, 1 P) ppm. ^{19}F NMR (376 MHz, CD_2Cl_2): δ = –72.7 (d, ^1J = 710.6 Hz, 6 F) ppm. HRMS (Maldi/TOF): calcd. for $C_{24}H_{27}N_2O$ $[M]^+$ 359.2123, found 359.2119. $C_{24}H_{27}F_6N_2OP$ (504.45): calcd. C 57.14, H 5.39, N 5.55; found C 57.22, H 5.44, N 5.13.

5-[3,5-Di(*tert*-butyl)methyl-2-hydroxyphenyl]-3,4-dihydro-4-isopropyl-2-mesityl-1*H*-imidazolin-1-ium Hexafluorophosphate (8): White solid (816 mg, 67% yield). $[\alpha]_D^{20}$ = –2.5 (*c* = 1, acetone); m.p. 95 °C. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.79 (s, 1 H, H-7), 7.32 (d, ^4J = 2.4 Hz, 1 H, H-18), 7.08 (d, ^4J = 2.4 Hz, 1 H, H-14), 6.91 (s, 2 H, H-3), 4.88 (d, ^2J = 14.4 Hz, 1 H, H-12), 4.40 (d, ^2J = 14.4 Hz, 1 H, H-12), 4.25 (m, 1 H, H-9), 3.92 (dd, ^2J = 11.9 Hz, ^3J = 4.0 Hz, 1 H, H-8), 3.77 (dd, ^2J = 11.9 Hz, ^3J = 9.5 Hz, 1 H, H-8), 2.40 (m, 1 H, H-10), 2.22 (s, 3 H, H-5), 2.15 (s, 6 H, H-6), 1.07 (s broad, 1 H, OH), 1.36 (s, 9 H, H-17), 1.22 (s, 9 H, H-21), 0.97 (d, ^3J = 6.8 Hz, 3 H, H-11), 0.87 (d, ^3J = 7.0, 3 H, H-11) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 158.6 (1 CH, C-7), 151.3 (1 C, C_{ar}), 144.7 (1 C, C_{ar}), 141.2 (1 C, C_{ar}), 136.9 (1 C, C_{ar}), 130.7 (1 C, C_{ar}), 130.4 (2 CH, C_{ar}), 129.8 (2 C, C_{ar}), 126.6 (1 CH, C_{ar}), 126.1 (1 CH, C_{ar}), 120.2 (1 C, C_{ar}), 65.4 (1 CH, C-9), 51.4 (1 CH_2, C-8), 48.0 (1 CH_2, C-12), 34.5 (1 C, C-20), 31.6 (3 CH_3, C-17), 30.4 (3 CH_3, C-21), 27.3 (1 CH, C-10), 21.1 (2 CH_3, C-11), 18.1 (1 CH_3, C-5), 14.5 (2 CH_3, C-6) ppm. ^{31}P NMR (162 MHz, CD_2Cl_2): δ = –710.2 Hz) ppm. ^{19}F NMR (376 MHz, CD_2Cl_2): δ = –72.7 (d, ^1J = –710.2 Hz, 6 F) ppm. HRMS (Maldi/TOF): calcd. for $C_{30}H_{45}N_2O$ $[M]^+$ 449.3532, found 449.3509. $C_{30}H_{45}F_6N_2OP$ (594.66): calcd. C 60.59, H 7.63, N 4.71; found C 60.97, H 7.69, N 4.75.

4,5-Dihydro-3-[1-(2-hydroxyphenyl)ethyl]-1-mesityl-1*H*-imidazolin-1-ium Hexafluorophosphate (9a): White solid (472 mg, 60% yield). $[\alpha]_D^{20}$ = –32.2 (*c* = 1, acetone); m.p. 183 °C. ^{1}H NMR [400 MHz, $(CD_3)_2CO$]: δ = 8.78 (s, 1 H, H-7), 7.52 (dd, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1 H, H_{ar}), 7.47 (m, 2 H, H_{ar}), 7.04 (s, 2 H, H-3), 7.18–7.08 (td, ^3J = 7.2 Hz, ^4J = 1.8 Hz, 1 H, H_{ar}), 5.37 (q, ^3J = 7.1 Hz, 1 H, H-10), 4.30 (m, 3 H, H-8, H-9), 4.09 (m, 1 H, H-9), 2.33 (s, 6 H, H-5), 2.30 (s, 3 H, H-1), 1.87 (d, ^3J = 7.1 Hz, 3 H, H-11) ppm. ^{13}C NMR [100 MHz, $(CD_3)_2CO$]: δ = 159.4 (1 CH, C-7), 157.2 (1 C, C-17), 141.2 (1 C, C_{ar}), 137.2 (2 C, C_{ar}), 132.7 (1 C, C_{ar}), 131.3 (1 CH, C_{ar}), 130.8 (2 CH, C_{ar}), 129.0 (1 CH, C_{ar}), 124.2 (1 C, C_{ar}), 120.8 (1 CH, C_{ar}), 117.7 (1 CH, C_{ar}), 55.3 (1 CH, C-10), 51.8 (1 CH_2, C-8), 47.9 (1 CH_2, C-9), 21.4 (1 CH_3, C-11), 18.0 (2 CH_3, C-5), 15.1 (1 CH_3, C-1) ppm. ^{31}P NMR [162 MHz, $(CD_3)_2CO$]: δ = –143.0 (sept, ^1J = –706.3 Hz, 1 P) ppm. ^{19}F NMR [376 MHz, $(CD_3)_2CO$]: δ = –75.8 (d, ^1J = –707.3 Hz, 6 F) ppm. HRMS (Maldi/TOF): calcd. for $C_{20}H_{25}N_2O$ $[C]^+$ 309.1967, found 309.1973.

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12e: $C_{16}H_{24}N_2 \cdot 1/2H_2O$, M_r = 506.76, monoclinic, *C*2, *a* = 23.516(5), *b* = 6.124(9), *c* = 12.726(2) Å, *V* = 1587(2) Å^{-3}, *Z* = 4, d_X = 1.061 Mg m^{-3}, λ(Mo-K_α) = 0.71073 Å, μ = 0.64 cm^{-1}, *F*(000) = 556, *T* = 293 K. The sample (0.55 × 0.45 × 0.40 mm) was studied with an automatic CAD4 NONIUS diffractometer with graphite-monochromatized Mo-K_α radiation. The cell parameters were obtained by fitting a set of 25 high-θ reflections. The data collection ($2\theta_{max}$ = 54°, scan $\omega/2\theta$ = 1, t_{max} = 60 s, *hkl* range: *h* 0,30, *k* 0,7, *l* –16,14) gave 1935 unique reflections from which 1494 had $I > 2.0\sigma(I)$. After Lorenz and polarization corrections, the structure was solved with SIR-97, which revealed the non-hydrogen atoms of the compound. After anisotropic refinement, a Fourier difference map revealed many hydrogen atoms. The whole structure was refined with SHELXL97 by the full-matrix least-squares techniques (use of *F* square magnitude); *x*, *y*, *z*, β_{ij} for C, O and N atoms, *x*, *y*, *z* in riding mode for H atoms; 168 variables and 1494 observations; calcd. $w = 1/[\sigma^2(F_o^2) + (0.14P)^2 + 0.35P]$ where $P = (F_o^2 + 2F_c^2)/3$ with the resulting R = 0.064, R_w = 0.178 and S_w = 1.034 (residual $\Delta\rho \leq 0.18$ e Å^{-3}).

28: $C_{13}H_{17}N_2 \cdot 2PF_6$, M_r = 346.26, orthorhombic, $P2_12_12_1$, *a* = 12.8406(4), *b* = 13.1442(4), *c* = 17.3827(4) Å, *V* = 2933.8(1) Å^{-3}, *Z* = 8, d_X = 1.568 Mg m^{-3}, λ(Mo-K_α) = 0.71073 Å, μ = 2.5 cm^{-1}, *F*(000) = 1424, *T* = 120 K. The sample (0.22 × 0.12 × 0.08 mm) was studied on a NONIUS Kappa CCD with graphite-monochromatized Mo-K_α radiation. The cell parameters were obtained with Denzo and Scalepack with 10 frames (ψ rotation: 1° per frame). The data collection ($2\theta_{max}$ = 54°, 173 frames via 1.8° ω rotation and 30 s per frame, *hkl* range: *h* –16,16, *k* –17,17, *l* –22,22) gave 37066 reflections. The data reduction with Denzo and Scalepack led to 6697 independent reflections from which 5029 had $I > 2.0\sigma(I)$. The structure was solved with SIR-97, which revealed the non-hydrogen atoms of the molecule. After anisotropic refinement, many hydrogen atoms were found with a Fourier difference map. The whole structure was refined with SHELXL97 by the full-matrix least-squares techniques (use of *F* square magnitude); *x*, *y*, *z*, β_{ij} for P, F, C and N atoms, *x*, *y*, *z* in riding mode for H atoms; 404 variables and 5029 observations with $I > 2.0\sigma(I)$; calcd. $w = 1/[\sigma^2(F_o^2) + (0.066P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$ with the resulting R = 0.045, R_w = 0.103 and S_w = 1.034, $\Delta\rho < 0.27$ e Å^{-3}.

30: $C_{16}H_{23}N_2 \cdot PF_6$, M_r = 388.33, orthorhombic, $P2_12_12_1$, *a* = 11.2502(2), *b* = 11.8523(2), *c* = 13.3138(3) Å, *V* = 1775.27(6) Å^{-3}, *Z* = 4, d_X = 1.453 Mg m^{-3}, λ(Mo-K_α) = 0.71073 Å, μ = 2.16 cm^{-1}, *F*(000) = 808, *T* = 120 K. The sample (0.45 × 0.32 × 0.30 mm) was studied with a NONIUS Kappa CCD with graphite-monochromatized Mo-K_α radiation. The cell parameters were obtained with Denzo and Scalepack with 10 frames (ψ rotation: 1° per frame). The data collection ($2\theta_{max}$ = 54°, 160 frames via 2.0° ω rotation and 12 s per frame, *hkl* range: *h* –14,14, *k* –15,15, *l* –17,17) gave 19823 reflections. The data reduction with Denzo and Scalepack led to 4075 independent reflections from which 3556 had $I > 2.0\sigma(I)$. The structure was solved with SIR-97, which revealed the non-hydrogen atoms of the structure. After anisotropic refinement, many hydrogen atoms were found with a Fourier difference map. The whole structure was refined with SHELXL97 by the full-matrix least-square techniques (use of *F* square magnitude); *x*, *y*, *z*, β_{ij} for P, C, O and F atoms, *x*, *y*, *z* in riding mode for H atoms; 227 variables and 3556 observations with $I > 2.0\sigma(I)$; calcd. $w = 1/[\sigma^2(F_o^2) + (0.084P)^2 + 1.17P]$ where $P = (F_o^2 + 2F_c^2)/3$ with the resulting R = 0.047, R_w = 0.124 and S_w = 1.061, $\Delta\rho < 0.73$ e Å^{-3}. The absolute configuration was unambiguously confirmed [Flack parameter: –0.02(9)].

5g: $C_{17}H_{27}N_2 \cdot PF_6$, M_r = 404.37, monoclinic, $P2_1$, *a* = 9.1683(2), *b* = 20.2115(7), *c* = 10.8752(3) Å, β = 101.599(2)°, *V* = 1974.1(1) Å^{-3}, *Z* = 4, d_X = 1.361 Mg m^{-3}, λ(Mo-K_α) = 0.71073 Å, μ = 1.97 cm^{-1},

$F(000)$ = 848, T = 120 K. The sample (0.35 × 0.32 × 0.12 mm) was studied on a NONIUS Kappa CCD with graphite-monochromatized Mo-K_α radiation. The cell parameters were obtained with Denzo and Scalepack with 10 frames (ψ rotation: 1° per frame). The data collection ($2\theta_{max}$ = 54°, 278 frames via 1.5° ω rotation and 10 s per frame, *hkl* range: *h* –11,11, *k* –26,26, *l* –14,14) gave 35228 reflections. The data reduction with Denzo and Scalepack led to 8929 independent reflections from which 5857 had $I > 2.0\sigma(I)$. The structure was solved with SIR-97, which revealed the non-hydrogen atoms of the molecule. After anisotropic refinement, many hydrogen atoms were found with a Fourier difference map. The whole structure was refined with SHELXL97 by the full-matrix least-squares techniques (use of F square magnitude); x, y, z, β_{ij} for P, C, F and N atoms, x, y, z in riding mode for H atoms; 470 variables and 5857 observations with $I > 2.0\sigma(I)$; calcd. $w = 1/[\sigma^2(F_o^2) + (0.15P)^2 + 0.48P]$ where $P = (F_o^2 + 2F_c^2)/3$ with the resulting R = 0.078, R_w = 0.204 and S_w = 1.044, $\Delta\rho < 0.81$ e Å^{-3}.

CCDC-227053 (for **12e**), -714010 (for **28**), -714009 (for **30**) and -227054 (for **5g**) contain the crystallographic data for this article. 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 www: http://www.ccdc.cam.ac.uk).

Supporting Information (see also the footnote on the first page of this article): Experimental procedures for the synthesis of ligands **5**, **6**, **7**, **8** and **9** and their full characterization data.

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[19] The remarkable benefit of using a bulkier *tert*-butyl group on the chelating side chain for the ligand **6** has been clearly demonstrated during the enantioselective formation of the *all*-quaternary carbon center derived from the addition of 3-substituted cyclohexenone, see ref.[13]
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