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Short Synthesis of Chiral 4-Substituted (*S*)-Imidazolinium Salts Bearing Sulfonates and Their Use in γ-Selective Reactions of Allylic Halides with Grignard Reagents

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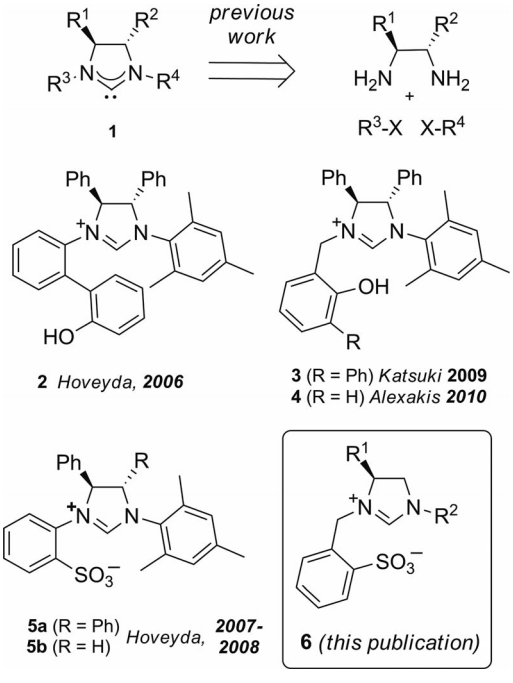
A one-pot reaction of Boc-protected amino alcohols and 2-sulfobenzoic anhydride followed by the addition of a wide variety of primary amines has allowed rapid access to diverse libraries of amidosulfonates 1,2-$C_6H_4(SO_3^-)$($COCHR^1$-$CH_2NH_2^+R^2$) (R^1 = Bn, *i*Pr, Ph; R^2 = aryl, CHMePh, 1-adamantyl), of which two examples have been characterised by X-ray crystallography. These reactions proceed by S_N2 opening of unisolated oxazoline intermediates. The amidosulfonates have been converted to imidazolinium sulfonate zwitterions (*N*-heterocyclic carbene precursors) in a two-step process, which involved reduction with BH_3·SMe_2 and cyclisation with $HC(OEt)_3$. Two examples (R^1 = Bn, R^2 = 2,6-*i*PrC_6H_3 and R^1 = *i*Pr, R^2 = 3,5-$Me_2C_6H_3$) have been crystallographically characterised, the latter as a PF_6 salt. The imidazolinium sulfonate zwitterions (1 mol-%) catalysed additions of RMgBr (R = alkyl) to (*E*)-ArC(R)=$CHCH_2$Br (R = H, Me). Additions to cinnamyl bromides showed high γ (S_N2') selectivity (up to 18.4:1) and provided significantly enantiomerically enriched products (up to 82 % *ee*).

Introduction

N-Heterocyclic carbene ligands (NHCs) are of high utility in contemporary catalytic chemistry.[1] These strongly retained spectator ligands can provide metal catalysts of exceptional activity and selectivity for a wide range of transformations, which include metathesis,[2] highly efficient palladium-catalysed C–C cross-coupling[3] and conjugate addition.[4] Free NHCs are themselves also active organocatalysts due to their powerful σ donor characteristics.[5] The majority of such NHCs are accessed by deprotonation of imidazolium-based precursor salts and in some cases both these and their metal complexes are commercially available. Chiral 4,5-substituted imidazoliniums **1** (Scheme 1) have proved very useful ligand motifs in modern asymmetric catalysis, especially those species that contain additional tethering donor groups.[6] Thus, Buchwald–Hartwig coupling has allowed the relatively efficient construction of **2**–**5a**[7] from commercial (*R*,*R*)-1,2-diphenylethylenediamine. However, in generalising such ligand families, quite significant synthetic effort can be involved in the preparation of parent chiral diamines that are not comercially available. For example, of the eight steps required to access highly useful **5b**, seven are to prepare the precursor diamine from 2,4,6-$Me_3C_6H_2NH_2$.[8] Very few publications deal with the formation of imidazolium NHC precursors by S_N2 substitution reactions using simple amines.[9] We conceived that



Scheme 1. Recent examples of NHC ligand precursors related to this work.

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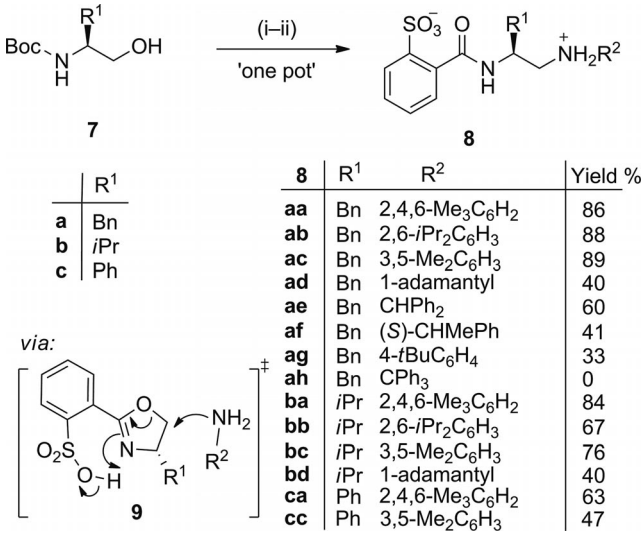
homologues of **5b**, i.e. **6**, might be rapidly prepared from commercial chiral, enantiopure 1,2-amino alcohol derivatives by such a route to provide an attractive addition to the ligand family shown in Scheme 1 and allow comparison of their efficacy in asymmetric catalysis.

Results and Discussion

Amido Sulfonic Acid Synthesis

We have previously demonstrated the multistep preparation of the amido sulfonic acids **8** from commercial Boc-protected amino alcohols **7** by isolation of oxazolines **9** and their subsequent reaction with two highly nucleophilic amines R^2NH_2 (R^2 = Bn, 2-$C_{10}H_7CH_2$) (Scheme 2).[10] We reasoned that **8** would be an efficient precursor to sulfonated chiral diamines for the synthesis of **6** if: (i) **9** did not have to be isolated, (ii) the opening of **9** showed very high generality for any primary amine and (iii) **8** could be reduced chemoselectively. Although it was anticipated that less nucleophilic amines would participate in such acid-induced oxazoline opening reactions, highly hindered anilines (which are likely to be the most suited to subsequent catalytic ligand applications) might be poor candidates for such S_N2 reactions. However, we were gratified to find that the opening of **9** is very general indeed. Even rather hindered anilines react smoothly with in situ-generated **9** to lead cleanly to **8** in moderate to very good yields (40–89%) under simple Dean–Stark conditions. A selection of these are shown in Scheme 2. For the most hindered systems, prolonged heating was required (up to 7 d but with acceptable yields) and amines with lower boiling points were avoided to prevent them from azeotroping out of the reaction mixture.



	R^1
a	Bn
b	*i*Pr
c	Ph

8	R^1	R^2	Yield %
aa	Bn	2,4,6-$Me_3C_6H_2$	86
ab	Bn	2,6-*i*$Pr_2C_6H_3$	88
ac	Bn	3,5-$Me_2C_6H_3$	89
ad	Bn	1-adamantyl	40
ae	Bn	$CHPh_2$	60
af	Bn	(*S*)-CHMePh	41
ag	Bn	4-*t*BuC_6H_4	33
ah	Bn	CPh_3	0
ba	*i*Pr	2,4,6-$Me_3C_6H_2$	84
bb	*i*Pr	2,6-*i*$Pr_2C_6H_3$	67
bc	*i*Pr	3,5-$Me_2C_6H_3$	76
bd	*i*Pr	1-adamantyl	40
ca	Ph	2,4,6-$Me_3C_6H_2$	63
cc	Ph	3,5-$Me_2C_6H_3$	47

Scheme 2. Synthesis of amido sulfonic acids. (i) 2-Sulfobenzoic anhydride, PhCl, 170 °C, 2–3 h. (ii), R^2NH_2, PhCl, 170 °C, 17 h–7 d.

The chemistry in Scheme 2 was extended to other hindered, nonaromatic amines including 1-adamantylamine (**8ad**, **8bd**). The only amines studied that did not undergo the S_N2 reaction cleanly were 2,4,6-tri-*tert*-butylaniline (which underwent subsequent acid-promoted stepwise de-*tert*-butylation to give mixtures, from which the only isolable compound was the 4-*tert*-butylaniline derivative **8ag**) and tritylamine, which was the only amine tried that gave no reaction. Compounds **8** were often crystalline, but required primary isolation by chromatography (CH_2Cl_2/MeOH, 19:1) to remove minor polar byproducts. Amides **8** eluted in a well defined manner and were often strongly fluorescent; the slightly visible bands simplified their chromatographic isolation. Typically **8** were obtained as colourless foams or crystals, both of which commonly contained occluded solvents. The connectivity in **8** was confirmed by X-ray crystallography, which also revealed the zwitterionic nature of these compounds. An extensive array of intra- and intermolecular hydrogen bonding was observed in two of the derivatives (Figures 1 and 2), which led to monomers or dimers in the solid state.

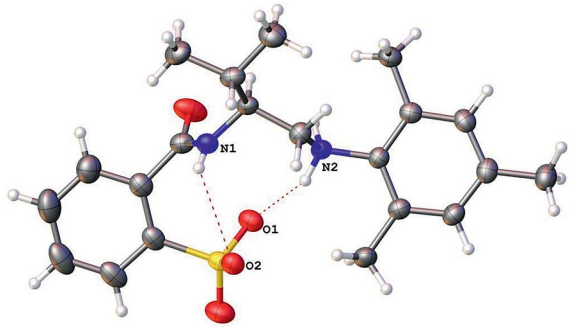


Figure 1. Molecular structure of **8ba**·$^1/_3$EtOH. Selected intramolecular hydrogen bonding interactions [Å]: N(1)···O(2) 3.1047(19), N(2)···O(1) 2.8384(19).

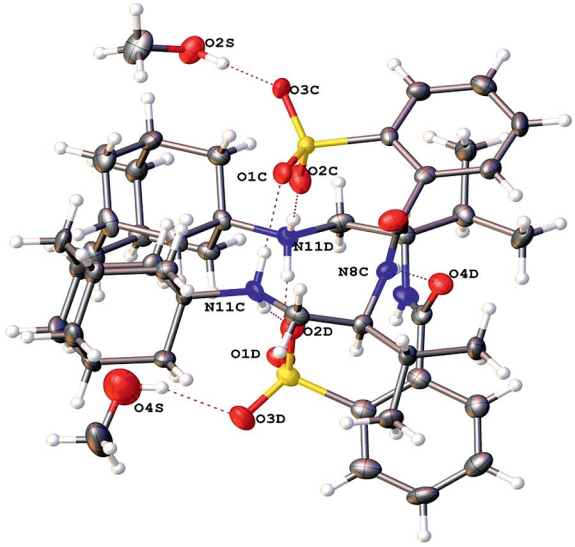
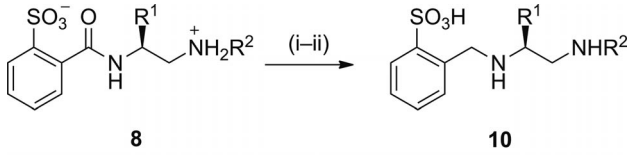


Figure 2. Molecular structure of the hydrogen bonded dimer (**8bd**·MeOH)$_2$. Selected hydrogen bonding interactions [Å]: N(8C)···O(4D) 2.756(5), N(11C)···O(1C) 2.832(5), N(11C)···O(2D) 2.823(5), N(11D)···O(2C) 2.909(5), N(11D)···O(1D) 2.838(5), O(2S)···O(3C) 2.796(5), O(4S)···O(3D) 2.726(8).

The new one-pot approach allowed rapid access to a diverse range of compounds and H bonding motifs as **8** was effectively prepared in a single step from commercially available reagents. This is a very powerful procedure for generating compound libraries. Recently, members of this library have been found to have activity against UDP-Gal*p* mutase.[11] This is a promising target enzyme in the mycobacterium that causes tuberculosis. Due to the evolution of resistant bacteria in this class there is a pressing need to attain new therapeutic agents in this field, and the simple synthesis of a diverse range of **8** provided by the one-pot procedure described here will prove vital in further screening.

Preparation of Diamino Sulfonic Acids

Reduction of **8** to the diamino sulfonic acids **10** was achieved by $BH_3{\cdot}SMe_2$ (Scheme 3).

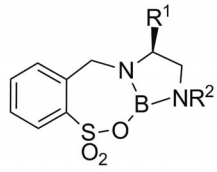


8 **10**

10	R^1	R^2	Yield/%
aa	Bn	2,4,6-$Me_3C_6H_2$	58
ab	Bn	2,6-*i*$Pr_2C_6H_3$	73
ae	Bn	$CHPh_2$	51
af	Bn	(*S*)-CHMePh	51
ba	*i*Pr	2,4,6-$Me_3C_6H_2$	67
bb	*i*Pr	2,6-*i*$Pr_2C_6H_3$	70
bc	*i*Pr	3,5-$Me_2C_6H_3$	83
bd	*i*Pr	1-adamantyl	43

Scheme 3. Reduction of **8** to **10**. (i) $BH_3{\cdot}SMe_2$, tetrahydrofuran, 60–90 °C, 3 d. (ii) MeOH, 90 °C, 2 h. Equivalent zwitterionic structures where either of the amines in **10** is protonated are equally valid.

Borane is the preferred reducing agent for the preparation of **10** as other reducing agents, such as $LiAlH_4$, required an aqueous work up, which led to the loss of the highly water soluble **10**. We speculate that borane reduction of **8** leads to the intermediate **11**, which is expected to be broken down under methanolysis. Subsequent distillation of the $B(OMe)_3$ coproduct and excess methanol could be achieved under vacuum, and the resultant solid **10** was purified by chromatography (CH_2Cl_2/MeOH, 19:1). This procedure is complicated by the near coelution of **8** and **10** under high polarity eluent conditions. Complete conversion had to be ensured in order to simplify the isolation of **10**. This can be achieved with excess borane and a long reaction time; 72 hours was found to be sufficient for the completion of all reactions. The best substrates for the reduction were those that have more hindered units in the R^2 group, e.g. **10ab** and **10bb**. Less hindered aryls and benzylic substituents led to more significant byproduct formation. It is presumed that **10** exist in equilibria with zwitterionic states where protonation of either of the amines is equally favoured. However, we were unable to crystallise an example of **10** to confirm this. As we do not know which of the amines is protonated in the solid state, the parent structure **10** is given in Scheme 3 for simplicity. These compounds were isolated as oils, from which occluded solvent was removed under prolonged exposure to high vacuum. In solution, rapid exchange of the NH and SO_3H protons with the solvent was apparent in their ^1H NMR spectra in [D_4]-MeOH.



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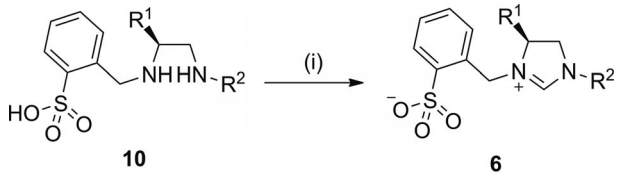
Imidazolinium Sulfonate Synthesis

Cyclisation of **10** to the imidazolinium sulfonates **6** proceeded cleanly under mild heating with $HC(OEt)_3$, and **6** were isolated as zwitterions by polar chromatography in good yields (Scheme 4). Generally, these sulfonates also occluded solvents, which were removed under high vacuum.



10 **6**

6	R^1	R^2	Yield/%
aa	Bn	2,4,6-$Me_3C_6H_2$	77
ab	Bn	2,6-*i*$Pr_2C_6H_3$	72
ae	Bn	$CHPh_2$	99
af	Bn	(*S*)-CHMePh	72
ba	*i*Pr	2,4,6-$Me_3C_6H_2$	90
bb	*i*Pr	2,6-*i*$Pr_2C_6H_3$	92
bd	*i*Pr	1-adamantyl	76

Scheme 4. Synthesis of **6**. (i) $(EtO)_3CH$, EtOH, 100 °C, 17 h. Compounds **6bc** (39%) and **6ca** (55%) were synthesised without purification of their precursor **10**, see text.

It was anticipated that reduction and cyclisation could be carried out without the need to purify **10** by chromatography. However, trace levels of borane produced byproducts, which limited the utility of this approach. For example, **6bc** (R^1 = *i*Pr, R^2 = 3,5-$Me_2C_6H_3$) was only isolated in a low yield (39%, over two steps) from the reaction mixture as its crystalline hexafluorophosphate salt. The situation was improved for more hindered systems; **6ca** (R^1 = Ph, R^2 = mesityl) was attained in 55% yield from **8ca** after chromatography without isolation of **10bc**. The major problem in these direct preparations of **6** from **8** was the formation of imidazolinidines by reduction by residual borane. Overall, intermediate isolation of **10** was the preferred approach. Crystallisation of **6**, in most cases, did not provide anything other than powdery solids. However, the most hin-

dered salt (**6ab**) crystallised as fine needles from EtOAc that contained traces of EtOH and water (Figure 3) and confirmed that the desired motif had been obtained.

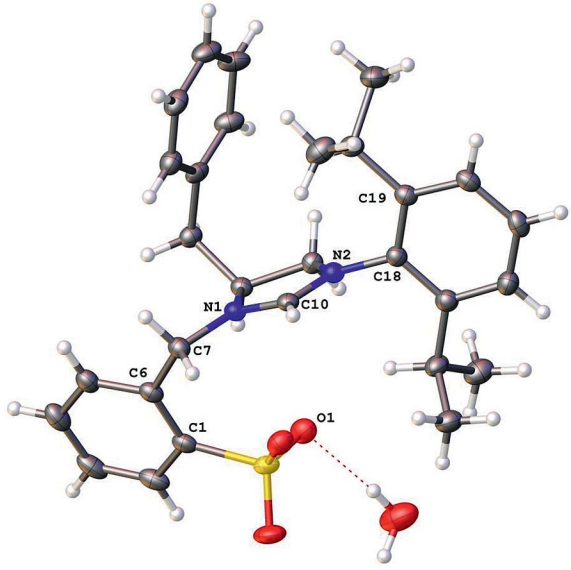


Figure 3. Molecular structure of **6ab**·H_2O. Selected torsion angles [°] and nonbonded distances [Å]: C(10)–N(2)–C(18)–C(19) 91.8, C(10)–N(1)–C(7)–C(6) 136.9, N(1)–C(7)–C(6)–C(1) 60.9; C(10)···O(1) 2.92.

We could not obtain crystals suitable for XRD of a less hindered example of **6** but we crystallised the related hexafluorophosphate adduct [H-**6bc**]PF_6 (Figure 4) by slow evaporation of a methanolic solution of **6bc** and NH_4PF_6. This salt adduct was formed by direct addition of NH_4PF_6 to the reaction mixture during the cyclisation reaction. In view of the very distinct difference in the asymmetric catalytic behaviour of **6ab** and **6bc** (see Table 2 later) it is instructive to compare their crystal structures. The most significant difference is in the placement of R^2 in **6ab** (2,6-$iPr_2C_6H_3$), which is essentially perpendicular to the plane of the imidazolinium, whereas it is almost coplanar in [H-**6bc**]PF_6 (3,5-$Me_2C_6H_3$). In both compounds the $–CH_2C_6H_4SO_3^-$ group is deflected to the bottom face of the imidazolimium core in order to minimise 1,2-steric interactions with R^1. There are, however, no clear factors that affect the positioning of the benzylic sulfonate ligand. The N–CH_2 torsion angle in **6ab** is marginally larger than that in H-**6bc**, but this is largely compensated by a reversed trend in the contiguous CH_2–C_{ipso} torsion angle. Thus, the positioning of this substituent, based on the X-ray data available, depends on the subtle interplay of both the R^1 and R^2 substituents. Hoveyda's more selective ligand, **5b**,[8] has a closer $SO_2O\cdots C_{im}$ contact (2.82 Å) than that seen in **6**.

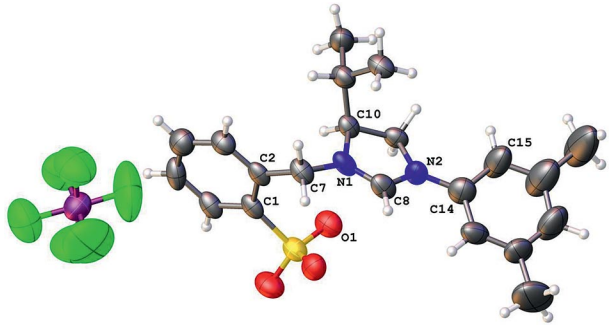
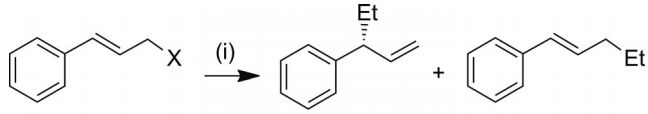


Figure 4. Molecular structure of [H-**6bc**]PF_6. Selected torsion angles [°] and nonbonded distances [Å]: C(8)–N(2)–C(14)–C(15) 154.3, C(8)–N(1)–C(7)–C(2) 133.0, N(1)–C(7)–C(2)–C(1) 58.6; C(8)···O(1) 3.07.

Asymmetric Catalysis

In view of the recent interest in using ligand **4** in "copper-free" NHC-catalysed additions of Grignard reagents to allylic halides,[12] we screened the ligand precursor **6ab** as a catalyst in the S_N2' addition of commercial solutions of EtMgBr to various (*E*)-cinnamyl electrophiles (Table 1). The presence of the $–CH_2C_6H_4SO_3^-$ donor was expected to lead to systems that showed significant enantioselectivity. Initial trials revealed Et_2O to be the best solvent and –15 °C to be an optimal temperature. To allow initial identification of the best leaving groups, reactions of (*E*)-PhCH=CHCH_2X (**12**) and EtMgBr were run under identical conditions (Table 1). Although cinnamyl bromide was clearly the best substrate, we initially found a slight variation of the *ee* values for the γ-product **13** based on both the age and quantity of the EtMgBr source used.[13] This effect was mirrored in the **13**:**14** regioselectivity (older bottles of EtMgBr, which contained more than trace amounts of EtOMgBr, as determined by Gilman titration, gave significantly inferior γ selectivities). Two solutions were found to overcome the detrimental effects of ROMgBr contamination: the use of 3 equiv. of freshly prepared Grignard reagents (see Entry 2) or alternatively to conduct the reaction in the presence of an excess of flame-dried $MgSO_4$ (0.5 equiv.). The latter is believed to coordinate the alkoxide and sequester it from the homogeneous reaction to the $MgSO_4$ slurry. Of the two techniques, the former was the most useful in the majority of cases.

Table 1. Leaving group optimisation. (i) EtMgBr (1.1 equiv.), diethyl ether, **6ab** (1 mol-%), –15 °C, 17 h.



12a–d (*R*)-**13d** **14d**

Entry	X	Conversion [%]	γ/α	*ee* [%]
1	Cl	74	9.4:1	44
2	Br	74	6–18.4:1	70–76
3	$OP(O)Ph_2$	46	4.0:1	54
4	$OP(O)(OEt)_2$	36	6.9:1	63

Using the optimal conditions, the ligand library **6** was tested for the addition of EtMgBr to (*E*)-cinnamyl bromide. This showed that **6ab** (R^1 = Bn, R^2 = 2,6-diisopropylphenyl) was the optimal promoter (Table 2). Further at-

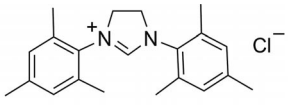
tempted optimisation by either increasing the loading of **6ab** to 3 mol-% or lowering the reaction temperature gave no benefit.

Table 2. Screening of **6aa**–**ca**. (i) EtMgBr (1.1 equiv.), diethyl ether, **6** (1 mol-%), –15 °C, 17 h.

6	R^1	R^2	Conversion [%]	*ee* [%]	γ/α
aa	Bn	2,4,6-$Me_3C_6H_2$	100	71	5.6:1
ab	Bn	2,6-*i*$Pr_2C_6H_3$	100	76	18.4:1
ae	Bn	$CHPh_2$	82	65	1.7:1
af	Bn	(*S*)-CHMePh	41	33	1:2.7
ba	*i*Pr	2,4,6-$Me_3C_6H_2$	100	70	2.8:1
bb	*i*Pr	2,6-*i*$Pr_2C_6H_3$	100	58	11.6:1
bc	*i*Pr	3,5-$Me_2C_6H_3$	97	9	1:2
bd	*i*Pr	1-adamantyl	44	28	1:6.9
ca	Ph	2,4,6-$Me_3C_6H_2$	100	36	1:1.6

In view of the crystal structures of **6ab** and [H-**6bc**]PF_6 we speculate that a perpendicularly-placed large aryl fragment in the R^2 sector plays a pivotal role to determine both the regio- and enantioselectivity (compare **6ab** and **6bc**, Table 2). Further increasing the size of R^2 reverses the regiochemistry (compare **6ab** and **6bd**, Table 2) and depresses the enantioselectivity, which suggests that the phenyl group of **12b** (X = Br; R^3, R^4 = H) is close to this quadrant in the selective transition state. However, appropriate placement of the $CH_2C_6H_4SO_3^-$ group for magnesium coordination is also critical, as branching in R^1 severely reduces the enantioselectivity (**6aa**, **6ba** and **6ca**, Table 2).

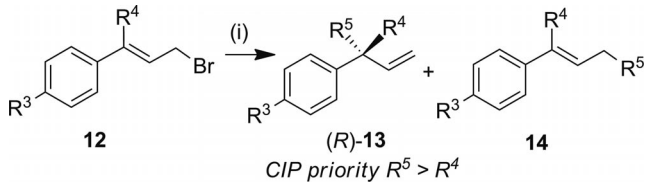
Optical rotation studies confirmed that **6ab** engenders the formation of (*R*)-**13**. Using the optimal ligand and conditions, a range of different Grignard reagents and substrates were tested (Table 3). These additions are also assigned to *Re* selectivity based on polarimetry results of the reaction mixtures. Racemic comparison mixtures that contained α-**14** and (±)-γ-**13** were prepared by equivalent reactions of R^5MgBr and **12** catalysed by achiral **SIMes**. These reactions provide high γ selectivities (of racemic materials). Interestingly, the mesityl groups of **SIMes** were also deployed perpendicular to the plane of the heterocycle (C–N_{ave} torsion angle 66.6°) in a similar manner to **6ab**.[14]



SIMes

A number of conclusions can be drawn from Table 3. Firstly, the cavity presented by the NHC ligand derived from **6ab** is not able to easily accommodate methylcinnamyl derivatives (R^4 = Me, compare Entries 1 and 2 with the rest of Table 3). Two possibilites are consistent with this observation: either the transition state is simply too cluttered to accept this substrate easily, or the enantioselectivity arises from a face–edge π stacking interaction between the ligand R^2 group and the aryl unit in **12**, which is perterbed by the presence of the γ-methyl group. The first possibility is supported by the fact that branching in the Grignard reagent is not well tolerated (Entries 10–14), and the latter proposal is supported by the fact that the presence of an electron-withdrawing CF_3 substituent in **12** typically has a somewhat positive effect on the enantioselectivity of the product. The behaviour of the methylcinnamyl bromide here is at odds with its normal behaviour observed by Alexakis[12] where the same substrate using **4** provided the highest level of γ selectivity.

Table 3. Scope and limitation of Grignard additions to allyl bromides. (i) R^5MgBr (3.0 equiv.), diethyl ether, **6ba** (1 mol-%), –15 °C, 17 h.



12 (*R*)-**13** **14**

CIP priority $R^5 > R^4$

Entry	R^3	R^4	R^5MgBr	Conversion [%]	γ/α	*ee* [%]
1	H	Me	Me	81	1.0:6.8	–
2	H	Me	Et	33	1.1:1	58
3	H	H	Me	99	1.5:1	73
4	H	H	Et	99	18.4:1	76
5	H	H	*n*Pr	99	5.8:1	71
6	H	H	*i*Pr	98	3.2:1	66
7	H	H	*n*Bu	99	8.3:1	78
8	H	H	*i*Bu	99	1.0:1.5	57
9	CF_3	H	Me	98	3.3:1	71
10	CF_3	H	Et	99	4.1:1	82
11	CF_3	H	*n*Pr	99	2.3:1	73
12	CF_3	H	*i*Pr	99	1.0:1.0	38
13	CF_3	H	*n*Bu	99	2.8:1	74
14	CF_3	H	*i*Bu	93	1.1:1.0	32

Conclusions

We have demonstrated a step-efficient method for the preparation of a new class of NHC-ligand precursors, which provides highly active catalysts (turnover number about 100) for γ selective additions to cinnamyl electrophiles (up to 18.4:1) without the use of transition metals. Such systems are of interest both because of the different method of activation they demonstrate (by Mg–NHC complexes rather than traditional transmetallation to transition metal complexes) and also because of their relevance to sustainable chemistry through the use of widely available "light" elements.

Experimental Section

General: The general experimental set up has been described previously.[10] Full descriptions of the preparative and catalytic procedures are given in the Supporting Information.

Formation of Amino Amido Sulfonic Acids (8): To a solution of 2-sulfobenzoic acid anhydride (1.1–1.3 equiv.) in chlorobenzene (50 mL per ca. 5 mmol) was added Boc-protected amino alcohol (1.0 equiv.) and the flask fitted with a Dean–Stark apparatus. The reaction mixture was heated to reflux (2–3 h, bath temperature

170 °C), allowed to cool (20–50 °C) and the required amine or aniline added (1.3–1.5 equiv.). The reaction mixture was heated to reflux for 17 h–7 d (bath temperature 170 °C). The mixture was allowed to cool and the solvent removed under vacuum. The resultant solid was typically purified by column chromatography using 2–5% methanol in dichloromethane as the eluent (**8aa**, **8ab**, **8ag**, **8ba** and **8bb** are slightly visible on SiO_2 due to natural fluorescence, which aided their separation. The R_f values in 5% methanol in dichloromethane are typically ≈ 0.35–0.45). The compounds readily occlude solvents, which were removed by prolonged drying under vacuum. The formation of **8ba** and **8bd** are representative.

(*S*)-2-[{1-(Mesitylamino)-3-methylbutan-2-yl}carbamoyl]benzenesulfonic Acid (8ba): Boc-(*L*)-valinol (1.92 g, 9.50 mmol), 2-sulfobenzonic acid anhydride (1.81 g, 9.83 mmol), and 2,4,6-trimethylaniline (1.47 g, 10.92 mmol) were heated to reflux for 2 d and provided **8ba** as a white powder (2.54 g, 66%), which crystallised as glistening colourless needles from EtOH/hexane; m.p. 196–198 °C. $[\alpha]_D$ = –43.6 (*c* = 1.08, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00 (d, *J* = 6.8 Hz, 3 H, CH*Me*$_\alpha$), 1.01 (d, *J* = 6.8 Hz, 3 H, CH*Me*$_\beta$), 2.02 (oct, *J* = 6.8 Hz, 1 H, C*H*CMe$_2$), 2.29 (s, 3 H, Ar*Me*), 2.52 (s, 6 H, 2× Ar*Me*), 3.29 (dd, *J* = 12.5, 3.6 Hz, 1 H, CHC*H*$_{2\alpha}$), 4.12 (app t, *J* = 12.5 Hz, 1 H, CHC*H*$_{2\beta}$), 4.37–4.47 (m, 1 H, C*H*NHCO), 6.93 (s, 2 H, Ar), 7.46–7.52 (m, 2 H, Ar), 7.63–7.68 (m, 1 H, Ar), 8.05–8.11 (m, 1 H Ar), 8.81 (d, *J* = 8.8 Hz, 1 H, N*H*$_{amine}$), 9.10 (br., 1 H, N*H*$_{amide}$), 10.80 (br., 1 H, SO_3*H*) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.8 (2× Ar*C*H$_3$), 18.9 (CH*C*H$_{3\alpha}$), 19.3 (CH*C*H$_{3\beta}$), 20.8 (Ar*C*H$_3$), 30.2 [*C*H(CH$_3$)$_2$], 53.8 (N*C*H), 55.5 (N*C*H$_2$), 127.7 (Ar-*C*H), 129.0 (Ar-*C*H), 130.3 (Ar-*C*H), 130.4 (Ar-*C*H), 130.8 (*ipso*-*C*, Ar), 130.9 (2× Ar-*C*H, *Ar*Me), 131.3 (2× *ipso*-*C*, Ar), 133.0 (*ipso*-*C*, Ar), 139.8 (*ipso*-*C*, Ar), 142.0 (*ipso*-*C*, Ar), 171.4 (C=O) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3775, 3683, 3620, 3456, 3009, 2976, 2895, 2412, 2248, 1885, 1642, 1602, 1522, 1476, 1423, 1334, 1239, 1046, 928, 877, 849, 660, 626 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{27}N_2O_4S$ [M – H]$^+$ 403.1697; found 403.1699. Crystallises from EtOH as **8ba**·$^1/_3$EtOH; $C_{21.7}H_{30}N_2O_{4.3}S$ (419.75): calcd. C 61.97, H 7.20, N 6.67; found C 61.96, H 7.33, N 6.71.

(*S*)-2-[{1-(Adamantan-1-ylamino)-3-methylbutan-2-yl}carbamoyl]-benzenesulfonic Acid (8bd): Boc-(*L*)-valinol (1.49 g, 7.33 mmol), 2-sulfobenzonic acid anhydride (1.36 g, 7.38 mmol), and adamantylamine (1.30 g, 8.61 mmol) were heated to reflux for 6 d and provided **8bd** as a white powder (1.24 g, 40%), which crystallised as small colourless needles from methanol; m.p. > 300 °C. $[\alpha]_D$ = –51.3 (*c* = 1.06, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90–0.97 (m, 6 H, CH*Me*$_2$), 1.54 (d$_{AB}$, J_{AB} = 12.6 Hz, 3 H, CHC*H*$_{2\alpha}$CH), 1.62 (d$_{AB}$, J_{AB} = 12.6 Hz, 3 H, CHC*H*$_{2\beta}$CH), 1.94 (app s, 6 H, C*H*$_2$), *overlapped by* 1.84–1.96 (m, 1 H, C*H*Me$_2$), 2.09 (s, 3 H, CH$_2$C*H*CH$_2$), 3.08–3.20 (br., m, 2 H, NC*H*$_2$), 4.35–4.55 (br., m, 1 H, NC*H*), 7.45–7.52 (m, 2 H, Ar), 7.60–7.65 (m, 1 H, Ar), 7.91 (br., s, 1 H, N*H*$_{amine}$), 8.13–8.15 (m, 1 H, Ar) overlapped by 8.17 (br., d, *J* = 9.2 Hz, 1 H, N*H*$_{amide}$), 8.54 (br., s, 1 H, SO_3*H*) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.0 [CH(Me)*C*H$_3$], 19.3 [CH(Me)*C*H$_3$], 29.0 (CH$_2$*C*HCH$_2$), 31.2 (*C*HMe$_2$), 35.4 (CH*C*H$_2$CH), 38.0 (CH*C*H$_2$CH), 41.2 (N*C*H$_2$CH), 52.4 (N*C*H), 58.6 [adamantyl-*C*, (CH)$_3$*C*NH], 127.8 (Ar-*C*H), 129.6 (Ar-*C*H), 130.3 (Ar-*C*H), 130.4 (Ar-*C*H), 133.5 [*ipso*-*C*, *Ar*C(=O)N], 141.9 (*ipso*-*C*, *Ar*SO$_3$), 169.8 (C=O) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3692, 3606, 3271, 3011, 2969, 2922, 2859, 2683, 2602, 2454, 2337, 1947, 1843, 1642, 1596, 1564, 1483, 1466, 1454, 1392, 1363, 1326, 1310, 1294, 1251, 1164, 1141, 1080, 1041, 1016, 980, 962, 939, 901, 872, 853, 660, 616 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{31}N_2O_4S$ [M – H]$^+$ 419.2010; found 419.2000. Crystallises from MeOH as **8bd**·MeOH; $C_{23}H_{36}N_2O_5S$ (452.61): calcd. C 61.03, H 8.02, N 6.19; found C 60.75, H 7.76, N 6.44.

Formation of Diamino Sulfonic Acids (10): In dried glassware under an argon atmosphere **8** (1 equiv.) was dissolved in dry tetrahydrofuran (10 mL per gram of **8**) and excess borane dimethylsulfide complex (6 mL per gram of **8**) was added. The reaction mixture was then heated to reflux (bath temperature ≈ 70 °C, ≈ 90 °C for adamantyl derivatives) for 3 d under an inert atmosphere, allowed to cool to ambient temperature and quenched with methanol at 0 °C. The solvent was removed under vacuum, and the resultant gummy solid redissolved in methanol (5 mL per expected mmol of product **10**) and heated to reflux for 2 h to hydrolyse the borates. The solvent was removed under vacuum to give oils or glassy foams. Purification was achieved by flash chromatography; typically a column of 6–9 cm high by 3.5 cm in diameter was needed to separate about 1.0 g of crude **10**. An eluent of 2–5% methanol in dichloromethane was used to obtain the products. The location of the diamino sulfonic acid was ascertained by TLC using 5% methanol in dichloromethane. Staining, first with ninhydrin (red/brown-green spots) then bleaching with potassium permanganate visualised the products. The R_f values in 5% methanol in dichloromethane are typically ≈ 0.3–0.45. Once the product **10** was isolated the column was flushed with methanol 40% in dichloromethane to ensure complete recovery. For the synthesis of **6**, chromatographic purification of **10** is preferred but not essential. Noncrystalline **10** typically occluded small amounts of dichloromethane (which did not affect their subsequent reactivity). Data for **10bc** are representative.

(*S*)-2-[{(1-{(3,5-Dimethylphenyl)amino}-3-methylbutan-2-yl)amino}-methyl]benzenesulfonic Acid (10bc): Using **8bc** (0.45 g, 1.15 mmol) provided **10bc** as a white powder (0.36 g, 83%); m.p. 180–182 °C. $[\alpha]_D$ = +57.1 (*c* = 0.40, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (d, *J* = 6.8 Hz, 3 H, CH*Me*$_\alpha$), 1.11 (d, *J* = 7.2 Hz, 3 H, CH*Me*$_\beta$), 1.62 (br., s, 1 H, N*H*), 2.00–2.11 (m, 1 H, C*H*Me$_2$), 2.30 (s, 6 H, 2× Ar*Me*), 3.23–3.33 (m, 1 H, NCHC*H*$_{2\alpha}$), 3.53–3.71 (m, 1 H, NCHC*H*$_{2\beta}$) overlapped by (m, 1 H, NC*H*CH$_2$), 4.30 (d, *J* = 13.0 Hz, 1 H, ArC*H*$_{2\alpha}$), 4.39 (d, *J* = 13.0 Hz, 1 H, ArC*H*$_{2\beta}$), 5.17 (br., s, 1 H, N*H*), 6.34 (s, 2 H, Ar), 6.47 (s, 1 H, Ar), 6.91 (app d, *J* = 7.6 Hz, 1 H, Ar), 7.33 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar), 7.40 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar), 8.04 (dd, *J* = 7.6, 1.2 Hz, 1 H, Ar), 8.62 (br., s, 1 H, SO_3 *H*) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.6 (CH*C*H$_{3\alpha}$), 18.3 (CH*C*H$_{3\beta}$), 21.6 (2× Ar*C*H$_3$), 28.6 (*C*HMe$_2$), 42.9 (N*C*H$_2$CHN), 50.6 (Ar*C*H$_2$), 61.4 (N*C*HCH$_2$), 110.7 (2× Ar-*C*H), 120.3 (Ar-*C*H), 127.0 (2× *ipso*-*C*, Ar), 128.5 (Ar-*C*H), 130.2 (Ar-*C*H), 130.9 (Ar-*C*H), 133.1 (Ar-*C*H), 139.3 (*ipso*-*C*, Ar), 144.4 (*ipso*-*C*, Ar), 146.7 (*ipso*-*C*, Ar) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3691, 3606, 3385, 3011, 2972, 2922, 2860, 1602, 1522, 1476, 1446, 1399, 1379, 1338, 1304, 1252, 1193, 1161, 1085, 1045, 1014, 964, 905, 826, 621, 606 cm^{-1}. HRMS (ESI): Calcd. for $C_{20}H_{27}N_2O_3S$ [M – H]$^+$ 375.1748; found 375.1753. **10bc**·0.1CH_2Cl_2: calcd. C 62.71, H 7.38, N 7.28; found C 62.45, H 7.52, N 7.06.

Formation of Imidazolinium Sulfonate Zwitterions (6): Distilled triethyl orthoformate (3 mL per 1 mmol of **10**) was added to a solution of **10** (1 equiv.) in ethanol (3 mL per 1 mmol of **10**). The reaction mixture was heated to reflux (17 h, bath temperature 80 °C). The ethanol was removed under vacuum, and residual orthoformate was decanted to give oily residues, which gave a foam-like solids under high vaccuum. Purification of **6** was achieved by column chromatography using 2–5% methanol in dichloromethane as the eluent (the R_f values in 5% methanol in dichloromethane are typically about 0.4–0.5) to provide colourless foams. Crystallisation was achieved in many cases by the slow evaporation of methanol, a mixture of chloroform or dichloromethane and ethyl acetate, which typically provided hydrated materials.

(*S*)-2-[(4-Benzyl-1-mesityl-4,5-dihydro-1*H*-imidazol-3-ium-3-yl)-methyl]benzenesulfonate (6aa): Using **10aa** (0.62 g, 1.42 mmol) provided **6aa** as a white powder (0.49 g, 77%); m.p. 279–280 °C. $[\alpha]_D$ = +107.5 (*c* = 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.02 (br., s, 3 H, ArMe_α), 2.21 (br., s, 3 H, ArMe_β), 2.276 (s, 3 H, Ar*Me*, *para*), 3.03 (dd, *J* = 14.0, 8.4 Hz, 1 H, PhC$H_{2\alpha}$), 3.32 (dd, *J* = 14.0, 4.4 Hz, 1 H, PhC$H_{2\beta}$), 3.59 (dd, *J* = 11.6, 7.7 Hz, 1 H, NCHC$H_{2\alpha}$), 4.14 (t, *J* = 11.6 Hz, 1 H, NCHC$H_{2\beta}$), 4.59 (dtd, *J* = 8.4, 7.7, 4.4 Hz, 1 H, NC*H*CH_2), 4.82 (d, *J* = 14.2 Hz, 1 H, ArC$H_{2\alpha}$N), 4.84 (d, *J* = 14.2 Hz, 1 H, ArC$H_{2\beta}$N), 6.84 (s, 2 H, Ar), 7.11–7.13 (m, 2 H, Ar), 7.24–7.39 (m, 5 H, Ar), 7.46 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar), 8.27 (dd, *J* = 7.6, 1.2 Hz, 1 H, Ar), 8.33 (s, 1 H, NC*H*N) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.7 (br., 2× Ar*C*H_3, *ortho*) 21.0 (Ar*C*H_3, *para*), 37.5 (Ph*C*H_2), 49.9 (Ar*C*H_2), 54.8 (NCH*C*H_2), 60.2 (N*C*HCH_2), 127.8 (Ar-*C*H), 128.2 (*ipso-C*, Ar), 129.2–129.6 (br., 2× Ar-*C*H) overlapped by [129.3 (2× Ar-*C*H), 129.3 (Ar-*C*H), 129.5 (2× Ar-*C*H)], 129.7 (Ar-*C*H), 129.8 (Ar-*C*H), 130.5 (*ipso-C*, Ar), 131.5 (Ar-*C*H), 134.1 (*ipso-C*, Ar), 140.0 (*ipso-C*, Ar), 146.5 (*ipso-C*, Ar), 148.0–156.0 (v. br, 2× *ipso-C*, ArMe), 159.4 (N*C*HN) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3691, 3606, 3440, 3064, 3010, 2928, 2465, 1637, 1604, 1496, 1480, 1455, 1372, 1300, 1267, 1192, 1142, 1088, 1021, 958, 855, 660, 619 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{27}N_2O_3S$ $[M - H]^+$ 447.1748; found 447.1747. Recrystallisation by slow evaporation of $CHCl_3$/EtOAc solutions gave a microcrystalline **10aa**·¾H_2O; $C_{26}H_{29.5}N_2O_{3.75}S$ (462.09): calcd. C 67.58, H 6.43, N 6.06; found C 67.47, H 6.36, N 6.05.

(*S*)-2-[{4-Benzyl-1-(2,6-diisopropylphenyl)-4,5-dihydro-1*H*-imidazol-3-ium-3-yl}methyl]benzenesulfonate (6ab): Using **10ab** (0.19 g, 0.40 mmol) provided **6ab** as a white powder (0.14 g, 72%); m.p. 200–205 °C. $[\alpha]_D$ = +45.0 (*c* = 0.50, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.15–1.21 (m, 12 H, 4× CH*Me*), 2.44 (quint, *J* = 6.8 Hz, 1 H, ArCH_αMe), 3.06 (dd, *J* = 14.0, 8.2 Hz, 1 H, PhC$H_{2\alpha}$), 3.34 (dd, *J* = 14.0, 4.4 Hz, 1 H, PhC$H_{2\beta}$), 3.43 (quint, *J* = 6.8 Hz, 1 H, ArCH_βMe), 3.69 (dd, *J* = 11.4, 7.6 Hz, 1 H, NC$H_{2\alpha}$), 4.18 (t, *J* = 11.4 Hz, 1 H, NC$H_{2\beta}$), 4.73 (dtd, *J* = 12.0, 7.6, 8.2, 4.4 Hz, 1 H, NC*H*CH_2), 4.84 (d, *J* = 14.0 Hz, 1 H, ArC$H_{2\alpha}$N), 5.92 (d, *J* = 14.0 Hz, 1 H, ArC$H_{2\beta}$N), 7.07–7.13 (m, 2 H, Ar), 7.17 (dd, *J* = 8.0, 1.6 Hz, 1 H, Ar), 7.22 (dd, *J* = 8.0, 1.2 Hz, 1 H, Ar), 7.26–7.32 (m, 1 H, Ar), 7.33–7.45 (m, 5 H, Ar), 7.53 (td, *J* = 8.0, 1.6 Hz, 1 H, Ar), 8.12 (s, 1 H, NC*H*N), 8.34 (dd, *J* = 8.0, 1.2 Hz, 1 H, Ar) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.2 (CH*C*$H_{3\alpha\alpha}$), 24.3 (CH*C*$H_{3\alpha\beta}$), 24.9 (CH*C*$H_{3\beta\alpha}$), 25.0 (CH*C*$H_{3\beta\beta}$), 27.8 (*C*H$Me_{2\alpha}$), 28.5 (*C*H$Me_{2\beta}$), 37.6 (Ph*C*H_2), 50.3 (Ar*C*H_2), 57.2 (N*C*H_2CH), 60.5 (N*C*H), 124.3 (Ar-*C*H), 125.4 (Ar-*C*H), 127.6 (*ipso-C*, Ar), 128.0 (Ar-*C*H), 129.4 (2× Ar-*C*H), 129.4 (2× Ar-*C*H), 129.6 (Ar-*C*H), 129.7 (Ar-*C*H), 129.8 (*ipso-C*, Ar), 130.2 (Ar-*C*H), 131.0 (Ar-*C*H), 131.2 (Ar-*C*H), 133.8 (*ipso-C*, Ar), 145.9 (*ipso-C*, Ar), 146.7 (*ipso-C*, Ar), 148.4 (*ipso-C*, Ar), 159.0 (N*C*HN) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3668, 3065, 3010, 2971, 2929, 2889, 2871, 2468, 1949, 1880, 1808, 1634, 1590, 1497, 1457, 1387, 1367, 1344, 1264, 1187, 1171, 1143, 1088, 1056, 1044, 1021, 990, 960, 935, 899, 866, 841, 660, 619 cm^{-1}. HRMS (ESI): calcd. for $C_{29}H_{33}N_2O_3S$ $[M - H]^+$ 489.2217; found 489.2223. Recrystallisation by slow evaporation of $CHCl_3$/EtOAc solutions gave needles of monohydrate that was readily dried to the hemihydrate **6aa**·½H_2O; $C_{29}H_{35}N_2O_{3.5}S$ (499.67): calcd. C 69.71, H 7.38, N 5.61; found C 69.56, H 7.16, N 5.59.

(*S*)-2-[(1-Benzhydryl-4-benzyl-4,5-dihydro-1*H*-imidazol-3-ium-3-yl)methyl]benzenesulfonate (6ae): Using **10ae** (0.20 g, 0.41 mmol) provided **6ae** as a white powder (0.17 g, 99%); m.p. 223–224 °C. $[\alpha]_D$ = +45.0 (*c* = 0.60, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.92 (dd, *J* = 14.0, 7.2 Hz, 1 H, PhC$H_{2\alpha}$), 3.05 (dd, *J* = 14.0, 4.4 Hz, 1 H, PhC$H_{2\beta}$), 3.39 (dd, *J* = 11.4, 6.4 Hz, 1 H, NC$H_{2\alpha}$), 3.83 (t, *J* = 11.4 Hz, 1 H, NC$H_{2\beta}$), 4.27–4.35 (m, 1 H, NC*H*CH_2), 4.51 (d, *J* = 14.0 Hz, ArC$H_{2\alpha}$N), 5.66 [s, 1 H, NC*H*(Ph)$_2$], 5.71 (d, *J* = 14.0 Hz, ArC$H_{2\beta}$N), 6.98–7.06 (m, 2 H, Ar), 7.09–7.18 (m, 3 H, Ar), 7.28–7.39 (m, 12 H, Ar), 7.43–7.48 (m, 1 H, Ar), 7.92 (s, 1 H, NC*H*N), 8.31 (dd, *J* = 8.0, 1.2 Hz, 1 H, Ar) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 37.3 (Ph*C*H_2), 50.3 (Ar*C*H_2), 53.0 (NCH_2CHN), 59.7 (N*C*HCH_2), 67.0 [N*C*H(Ph$_2$)], 127.7 (Ar-*C*H), 127.9 (*ipso-C*, Ar), 128.3 (2× Ar-*C*H), 128.5 (2× Ar-*C*H), 129.0 (Ar-*C*H), 129.0 (Ar-*C*H), 129.2 (2× Ar-*C*H), 129.3 (4× Ar-*C*H), 129.4 (2× Ar-*C*H), 129.6 (Ar-*C*H), 129.7 (Ar-*C*H), 129.9 (Ar-*C*H), 131.3 (Ar-*C*H), 134.2 (*ipso-C*, Ar), 135.4 (*ipso-C*, Ar), 135.6 (*ipso-C*, Ar), 146.2 (*ipso-C*, Ar), 159.1 (N*C*HN) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3693, 3672, 3606, 3442, 3109, 3090, 3066, 3011, 2935, 2887, 2857, 2467, 2254, 1955, 1900, 1814, 1702, 1641, 1604, 1586, 1497, 1474, 1454, 1372, 1349, 1331, 1302, 1274, 1192, 1143, 1087, 1021, 1004, 945, 909, 882, 867, 831, 660, 619 cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{27}N_2O_3S$ $[M - H]^+$ 495.1748; found 495.1770. Recrystallisation by slow evaporation of $CHCl_3$/EtOAc solutions gave microcrystals of a hydrate **6ae**·1½H_2O; $C_{29}H_{35}N_2O_{3.5}S$ (499.67): calcd. C 69.71, H 7.38, N 5.61; found C 69.56, H 7.16, N 5.59.

2-[({*S*}-4-Benzyl-1-{(*S*)-1-phenylethyl}-4,5-dihydro-1*H*-imidazol-3-ium-3-yl)methyl]benzenesulfonate (6af): Using **10af** (0.15 g, 0.35 mmol) provided **6af** as a white powder (0.11 g, 72%); m.p. 250 °C (dec). $[\alpha]_D$ = +50.7 (*c* = 0.30, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.72 (d, *J* = 6.8 Hz, 3 H, CH*Me*), 2.77 (dd, *J* = 13.6, 8.8 Hz, 1 H, PhC$H_{2\alpha}$), 3.14–3.21 (m, 1 H, PhC$H_{2\beta}$) overlapped by (m, 1 H, NC$H_{2\alpha}$CH), 3.64 (t, *J* = 11.6 Hz, 1 H, NC$H_{2\beta}$CH), 4.20 (dtd, *J* = 11.6, 8.8, 4.4 Hz, 1 H, NC*H*CH_2), 4.52 (d, *J* = 14.4 Hz, 1 H, ArC$H_{2\alpha}$N), 4.79 [q, *J* = 6.8 Hz, 1 H, ArC*H*(Me)N], 5.97 (d, *J* = 14.4 Hz, 1 H, ArC$H_{2\beta}$N), 6.93–6.98 (m, 2 H, Ar), 7.12 (dd, *J* = 7.6, 0.8 Hz, 1 H, Ar), 7.24–7.39 (m, 9 H, Ar), 7.48 (td, *J* = 6.4, 1.6 Hz, 1 H, Ar), 8.32 (dd, *J* = 8.0, 1.2 Hz, 1 H, Ar), 8.88 (s, 1 H, NC*H*N) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 19.4 (CH*C*H_3), 37.7 (Ph*C*H_2), 49.7 (Ar*C*H_2), 51.1 (N*C*H_2CH), 58.2 [Ph*C*H(CH$_3$)-N], 29.3 (N*C*HCH_2), 127.0 (2× Ar-*C*H), 127.6 (Ar-*C*H), 128.6 (*ipso-C*, Ar), 128.7 (Ar-*C*H), 129.1 (2× Ar-*C*H), 129.2 (2× Ar-*C*H), 129.2 (2× Ar-*C*H), 129.6 (Ar-*C*H), 129.7 (2× Ar-*C*H), 131.4 (Ar-*C*H), 134.4 (*ipso-C*, Ar), 137.6 (*ipso-C*, Ar), 146.3 (*ipso-C*, Ar), 158.3 (N*C*HN) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3691, 3606, 3450, 3089, 3066, 3011, 2932, 2858, 2466, 2338, 1953, 1886, 1811, 1642, 1603, 1511, 1497, 1456, 1444, 1386, 1375, 1355, 1304, 1285, 1268, 1192, 1143, 1117, 1087, 1047, 1021, 959, 909, 831, 660, 619 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{25}N_2O_3S$ $[M - H]^+$ 433.1591; found 433.1600. Recrystallisation by slow evaporation of $CHCl_3$/EtOAc solutions gave microcrystals of a monohydrate **6af**·H_2O; $C_{25}H_{28}N_2O_4S$ (452.57): calcd. C 66.35, H 6.24, N 6.19; found C 66.22, H 6.07, N 6.14.

(*S*)-2-[(4-Isopropyl-1-mesityl-4,5-dihydro-1*H*-imidazol-3-ium-3-yl)-methyl]benzenesulfonate (6ba): Using **10ba** (0.23 g, 0.58 mmol) provided **6ba** (0.21 g, 90%) as a olourless light foam-like solid; m.p. 243–245 °C. $[\alpha]_D$ = +28.3 (*c* = 1.04 in methanol). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 7.0 Hz, 3 H, CHMe_α), 1.11 (d, *J* = 7.0 Hz, 3 H, CHMe_β), 2.24 (s, 6 H, 2× Ar*Me*, *ortho*), 2.28 (s, 3 H, Ar*Me*, *para*) 2.45–2.49 (m, 1 H, C*H*Me$_2$), 3.68 (dd, *J* = 12.5, 3.4 Hz, 1 H, NC$H_{2\alpha}$CH), 4.13 (dd, *J* = 12.5, 11.8 Hz, 1 H, NC$H_{2\beta}$CH), 4.35 (ddd, *J* = 12.5, 11.8, 3.4 Hz, 1 H, NC*H*), 4.59 (d, *J* = 14.0 Hz, 1 H, ArC$H_{2\beta}$), 5.79 (d, *J* = 14.0 Hz, 1 H, ArC$H_{2\alpha}$), 6.91 (br., s, 2 H, Ar), 7.25 (dd, *J* = 7.4, 1.4 Hz, 1 H, Ar), 7.32 (td, *J* = 7.4, 1.4 Hz, 1 H, Ar), 7.39 (td, *J* = 7.4, 1.4 Hz, 1 H, Ar), 8.19 (dd, *J* = 7.4, 1.4 Hz, 1 H, Ar), 8.32 (s, 1 H, NC*H*N) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.6 (CH*C*$H_{3\alpha}$), 18.1 (CH*C*$H_{3\beta}$), 18.2 (2× Ar*C*H_3, *ortho*), 21.0 (2× Ar*C*H_3, *para*), 26.6 (*C*HMe$_2$), 49.6 (Ar*C*H_2), 50.5 (N*C*H_2CH), 64.2 (N*C*HCH$_2$), 128.2 (*ipso-C*, Ar), 129.2 (Ar-*C*H), 129.6 (Ar-*C*H), 129.7 (Ar-*C*H), 130.1 (br., 2×

Ar-*C*H), 130.8 (*ipso*-*C*, Ar), 131.5 (Ar-*C*H), 134.8 (br., *ipso*-*C*, Ar), 136.9 (br., *ipso*-*C*, Ar), 139.9 (*ipso*-*C*, Ar), 146.4 (*ipso*-*C*, Ar), 159.7 (N*C*HN) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3434, 3060, 3008, 2932, 2877, 1718, 1639, 1508, 1466, 1445, 1395, 1373, 1335, 1268, 1193, 1142, 1087, 1021, 986, 956, 855, 833, 660, 619 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{27}N_2O_3S$ $[M - 2H]^+$ 399.1748; found 399.1753. Recrystallisation by slow evaporation of $CHCl_3$/EtOAc solutions gave microcrystals of a monohydrate **6ba**·H_2O; $C_{25}H_{28}N_2O_4S$ (452.57): calcd. C 63.13, H 7.22, N 6.69; found C 63.02, H 7.18, N 6.51.

(*S*)-2-[{1-(2,6-Diisopropylphenyl)-4-isopropyl-4,5-dihydro-1*H*-imidazol-3-ium-3-yl}methyl]benzenesulfonate (6bb): Using **10bb** (1.12 g, 2.60 mmol) provided **6bb** (1.07 g, 92%) as a white foam-like solid; m.p. 155–157 °C. $[\alpha]_D$ = +53.5 (*c* = 0.11 in chloroform). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.8 Hz, 3 H, CHCH*Me*$_\alpha$), 1.15 (d, *J* = 6.8 Hz, 3 H, CHCH*Me*$_\beta$), 1.24 (d, *J* = 6.8 Hz, 3 H, ArCH*Me*$_{\alpha\alpha}$), 1.27 (d, *J* = 6.8 Hz, 3 H, ArCH*Me*$_{\alpha\beta}$), 1.29 (d, *J* = 6.8 Hz, 3 H, ArCH*Me*$_{\beta\alpha}$), 1.31 (d, *J* = 6.8 Hz, 3 H, ArCH*Me*$_{\beta\beta}$), 2.43–2.53 (m, 1 H, CHC*H*Me$_2$), 2.80 (septet, *J* = 6.8 Hz, 1 H, ArC*H*Me$_{2\alpha}$), 3.53 (septet, *J* = 6.8 Hz, 1 H, ArC*H*Me$_{2\beta}$), 3.72 (dd, *J* = 11.8, 9.6 Hz, 1 H, NCHC*H*$_{2\alpha}$), 4.17 (t, *J* = 11.8 Hz, 1 H, NCHC*H*$_{2\beta}$), 4.46–4.53 (m, 1 H, NC*H*CH$_2$), 4.60 (d, *J* = 14.0 Hz, ArC*H*$_{2\alpha}$), 4.81 (d, *J* = 14.0 Hz, ArC*H*$_{2\beta}$), 7.21–7.26 (m, 2 H, Ar), 7.24–7.30 (m, 1 H, Ar), 7.36–7.42 (m, 1 H, Ar), 7.43–7.47 (m, 1 H, Ar), 7.48–7.52 (m, 1 H, Ar), 8.11 (s, 1 H, NC*H*N), 8.31–8.34 (m, 1 H, Ar) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.4 (CHCH*C*H$_{3\alpha}$), 18.2 (CHCH*C*H$_{3\beta}$), 24.1 (ArCH*C*H$_{3\alpha\alpha}$), 24.5 (ArCH*C*H$_{3\alpha\beta}$), 24.6 (ArCH*C*H$_{3\beta\alpha}$), 25.0 (ArCH*C*H$_{3\beta\beta}$), 26.5 (CH*C*HMe$_2$), 27.8 (Ar*C*$_\alpha$HMe$_2$), 28.6 (Ar*C*$_\beta$HMe$_2$), 49.5 (Ph*C*H$_2$), 53.2 (NCH*C*H$_2$), 64.5 (N*C*HCH$_2$), 124.3 (Ar-*C*H), 125.3 (Ar-*C*H), 128.0 (*ipso*-*C*, Ar), 129.2 (Ar-*C*H), 129.7 (Ar-*C*H), 129.7 (Ar-*C*H), 130.2 (*ipso*-*C*, Ar), 130.9 (Ar-*C*H), 131.4 (Ar-*C*H), 145.9 (*ipso*-*C*, Ar), 146.5 (*ipso*-*C*, Ar), 148.2 (*ipso*-*C*, Ar), 159.5 (N*C*HN) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3689, 3010, 2969, 2931, 2873, 2361, 2338, 1639, 1506, 1465, 1444, 1388, 1372, 1337, 1194, 1142, 1103, 1087, 1056, 1021, 928, 834, 662, 619 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{33}N_2O_3S$ $[M - H]^+$ 411.2217; found 411.2200. Recrystallisation by slow evaporation of $CHCl_3$/EtOAc solutions gave microcrystals of a monohydrate **6bb**·H_2O; $C_{25}H_{36}N_2O_4S$ (460.63): calcd. C 65.19, H 7.88, N 6.08; found C 65.03, H 7.82, N 5.76.

(*S*)-2-[{1-(3,5-Dimethylphenyl)-4-isopropyl-4,5-dihydro-1*H*-imidazol-3-ium-3-yl}methyl]benzenesulfonate (6bc): Using **8bc** (1.34 g, 3.45 mmol), without purification of intermediate **10bc**, provided **6bc** (0.52 g, 39%) as a white foam-like solid; m.p. 231 °C. $[\alpha]_D$ = –125.8 (*c* = 1.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.91 (d, *J* = 7.2 Hz, 3 H, CH*Me*$_\alpha$), 0.97 (d, *J* = 6.8 Hz, 3 H, CH*Me*$_\beta$), 2.25 (s, 6 H, 2× Ar*Me*) overlapped by 2.24–2.36 (m, 1 H, C*H*Me$_2$), 3.88 (dd, *J* = 10.4, 6.8 Hz, 1 H, NC*H*$_{2\alpha}$), 4.13–4.18 (m, 1 H, NC*H*CH$_2$N), 4.25–4.30 (m, 1 H, NC*H*$_{2\beta}$), 4.52 (d, *J* = 14.2 Hz, 1 H, ArC*H*$_{2\alpha}$N), 5.95 (d, *J* = 14.2 Hz, 1 H, ArC*H*$_{2\beta}$N), 6.78 (s, 1 H, Ar), 6.91 (s, 2 H, Ar), 7.22 (dd, *J* = 7.2, 1.2 Hz, 1 H, Ar), 7.35 (td, *J* = 7.2, 1.2 Hz, 1 H, Ar), 7.43 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar), 8.25 (dd, *J* = 7.6, 1.2 Hz, 1 H, Ar), 9.33 (NC*H*N) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.2 (CH*C*H$_3$), 17.9 (CHCH$_3$), 21.2 (2× Ar*C*H$_3$), 26.9 (*C*HMe$_2$), 48.7 (NCH*C*H$_2$N), 50.0 (Ar*C*H$_2$), 63.5 (N*C*HCH$_2$N), 115.6 (2× Ar-*C*H), 128.1 (*ipso*-*C*, Ar), 128.6 (Ar-*C*H), 129.4 (Ar-*C*H), 129.7 (Ar-*C*H), 129.8 (Ar-*C*H), 131.5 (Ar-*C*H), 135.7 (*ipso*-*C*, Ar), 139.4 (*ipso*-*C*, Ar), 139.9 (*ipso*-*C*, Ar), 146.0 (*ipso*-*C*, Ar), 156.0 (N*C*HN) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3691, 3607, 3411, 3010, 2973, 2934, 2878, 2739, 2465, 2337, 1943, 1834, 1637, 1616, 1599, 1517, 1472, 1445, 1396, 1375, 1344, 1330, 1271, 1192, 1143, 1114, 1087, 1067, 1021, 958, 917, 881, 837, 660, 620, 605 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{26}N_2NaO_3S$ $[M + Na]^+$ 409.1556; found 409.1556. Recrystallisation by slow evaporation of $CHCl_3$/EtOAc solutions gave microcrystals of a monohydrate **6bc**·H_2O; $C_{21}H_{28}N_2O_4S$ (404.52): calcd. C 62.35, H 6.98, N 6.93; found C 62.60, H 6.92, N 6.61. The compound could only be crystallised by partial conversion to its hexafluorophosphate salt, H-**6bc**·PF_6.

(*S*)-2-[{1-(Adamantan-1-yl)-4-isopropyl-4,5-dihydro-1*H*-imidazol-3-ium-3-yl}methyl]benzenesulfonate (6bd): Using **10bd** (0.20 g, 0.50 mmol) provided **6bd** (0.127 g, 76%) as a colourless solid; m.p. 277 °C. $[\alpha]_D$ = –13.2 (*c* = 0.79, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 6.8 Hz, 3 H, CH*Me*$_\alpha$), 0.92 (d, *J* = 6.0 Hz, 3 H, CH*Me*$_\beta$), 1.68 [d, *J* = 12.6 Hz, 3 H, (CH)C*H*$_{2\alpha\alpha}$(CH)], 1.73 [d, *J* = 12.6 Hz, 3 H, (CH)C*H*$_{2\alpha\beta}$(CH)], 1.93 [d, *J* = 11.4 Hz, 3 H, (CH)C*H*$_{2\beta\alpha}$(CH)], 1.99 [d, *J* = 11.4 Hz, 3 H, (CH)C*H*$_{2\beta\beta}$(CH)], 2.20 [s, 3 H, (C*H*)CH$_2$(C*H*)], 2.23–2.32 (m, 1 H, C*H*Me$_2$), 3.52 (dd, *J* = 10.4, 6.6 Hz, 1 H, NC*H*$_{2\alpha}$), 3.85 (dd, *J* = 12.2, 10.4 Hz, 1 H, NCHC*H*$_{2\beta}$) overlapped by 3.94 (ddd, *J* = 12.2, 6.6, 3.2 Hz, 1 H, C*H*CH$_2$), 4.34 (d, *J* = 14.2 Hz, 1 H, ArC*H*$_{2\alpha}$N), 5.82 (d, *J* = 14.2 Hz, 1 H, ArC*H*$_{2\beta}$N), 7.17 (dd, *J* = 7.6, 1.2 Hz, 1 H, Ar), 7.34 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar), 7.44 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar), 8.28 (dd, *J* = 7.6, 1.2 Hz, 1 H, Ar), 8.44 (s, 1 H, NC*H*N) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.1 (CH*C*$_\alpha$H$_3$), 17.9 (CH*C*$_\beta$H$_3$), 27.0 (*C*HMe$_2$), 29.0 [3 × (CH$_2$)$_3$*C*H(CH$_2$)$_3$], 35.6 (3 × CH*C*$_\alpha$H$_2$CH), 40.5 (3 × CH*C*$_\beta$H$_2$CH), 43.9 (NCH*C*H$_2$), 49.4 (Ar*C*H$_2$), 56.8 [adamantyl-*C*, (CH$_2$)$_3$*C*N], 62.3 (N*C*HCH$_2$), 128.5 (*ipso*-*C*, Ar), 129.6 (2× Ar-*C*H), 129.6 (Ar-*C*H), 131.2 (Ar-*C*H), 146.3 (*ipso*-*C*, Ar), 156.2 (N*C*HN) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3668, 3408, 3125, 3063, 3011, 2973, 2921, 2878, 2858, 2686, 2462, 2361, 2339, 1940, 1834, 1639, 1576, 1505, 1472, 1453, 1395, 1365, 1347, 1308, 1287, 1265, 1192, 1142, 1117, 1097, 1086, 1047, 1020, 984, 958, 909, 881, 831, 660, 645, 619 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{31}N_2O_3S$ $[M - H]^+$ 415.2061; found 415.2080. The compound was crystallised (microneedles, $CHCl_3$/EtOAc) as its NaOH adduct **6ba**·NaOH; $C_{23}H_{33}N_2NaO_4S$ (456.57): calcd. C 60.50, H 7.29, N 6.14; found C 60.82, H 7.47, N 6.12.

(*S*)-2-[(1-Mesityl-4-phenyl-4,5-dihydro-1*H*-imidazol-3-ium-3-yl)-methyl]benzenesulfonate (6ca): Using using **8ca** (1.44 g, 3.29 mmol), without purification of intermediate **10ca**, provided **6ca** (0.79 g, 55%) as a white solid; m.p. 263–270 °C. $[\alpha]_D$ = +7.2 (*c* = 1.15, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.26 (br., s, 3 H, Ar*Me*$_\alpha$, *ortho*) overlapped by 2.30 (s, 3 H, Ar*Me*, *para*) and overlapped by 2.38 (br., s, 3 H, Ar*Me*$_\beta$, *ortho*), 3.78 (dd, *J* = 11.6, 9.4 Hz, 1 H, NC*H*$_{2\alpha}$), 4.35 (d, *J* = 14.0 Hz, 1 H, ArC*H*$_{2\alpha}$N), 4.56 (t, *J* = 11.6 Hz, 1 H, NC*H*$_{2\beta}$), 5.29 (dd, *J* = 9.4, 2.8 Hz, 1 H, NC*H*CH$_2$), 5.81 (d, *J* = 14.0 Hz, 1 H, ArC*H*$_{2\beta}$N), 6.62 (dd, *J* = 7.2, 0.8 Hz, 1 H, Ar), 6.90 (br., s, 2 H, Ar), 7.20 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar), 7.33–7.35 (m, 2 H, Ar), 7.42 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar), 7.50–7.55 (m, 3 H, Ar), 8.267 (dd, *J* = 7.6, 1.2 Hz, 1 H, Ar), 8.70 (s, 1 H, NC*H*N) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.0 (br., 2× Ar*C*H$_3$, *ortho*), 21.0 (Ar*C*H$_3$, *para*), 49.8 (Ar*C*H$_2$), 59.0 (NCH*C*H$_2$), 63.3 (N*C*HCH$_2$), 127.4 (2× Ar-*C*H), 127.8 (*ipso*-*C*, Ar), 129.0 (Ar-*C*H), 129.4 (Ar-*C*H), 129.6 (Ar-*C*H), 129.8 (2× Ar-*C*H), 129.8 (3× Ar-*C*H), 130.5 (*ipso*-*C*, Ar), 132.1 (Ar-*C*H), 135.1 (*ipso*-*C*, Ar), 135.9 (*ipso*-*C*, Ar), 137.1 (*ipso*-*C*, Ar), 140.0 (*ipso*-*C*, Ar), 146.2 (*ipso*-*C*, Ar), 160.2 (N*C*HN) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3691, 3606, 3416, 3093, 3064, 3011, 2467, 1957, 1636, 1496, 1480, 1457, 1445, 1372, 1329, 1265, 1192, 1142, 1088, 1021, 957, 909, 868, 855, 833, 660, 619 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{26}N_2NaO_3S$ $[M + Na]^+$ 457.1556; found 457.1558. Recrystallisation by slow evaporation of CH_2Cl_2/EtOAc solutions gave microcrystals of **6ca**·¾CH_2Cl_2; $C_{25.7}H_{27.5}Cl_{1.5}N_2O_3S$ (497.65): calcd. C 62.07, H 5.56, N 5.62; found C 62.28, H 5.76, N 5.38.

Allylic Substitution Reaction of Cinnamyl Derivatives Using Grignard Reagents: In flame-dried glassware (typically carousel reactor

tubes) under argon, **6** (5.3 μmol) and any additive (if required) were suspended in dry diethyl ether (1.0 mL), to which was added a solution of the appropriate cinnamyl derivative (0.53 mmol) in Et_2O (1.0 mL). The reaction mixture was stirred (10–15 min) at room temperature before being cooled to –15 °C and stirred for a further 10 min. The alkylmagnesium bromide (3.0 equiv.) was added dropwise (over 2–4 min). The colourless reaction mixture was then stirred (200 rpm, 17 h) at –15 °C, quenched by addition of saturated, acidified NH_4Cl solution and stirred (30–60 min) whilst being warmed to room temperature. The organic layer was extracted into Et_2O, dried (Na_2SO_4) and filtered though a plug of silica before the solvent was removed in vacuo. Purification by column chromatography (pentane as eluent) gave a mixture of α and γ products. Yields and conversions (Table 3) were determined by isolation, NMR spectroscopy or GC, against an internal standard, as appropriate, *ee* values were determined by chiral GC using a Chiracil-Dex-CB column. Details of the known products are given in the Supporting Information.

CCDC-843838 (for **6ab**), -843839 (for [H-**6bc**]PF_6), -843836 (for **8ba**) and -843837 (for **8bd**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Full experimental procedures and spectroscopic data for all compounds.

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[1] For general overviews, see: a) *N-Heterocyclic Carbenes in Transition Metal Catalysis, Topics in Organometallic Chemistry* (Ed.: F. Glorius), vol. 21, Springer-Verlag, Berlin/Heidelberg, **2007**; b) *N-Heterocyclic Carbenes in Synthesis* (Ed.: S. P. Nolan), Wiley-VCH, Weinheim, Germany, **2006**; c) *N-Heterocyclic Carbenes* (Ed.: S. Díez-González), RSC Publishing, Cambridge, UK, **2010**. For steric factors, see: d) T. Dröge, F. Glorius, *Angew. Chem. Int. Ed.* **2010**, *49*, 6940–6952. For electronic factors, see: e) H. Jacobsen, A. Correa, A. Poater, C. Costabile, L. Cavallo, *Coord. Chem. Rev.* **2009**, *253*, 687–703.

[2] For a comprehensive review, see: a) . G. C. Vougioukalakis, R. H. Grubbs, *Chem. Rev.* **2010**, *110*, 1746–1787. For recent developments in chiral Ru complexes see: S. Tiede, A. Berger, D. Schlesiger, D. Rost, A. Lühl, S. Blechert, *Angew. Chem. Int. Ed.* **2010**, *49*, 3972–3975.

[3] For a review of commercial PEPPSI catalysts: a) E. A. B. Kantchev, C. J. O'Brien, M. G. Organ, *Aldrichim. Acta* **2006**, *39*, 97–111. For alternatives and recent developments, see: b) C. Lohre, T. Dröge, C. Wang, F. Glorius, *Chem. Eur. J.* **2011**, *17*, 6052–6055; c) F. Godoy, C. Segarra, M. Poyatos, E. Peris, *Organometallics* **2011**, *30*, 684–688; d) Z. Xi, B. Liu, W. Chen, *J. Org. Chem.* **2008**, *73*, 3954–3957.

[4] For an overview see: a) J. Wencel, M. Mauduit, H. Hénon, S. Kehrli, A. Alexakis, *Aldrichim. Acta* **2009**, *42*, 43–50; b) For recent developments, see: S. Kehrli, D. Martin, D. Rix, M. Mauduit, A. Alexakis, *Chem. Eur. J.* **2010**, *16*, 9890–9904; c) K. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2009**, *131*, 4455–4462.

[5] For recent reviews in this area, see: a) A. T. Biju, N. Kuhl, F. Glorius, *Acc. Chem. Res.* **2011**, DOI: 10.1021/ar2000716; b) N. Marion, S. Díez-González, S. P. Nolan, *Angew. Chem.* **2007**, *119*, 3046; *Angew. Chem. Int. Ed.* **2007**, *46*, 2988–3000; c) D. Enders, K Breuer, in: *Comprehensive Asymmetric Catalysis*, vol. 3 (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, Germany, **1999**, p. **1093**; d) D. Enders, T. Balensiefer, O. Niemeier, M. Christmann, in: *Enantioselective Organocatalysis: Reactions and Experimental Procedures* (Ed.: P. I. Dalko), Wiely-VCH, Weinheim, Germany, **2007**, p. 331; e) D. Enders, O. Niemeier, A. Henseler, *Chem. Rev.* **2007**, *107*, 5606; f) V. Nair, S. Vellalath, B. P. Babu, *Chem. Soc. Rev.* **2008**, *37*, 2691.

[6] For an overview, see: a) S. T. Liddle, I. S. Edworthy, P. L. Arnold, *Chem. Soc. Rev.* **2007**, *36*, 1732–1744; b) for use in allylic Cu catalysis, see: T. Jennequin, J. Wencel-Delord, D. Rix, J. Daubignard, C. Crevisy, M. Mauduit, *Synlett* **2010**, 1661–1665. For use in conjugate addition Cu catalysis, see: M. Tissot, A. Pérez Hernández, D. Müller, M. Mauduit, A. Alexakis, *Org. Lett.* **2011**, *13*, 1524–1527.

[7] For an overview of NHC precursor routes, see: a) L. Benhamou, E. Chardon, G. Lavigne, S. Bellemin-Laponnaz, V. César, *Chem. Rev.* **2011**, *111*, 2705–2733; b) for synthesis of **2**, see: J. J. Van Veldhuizen, J. E. Campbell, R. E. Giudici, A. H. Hoveyda, *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882; c) for synthesis of **3**, see: T. Uchida, T. Katsuki, *Tetrahedron Lett.* **2009**, *50*, 4741–4743; d) for synthesis of **4**, see: O. Jackowski, A. Alexakis, *Angew. Chem.* **2010**, *122*, 3418; *Angew. Chem. Int. Ed.* **2010**, *49*, 3346–3350; e) for synthesis of **5a**, see: M. K. Brown, T. L. May, C. A. Baxter, A. H. Hoveyda, *Angew. Chem.* **2007**, *119*, 1115; *Angew. Chem. Int. Ed.* **2007**, *46*, 1097–1100.

[8] For synthesis of **5b**, see: Y. Lee, K. Akiyama, D. G. Gillingham, M. K. Brown, A. H. Hoveyda, *J. Am. Chem. Soc.* **2008**, *130*, 446–447.

[9] For a rare example, see: a) B. A. Bhanu Prasad, S. R. Gilbertson, *Org. Lett.* **2009**, *11*, 3710–3713. For a related system see: b) A. Fürstner, M. Alcarazo, V. César, C. W. Lehmann, *Chem. Commun.* **2006**, 2176–2178.

[10] a) R. I. Robinson, J. C. Stephens, S. M. Worden, A. J. Blake, C. Wilson, S. Woodward, *Eur. J. Org. Chem.* **2004**, 4596–4605. For Lewis-acid-promoted opening of oxazolines, see: b) M. J. Fazio, *J. Org. Chem.* **1984**, *49*, 4889–4893.

[11] S. Karunan Partha, A. Sadeghi-Khomami, S. Cren, R. I. Robinson, S. Woodward, K. Slowski, L. Berast, B. Zheng, N. R. Thomas, D. A. R. Sanders, *Molecular Informatics* **2011**, DOI: 10.1002/minf.201100085 further screening of an enlarged library is underway.

[12] a) Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2006**, *128*, 15604–15605; b) O. Jackowski, A. Alexakis, *Angew. Chem.* **2010**, *122*, 3418; *Angew. Chem. Int. Ed.* **2010**, *49*, 3346–3350; c) Y. Lee, B. Li, A. H. Hoveyda, *J. Am. Chem. Soc.* **2009**, *131*, 11625–11633.

[13] A similar effect has been noticed in organoaluminium chemistry, see: P. K. Fraser, S. Woodward, *Chem. Eur. J.* **2003**, *9*, 776–783.

[14] a) Data taken from the X-ray structure "RUYTUB", see: B. F. Straub, M. Wrede, K. Schmid, F. Rominger, *Eur. J. Inorg. Chem.* **2010**, 1907–1911 and http://webcsd.ccdc.cam.ac.uk/; b) for a recent example of chiral symmetrical NHC analogues in this chemistry, see: J.-N. Levy, C. Latham, L. Roisin, N. Kandziora, P. Di Fruscia, A. J. P. White, S. Woodward, M. J. Fuchter, *Org. Biomol. Chem.* **2011**, DOI: 10.1039/C1OB06780J.

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