# Graphical Abstract

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**_N_-(Alkylsulfamoyl)aldimines: easily deprotected precursors for diarylmethylamine synthesis**

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Rosemary H. Crampton,[a] Martin Fox[b] and Simon Woodward*[a]
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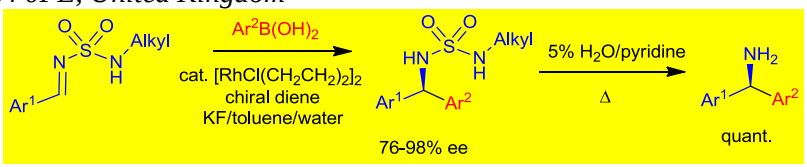

# Stereochemistry Abstract

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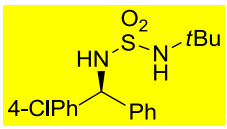
Rosemary H. Crampton, Martin Fox and Simon Woodward




$C_{17}H_{21}ClN_2O_2S$

(*S*)-*N*-*tert*-Butyl-*N'*-(4-chlorophenyl)(phenyl)methylsulfamide

E.e. = 81%
$[\alpha]_D$ = −1.9 (*c* = 1.09, $CHCl_3$)
Source of chirality: Asymmetric catalysis
Absolute configuration: 1*S*

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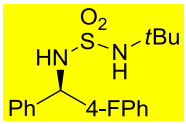


$C_{17}H_{21}FN_2O_2S$

(*R*)-*N*-*tert*-Butyl-*N*'-(4-fluorophenyl)(phenyl)methylsulfamide

E.e. = 95%
$[\alpha]_D$ = +0.5 (*c* = 0.97, $CHCl_3$)
Source of chirality: Asymmetric catalysis
Absolute configuration: 1*R*

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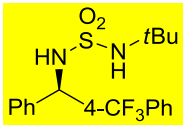


E.e. = 98%
$[\alpha]_D$ = −3.7 (*c* = 1.35, $CHCl_3$)
Source of chirality: Asymmetric catalysis
Absolute configuration: 1*R*

$C_{18}H_{21}F_3N_2O_2S$

(*R*)-*N*-*tert*-Butyl-*N*'-(*R*)-(4-trifluoromethylphenyl)(phenyl)methylsulfamide

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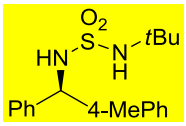
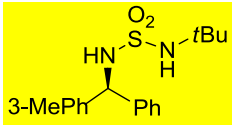



E.e. = 95%
$[\alpha]_D^{25}$ = +3.9 (*c* = 0.99 in $CHCl_3$)
Source of chirality: Asymmetric catalysis
Absolute configuration: 1*R*

$C_{18}H_{24}N_2O_2S$

(*R*)-*N*-*tert*-Butyl-*N'*-(4-methylphenyl)(phenyl)methylsulfamide

Rosemary H. Crampton, Martin Fox and Simon Woodward

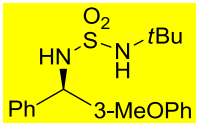



E.e = 85%
$[\alpha]_D$ = −2.0 (*c* = 1.10, $CHCl_3$)
Source of chirality: Asymmetric catalysis
Absolute configuration: 1*S*

$C_{18}H_{24}N_2O_2S$

(*S*)-*N*-*tert*-Butyl-*N'*-(3-methylphenyl)(phenyl)methylsulfamide

Rosemary H. Crampton, Martin Fox and Simon Woodward




$C_{18}H_{24}N_2O_3S$

(*R*)-*N*-*tert*-Butyl-*N'*-(3-methoxyphenyl)(phenyl)methylsulfamide

E.e. = 97%
$[\alpha]_D = -1.0$ (*c* = 1.26, $CHCl_3$)
Source of chirality: Asymmetric catalysis
Absolute configuration: 1*R*

Tetrahedron: *Asymmetry*
journal homepage: www.elsevier.com/locate/tetasy

# *N*-(Alkylsulfamoyl)aldimines: easily deprotected precursors for diarylmethylamine synthesis

Rosemary H. Crampton,[a] Martin Fox[b] and Simon Woodward[a*]
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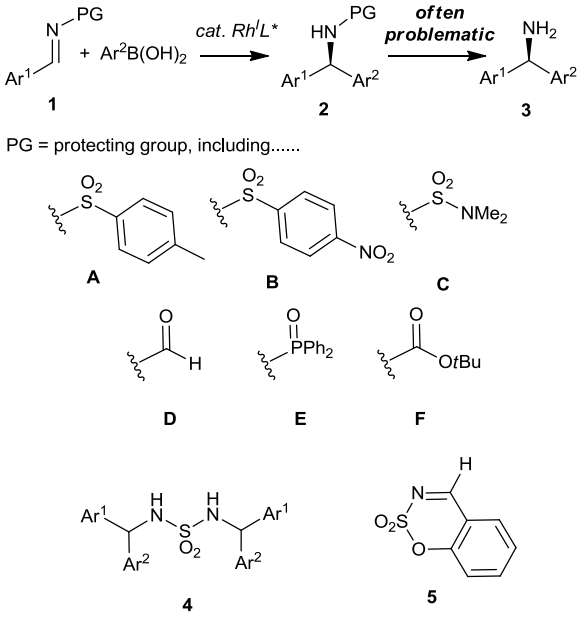
ABSTRACT

Sequential reaction of chlorosulfonyl isocyanate with *t*-BuOH, *t*-BuNH$_2$ and TFA allows formation of $H_2NSO_2NHBu^t$. Condensation of the latter with $Ar^1CHO$, in the presence of $Ti(OEt)_4$ provides the activated imines $Ar^1CH{=}NSO_2NHBu^t$ (59-89%). Commercially available boronic acids add to these imines with good setereoselectivity (76-98% *ee*) using readily available diene ligands. Simple deprotection with 5% w/w water in pyridine affords free $Ar^1CHNH_2Ar^2$.

## 1. Introduction

In the decade or so since Miyaura introduced rhodium-catalysed addition of arylboron reagents to activated imines (2000)[1] a large range of catalytic systems and have been developed and the attainment of highly enantioselective (>90% *ee*) versions can be assured in many cases.[2] A more pressing problem in this area is to attaining protecting groups that simultaneously strongly activate imine **1** to addition but also allow mild deprotection of the addition products **2** to the commercially interesting diarylmethylamines **3** (Scheme 1).[3] *N*-Tosyl protected imines (**A**) are widely used but the harsh (acidic or highly reducing) removal conditions required for **2** cleave many other groups.[4] *N*-Nosylarylimines (**B**) offer improvements but any functionalities in **3** must be tolerant to strong nucleophiles (e.g. PhSH).[5] *N*,*N*-Dimethylsulfamoyl protected imines (**C**) are robust but can require transamination under forcing microwave promotion to effect their removal.[6] Formyl protection (**D**) does offer deprotection under mildly acidic conditions, but in this case the imines need to be stored as their sulfinate adducts to avoid their decomposition.[7] *N*-diphenylphosphinoyl groups (**E**) have been popularized by Ellman and others, but add significantly to the imine mass.[n8] Finally, Boc protection (**F**) can be used, but this is sometimes too labile.[n9] In seeking to balance the requirements of imine activation, protecting group stability and ease of removal we have suggested that the use of a simple $–SO_2–$ function can be effective, as in **4**, that can be removed under mildly basic conditions (5% water in pyridine) – conditions complementary to groups **A-D**.[10] However, the presence of two stereocentres in **4** complicates their *ee* assay. To avoid such issues we proposed that the use of a simple 'dummy' amine in the sulfamoyl group $–SO_2NHR$ should prove useful. Recently, Lam used the substrates **5** which are restricted to the use of salicyladehyde derived aldimines.[11] This prompts us to disclose our own approach here which places no restrictions on $Ar^1$.




**Scheme 1.** Typical approached to 2-arylethylamines.

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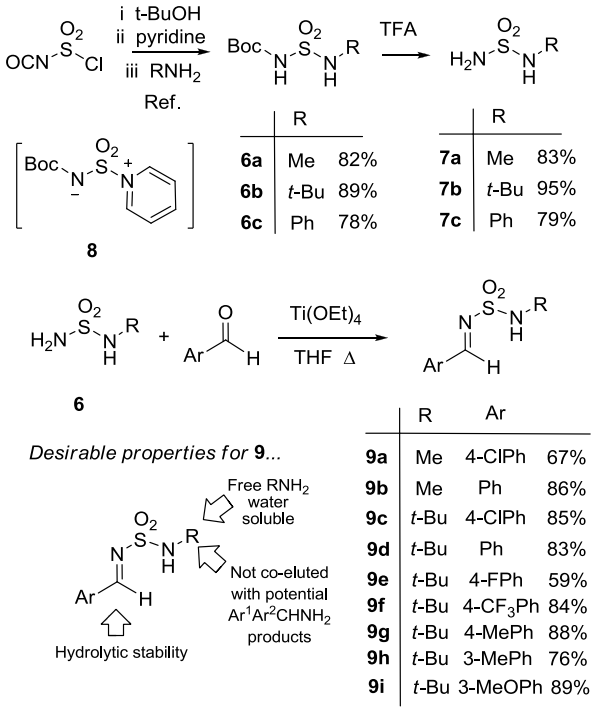
## 2. Results and Discussion

### 2.1 Synthesis of sulfamyl imine acceptors 9

An efficient route to the required imines **9** (Scheme 2) uses the chemistry of Masui[12] to access the intermediate sulfamides **7** directly from *N*-alkylsulfamoylcarbamates **6**. The latter are easily prepared by sequential of *tert*-BuOH and aqueous solutions of $RNH_2$ to widely available chlorosulfonyl isocyanate; chemistry which presumably proceeds *via* the Burgess-like intermediate **8**. No extensive purification of intermediates **6** is necessary prior to hydrolysis but representative **6b** was fully characterised as it is a new chemical entity compared to **6a** and **6c**.[12-14] Conversion of **6** to **7** was simply attained by treatment with TFA in $CH_2Cl_2$ at ambient temperature affording known **7** in 79-95% yield.[14,15] Preliminary trials using PhCHO revealed that the imines **9** were best prepared by $Ti(OEt)_4$ induced dehydrations, other conditions (cat. $H^+$/Dean-Stark, $MgSO_4$, $CuSO_4$) affording low/trace yields.




| | R | | | R | |
|---|---|---|---|---|---|
| **6a** | Me | 82% | **7a** | Me | 83% |
| **6b** | *t*-Bu | 89% | **7b** | *t*-Bu | 95% |
| **6c** | Ph | 78% | **7c** | Ph | 79% |

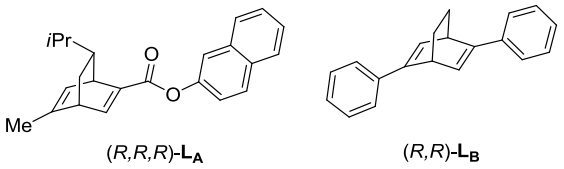
| | R | Ar | |
|---|---|---|---|
| **9a** | Me | 4-ClPh | 67% |
| **9b** | Me | Ph | 86% |
| **9c** | *t*-Bu | 4-ClPh | 85% |
| **9d** | *t*-Bu | Ph | 83% |
| **9e** | *t*-Bu | 4-FPh | 59% |
| **9f** | *t*-Bu | 4-$CF_3$Ph | 84% |
| **9g** | *t*-Bu | 4-MePh | 88% |
| **9h** | *t*-Bu | 3-MePh | 76% |
| **9i** | *t*-Bu | 3-MeOPh | 89% |

**Scheme 2.** Preparation of activated imines used in this study.

Investigation of an extensive range of R-substituents in **9**[14] indicated that the *tert*-butyl 'dummy group' was superior to all others for the following reasons - (i) While the $SO_2NHBu^t$ group is easily removed under the same conditions as **4** deprotection[10] (mild pyridine reflux with 5% w/w water) the compounds are hydrolytically robust in routine usage (much more so than the methyl derivatives **9a-b**). (ii) The released *t*-$BuNH_2$ is water soluble facilitating its simple separation; other substituents (e.g. benzyl or aryl derivatives) require chromatographic separations. (iii) The *tert*-butyl derivatives **9c-9i** were frequently found to be crystalline entities facilitating purification. Surprisingly, given these highly attractive features, the protecting group in acyclic **9** appears not to have been used in additions to imines before as far as we can tell – although it is clearly closely related to $RCH{=}NSO_2NR_2$ structures.[6]

### 2.2. Catalytic 1,2-arylboron additions sulfamyl imines 9

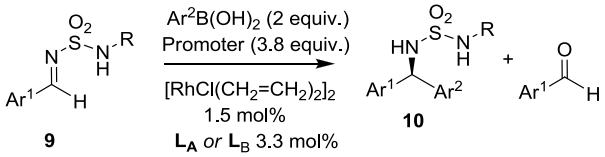
Our aim was to obtain a system that would enable simple access to a wide range of protecting group free diaryl amines **3** using simple and widely available (commercial) reagents. Among the bewildering array of ligands and organoboron sources for catalytic asymmetric additions to imines the most readily available are simple boronic acids ($ArB(OH)_2$) and the commercialised ligands $\mathbf{L_A}$-$\mathbf{L_B}$ (Scheme 3) in the presence of the widely available rhodium source $[RhCl(CH_2{=}CH_2)_2]_2$.




**Scheme 3.** Chiral ligands used in this study.

Initial optimisation concentrated on imines **9a-d** as representative examples of electron neutral and moderately electron deficient imines in the presence of the $Rh^I$-L based catalyst (3 mol% based on **9** using $\mathbf{L_A}$ or $\mathbf{L_B}$). The biphasic conditions of Zhou[16] proved most appropriate for use of boronic acids (Table 1).

**Table 1.** Optimisation of catalytic $ArB(OH)_2$ addition to **9**.[a]



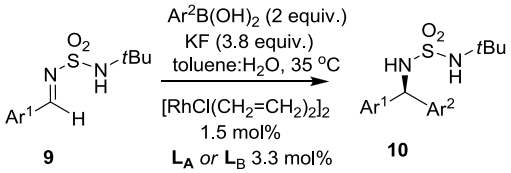
| Run | $Ar^1$ | R | $Ar^2$ | Solvent and base | Yield **10** (*ee*)/% | Hydrol. /% |
|---|---|---|---|---|---|---|
| | | | Using ligand $\mathbf{L_A}$ | | | |
| 1 | Ph | Me | 4-ClPh | $CH_2Cl_2$ KF | 79 (*85*) | 13 |
| 2 | Ph | Me | 4-ClPh | toluene KF | 73 (*84*) | 15 |
| 3 | 4-ClPh | Me | Ph | $CH_2Cl_2$ KF | 42 (*n/d*) | 17 |
| 4 | 4-ClPh | Me | Ph | toluene $K_2CO_3$ | 87 (*71*) | 7 |
| 5 | Ph | *t*Bu | 4-ClPh | toluene KF | 83 (*86*) | <2 |
| 6 | 4-ClPh | *t*Bu | Ph | toluene KF | 89 (*81*) | <2 |
| | | | Using ligand $\mathbf{L_B}$ | | | |
| 7 | Ph | Me | 4-ClPh | $CH_2Cl_2$ KF | 82 (*91*) | 2 |
| 8 | 4-ClPh | Me | Ph | $CH_2Cl_2$ KF | 6 (*n/d*) | 92 |
| 9 | Ph | *t*Bu | 4-ClPh | toluene KF | 84 (*94*) | 0 |
| 10 | 4-ClPh | *t*Bu | Ph | toluene KF | 17 (*n/d*) | 69 |

[a] Reactions were carried out using **9** (0.5 mmol), $Ar^2B(OH)_2$ (1.0 mmol), $[RhCl(C_2H_4)_2]_2$ (1.5 mol%), $\mathbf{L_A}$ (3.3 mol%) and a base (3.8 equiv.) in solvent (1 mL) plus water (1 mL) for 16 h at 35 °C. Yields were determined by isolation, except runs 3, 8 and 10 which were from $^1$H NMR conversions. Enantioselectivities were determined by HPLC as described in Section 4.5.

While interesting levels of enantioselectivity (84-91%) were realised in 4-ClPhB$(OH)_2$ additions to *N*-methyl/phenyl substituted **9b** (Runs 1-2 and 7), additions to more electron deficient **9a** uniformly resulted in lower *ee* values and appreciable hydrolysis to 4-ClPhCHO together with additional byproducts (Runs 3-4 and 8). The presence of these species prevented accurate *ee* assay on the small amounts of **10** formed. Despite systematic variation of the reaction conditions (solvent, base and catalyst types) no overall system could be identified to completely inhibit hydrolysis of the *N*-methyl derivatives **9a-b**. Potassium carbonate was useful in some cases (Run 4) but synthetically useful levels of enantioselectivity could not be realised. Attention was switched to the *N-tert*-butyl derivatives **9c-d**. While high *ee* values were realised (81-94%) unusual system dependent hydrolysis was observed (Runs 5-6 and 9-10 highlighted). While that based on Hayashi's (*R,R*)-bod ligand $\mathbf{L_B}$ gave an optimal *ee* for 4-ClPhB$(OH)_2$ addition to **9d**, the same catalyst reproducibly only promoted extensive hydrolysis of **9c**. Intermediate results were attained with $\mathbf{L_A}$ (Runs 5-6). The yields attained of additions products**10** are a composite of: (i) imine electrophilicity (promoting both addition and hydrolysis), (ii) steric/electronic nature of the arylboronic acid (controlling the rate of catalyst loading and hydrodeboration), (iii) ligand affects controlling the rate of catalyst loading and addition.[4] Disentangling these factors for a given system is not easy. While the results using *N-tert*-butyl derivatives **9c-d** were encouraging they raise two key questions: (i) given the tendency of these starting materials to show catalyst system dependent hydrolysis does a wide enough range of synthetic utility exist? and is any pattern of reactivity apparent? (ii) Are the final products **10** easily deprotected and does this result in any stereochemical erosion of the *ee* realised in the catalytic addition? The first of these questions is addressed in Table 2 and Scheme 4.

For additions to phenyl-based **9d** addition of a significant range of $Ar^2B(OH)_2$ was tolerated regardless of the ligand used. One exception to this was addition of 3-MePhB$(OH)_2$ where almost complete hydrolysis of the starting imine was observed generating **10e** in very low yield (7%) when using $\mathbf{L_B}$. For the substituted imines **9c** and **9e-h** there were very significant issues of hydrolysis in systems using $\mathbf{L_B}$. Systems that are intolerant of this ligand (<20% yield of **10**) are summarised in Scheme 4. We could realise no useful addition yields to the 4-MePh imine **9g** with either $\mathbf{L_A}$ or $\mathbf{L_B}$.

**Table 2.** Tolerated combinations of $ArB(OH)_2$ and **9**.[a]




**9** **10**

| **9** | $Ar^1$ | $Ar^2$ | L used | **10** | Yield (*ee*)/% |
|---|---|---|---|---|---|
| **9c** | 4-ClPh | Ph | $\mathbf{L_A}$ | (*S*)-**10a** | 89 (*81*) |
| **9d** | Ph | 4-ClPh | $\mathbf{L_A}$ | (*R*)-**10a** | 83 (*86*) |
| **9d** | Ph | 4-ClPh | $\mathbf{L_B}$ | (*R*)-**10a** | 84 (*94*) |
| **9d** | Ph | 4-FPh | $\mathbf{L_A}$ | (*R*)-**10b** | 42 (*87*) |
| **9d** | Ph | 4-FPh | $\mathbf{L_B}$ | (*R*)-**10b** | 90 (*95*) |
| **9d** | Ph | 4-$CF_3$Ph | $\mathbf{L_A}$ | (*R*)-**10c** | 32 (*90*) |
| **9d** | Ph | 4-$CF_3$Ph | $\mathbf{L_B}$ | (*R*)-**10c** | 84 (*98*) |
| **9d** | Ph | 4-MePh | $\mathbf{L_A}$ | (*R*)-**10d** | 68 (*78*) |
| **9d** | Ph | 4-MePh | $\mathbf{L_B}$ | (*R*)-**10d** | 71 (*95*) |
| **9d** | Ph | 3-MePh | $\mathbf{L_A}$ | (*R*)-**10e** | 35 (*76*) |
| **9d** | Ph | 3-MeOPh | $\mathbf{L_A}$ | (*R*)-**10f** | 37 (*84*) |
| **9d** | Ph | 3-MeOPh | $\mathbf{L_B}$ | (*R*)-**10f** | 91 (*97*) |
| **9e** | 4-FPh | Ph | $\mathbf{L_A}$ | (*S*)-**10b** | 41 (*80*) |
| **9f** | 4-$CF_3$Ph | Ph | $\mathbf{L_A}$ | (*S*)-**10c** | 71 (*78*) |
| **9h** | 3-MePh | Ph | $\mathbf{L_A}$ | (*S*)-**10e** | 53 (*85*) |
| **9h** | 3-MeOPh | Ph | $\mathbf{L_A}$ | (*S*)-**10f** | 34 (*86*) |

[a] Reactions were carried out using **9** (0.5 mmol), $Ar^2B(OH)_2$ (1.0 mmol), $[RhCl(C_2H_4)_2]_2$ (1.5 mol%), $\mathbf{L_A}$ or $\mathbf{L_B}$ (3.3 mol%) and KF (3.8 equiv.) in toluene:water (2 mL, 1:1) for 16 h at 35 °C. Yields were determined by isolation. Enantioselectivities were determined by HPLC as described in Section 4.5.

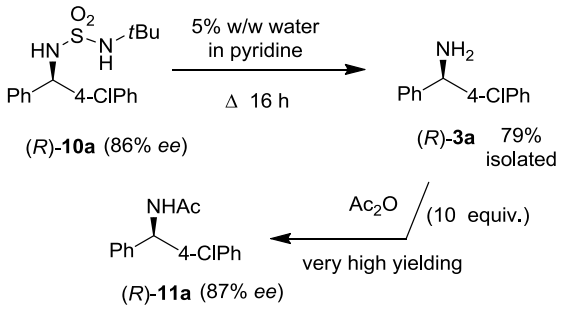
*Non-tolerated imine/boronic acid combinations for* $\mathbf{L_B}$...

| | | | |
|---|---|---|---|
| 4-ClPh / Ph | Ph / 3-MePh | 4-FPh / Ph | 3-MeOPh / Ph |
| 17% yield | 7% yield | 12% yield | 19% yield |
| 4-$CF_3$Ph / Ph | 4-MePh / Ph | 3-MePh / Ph | ....*Yields of* ***10*** |
| 17% yield | 12% yield | 7% yield | |

**Scheme 4.** Imine/boronic acid combinations leading to extensive imine hydrolysis (isolated yields of **10** given).

### 2.3. Deprotection of sulfamide addition products 10

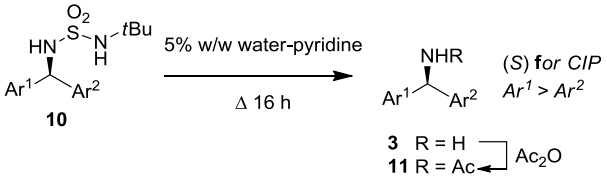
The principal reason for the development of our monoalkyl sulfamide addition products **10** was that they would undergo facile deprotection to the free diarylmethylamines **3** under mild basic conditions with good recovery and no racemisation. In a trial (*R*)-**10a** (86% *ee*) was subjected to aqueous pyridine deprotection protocol (Scheme 5). Pleasingly this provided a very high yielding conversion to the free amine (*R*)-**3a** with literature properties that could be isolated in 79% yield. Such species are not commonly isolated due to polarity/basicity issues resulting in material loss. More conveniently, direct treatment of the reaction mixture containing (*R*)-**3a** with excess $Ac_2O$ resulted in *in situ* protecting group exchange to (*R*)-**11a** (87% *ee*) allowing us to confirm that essentially no racemisation had taken place within the error on the HPLC assay (±1%). In fact *ee* measurement on **11** was by far the most convenient method in all cases.




**Scheme 5.** Representative conditions for racemisation-free deprotection of **10** and protecting group exchange.

Application of the tested deprotection strategy across the range of compounds allowed facile access to the full range of deprotected primary amines (Table 3) without degradation of enantioselectivity. While conversion of **10** to **3** was very high yielding isolation of the amines was simplified by formation of their acetamides (in an analogous way to Scheme 5). All of the compounds had properties identical to materials provided by our previous deprotections of **4**.[10] Summary conditions for the *ee* determinations are given in the Experimental Section (Table 4).

**Table 3.** Mild base-promoted deprotection of **10**.[a]




| **3** | $Ar^1$ | $Ar^2$ | Chirality | Yield **11**/% | *Ee* **11**/% |
|---|---|---|---|---|---|
| **3a** | Ph | 4-ClPh | *R* | 79 | 86 |
| **3b** | Ph | 4-FPh | *R* | 88 | 87 |
| **3c** | Ph | 4-$CF_3$Ph | *R* | 99 | 98 |
| **3d** | Ph | 4-MePh | *R* | 78 | 95 |
| **3e** | 3-MePh | Ph | *S* | 78 | 85 |
| **3f** | Ph | 3-MeOPh | *R* | 73 | 97 |

[a] Reactions were carried out using isolated samples of **10** prepared from **9** (0.5 mmol).

## 3. Conclusions

In conclusion the *N-tert*-butyl-sulfamyl group has been developed as a new activating group for imines. The imines are simply prepared by condensation of the *N-tert*-butyl-sulfamide and an arylaldehyde in the presence of $Ti(OEt)_4$. The required *N-tert*-butyl-sulfamide can be readily prepared from *tert*-$BuNH_2$ and chlorosulfonyl isocyanate in two high yielding steps. Rhodium catalysed addition of aryl boronic acids proceeds in varying yields; the optimum yield being achieved with the $\mathbf{L_B}$ ligand and the unsubstituted benzaldehyde derived imine **9d**. These aryl additions give enantioenriched sulfamides with excellent enantiomeric excess. However, in some cases extensive hydrolysis of the precursor imine is observed. This could be moderated by use of ligand $\mathbf{L_A}$. Deprotection of the resultant addition products with 5% w/w water in pyridine is very high yielding and proceeds without loss of enantiomeric excess. Overall the procedure is complementary to existing routes to **3** that normally require rather harsher deprotection strategies under either acidic or reductive conditions, or in the presence of strong nucleophiles.

## 4. Experimental

### 4.1 General

The general instrumentation used has been described previously.[10,14] All reactions involving air sensitive materials were carried out under argon using standard Schlenk techniques. Ligands $\mathbf{L_A}$-$\mathbf{L_B}$ were commercial products or prepared by literature procedures.[17]

### 4.2 Representative preparation of *N*-alkylsulfamoylcarbamates *tert*-Butyl *N*-*tert*-butylsulfamoylcarbamate 6b

Chlorosulfonyl isocyanate (8.7 mL, 0.1 mol, 1 equiv.) in toluene (10 mL) was added dropwise to a stirred solution of *tert*-butanol (9.4 mL, 0.1 mol, 1 equiv.) in toluene (100 mL) at 3 °C over 30 min. The colourless suspension was stirred at 3 °C for 45 min, then pyridine (17.7 mL, 0.22 mol, 2.2 equiv.) was added dropwise over 15 min and the suspension stirred at 7 °C for 60 min. *tert*-Butylamine (40-70 wt. % in $H_2O$, 0.6 mol, 6 equiv.) was added dropwise at 5 °C over 30 min and the biphasic mixture was stirred for 2 h at 5 °C. The layers were separated, the aqueous was washed with toluene (100 mL). The combined organics were washed with water (100 mL). The combined aqueous were acidified with 2 M HCl to pH 1 and the precipitate was collected by filtration to afford the product **6b** as a colourless crystalline solid (4.51 g, 89%). $R_f$ 0.69 (5% MeOH/$CH_2Cl_2$); m.p. 151 °C dec.; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3401, 2939, 1737, 1435, 1403, 1143; $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 7.11 (s, 1 H, NHBoc), 5.03 (s, 1 H, N*H*C($CH_3$)$_3$)), 1.50 (s, 9 H, COOC($CH_3$)$_3$), 1.36 (s, 9 H, NHC(*$CH_3$*)$_3$); $^{13}$C NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 150.2 (C), 83.5 (C), 55.0 (C), 29.4 ($CH_3$), 28.1 ($CH_3$); HRMS (ESI Positive) calcd. for $C_9H_{20}N_2O_4S$, [M+Na] 275.1036, found 275.1042; Anal. Calc. for $C_9H_{20}N_2O_4S$: C, 42.84; H, 7.99; N, 11.10%. Found: C, 42.62; H, 7.97; N, 11.05%. Other derivatives of **6** were prepared in analogous manner and had literature properties.[13,14]

### 4.3 General procedure for formation of sulfamides 7

Trifluoroacetic acid (240 mmol) in $CH_2Cl_2$ (20 mL) was added dropwise to a stirred suspension of *N*-alkylsulfamoylcarbamate **6** (80 mmol) in $CH_2Cl_2$ (100 mL) at 0 °C. The solution was stirred overnight and allowed to warm to ambient temperature. The solution was concentrated *in vacuo* and the residue was taken up in EtOAc (75 mL), washed with sat. $NaHCO_3$ solution (2 × 50 mL), dried ($Na_2SO_4$) and concentrated to a colourless oil. Compound **7b** required no purification. All other species were isolated by column chromatography (5% MeOH/$CH_2Cl_2$) as crystalline solids or pale oils with literature properties.[14,15] $R_f$ **7a** 0.24 (10:1 $CH_2Cl_2$:MeOH), $^1$H NMR (400.1 MHz, acetone-$d_6$) $\delta_H$ 5.81 (br s, 2 H, $NH_2$), 5.51 (br s, 1 H, $NHCH_3$), 2.71 (d, $J$ = 5.2 Hz, 3 H, $NHCH_3$); **7b** $R_f$ 0.16 (5% MeOH/$CH_2Cl_2$), $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 6.40 (br s, 2H, $NH_2$), 6.30 (br s, 1H, N*H*C($CH_3$)$_3$), 1.24 (s, 9H, C($CH_3$)$_3$); $R_f$ **7c** 0.22 (5% MeOH/$CH_2Cl_2$), $^1$H NMR (400.1 MHz, DMSO-$d_6$) $\delta_H$ 9.46 (s, 1 H, NHPh), 7.28-7.23 (m, 2 H, $CH_{aryl}$), 7.17-7.14 (m, 2 H, $CH_{aryl}$), 7.06 (br s, 2 H, $NH_2$) 6.96 (tt, $J$ = 7.2, 1.1 Hz, 1 H, $CH_{aryl}$).

### 4.4 General Method for synthesis of sulfamyl imines 9

*N*-Alkylsulfamide **7** (3.63 mmol, 1 equiv.) was added to a stirred solution of arylaldehyde (4.00 mmol, 1.1 equiv.) and $Ti(OEt)_4$ (1.95g, 7.26 mmol, 2 equiv.) in THF (10 mL). The solution was stirred at reflux for 7 h. Allowed to cool then poured into stirred brine (100 mL), EtOAc (50 mL) was added and the mixture stirred vigorously. The mixture was then filtered through Celite® and flushed with further EtOAc. The filtrate was separated and the aqueous was back extracted with EtOAc (50 mL). The combined organics were washed with brine (50 mL), dried ($Na_2SO_4$) and concentrated to a cream solid. Purification by column chromatography or trituration gave the product as a colourless to cream solids (yellow for **9f**).

#### 4.4.1 *N*-Methyl-*N′*-[4-chlorophenylmethylidene]sulfamide 9a

Prepared from **7a** (1.10 g, 10 mmol) and 4-chlorobenzaldehyde (1.55 g, 11 mmol) and purified by column chromatography (2:1 pet. ether:EtOAc) to give a colourless solid (1.60 g, 67%). $R_f$ 0.23 (2:1 pet. ether:EtOAc); m.p. 135-137 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3388, 1611, 1594, 1338, 1162, 842; $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 8.88 (s, 1 H, N=CH), 7.88 (dt, $J$ = 8.4, 2.3 Hz, 2 H, $CH_{aryl}$), 7.50 (dt, $J$ = 8.4, 2.2 Hz, 2 H, $CH_{aryl}$), 4.44 (br q, $J$ = 5.2 Hz, 1 H, NH), 2.84 (q, $J$ = 5.2 Hz, 3 H, $CH_3$); $^{13}$C NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 168.5 (CH), 141.1 (C), 132.0 (CH), 130.8 (C), 129.6 (CH), 29.9 ($CH_3$); HRMS (ESI Positive) calcd. for $C_8H_9N_2O_2S$, [M+Na] 254.9965, found 254.9974; Anal. Calc. for $C_8H_9N_2O_2S$: C, 41.29; H, 3.90; N, 12.04%. Found: C, 41.24; H, 3.86; N, 11.82%.

#### 4.4.2 *N*-Methyl-*N′*-[phenylmethylidene]sulfamide 9b

Prepared from **7a** (3.30 g, 30 mmol) and benzaldehyde (3.37 mL, 33 mmol), trituration with hexanes gave a cream solid (5.09 g, 86%). $R_f$ 0.19 (4:1 pet. ether:EtOAc); m.p. 127-130 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3386, 1610, 1578, 1336, 1161, 842; $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 8.93 (s, 1 H, N=CH), 7.96-7.93 (m, 2 H, $CH_{aryl}$), 7.64 (tt, $J$ = 1.6, 7.4 Hz, 1 H, $CH_{aryl}$), 7.55-7.51 (m, 2 H, $CH_{aryl}$), 4.42 (d, $J$ = 5.2 Hz, 1 H, N*H*$CH_3$), 2.84 (d, $J$ = 5.2 Hz, 3 H, NH*$CH_3$*); $^{13}$C NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 170.0 (CH), 134.6 (CH), 132.3 (C), 130.9 (CH), 129.2 (CH), 29.9 ($CH_3$); HRMS (ESI Positive) calcd. for $C_8H_{10}N_2O_2S$, [M+Na] 221.0355, found 221.0359; Anal. Calc. for $C_8H_{10}N_2O_2S$: C, 48.47; H, 5.08; N, 14.13%. Found: C, 48.28; H, 5.14; N, 13.99%.

#### 4.4.3 *N*-*tert*-Butyl-*N′*-[4-chlorophenylmethylidene]sulfamide 9c

Prepared from **7b** (1.40 g, 9.2 mmol) and 4-chlorobenzaldehyde (1.42 g, 10.1 mmol) purified by column chromatography (4:1 pet. ether:EtOAc) to give a colourless solid (1.21 g, 85%). $R_f$ 0.32 (4:1 pet. ether:EtOAc); m.p. 111-114 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3386, 2980, 1614, 1595, 1334, 1150, 999, 868; $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 8.87 (s, 1 H, N=CH), 7.85 (dt, $J$ = 8.4, 2.1 Hz, 2 H, $CH_{aryl}$), 7.49 (dt, $J$ = 8.4, 2.0 Hz, 2 H, $CH_{aryl}$), 4.46 (s, 1 H, N*H*C($CH_3$)$_3$)), 1.39 (s, 9 H, C($CH_3$)$_3$); $^{13}$C NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 166.4 (CH), 140.7 (C), 131.8 (CH), 131.1 (C), 129.6 (CH), 55.1 (C), 30.2 ($CH_3$); HRMS (ESI Positive) calcd. for $C_{11}H_{15}ClN_2O_2S$, [M+Na] 297.0435,

found 297.0441; Anal. Calc. for $C_{11}H_{15}ClN_2O_2S$: C, 48.08; H, 5.50; N, 10.20%. Found: C, 48.05; H, 5.48; N, 10.21%.

#### 4.4.4 *N*-*tert*-Butyl-*N'*-[phenylmethylidene]sulfamide 9d

Prepared from **7b** (1.14 g, 7.50 mmol) and benzaldehyde (0.84 mL, 8.25 mmol) purified by column chromatography (4:1 pet. ether:EtOAc) to give a colourless solid (1.49 g, 83%). $R_f$ 0.33 (4:1 pet. ether:EtOAc); m.p. 103-106 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3386, 2980, 1613, 1576, 1391, 1333, 1150, 998, 864; $^1H$ NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 8.92 (s, 1 H, N=CH), 7.93-7.91 (m, 2 H, $CH_{aryl}$), 7.62 (tt, *J* = 7.4, 1.5 Hz, 1 H, $CH_{aryl}$), 7.53-7.49 (m, 2 H, $CH_{aryl}$), 4.50 (s, 1 H, N*H*C$(CH_3)_3$)), 1.39 (s, 9H, C$(CH_3)_3$); $^{13}C$ NMR (100.6 MHz, CDCl3) $\delta_C$ 167.8 (CH), 134.2 (CH), 132.7 (C), 130.7 (CH), 129.1 (CH), 55.0 (C), 30.2 ($CH_3$); HRMS(ESI Positive) calcd. for $C_{11}H_{16}N_2O_2S$, [M+Na] 263.0825, found 263.0815. Anal. Calc. for $C_{11}H_{16}N_2O_2S$: C, 54.98; H, 6.71; N, 11.66%. Found: C, 54.82; H, 6.68; N, 11.71%.

#### 4.4.5 *N*-*tert*-Butyl-*N'*-[4-fluorophenylmethylidene]sulfamide 9e

Prepared from **7b** (1.14 g, 7.50 mmol) and 4-fluorobenzaldehyde (0.88 ml, 8.25 mmol) purified by column chromatography (4:1 pet. ether:EtOAc) to afford a cream solid (1.15 g, 59%). $R_f$ 0.31 (4:1 pet. ether:EtOAc); M.p. 103-105 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3386, 2939, 1601, 1510, 1333, 1242, 1149, 999; $^1H$ NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 8.88 (s, 1 H, N=CH), 7.96-7.91 (m, 2 H, $CH_{aryl}$), 7.22-7.17 (m, 2 H, $CH_{aryl}$), 4.63 (s, 1 H, N*H*C$(CH_3)_3$)), 1.39 (s, 9 H, C$(CH_3)_3$); $^{13}C$ NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 166.4 (C, d, $^1J_{CF}$ = 256 Hz), 166.3 (CH), 133.1 (CH, d, $^3J_{CF}$ = 10.2 Hz), 129.0 (C), 116.6 (CH, d, $^2J_{CF}$ = 21.8 Hz), 55.0 (C), 30.1 ($CH_3$); $^{19}F$ NMR (376.5 MHz, $CDCl_3$) $\delta_F$ −102.5; HRMS (ESI Positive) calcd. for $C_{11}H_{15}FN_2O_2S$, [M+Na] 281.0730, found 281.0724. Anal. Calc. for $C_{11}H_{15}FN_2O_2S$: C, 51.15; H, 5.85; N, 10.84%. Found: C, 51.10; H, 5.85; N, 10.84%.

#### 4.4.6 *N*-*tert*-Butyl-*N'*-[4-(trifluoromethyl)phenylmethylidene]sulfamide 9f

Prepared from 7b (1.14 g, 7.50 mmol) and 4-(trifluoromethyl)benzaldehyde (1.13 mL, 8.25

mmol) purified by column chromatography (2:1 pet. ether:EtOAc) to give the product as a yellow solid (1.93 g, 84%). $R_f$ 0.27 (4:1 pet. ether:EtOAc); m.p. 103-106 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3386, 2980, 1619, 1324, 1175, 1151, 1000; $^1H$ NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 8.96 (s, 1 H, N=CH), 8.04 (d, *J* = 8.0 Hz, 2 H, CHaryl), 7.77 (d, *J* = 8.0 Hz, 2 H, $CH_{aryl}$), 4.68 (s, 1 H, N*H*C$(CH_3)_3$), 1.40 (s, 9 H, C$(CH_3)_3$); $^{13}C$ NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 166.1 (CH), 135.7 (C), 135.3 (C, q, $^2J_{CF}$ = 32.8 Hz), 130.7 (CH), 126.1 (CH, q, $^3J_{CF}$ = 3.8 Hz), 123.4 (C, q, $^1J_{CF}$ = 271 Hz), 55.2 (C), 30.1 ($CH_3$); $^{19}F$ NMR (376.5 MHz, $CDCl_3$) $\delta_F$ −63.3; HRMS (ESI Positive) calcd. for $C_{12}H_{15}F_3N_2O_2S$, [M+Na] 331.0699, found 331.0689. Anal. Calc. for $C_{12}H_{15}F_3N_2O_2S$: C, 46.75; H, 4.90; N, 9.09%. Found: C, 46.70; H, 4.88; N, 8.97%.

#### 4.4.7 *N*-*tert*-Butyl-*N'*-[4-methylphenylmethylidene]sulfamide 9g

Prepared from **7b** (1.14 g, 7.50 mmol) and *p*-tolualdehyde (0.98 ml, 8.25 mmol) purified by column chromatography (4:1 pet. ether:EtOAc) to afford a cream solid (1.69 g, 88%). $R_f$ 0.39 (4:1 pet. ether:EtOAc); m.p. 131-134 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3386, 2979, 1603, 1569, 1332, 1148, 998, 872; $^1H$ NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 8.87 (s, 1 H, N=CH), 7.81 (d, *J* = 8.0 Hz, 2 H, $CH_{aryl}$), 7.31 (d, *J* = 8.0 Hz, 2 H, $CH_{aryl}$), 4.38 (br s, 1 H, N*H*C$(CH_3)_3$)), 2.45 (s, 3 H, Ar$CH_3$), 1.38 (s, 9 H, C$(CH_3)_3$); $^{13}C$ NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 167.7 (CH), 145.5 (C), 130.8 (CH), 130.1 (C), 129.9 (CH), 54.9 (C), 30.1 ($CH_3$), 21.9 ($CH_3$); HRMS (ESI Positive) calcd. for $C_{12}H_{18}N_2O_2S$, [M+Na] 277.0981, found 277.0982. Anal. Calc. for $C_{12}H_{18}N_2O_2S$: C, 56.67; H, 7.13; N, 11.01%. Found: C, 56.70; H, 7.13; N, 10.92%.

#### 4.4.8 *N*-*tert*-Butyl-*N'*-[3-methylphenylmethylidene]sulfamide 9h

Prepared from **7b** (1.14 g, 7.50 mmol) and *m*-tolualdehyde (0.97 mL, 8.25 mmol) purified by column chromatography (4:1 pet. ether:EtOAc) to give a cream solid (1.44 g, 76%). $R_f$ 0.26 (4:1 pet. ether:EtOAc); m.p. 85-88 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3386, 2937, 1583, 1391, 1333, 1149, 997; $^1H$ NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 8.88 (s, 1 H, N=CH), 7.73-7.69 (m, 2 H, $CH_{aryl}$), 7.44-7.37 (m, 2 H, $CH_{aryl}$), 4.51 (br s, 1 H, NH), 2.42 (s, 3 H, Ar$CH_3$), 1.39 (s, 9 H, C$(CH_3)_3$); $^{13}C$ NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 168.1 (CH), 139.0 (C), 135.2 (CH), 132.6 (C), 130.9 (CH), 129.0 (CH), 128.2 (CH), 55.0 (C), 30.2 ($CH_3$), 21.2 ($CH_3$); HRMS (ESI Positive) calcd. for $C_{12}H_{18}N_2O_2S$, [M+H] 277.0981, found 277.0989. Anal. Calc. for $C_{12}H_{18}N_2O_2S$: C, 56.67; H, 7.13; N, 11.01%. Found: C, 56.58; H, 7.13; N, 11.01%.

#### 4.4.9 *N*-*tert*-Butyl-*N'*-[3-methoxyphenylmethylidene]sulfamide 9i

Prepared from **7b** (1.14 g, 7.50 mmol) and 3-methoxybenzaldehyde (1.00 ml, 8.25 mmol) purified by column chromatography (4:1 pet. ether:EtOAc) to afford a cream solid (1.80 g, 89%). $R_f$ 0.26 (4:1 pet. ether:EtOAc); m.p. 90-93 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3386, 2941, 1581, 1333, 1150, 998, 869; $^1H$ NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 8.87 (s, 1 H, N=CH), 7.48-7.39 (m, 3 H, $CH_{aryl}$), 7.16 (ddd, *J* = 8.0, 2.8, 1.6 Hz, 1 H, $CH_{aryl}$), 4.57 (br s, 1 H, N*H*C$(CH_3)_3$)), 3.87 (s, 3 H, $OCH_3$), 1.39 (s, 9 H, C$(CH_3)_3$); $^{13}C$ NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 167.8 (CH), 160.1 (C), 134.0 (C), 130.1 (CH), 124.4 (CH), 121.1 (CH), 113.4 (CH), 55.5 ($CH_3$), 55.0 (C), 30.1 ($CH_3$); HRMS (ESI Positive) calcd. for $C_{12}H_{18}N_2O_3S$, [M+Na] 293.0930, found 293.0927. Anal. Calc. for $C_{12}H_{18}N_2O_3S$: C, 53.31; H, 6.71; N, 10.36%. Found: C, 53.26; H, 6.67; N, 10.24%.

### 4.5 General method for rhodium catalysed boronic acid addition to sulfamyl imines 9

A flame dried Schlenk was charged with $[RhCl(C_2H_4)_2]_2$ (2.9 mg, 7.5 μmol, 1.5 mol%), ligand (16.5 μmol, 3.3 mol%) and toluene (0.4 mL), the orange solution was stirred at

ambient temperature for 10 min. Toluene (0.6 mL), water (1 mL), $Ar^2B(OH)_2$ (1 mmol, 2 equiv.), KF (110.4 mg, 1.9 mmol, 3.8 equiv.) and sulfamyl imine **9** (0.5 mmol, 1 equiv.) were added sequentially. The biphasic mixture was gently stirred at 35 °C for 16 h. Water (10 mL) added and washed with $CH_2Cl_2$ (2 × 20 mL). The combined organics were washed with brine (10 mL), dried ($Na_2SO_4$) and concentrated. If necessary, undesired by-products could be removed by stirring residue in 1:1 $CH_2Cl_2$:2 M HCl (10 mL). Purification by column chromatography gave the final products **10** (see individual conditions).

Authentic racemic samples of **10** were prepared by PhMgCl (4.0 equiv.) addition to **9** (0.50 mmol) in THF (10 mL) at 0 °C. The reactions were allowed to come to ambient temperature while being stirred (18 h) followed by standard workup. Alternatively $Ar^2Li$ was pre-formed in THF at -78 °C and treated with **9d** (3 h, -78 °C) followed by aqueous quench and an identical workup.

#### 4.5.1 (*S*)-*N*-*tert*-Butyl-*N*'-(4-chlorophenyl)(phenyl)methylsulfamide (*S*)-10a

Prepared from **9c** (137.4 mg, 0.50 mmol) using $\mathbf{L_A}$ and purified by column chromatography (4:1 pet. ether:EtOAc) to give a white solid (156.8 mg, 89%); Rf 0.29 (4:1 pet. ether:EtOAc); m.p. 157-159 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3383, 2980, 1491, 1324, 1145; $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 7.36-7.26 (m, 9 H, $CH_{aryl}$), 5.59 (d, *J* = 6.7 Hz, 1 H, NHC*H*), 4.85 (d, *J* = 6.7 Hz, 1 H, N*H*CH), 4.02 (s, 1 H, N*H*C$(CH_3)_3$), 1.18 (s, 9 H, C$(CH_3)_3$); $^{13}$C NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 140.9 (C), 140.0 (C), 133.2 (C), 128.8 (CH), 128.7 (CH), 128.6 (CH), 127.8 (CH), 127.4 (CH), 60.8 (CH), 54.2 (C), 29.5 ($CH_3$); HRMS (ESI Positive) calcd. for $C_{17}H_{21}ClN_2O_2S$, [M+Na] 375.0904, found 375.0916. Anal. Calc. for $C_{17}H_{21}ClN_2O_2S$: C, 57.86; H, 6.00; N, 7.94%. Found: C, 57.63; H, 6.02; N, 7.77%. HPLC: Daicel Chiralpak OD-H, 95:5 hexanes:*i*PrOH; 1.0 mL/min; 200 nm; (*S*)-enantiomer $t_S$ = 22.2 min, (*R*)-enantiomer $t_R$ = 30.1 min; $[\alpha]_D$ = −1.9 (*c* = 1.09, $CHCl_3$, for 81% *ee* material). A sample of (*R*)-**10a** (83% yield, 94% *ee*) was prepared from **9d** and $\mathbf{L_B}$ which showed equivalent properties aside from its optical rotation.

#### 4.5.2 (*R*)-*N*-*tert*-Butyl-*N*'-(4-fluorophenyl)(phenyl)methylsulfamide (*R*)-10b

Prepared from **9d** (120 mg, 0.50 mmol) using $\mathbf{L_B}$ and purified by column chromatography (4:1 pet. ether:EtOAc) to give a colourless solid (151 mg, 90%). $R_f$ 0.25 (4:1 pet. ether:EtOAc); m.p. 133-135 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3383, 2980, 1606, 1510, 1322, 1144, 991; $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 7.36-7.26 (m, 7 H, $CH_{aryl}$), 7.04-6.98 (m, 2 H, $CH_{aryl}$), 5.60 (d, *J* = 6.8 Hz, 1 H, NHC*H*), 4.89 (d, *J* = 6.8 Hz, 1 H, N*H*CH), 4.05 (s, 1 H, N*H*C$(CH_3)_3$), 1.17 (s, 9 H, C$(CH_3)_3$); $^{13}$C NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 162.1 (C, d, $^1J_{CF}$ = 246 Hz), 141.1 (C), 137.1 (C, d, $^4J_{CF}$ = 2.9 Hz), 129.2 (CH, d, $^3J_{CF}$ = 8.8 Hz), 128.8 (CH), 127.9 (CH), 127.4 (CH), 115.5 (CH, d, $^2J_{CF}$ = 20.3 Hz), 61.0 (CH), 54.4 (C), 29.5 ($CH_3$); $^{19}$F NMR (376.5 MHz, $CDCl_3$) $\delta_F$ −114.1; HRMS (ESI Positive) calcd. for $C_{17}H_{21}FN_2O_2S$, [M+Na] 359.1200, found 359.1197; Anal. Calc. for $C_{17}H_{21}FN_2O_2S$: C, 60.69; H, 6.29; N, 8.33%. Found: C, 60.58; H, 6.26; N, 8.22%; HPLC: Daicel Chiralpak OD-H, 95:5 hexanes:*i*PrOH; 1.0 mL/min; 200 nm; (*S*)-enantiomer $t_S$ = 20.1 min, (*R*)-enantiomer $t_R$ = 25.2 min; $[\alpha]_D$ = +0.5 (*c* = 0.97, $CHCl_3$, for 95% *ee* material). A sample of (*S*)-**10b** (41% yield, 80% *ee*) was prepared from **9e** and $\mathbf{L_A}$ which showed equivalent properties aside from its optical rotation.

#### 4.5.3 (*R*)-*N*-*tert*-Butyl-*N*'-(4-trifluoromethylphenyl)(phenyl)methylsulfamide (*R*)-10c

Prepared from **9d** (120 g, 0.50 mmol) using $\mathbf{L_B}$ and purified by column chromatography (4:1 pet. ether:EtOAc) to give a colourless solid (162 mg, 84%). $R_f$ 0.13 (4:1 pet. ether:EtOAc); M.p. 140-143 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3382, 2979, 1421, 1326, 1169, 1144, 991; $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 7.60 (d, *J* = 8.0 Hz, 2 H, $CH_{aryl}$), 7.49 (d, *J* = 8.8 Hz, 2 H, $CH_{aryl}$), 7.40-7.28 (m, 5 H, $CH_{aryl}$), 5.67 (d, *J* = 6.4 Hz, 1 H, C*H*NH), 4.83 (d, *J* = 6.8 Hz, 1 H, CHN*H*), 3.98 (s, 1 H. N*H*C$(CH_3)_3$), 1.19 (s, 9 H, C$(CH_3)_3$); $^{13}$C NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 145.3 (C), 140.6 (C), 129.8 (C, q, $^2J_{CF}$ = 32 Hz), 128.9 (CH), 128.2 (CH), 127.8 (CH), 127.5 (CH), 125.5 (CH, q, $^3J_{CF}$ = 3.6 Hz), 124.0 (C, q, $^1J_{CF}$ = 271 Hz), 61.2 (CH), 54.4 (C), 29.5 ($CH_3$); $^{19}$F NMR (376.5 MHz, $CDCl_3$) $\delta_F$ −62.5; HRMS (ESI Positive) calcd. for $C_{18}H_{21}F_3N_2O_2S$, [M+Na] 409.1168, found 409.1167. Anal. Calc. for $C_{18}H_{21}F_3N_2O_2S$: C, 55.95; H, 5.48; N, 7.25%. Found: C, 55.95; H, 5.47; N, 7.12%; HPLC: Daicel Chiralpak OD-H, 95:5 hexanes:*i*PrOH; 1.0 mL/min; 200 nm; (*S*)-enantiomer $t_S$ = 13.6 min, (*R*)-enantiomer $t_R$ = 22.1 min; $[\alpha]_D$ = −3.7 (*c* = 1.35, $CHCl_3$, for 98% *ee* material). A sample of (*S*)-**10c** (71% yield, 78% *ee*) was prepared from **9f** and $\mathbf{L_A}$ which showed equivalent properties aside from its optical rotation.

#### 4.5.4 (*R*)-*N*-*tert*-Butyl-*N*'-(4-methylphenyl)(phenyl)methylsulfamide (*R*)-10d

Prepared from **9d** (127 mg, 0.50 mmol) using $\mathbf{L_B}$ and purified by column chromatography (4:1 pet. ether:EtOAc) to give a colourless solid (119 mg, 71%). $R_f$ 0.33 (4:1 pet. ether:EtOAc); m.p. 147-149 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3384, 3011, 1321, 1144, 990; $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 7.34-7.32 (m, 4 H, $CH_{aryl}$), 7.30-7.25 (m, 1 H, $CH_{aryl}$), 7.22-7.20 (m, 2 H, $CH_{aryl}$), 7.15-7.13 (m, 2 H, $CH_{aryl}$), 5.59 (d, *J* = 6.4 Hz, 1 H, NHC*H*), 4.74 (d, *J* = 6.4 Hz, 1 H, N*H*CH), 3.84 (br s, 1 H, N*H*C$(CH_3)_3$), 2.33 (s, 3 H, Ar$CH_3$), 1.17 (s, 9 H, C$(CH_3)_3$); $^{13}$C NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 141.4 (C), 138.3 (C), 137.5 (C), 129.4 (CH), 128.7 (CH), 127.6 (CH), 127.5 (CH), 127.4 (CH), 61.5 (CH), 54.3 (C), 29.6 ($CH_3$), 21.0 ($CH_3$); HRMS (ESI Positive) calcd. for $C_{18}H_{24}N_2O_2S$, [M+Na] 355.1451, found 355.1450. Anal. Calc. for $C_{18}H_{24}N_2O_2S$: C, 65.05; H, 7.28; N, 8.43%. Found: C, 64.98; H, 7.30; N, 8.20%; HPLC: Daicel Chiralpak OD-H, 95:5 hexanes:*i*PrOH; 1.0 mL/min; 200 nm; (*S*)-enantiomer $t_S$ = 21.1 min, (*R*)-enantiomer $t_R$ = 26.1 min. $[\alpha]_D$ = +3.9 (*c* = 0.99, $CHCl_3$, for 95% *ee* material).

#### 4.5.5 (*S*)-*N*-*tert*-Butyl-*N*'-(3-methylphenyl)(phenyl)methylsulfamide (*S*)-10e

Prepared from **9h** (120 mg, 0.50 mmol) and $\mathbf{L_A}$ purified by column chromatography (4:1 pet. ether:EtOAc) to give a colourless solid (89 mg, 54%). $R_f$ 0.30 (4:1 pet. ether:EtOAc); m.p. 90-93 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3384, 2978, 1391, 1324, 1144, 990; $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 7.34-7.19 (m, 6 H, $CH_{aryl}$), 7.14-7.06 (m, 3 H, $CH_{aryl}$), 5.57 (d, $J$ = 6.8 Hz, 1 H, C*H*NH), 4.91 (d, $J$ = 6.4 Hz, 1 H, CHN*H*), 4.05 (s, 1 H, N*H*C$(CH_3)_3$), 2.32 (s, 3 H, Ar$CH_3$), 1.15 (s, 9 H, C(C*H*$_3)_3$); $^{13}$C NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 141.4 (C), 141.2 (C), 138.3 (C), 128.60 (CH), 128.55 (CH), 128.4 (CH), 128.2 (CH), 127.6 (CH), 127.5 (CH), 124.5 (CH), 61.6 (CH), 54.2 (C), 29.5 ($CH_3$), 21.4 ($CH_3$); HRMS (ESI Positive) calcd. for $C_{18}H_{24}N_2O_2S$, [M+Na] 355.1451, found 355.1450. Anal. Calc. for $C_{18}H_{24}N_2O_2S$: C, 65.03; H, 7.28; N, 8.43%. Found: C, 65.03; H, 7.28; N, 8.41%; HPLC: Daicel Chiralpak AD, 95:5 hexanes:*i*PrOH; 1.0 mL/min; 200 nm; (*S*)-enantiomer $t_S$ = 26.3 min, (*R*)-enantiomer $t_R$ = 35.6 min. $[\alpha]_D$ = −2.0 (*c* = 1.10, $CHCl_3$, for 85% *ee* material). A sample of (*R*)-**10e** (35% yield, 76% *ee*) was prepared from **9d** and $\mathbf{L_A}$ which showed equivalent properties aside from its optical rotation.

### 4.5.6 (*R*)-*N*-*tert*-Butyl-*N*'-(3-methoxyphenyl)(phenyl)methylsulfamide (*R*)-10f

Prepared from **9d** (120 mg, 0.50 mmol) and $L_B$ purified by column chromatography (4:1 pet. ether:EtOAc) to give a colourless solid (158 mg, 91%). $R_f$ 0.28 (4:1 pet. ether:EtOAc); m.p. 100-103 °C; IR ($CHCl_3$) $\nu_{max}/cm^{-1}$ 3383, 2969, 1600, 1321, 1240, 1042; $^1$H NMR (400.1 MHz, $CDCl_3$) $\delta_H$ 7.34-7.32 (m, 6 H, $CH_{aryl}$), 6.92-6.88 (m, 2 H, $CH_{aryl}$), 6.82-6.80 (m, 1 H, $CH_{aryl}$), 5.59 (d, $J$ = 6.4 Hz, 1 H, NHC*H*), 4.80 (d, $J$ = 6.8 Hz, 1 H, N*H*CH), 3.91 (br s, 1 H, N*H*C$(CH_3)_3$), 3.78 (s, 3 H, $OCH_3$), 1.18 (s, 9 H, C$(CH_3)_3$); $^{13}$C NMR (100.6 MHz, $CDCl_3$) $\delta_C$ 159.8 (C), 142.9 (C), 141.2 (C), 129.7 (CH), 128.6 (CH), 127.6 (CH), 127.5 (CH), 119.8 (CH), 113.4 (CH), 112.9 (CH), 61.6 (CH), 55.2 ($CH_3$), 54.2 (C), 29.5 ($CH_3$); HRMS (ESI Positive) calcd. for $C_{18}H_{24}N_2O_3S$, [M+Na] 371.1400, found 371.1390. Anal. Calc. for $C_{18}H_{24}N_2O_3S$: C, 62.04; H, 6.94; N, 8.04%. Found: C, 61.90; H, 6.91; N, 8.06%; HPLC: Daicel Chiralpak AD, 95:5 hexanes:*i*PrOH; 0.5 mL/min; 200 nm; (*S*)-enantiomer $t_S$ = 95.6 min, (*R*)-enantiomer $t_R$ = 104.0 min. $[\alpha]_D$ = −1.0 (*c* = 1.26, $CHCl_3$, for 97% *ee* material). A sample of (*S*)-**10f** (34% yield, 86% *ee*) was prepared from **9h** and $\mathbf{L_A}$ which showed equivalent properties aside from its optical rotation.

### 4.6 Deprotection and acetylation of sulfamides 10, formation of 3 and 11

A solution of the sulfamide **10** (typically *ca*. 0.4 mmol) in 5% water-pyridine (10 mL) was stirred at reflux overnight. Removal of the solvents afforded the amines **3** directly. Alternatively, the solution was allowed to cool and acetic anhydride (10 eq) was added, stirred at ambient temperature for 7 h. Subsequently 1 M HCl (20 mL) was added and the mixture extracted with $Et_2O$ (2 × 15 mL). The combined organic extracts were washed with 2 M HCl (2 × 20 mL), water (20 mL) and brine (20 mL), dried ($Na_2SO_4$) and concentrated to give the product with no further purification necessary. Full data for both the amines[7,14] and their acyl derivatives[14,18] are available. Summary data for the *ee* assays on the acetamides **11** are given in Table 4.

**Table 4.** Enantiopurity determination using **11**.[a]

| **3** | $Ar^1$ | $Ar^2$ | HPLC conditions[b] | $[\alpha]_D$ **11**/%[c] |
|---|---|---|---|---|
| **11a** | Ph | 4-ClPh | OD, 95:5, 1 mL min$^{-1}$ $t_S$ = 22.2, $t_R$ = 33.6 min | -1.1 (*R*, *c* = 1.3, 87% *ee*)[d] |
| **11b** | Ph | 4-FPh | OD, 95:5, 1 mL min$^{-1}$ $t_S$ = 8.8, $t_R$ = 13.6 min | -1.2 (*R*, *c* = 1.1, 95% *ee*) |
| **11c** | Ph | 4-$CF_3$Ph | OD-H, 90:10, 1 mL min$^{-1}$ $t_S$ = 6.6, $t_R$ = 11.0 min | +33.6 (*S*, *c* = 0.62, 89% *ee*)[e] |
| **11d** | Ph | 4-MePh | OD-H, 90:10, 1 mL min$^{-1}$ $t_S$ = 8,0, $t_R$ = 10.1 min | -1.7 (*R*, *c* = 1.0, 97% *ee*) |
| **11e** | 3-MePh | Ph | AH-H+AD in series, 95:5, 1 mL min$^{-1}$ $t_S$ = 27.6, $t_R$ = 32.0 min | +1.3 (*S*, *c* = 1.1, 85% *ee*) |
| **11f** | Ph | 3-MeOPh | OD, 95:5, 1 mL min$^{-1}$ $t_S$ = 13.7, $t_R$ = 27.9 min | n/d |

[a] Carried out on acetamides prepared directly from *in situ* **3** (0.3-0.5 mmol) by the chemistry of Table 4.
[b] Data in the form: column type, ratio of hexanes:*iso*-PrOH, flow rate, enantiomer elution order. A detector wavelength of 200 nm was used in all cases.
[c] At ambient temperature in $CHCl_3$ unless otherwise stated.
[d] In EtOH.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