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

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

[a] *School of Chemistry, The University of Nottingham, University Park, Nottingham NG7 2RD, United Kingdom*
[b] *Chirotech Technology Centre, Dr. Reddy's Laboratories EU Ltd, Unit 410 Cambridge Science Park, Milton Road, Cambridge CB4 0PE, United Kingdom*

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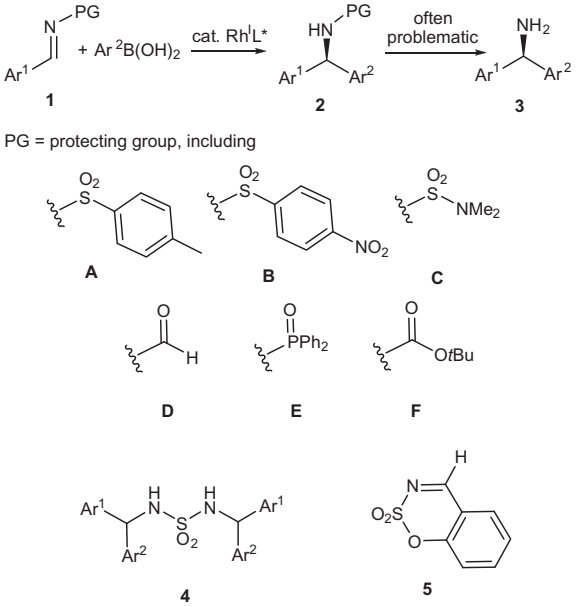
ABSTRACT

The 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 stereoselectivity (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

Over the last decade or so since Miyaura introduced the rhodium-catalysed addition of arylboron reagents to activated imines (2000)[1] a large range of catalytic systems 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 obtain protecting groups that simultaneously strongly activate imine **1** to addition reactions, but also allow for mild deprotection of the addition products **2** to the commercially interesting diarylmethylamines **3** (Scheme 1).[3] *N*-Tosyl protected imines **A** are used widely 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 conditions 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 decomposition.[7] *N*-Diphenylphosphinoyl groups **E** have been popularised by Ellman and others, but add significantly to the imine mass.[8] Finally, Boc protection **F** can be used, but this group is sometimes too labile.[9] 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**, and can be removed under mildly basic conditions (5% water in pyridine), conditions that are complementary to groups **A**–**D**.[10] However, the presence of two stereocentres in **4** complicates their *ee* assay. In order 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 substrates **5**, which are restricted to the use of salicyladehyde derived aldimines.[11] This prompted us to disclose our own approach which places no restrictions on Ar^1.



Scheme 1. Typical approach to 2-arylethylamines.

* Corresponding author. Fax: +44 115 9513564.
E-mail address: simon.woodward@nottingham.ac.uk (S. Woodward).

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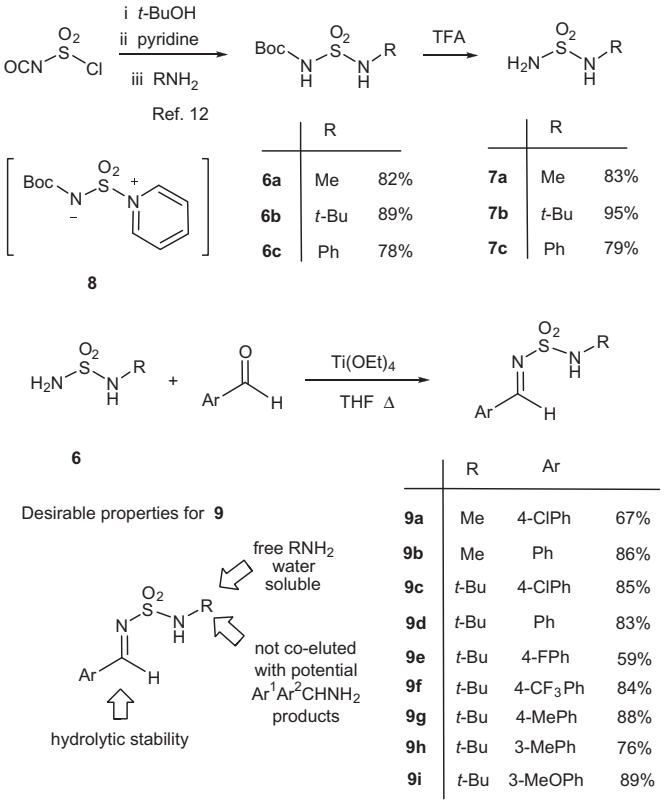
2. Results and discussion

2.1. Synthesis of sulfamyl imine acceptors 9

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

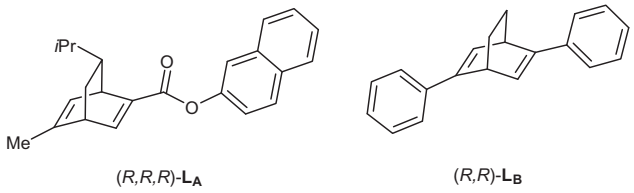
	R	Ar	
9a	Me	4-ClPh	67%
9b	Me	Ph	86%
9c	*t*-Bu	4-ClPh	85%
9d	*t*-Bu	Ph	83%
9e	*t*-Bu	4-FPh	59%
9f	*t*-Bu	4-CF_3Ph	84%
9g	*t*-Bu	4-MePh	88%
9h	*t*-Bu	3-MePh	76%
9i	*t*-Bu	3-MeOPh	89%

Scheme 2. Preparation of activated imines used herein.

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 can be easily removed under the same conditions as the deprotection of **4**[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, thus facilitating its simple separation; other substituents (e.g., benzyl or aryl derivatives) required chromatographic separations; and (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** does not appear to have been used in additions to imines, although it is clearly closely related to $RCH{=}NSO_2NR_2$ structures.[6]

2.2. Catalytic 1,2-arylboron additions to 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 array of ligands and organoboron sources used 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 a widely available rhodium source $[RhCl(CH_2{=}CH_2)_2]_2$.

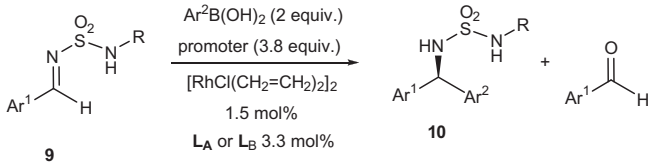


Scheme 3. Chiral ligands used herein.

Our 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 to be the most appropriate for the use of boronic acids (Table 1).

While interesting levels of enantioselectivity (84–91%) were realised in the 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 by-products (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 the 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. We then turned our attention 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). While the system 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 promoted extensive hydrolysis of **9c**. Moderate results were attained with $\mathbf{L_A}$ (runs 5–6). The yields attained of addition products **10** are a composite of: (i) imine electrophilicity (promoting both the addition and hydrolysis); (ii) steric/electronic nature of the arylboronic acid (controlling the rate of catalyst loading and hydrodeboration); and (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 did 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.

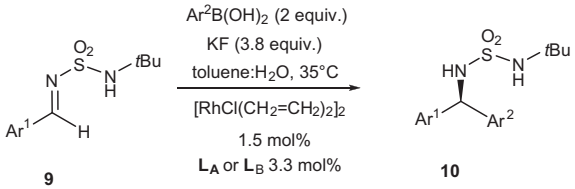
Table 1
Optimisation of catalytic $ArB(OH)_2$ addition to **9**[a]



Run	Ar^1	R	Ar^2	Solvent and base	Yield **10** (*ee*) (%)	Hydrol (%)
Using ligand 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 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 %), L_A (3.3 mol %) and a base (3.8 equiv) in solvent (1 mL) and water (1 mL) for 16 h at 35 °C. Yields were determined by isolation, except for runs 3, 8 and 10, which were determined from ^{1}H NMR conversions. Enantioselectivities were determined by HPLC as described in Section 4.5.

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



9	Ar^1	Ar^2	L used	10	Yield (*ee*) (%)
9c	4-ClPh	Ph	L_A	(*S*)-**10a**	89 (81)
9d	Ph	4-ClPh	L_A	(*R*)-**10a**	83 (86)
9d	Ph	4-ClPh	L_B	(*R*)-**10a**	84 (94)
9d	Ph	4-FPh	L_A	(*R*)-**10b**	42 (87)
9d	Ph	4-FPh	L_B	(*R*)-**10b**	90 (95)
9d	Ph	4-CF_3Ph	L_A	(*R*)-**10c**	32 (90)
9d	Ph	4-CF_3Ph	L_B	(*R*)-**10c**	84 (98)
9d	Ph	4-MePh	L_A	(*R*)-**10d**	68 (78)
9d	Ph	4-MePh	L_B	(*R*)-**10d**	71 (95)
9d	Ph	3-MePh	L_A	(*R*)-**10e**	35 (76)
9d	Ph	3-MeOPh	L_A	(*R*)-**10f**	37 (84)
9d	Ph	3-MeOPh	L_B	(*R*)-**10f**	91 (97)
9e	4-FPh	Ph	L_A	(*S*)-**10b**	41 (80)
9f	4-CF_3Ph	Ph	L_A	(*S*)-**10c**	71 (78)
9h	3-MePh	Ph	L_A	(*S*)-**10e**	53 (85)
9h	3-MeOPh	Ph	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 %), L_A or 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.

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

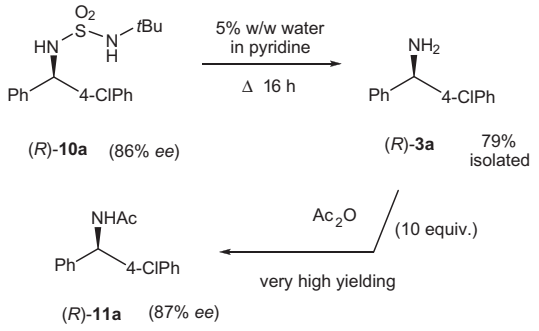
Non-tolerated imine/boronic acid combinations for L_B

4-ClPh / Ph	Ph / 3-MePh	4-FPh / Ph	3-MeOPh / Ph
17% yield	7% yield	12% yield	19% yield
4-CF_3Ph/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 main 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 run, (*R*)-**10a** (86% *ee*) was subjected to an aqueous pyridine deprotection protocol (Scheme 5). This provided a very high yielding

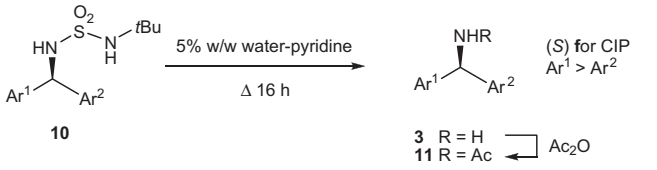


Scheme 5. Representative conditions for the racemisation-free deprotection of **10** and protecting group exchange.

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, the direct treatment of the reaction mixture containing (*R*)-**3a** with excess Ac_2O resulted in the 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, the *ee* measurement on **11** was by far the most convenient method in all cases.

Application of the deprotection strategy across a range of compounds allowed facile access to a full range of deprotected primary amines (Table 3) without degradation of the enantioselectivity. While conversion of **10**–**3** was very high yielding, isolation of the amines was simplified by the 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 Section 4 (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_3Ph	(*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. Conclusion

In conclusion, an *N*-*tert*-butyl-sulfamyl group has been developed as a new activating group for imines. The imines are prepared by condensation of *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. The rhodium catalysed addition of aryl boronic acids proceeded in varying yields; the optimum yield was 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 the 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 a loss of enantiomeric excess. Overall the procedure is complementary to existing routes to **3** that normally require 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. Next, *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 and the aqueous phase was washed with toluene (100 mL). The combined organic phases 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); mp 151 °C dec; IR ($CHCl_3$) ν_{max}/cm^{-1} 3401, 2939, 1737, 1435, 1403, 1143; ^1H NMR (400.1 MHz, $CDCl_3$) δ_H 7.11 (s, 1H, NHBoc), 5.03 (s, 1H, N*H*C(CH_3)$_3$)), 1.50 (s, 9H, COOC(CH_3)$_3$), 1.36 (s, 9H, NHC(*C*H_3)$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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 properties that matched the literature.[13,14]

4.3. General procedure for the 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**

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 (*c* 1.3) 87% *ee* (*R*)[d]
11b	Ph	4-FPh	OD, 95:5, 1 mL min^{-1} t_S = 8.8, t_R = 13.6 min	−1.2 (*c* 1.1) 95% *ee* (*R*)
11c	Ph	4-CF_3Ph	OD-H, 90:10, 1 mL min^{-1} t_S = 6.6, t_R = 11.0 min	+33.6 (*c* 0.62) 89% *ee* (*S*)[e]
11d	Ph	4-MePh	OD-H, 90:10, 1 mL min^{-1} t_S = 8,0, t_R = 10.1 min	−1.7 (*c* 1.0) 97% *ee* (*R*)
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 (*c* 1.1) 85% *ee* (*S*)
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.
[e] Literature value, ref. 18b.

(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) δ_H 5.81 (brs, 2H, NH_2), 5.51 (brs, 1H, $NHCH_3$), 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, $CDCl_3$) δ_H 6.40 (brs, 2H, NH_2), 6.30 (brs, 1H, N*HC*$(CH_3)_3$), 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) δ_H 9.46 (s, 1H, NHPh), 7.28–7.23 (m, 2H, CH_{aryl}), 7.17–7.14 (m, 2H, CH_{aryl}), 7.06 (brs, 2H, NH_2) 6.96 (tt, J = 7.2, 1.1 Hz, 1H, CH_{aryl}).

4.4. General method for the 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)$_4$ (1.95 g, 7.26 mmol, 2 equiv) in THF (10 mL). The solution was stirred at reflux for 7 h, allowed to cool and then poured into stirred brine (100 mL), EtOAc (50 mL) was added and the mixture was stirred vigorously. The mixture was then filtered through Celite® and flushed with further EtOAc. The filtrate was separated and the aqueous layer was back extracted with EtOAc (50 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4) and concentrated to a cream solid. Purification by column chromatography or trituration gave the products as 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); mp 135–137 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3388, 1611, 1594, 1338, 1162, 842; ^{1}H NMR (400.1 MHz, $CDCl_3$) δ_H 8.88 (s, 1H, N=CH), 7.88 (dt, J = 8.4, 2.3 Hz, 2H, CH_{aryl}), 7.50 (dt, J = 8.4, 2.2 Hz, 2H, CH_{aryl}), 4.44 (br q, J = 5.2 Hz, 1H, NH), 2.84 (q, J = 5.2 Hz, 3 H, CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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); mp 127–130 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3386, 1610, 1578, 1336, 1161, 842; ^{1}H NMR (400.1 MHz, $CDCl_3$) δ_H 8.93 (s, 1H, N=CH), 7.96–7.93 (m, 2H, CH_{aryl}), 7.64 (tt, J = 1.6, 7.4 Hz, 1H, CH_{aryl}), 7.55–7.51 (m, 2H, CH_{aryl}), 4.42 (d, J = 5.2 Hz, 1H, N*H*CH_3), 2.84 (d, J = 5.2 Hz, 3 H, NH*CH*$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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); mp 111–114 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3386, 2980, 1614, 1595, 1334, 1150, 999, 868; ^{1}H NMR (400.1 MHz, $CDCl_3$) δ_H 8.87 (s, 1H, N=CH), 7.85 (dt, J = 8.4, 2.1 Hz, 2H, CH_{aryl}), 7.49 (dt, J = 8.4, 2.0 Hz, 2H, CH_{aryl}), 4.46 (s, 1H, N*HC*$(CH_3)_3$)), 1.39 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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); mp 103–106 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3386, 2980, 1613, 1576, 1391, 1333, 1150, 998, 864; ^{1}H NMR (400.1 MHz, $CDCl_3$) δ_H 8.92 (s, 1H, N=CH), 7.93–7.91 (m, 2H, CH_{aryl}), 7.62 (tt, J = 7.4, 1.5 Hz, 1H, CH_{aryl}), 7.53–7.49 (m, 2H, CH_{aryl}), 4.50 (s, 1H, N*HC*$(CH_3)_3$)), 1.39 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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); mp 103–105 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3386, 2939, 1601, 1510, 1333, 1242, 1149, 999; ^{1}H NMR (400.1 MHz, $CDCl_3$) δ_H 8.88 (s, 1H, N=CH), 7.96–7.91 (m, 2H, CH_{aryl}), 7.22–7.17 (m, 2H, CH_{aryl}), 4.63 (s, 1H, N*HC*$(CH_3)_3$)), 1.39 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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, $CDCl_3$) δ_F −102.5; HRMS (ESI Positive) calcd for $C_{11}H_{15}FN_2O_2S$, [M+Na] 281.0730, found 281.0724. Anal. Calcd 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); mp 103–106 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3386, 2980, 1619, 1324, 1175, 1151, 1000; ^{1}H NMR (400.1 MHz, $CDCl_3$) δ_H 8.96 (s, 1H, N=CH), 8.04 (d, J = 8.0 Hz, 2H, CH_{aryl}), 7.77 (d, J = 8.0 Hz, 2H, CH_{aryl}), 4.68 (s, 1H, N*HC*$(CH_3)_3$), 1.40 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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, $CDCl_3$) δ_F −63.3; HRMS (ESI Positive) calcd for $C_{12}H_{15}F_3N_2O_2S$, [M+Na] 331.0699, found 331.0689. Anal. Calcd 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); mp 131–134 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3386, 2979, 1603, 1569, 1332, 1148, 998, 872; ^{1}H NMR (400.1 MHz, $CDCl_3$) δ_H 8.87 (s, 1H, N=CH), 7.81 (d, J = 8.0 Hz, 2H, CH_{aryl}), 7.31 (d, J = 8.0 Hz, 2H, CH_{aryl}), 4.38 (brs, 1H, N*HC*$(CH_3)_3$)), 2.45 (s, 3 H, $ArCH_3$), 1.38 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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); mp 85–88 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3386, 2937, 1583, 1391, 1333, 1149, 997; ^1H NMR (400.1 MHz, $CDCl_3$) δ_H 8.88 (s, 1H, N=CH), 7.73–7.69 (m, 2H, CH_{aryl}), 7.44–7.37 (m, 2H, CH_{aryl}), 4.51 (brs, 1H, NH), 2.42 (s, 3 H, $ArCH_3$), 1.39 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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); mp 90–93 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3386, 2941, 1581, 1333, 1150, 998, 869; ^1H NMR (400.1 MHz, $CDCl_3$) δ_H 8.87 (s, 1H, N=CH), 7.48–7.39 (m, 3 H, CH_{aryl}), 7.16 (ddd, J = 8.0, 2.8, 1.6 Hz, 1H, CH_{aryl}), 4.57 (brs, 1H, N*H*C$(CH_3)_3$)), 3.87 (s, 3 H, OCH_3), 1.39 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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 the 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) was then added and washed with CH_2Cl_2 (2 × 20 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4) and concentrated. If necessary, undesired by-products could be removed by stirring the 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 return to ambient temperature while being stirred (18 h) followed by standard work-up. Alternatively Ar^2Li was pre-formed in THF at −78 °C and treated with **9d** (3 h, −78 °C) followed by aqueous quenching 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%); R_f 0.29 (4:1 pet. ether/EtOAc); mp 157–159 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3383, 2980, 1491, 1324, 1145; ^1H NMR (400.1 MHz, $CDCl_3$) δ_H 7.36–7.26 (m, 9H, CH_{aryl}), 5.59 (d, J = 6.7 Hz, 1H, NHC*H*), 4.85 (d, J = 6.7 Hz, 1H, N*H*CH), 4.02 (s, 1H, N*H*C$(CH_3)_3$), 1.18 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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 specific 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); mp 133–135 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3383, 2980, 1606, 1510, 1322, 1144, 991; ^1H NMR (400.1 MHz, $CDCl_3$) δ_H 7.36–7.26 (m, 7 H, CH_{aryl}), 7.04–6.98 (m, 2H, CH_{aryl}), 5.60 (d, J = 6.8 Hz, 1H, NHC*H*), 4.89 (d, J = 6.8 Hz, 1H, N*H*CH), 4.05 (s, 1H, N*H*C$(CH_3)_3$), 1.17 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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, $CDCl_3$) δ_F −114.1; HRMS (ESI Positive) calcd for $C_{17}H_{21}FN_2O_2S$, [M+Na] 359.1200, found 359.1197; Anal. Calcd 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 specific 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); mp 140–143 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3382, 2979, 1421, 1326, 1169, 1144, 991; ^1H NMR (400.1 MHz, $CDCl_3$) δ_H 7.60 (d, J = 8.0 Hz, 2H, CH_{aryl}), 7.49 (d, J = 8.8 Hz, 2H, CH_{aryl}), 7.40–7.28 (m, 5 H, CH_{aryl}), 5.67 (d, J = 6.4 Hz, 1H, C*H*NH), 4.83 (d, J = 6.8 Hz, 1H, CHN*H*), 3.98 (s, 1H, N*H*C$(CH_3)_3$), 1.19 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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, $CDCl_3$) δ_F −62.5; HRMS (ESI Positive) calcd for $C_{18}H_{21}F_3N_2O_2S$, [M+Na] 409.1168, found 409.1167. Anal. Calcd 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 specific 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); mp 147–149 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3384, 3011, 1321, 1144, 990; ^1H NMR (400.1 MHz, $CDCl_3$) δ_H 7.34–7.32 (m, 4 H, CH_{aryl}), 7.30–7.25 (m, 1H, CH_{aryl}), 7.22–7.20 (m, 2H, CH_{aryl}), 7.15–7.13 (m, 2H, CH_{aryl}),

5.59 (d, J = 6.4 Hz, 1H, NHC*H*), 4.74 (d, J = 6.4 Hz, 1H, N*H*CH), 3.84 (brs, 1H, N*H*C(CH_3)$_3$), 2.33 (s, 3 H, ArCH_3), 1.17 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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); mp 90–93 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3384, 2978, 1391, 1324, 1144, 990; ^{1}H NMR (400.1 MHz, $CDCl_3$) δ_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, 1H, C*H*NH), 4.91 (d, J = 6.4 Hz, 1H, CHN*H*), 4.05 (s, 1H, N*H*C(CH_3)$_3$), 2.32 (s, 3 H, ArCH_3), 1.15 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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 specific rotation.

4.5.6. (*R*)-*N*-*tert*-Butyl-*N*′-(3-methoxyphenyl)(phenyl) methylsulfamide (*R*)-10f

Prepared from **9d** (120 mg, 0.50 mmol) and $\mathbf{L_B}$ and 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); mp 100–103 °C; IR ($CHCl_3$) ν_{max}/cm^{-1} 3383, 2969, 1600, 1321, 1240, 1042; ^{1}H NMR (400.1 MHz, $CDCl_3$) δ_H 7.34–7.32 (m, 6 H, CH_{aryl}), 6.92–6.88 (m, 2H, CH_{aryl}), 6.82–6.80 (m, 1H, CH_{aryl}), 5.59 (d, J = 6.4 Hz, 1H, NHC*H*), 4.80 (d, J = 6.8 Hz, 1H, N*H*CH), 3.91 (brs, 1H, N*H*C(CH_3)$_3$), 3.78 (s, 3 H, OCH_3), 1.18 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_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. Calcd 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 specific rotation.

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

A solution of 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 equiv) was added and 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.

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