Asymmetric synthesis of new chiral *N*-sulfinyl 2,2-disubstituted aziridines by Grignard additions across α-chloro *N*-sulfinyl ketimines†‡

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Reaction of chiral α-chloro *N*-*tert*-butanesulfinyl ketimines with Grignard reagents afforded new chiral *N*-sulfinyl 2,2-disubstituted aziridines in good to excellent diastereomeric ratio (dr up to 98 : 2). The 1,2,2-trisubstituted aziridines were isolated in high overall yield (51–85%) and with excellent enantiomeric excess (>98% ee). The stereoselectivity obtained in the Grignard addition is rationalized by the coordinating ability of the α-chloro atom resulting in the opposite stereochemical outcome as observed for nonfunctionalized *N*-sulfinyl ketimines.

Introduction

Terminal aziridines are particularly useful synthetic intermediates owing to the ease, generality, and predictable regioselectivity of their ring opening reactions with nucleophiles.[1] Since chiral aziridines are key substrates in the synthesis of a number of useful alkaloids, amino acids and β-lactam antibiotics and are used as chiral auxiliaries and ligands, they have received increasing attention in recent years.[2,3] The development of an efficient synthesis of a wide variety of chiral aziridines with a stereogenic quaternary carbon center at the 2-position represents an important challenge in this field. The reported methods, leading to chiral 2,2-disubstituted aziridines, suffer from several drawbacks. Some entries based on the cyclization of specific chiral α-quaternary amino alcohol or amino thioether intermediates require multistep synthesis and transformation of the chiral substrates.[4,5] The lithiation/alkylation of chiral 2-phenylaziridines is rather limited in scope.[6] Direct aziridinations of 1,1-disubstituted alkenes or Corey–Chaykovsky aziridinations of ketimines into chiral 2,2-disubstituted aziridines suffer from poor stereoselectivity or yield.[7,8] The 1,2-nucleophilic addition of organometallics across chiral ketimines derived from α-halo ketones would form an attractive general two-step pathway to various chiral 2,2-disubstituted aziridines from readily available achiral compounds, if undesired reactions, such as substitutions and dehydrohalogenations, could be avoided and high stereoselectivity could be obtained. α-Halogenated imines have drawn great attention as versatile intermediates for the synthesis of biologically active compounds.[9] α-Chloro imines can be easily synthesized by condensation of α-chloro aldehydes or α-chloro ketones with primary amines in the absence (aldehydes) or presence (ketones) of titanium(IV) chloride.[10] Alternatively, imines can be halogenated at the α-position by *N*-halosuccinimides.[10b,10c,11]

Cyclization of these α-halo imines by nucleophilic addition and subsequent ring closure provides a ready access to a great variety of aziridines.[10,11e] The activation of the imino function with a chiral, easily deprotected *N*-substituent for nucleophilic addition in a stereoselective way, has received considerable attention. In the synthesis of chiral amines, amino alcohols, amino acids and other interesting compounds, the stereoselective addition of organometallics across *N*-sulfinyl imines, pioneered by Davis[12] and Ellman,[13] has proven to be a straightforward method.[14] Despite the advantageous reactivity of known *N*-alkyl and *N*-aryl halogenated imines, the use of halogenated *N*-sulfinyl imines was longtime limited to some fluorinated examples,[15] and a few examples of chloro or bromo *N*-sulfinyl imines,[16] without a thorough study of their reactivity. In response, recently, our research group and others prepared a variety of chiral aziridines with very good stereoselectivity starting from α-chlorinated *N*-*tert*-butanesulfinyl imines.[17] However, the synthesis of chiral *N*-sulfinylaziridines with a quaternary carbon at the 2-position has been limited to the addition of dimethylphosphite,[17f] and AllylMgCl across aliphatic *N*-sulfinyl α,α-dialkyl-α-chloro ketimines.[17d] In the latter case, the use of Grignard reagents, different from AllylMgCl, afforded chiral cyclopropylamines *via* competitive 1,3-dehydrohalogenation and subsequent addition of the Grignard reagent across the intermediate cyclopropylideneamine.[17d] Therefore, it was envisioned that the use of arylated α-halo *N*-*tert*-butanesulfinyl ketimines, lacking acidic protons in the α′-position, would result in the synthesis of chiral aziridines with a quaternary center after nucleophilic addition of organometallics. Also, the Grignard addition across the α-chloro ketimine derived from α-chloroacetone, lacking alkyl groups which stabilize the reactive intermediates in the formation of cyclopropylamines, would result in the synthesis of chiral 2,2-disubstituted aziridines. Herein, therefore, highly diastereoselective Grignard addition reactions across α-chloro *N*-*tert*-butanesulfinyl ketimines in the preparation of the corresponding chiral *N*-sulfinyl 2,2-disubstituted aziridines as new chiral building blocks are described.

Results and discussion

The Grignard addition across aromatic α-chloro *N*-*tert*-butanesulfinyl ketimines **1** was optimized by systematically

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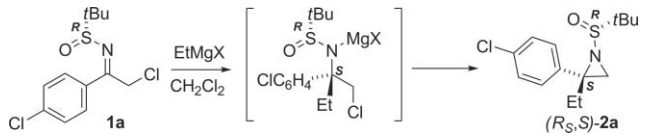
Table 1 Optimization of the Grignard addition of EtMgX across ketimine **1a** in the synthesis of *N*-*tert*-butanesulfinyl 2-ethyl-2-(4-chlorophenyl)aziridine **2a**



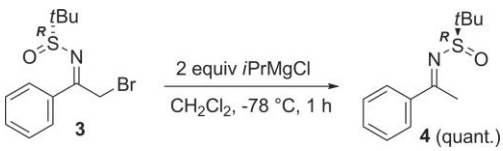
Entry	EtMgX (equiv)	T/°C	Time/h	Conversion of **1a** into **2a** (%)[a]	dr[a]
1	1.05 (X = Br)	−78 (−40)	2 (4)	51	70/30
2	2.0 (X = Br)	−78 (−40)	2 (4)	79	81/19
3	10.0 (X = Br)	−78 (−40)	2 (4)	71[b]	88/12
4	2.0 (X = Br)	−78 (0)	1 (2)	93	84/16
5	2.0 (X = Cl)	−78 (0)	1 (2)	98	84/16
6	4.0 (X = Cl)	−78 (0)	1 (2)	100	86/14[c]
7	2.0 (X = Cl)[d]	−78	1	89	21/79
8	—[e]	−78 to rt	1	—	—

[a] Determined *via* ^{1}H NMR analysis of the crude reaction mixture. [b] More unidentified side products were observed in the crude reaction mixture. [c] The major diastereomer could be isolated by flash chromatography leading to a yield of 62% for enantiopure (R_S,*S*)-**2a**. [d] 2.3 equiv Me_2Zn was added and THF was used instead of CH_2Cl_2. [e] Reaction conditions: 1.2 equiv $EtCeCl_2$, THF/DMPU (10 : 1).

changing the reaction conditions in the Grignard addition of EtMgX (X = Br, Cl) across (R_S)-*N*-[2-chloro-1-(4-chlorophenyl)-ethylidene]-*tert*-butanesulfinamide **1a** for the synthesis of chiral *N*-*tert*-butanesulfinyl 2-ethyl-2-(4-chlorophenyl)aziridine **2a** (Table 1). As recently described by our research group, the synthesis of the aromatic α-chloro *N*-*tert*-butanesulfinyl ketimines **1** was performed by condensation of the appropriate phenacyl chlorides with (R_s)-*tert*-butanesulfinamide in the presence of 2 equivalents of $Ti(OEt)_4$ in THF in 88–89% yield.[17a]

The initial reaction conditions involved the dropwise addition of 1.05 equivalents of EtMgBr to ketimine **1a** at −78 °C in CH_2Cl_2 and consecutive stirring for 2 h at −78 °C followed by 4 h at −40 °C (entry 1). After aqueous workup, a conversion of 51% of ketimine **1a** into aziridine **2a** was observed with a moderate diastereoselectivity (dr 70/30). The addition of 2.0 equivalents EtMgBr to ketimine **1a** under similar conditions resulted in 79% conversion to aziridine **2a** with enhanced diastereoselectivity (dr 81/19) (entry 2). Increasing the excess of EtMgBr (10 equiv), gave an even higher diastereoselectivity (dr 88/12), but the amount of aziridine **2a** (71%) present in the reaction mixture was lower due to the formation of unidentified side products (entry 3). Repeating the reaction with 2.0 equivalents EtMgBr at elevated temperature, *i.e.* at −78 °C for 1 h and 2 h at 0 °C, led to an increase of the conversion of ketimine **1a** into aziridine **2a** (93%) and a higher diastereoselectivity (dr 84/16) (entry 4). Thankfully, the use of EtMgCl instead of EtMgBr led to an almost full conversion of ketimine **1a** into aziridine **2a** (98%), while maintaining the diastereoselectivity (entry 5). Finally, optimal reaction conditions involved increasing the amount of Grignard reagent to 4.0 equivalents of EtMgCl, leading to a full conversion of ketimine **1a** into aziridine **2a** with a slightly higher diastereoselectivity (dr 86 : 14) (entry 6). The major diastereomer could be isolated by flash chromatography leading to a yield of 62% for enantiopure (R_S,*S*)-**2a** (>98% ee), while the minor diastereomer could not be obtained in pure form. In an attempt to improve the stereoselectivity of the addition further, ketimine **1a** was treated with the triorganozincate $EtMe_2ZnMgCl$, prepared *via* addition of Me_2Zn to the Grignard reagent, according to a recently reported procedure (entry 7).[18] Unfortunately, the formation of aziridine **2a** was not complete and a lower reversed diastereoselectivity (dr 21/79) was observed. In a last attempt, using the organocerium reagent $EtCeCl_2$ instead of EtMgCl, a complex reaction mixture was obtained (entry 8).[17e]

In order to explore the scope of the Grignard addition across aromatic α-halo *N*-*tert*-butanesulfinyl ketimines **1**, a variety of different Grignard reagents and substrates were evaluated. First, the substrate was altered from α-chloro ketimine **1a** to the corresponding α-bromo ketimine, *i.e.* (R_S)-*N*-[2-bromo-1-phenylethylidene]-*tert*-butanesulfinamide **3**. Addition of various amounts of EtMgBr (1–2 equiv) to the α-bromo *N*-*tert*-butanesulfinyl ketimine **3** at various temperatures (–97 to –40 °C) only led to small amounts of aziridine **2d** (0–22%), while debromination of the α-bromo ketimine **3** predominantly occurred, leading to the corresponding *N*-(1-phenylethylidene)-*tert*-butanesulfinamide **4** (78–88%). The addition of Lewis acids ($MgBr_2$, $Ti(OEt)_4$) did not suppress this reduction to imine **4**. Moreover, with *i*PrMgCl (2 equiv, −78 °C, 1 h) as the organometallic reagent a quantitative debromination to ketimine **4** was observed (Scheme 1). This debromination probably results from halogen/metal exchange leading to the Grignard derivative of imine **3**, followed by protonation upon work-up.[19]



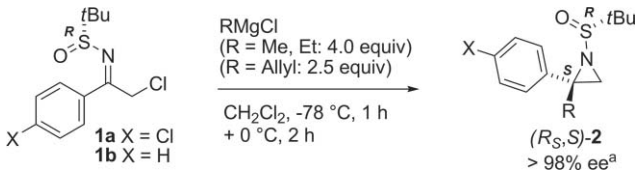
Scheme 1 Debromination of α-bromo ketimine **3** to *N*-(1-phenylethylidene)-*tert*-butanesulfinamide **4**.

The optimized reaction conditions, found in the addition of EtMgCl across ketimine **1a**, were also applied in the addition of MeMgCl and AllylMgCl across aromatic α-chloro *N*-*tert*-butanesulfinyl ketimines **1a** and **1b** (Table 2). The corresponding chiral *N*-sulfinyl 2-alkyl- and 2-allyl-2-arylaziridines **2** were synthesized with good to excellent diastereoselectivity (dr up to 98/2) and isolated in high overall yield (51–85%) with excellent enantiomeric purity (>98% ee) (Table 2). As compared to the reactions with EtMgCl and MeMgCl, the reaction with AllylMgCl proceeded slightly faster, so that the use of 2.5 equivalents of AllylMgCl was sufficient for full conversion of **1a** and **1b** to the corresponding *N*-sulfinyl 2-allyl-2-arylaziridines **2c** and **2f** (entries 3 and 6).

The enantiomeric excess of aziridines (R_S,*S*)-**2** was determined by comparing ^{1}H NMR data obtained from the addition of (*R*)-Pirkle's alcohol, as a chiral shift reagent,[20] to racemic mixtures of aziridines **2**, prepared with *rac*-*tert*-butanesulfinamide as starting material, and from the addition of *R*-Pirkle's alcohol to the chiral prepared aziridines (R_S,*S*)-**2**. From these experiments an enantiomeric excess of >98% ee for aziridines (R_S,*S*)-**2** was concluded.

To determine the absolute stereochemistry of *N*-sulfinyl-aziridines **2**, *N*-sulfonylaziridines **5** and *N*-sulfonyl β-amino alcohols **6**, some of which are reported in the literature,[6,21] were synthesized with *m*-CPBA in CH_2Cl_2 (Table 3). The

Table 2 Reaction of RMgCl with ketimines **1a** and **1b**



Entry	Imine	R	Product	dr[b]	Yield (%)[c]
1	**1a**	Et	**2a**	86/14	(*R*$_S$,*S*)-**2a** (62)[d]
2	**1a**	Me	**2b**	94/6	(*R*$_S$,*S*)-**2b** (72)[e]
3	**1a**	Allyl[f]	**2c**	90/10	(*R*$_S$,*S*)-**2c** (51)[g]
4	**1b**	Et	**2d**	89/11	(*R*$_S$,*S*)-**2d** (67)[h]
5	**1b**	Me	**2e**	98/2	(*R*$_S$,*S*)-**2e** (61)[i]
6	**1b**	Allyl[f]	**2f**	94/6	(*R*$_S$,*S*)-**2f** (85)

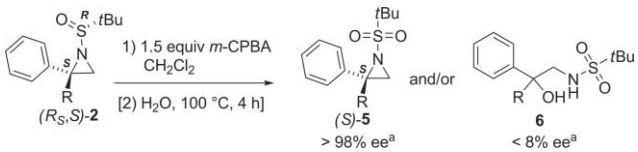
[a] Determined by ^{1}H NMR analysis with Pirkle's alcohol. [b] Determined *via* ^{1}H NMR analysis of the crude reaction mixture. [c] Yield of major isomer after flash chromatography. [d] Additionally a mixture of diastereomers (dr 68/32) was isolated in 16% yield. [e] Additionally a mixture of diastereomers (dr 83/17) was isolated in 16% yield. [f] 2.5 equiv AllylMgCl was used. [g] Additionally a mixture of diastereomers (dr 76/24) was isolated in 22% yield. [h] Additionally a mixture of diastereomers (dr 38/62) was isolated in 17% yield. [i] Additionally a mixture of diastereomers (dr 87/13) was isolated in 7% yield.

(*R*)-enantiomer of *N*-sulfonylaziridine **5e** (R = Me) is a known compound in the literature.[6] Therefore *N*-sulfinylaziridine (*R*$_S$,*S*)-**2e** was treated with 1.5 equivalents of *m*-CPBA (70–75% in balance with H_2O) in CH_2Cl_2 at room temperature for 15 min to achieve the oxidation of the sulfinyl group. Unfortunately, no formation of sulfonylaziridine (*S*)-**5e** was observed. Instead full conversion to *N*-sulfonyl β-amino alcohol **6e** was achieved due to ring opening with H_2O after the oxidation (entry 1). After recrystallization in diethyl ether, the pure *N*-sulfonyl β-amino alcohol **6e** was isolated in 87% yield. In a second attempt, the oxidation was performed at lower temperature, *i.e.* adding *m*-CPBA at −78 °C, followed by stirring for 0.5 h at 0 °C, leading to a full conversion of *N*-sulfinylaziridine (*R*$_S$,*S*)-**2e** to *N*-sulfonylaziridine (*S*)-**5e** in 94% yield (entry 2).

Because chiral *N*-sulfonyl β-amino alcohols (*S*)-**6d** and (*S*)-**6f** are also known compounds in literature,[21] attempts were made to achieve their synthesis. Aziridine (*R*$_S$,*S*)-**2d** was treated with *m*-CPBA under similar conditions as in the synthesis of *N*-sulfonyl β-amino alcohol **6e** (entry 1), leading, unfortunately, to a mixture of sulfonylaziridine (*S*)-**5d** and *N*-sulfonyl β-amino alcohol **6d** (ratio: 47/53) (entry 3). To achieve a full conversion to *N*-sulfonyl β-amino alcohol **6d**, the mixture of (*S*)-**5d** and **6d** was dissolved in H_2O and stirred for 4 h at 100 °C, leading to *N*-sulfonyl β-amino alcohol **6d** in 88% yield after purification by flash chromatography (entry 4). When aziridine (*R*$_S$,*S*)-**2f** was treated with *m*-CPBA at room temperature for 15 min, no ring opening was observed and *N*-sulfonylaziridine (*S*)-**5f** was isolated in 85% yield (entry 5). To drive the reaction towards the formation of *N*-sulfonyl β-amino alcohol **6f** water was added to the solvent (CH_2Cl_2) in a 3 : 2 CH_2Cl_2–H_2O ratio. Still no ring opening was observed and only *N*-sulfonylaziridine (*S*)-**5f** was isolated in 76% yield (entry 6). Finally, after the oxidation of *N*-sulfinylaziridine (*R*$_S$,*S*)-**2f** to *N*-sulfonylaziridine (*S*)-**5f** with *m*-CPBA, the oxidized aziridine (*S*)-**5f** was dissolved in water and stirred for 4 h at 100 °C. In this way the ring opened *N*-sulfonyl β-amino alcohol **6f** was obtained in 71% yield after purification by flash chromatography (entry 7). Noteworthy, *N*-sulfonylaziridine **5e** (R = Me) was more prone towards ring opening to *N*-sulfonyl β-amino alcohols **6** than *N*-sulfonylaziridines **5d** (R = Et) and **5f** (R = Allyl). Probably, steric hindrance forms the determining factor in the ease of ring opening. The enantiomeric excess of the synthesized *N*-sulfonylaziridines (*S*)-**5** and *N*-sulfonyl β-amino alcohols **6** was determined by ^{1}H NMR analysis with Pirkle's alcohol and an enantiomeric excess of >98% for *N*-sulfonylaziridines (*S*)-**5** was concluded. Unfortunately, racemisation occurred during the ring opening reaction of *N*-sulfonylaziridines (*S*)-**5** with water leading to the formation of *N*-sulfonyl β-amino alcohols **6**, with a low enantiomeric purity (<8% ee). Nevertheless, comparison of the optical rotation of *N*-sulfonylaziridine (*S*)-**5e** ([α]$_D$ (*S*)-**5e** +136.6 (*c* 1.0, $CHCl_3$) *vs.* (*R*)-**5e** −142.5 (*c* 1.3, $CHCl_3$) in Lit.[6]), confirmed the assigned absolute stereochemistry of the *N*-sulfinyl aziridines (*R*$_S$,*S*)-**2**. It is interesting to mention that the (*R*)-enantiomer of *N*-sulfonylaziridine **5e** was regioselectively ring opened at the benzylic position using aniline without loss of stereochemical integrity.[6]

In order to expand the scope of the Grignard addition across α-chloro *N*-*tert*-butanesulfinyl ketimines, non-aromatic α-chloro

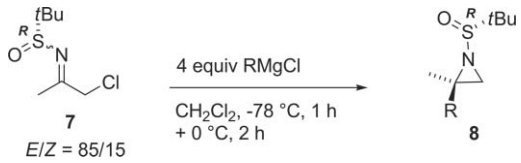
Table 3 Synthesis of chiral *N*-sulfonylaziridines **5** and *N*-sulfonyl β-amino alcohols **6** starting from *N*-sulfinylaziridines **2**



Entry	R	Reaction conditions	Result[b]
1	Me	1) rt, 15 min, 2) -	**6e** (87%)[c]
2	Me	1) −78 to 0 °C, 0.5 h, 2) -	(*S*)-**5e** (94%)[c]
3	Et	1) rt, 15 min, 2) -	(*S*)-**5d** (47%), **6d** (53%)
4	Et	1) rt, 15 min, 2) H_2O, 100 °C, 4 h	**6d** (88%)[c]
5	Allyl	1) rt, 15 min, 2) -	(*S*)-**5f** (85%)[c]
6	Allyl	1) CH_2Cl_2–H_2O (3 : 2), rt, 15 min, 2) -	(*S*)-**5f** (76%)[c]
7	Allyl	1) rt, 15 min, 2) H_2O, 100 °C, 4 h	**6f** (71%)[c]

[a] Determined by ^{1}H NMR analysis with Pirkle's alcohol. [b] Determined *via* ^{1}H NMR analysis of the crude reaction mixture. [c] Isolated yield.

Table 4 Reaction of RMgCl with ketimine **7**



Entry	R	Product	dr[a]	Yield (%)[b]
1	Me	**8a**	—	(R_S)-**8a** (52)
2	Et	**8b**	92/8	(R_S,R)-**8b** (57)[c]
3	Allyl	**8c**	90/10	(R_S,R)-**8c** (59)[d]

[a] Determined *via* ^{1}H NMR analysis of the crude reaction mixture. [b] Yield of the major isomer after flash chromatography. [c] The diastereomers could not be separated *via* flash chromatography resulting in **8b** (57%, dr 92/8). [d] Additionally a mixture of diastereomers **8c** (dr 76/24) was isolated in 7% yield.

ketimine **7** was used in the synthesis of chiral aziridines **8** (Table 4). The synthesis of ketimine **7** was performed by condensation of α-chloroacetone with (R_s)-*tert*-butanesulfinamide in the presence of 2 equivalents of $Ti(OEt)_4$ in THF in 63% yield.[17a,17f] The optimized reaction conditions, found in the addition of EtMgCl across ketimine **1a** (Table 1), were also applied in the addition of Grignard reagents across α-chloro ketimine **7**. In contrast with the Grignard addition across aliphatic *N*-sulfinyl α,α-dialkyl-α-chloro ketimines where chiral cyclopropylamines were formed *via* competitive 1,3-dehydrohalogenation and subsequent addition of the Grignard reagent across the intermediate cyclopropylideneamine,[17d] the Grignard addition across ketimine **7** afforded to our satisfaction the corresponding *N*-sulfinyl 2-alkyl- and 2-allyl-2-methylaziridines **8** with high diastereoselectivity (dr up to 92/8) and acceptable isolated yields (52–59%) (Table 4).

The addition of EtMgCl across ketimine **7** led to the formation of aziridine **8b** in good diastereoselectivity (dr 92/8), but unfortunately the diastereomers could not be separated by flash chromatography. These results demonstrate the importance of the presence of alkyl groups at the α-carbon center of α-chloro ketimines in the synthesis of the corresponding chiral cyclopropylamines by reaction with Grignard reagents. The alkyl groups could play an important role in stabilizing the positive charge at the α-position of the α,α-dialkyl-α-chloro ketimines after cleavage of chloride from the initially formed 1-azaallylic anion, en route to the intermediate cyclopropylideneamine.[17d] Such more substituted zwitterionic species or cyclopropylideneamines are more stable and favor the Favorskii-rearrangement.[22]

In analogy with the synthesis of chiral aziridines from chiral α-chloro aldimines,[17c] the stereoselectivity of the reaction of chiral α-chloro *N*-*tert*-butanesulfinyl ketimines **1** and **7** with Grignard reagents is opposite to the one that is predicted *via* the chelation-controlled transition state **A** (Fig. 1), which is the general intermediate proposed for non-functionalized *N*-sulfinyl imines.[12,13,23] The stereoselectivity obtained in the Grignard additions across α-chloro ketimines **1** and **7** is opposite to the reported stereoselectivity obtained in the Grignard addition of AllylMgBr across nonfunctionalized imine **4**.[13a]

The reversal of the stereochemical outcome of the reaction is attributed to the α-coordinating ability of the chlorine atom with the metal of the incoming nucleophile as depicted in transition

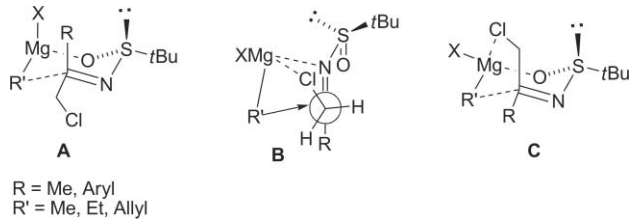


Fig. 1 Proposed transition states during the reaction of chiral α-chloro *tert*-butanesulfinyl ketimines **1** and **7** with Grignard reagents.

state **B** (Fig. 1). The coordinating α-chloro group seems to override the chelation of the sulfinyl oxygen (transition state **A**) and allows the sulfinimine to react in the preferred conformation wherein the S–O bond and the lone pair of electrons on the nitrogen atom are antiperiplanar.[14] Transition state **C** is less likely as this would involve *E*- to *Z*-imine isomerisation during the reaction.[24] The reversal of selectivity is analogous to the results obtained with other *N*-sulfinyl imines containing an α-coordinating group, such as a nitrogen or oxygen atom.[23a,25]

Conclusions

In conclusion, an efficient strategy for the asymmetric synthesis of *N*-sulfinyl 2,2-disubstituted aziridines was developed. Upon treatment of α-chloro *N*-*tert*-butanesulfinyl ketimines with Grignard reagents, chiral *N*-sulfinyl 2,2-disubstituted aziridines were synthesized with good to excellent diastereoselectivity *via* 1,2-addition across the imino function and subsequent ring closure. The *N*-sulfinyl aziridines were isolated in high overall yield (51–85%) and with excellent enantiomeric excess (>98% ee). It was found that α-chloro *N*-*tert*-butanesulfinyl ketimines are the preferred α-halo ketimines for aziridine formation as the corresponding α-bromo derivatives mainly led to the debrominated ketimines upon treatment with Grignard reagents. The oxidation of the synthesized *N*-sulfinyl aziridines to the corresponding *N*-sulfonyl aziridines was possible without loss of enantiomeric purity and allowed the determination of the stereochemical outcome of the Grignard additions. The stereoselectivity obtained in the Grignard addition was rationalized by the coordinating ability of the α-chloro atom resulting in the opposite stereochemical outcome as observed for nonfunctionalized *N*-sulfinyl ketimines.

Experimental

General methods

Tetrahydrofuran (THF) was freshly distilled under a nitrogen atmosphere from sodium/benzophenone ketyl, whereas dichloromethane (CH_2Cl_2) was distilled from calcium hydride. All other chemicals were of commercial grade and used without further purification. Petroleum ether refers to the 40–60 °C boiling fraction. ^{1}H NMR (300 MHz), ^{13}C NMR (75 MHz) spectra were recorded in deuterated solvents with tetramethylsilane (TMS, $\delta =$ 0 ppm) as internal standard. Mass spectra were recorded using a direct inlet system (ESI, 4000 V). IR spectra were obtained from samples in neat form with an ATR (attenuated total reflectance) accessory. The purification of the reaction mixtures was performed by column chromatography over silica gel (particle size 0.035–0.070 mm, pore diameter *ca.* 6 nm). Melting points of crystalline

compounds were determined with a Büchi 540 apparatus. Elemental analyses were performed using a Perkin-Elmer 2400 (Series II, CHNS/O) elementary analyzer. Aromatic *tert*-butanesulfinyl α-halo ketimines were prepared as previously described.[17a] (R_s)-*tert*-Butanesulfinamide is commercially available (>98% ee).

Synthesis of chiral *N*-sulfinyl 2-alkyl and 2-allyl-2-arylaziridines 2

The synthesis of (R_s,*S*)-1-(*tert*-butylsulfinyl)-2-(4-chlorophenyl)-2-methylaziridine (R_s,*S*)-**2b** is representative. In a flame-dried flask a 0.5 M solution of α-chloro *N*-*tert*-butanesulfinyl ketimine **1a** (1 equiv, 1.70 g, 5.82 mmol) in dry CH_2Cl_2 under nitrogen atmosphere was prepared. The stirred solution was cooled to −78 °C before 4.0 equivalents of a 3 M solution of MeMgCl (4.0 equiv, 7.76 mL, 23.28 mmol) in THF was added dropwise. The reaction was stirred for 1 h at −78 °C followed by stirring at 0 °C for 2 h. The reaction was quenched at this temperature by addition of a saturated solution of NH_4Cl (5 mL) and diluted with saturated aqueous $NaHCO_3$ (20 mL) and EtOAc (20 mL) at room temperature. The aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic layers were dried ($MgSO_4$, containing a trace of K_2CO_3), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography to yield 1.14 g (4.20 mmol) of pure (R_s,*S*)-1-(*tert*-butylsulfinyl)-2-(4-chlorophenyl)-2-methylaziridine (R_s,*S*)-**2b** (72% yield). Additionally a mixture of diastereomers **2b** (dr 83/17) was isolated in 16% yield.

(R_s,*S*)-1-(*tert*-Butylsulfinyl)-2-(4-chlorophenyl)-2-ethylaziridine (R_s,*S*)-2a. R_f 0.39 (petroleum ether/Et_2O 1 : 1). Yellow crystals, yield 62% (+ 16% dr 68/32). $[\alpha]_D$ −310.3 (*c* 0.3, MeOH). Mp 59.8–60.2 °C. ee > 98%. ν_{max}/cm^{-1} 819, 925, 1073, 1090, 2926, 2964. δ_H(300 MHz, $CDCl_3$; Me_4Si) 0.84 (3H, t, J = 7.2 Hz), 1.19 (9H, s), 1.63 (1H, d × q, J = 14.0, 7.2 Hz), 2.02 (1H, s), 2.06 (1H, d × q, J = 14.0, 7.2 Hz), 2.98 (1H, s), 7.24–7.33 (4H, m). δ_C(75 MHz, $CDCl_3$) 9.6, 22.7, 28.9, 32.8, 48.4, 57.3, 128.6 (2C), 130.6 (2C), 134.1, 135.1. MS (ES, pos. mode) *m*/*z* (%): 286/288 (M + H$^+$, 100). Anal. Calcd for $C_{14}H_{20}ClNOS$: C 58.83; H 7.05; N 4.90. Found: C 58.59; H 6.91; N 4.63%.

(R_s,*S*)-1-(*tert*-Butylsulfinyl)-2-(4-chlorophenyl)-2-methylaziridine (R_s,*S*)-2b. R_f 0.50 (petroleum ether/Et_2O 1 : 1). Yellow crystals, yield 72% (+ 16% dr 83/17). $[\alpha]_D$ −263.5 (*c* 0.4, MeOH). Mp 64.5–65.0 °C. ee > 98%. ν_{max}/cm^{-1} 892, 1012, 1075, 1087, 1493, 2926, 2957, 2976. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.23 (9H, s), 1.66 (3H, s), 2.13 (1H, s), 3.05 (1H, s), 7.28–7.38 (4H, m). δ_C(75 MHz, $CDCl_3$) 22.7, 25.9, 31.7, 44.4, 57.2, 128.7 (2C), 129.7 (2C), 134.0, 136.7. MS (ES, pos. mode) *m*/*z* (%): 272/274 (M + H$^+$, 100). Anal. Calcd for $C_{13}H_{18}ClNOS$: C 57.45; H 6.67; N 5.15. Found: C 57.18; H 6.45; N 4.93%.

(R_s,*S*)-1-(*tert*-Butylsulfinyl)-2-allyl-2-(4-chlorophenyl)aziridine (R_s,*S*)-2c. Prepared with 2.5 equivalents of AllylMgCl. R_f 0.47 (petroleum ether/Et_2O 1 : 1). Yellow crystals, yield 51% (+ 22% dr 76/24). $[\alpha]_D$ −279.2 (*c* 0.6, MeOH). Mp 43.3–43.6 °C. ee > 98%. ν_{max}/cm^{-1} 818, 923, 1072, 1357, 1493, 2977. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.19 (9H, s), 2.10 (1H, s), 2.41 and 2.72 (2H, d × d, J = 14.3, 7.2 Hz), 3.00 (1H, s), 4.94–5.06 (2H, m), 5.58–5.72 (1H, m), 7.22–7.34 (4H, m). δ_C(75 MHz, $CDCl_3$) 22.7, 28.7, 44.0, 46.8, 57.4, 118.6, 128.6 (2C), 130.6 (2C), 132.9, 134.3, 134.9. MS (ES, pos. mode) *m*/*z* (%): 298/300 (M + H$^+$, 100). Anal. Calcd for $C_{15}H_{20}ClNOS$: C 60.49; H 6.77; N 4.70. Found: C 60.33; H 6.59; N 4.51%.

(R_s,*S*)-1-(*tert*-Butylsulfinyl)-2-ethyl-2-phenylaziridine (R_s,*S*)-2d. R_f 0.33 (petroleum ether/Et_2O 7 : 3). Yellow crystals, yield 67% (+ 17% dr 38/62). $[\alpha]_D$ −410.4 (*c* 0.4, MeOH). Mp 44.5–44.9 °C. ee > 98%. ν_{max}/cm^{-1} 760, 915, 1071, 1360, 1449, 2962. δ_H(300 MHz, $CDCl_3$; Me_4Si) 0.85 (3H, t, J = 7.2 Hz), 1.19 (9H, s), 1.65 (1H, d × q, J = 14.0, 7.2 Hz), 2.04 (1H, s), 2.11 (1H, d × q, J = 14.0, 7.2 Hz), 3.03 (1H, s), 7.24–7.40 (5H, m). δ_C(75 MHz, $CDCl_3$) 9.7, 22.8, 29.1, 32.9, 49.1, 57.1, 128.1, 128.3 (2C), 129.2 (2C), 136.5. MS (ES, pos. mode) *m*/*z* (%): 252 (M + H$^+$, 100). Anal. Calcd for $C_{14}H_{21}NOS$: C 66.89; H 8.42; N 5.57. Found: C 66.54; H 8.19; N 5.57%.

(R_s,*S*)-1-(*tert*-Butylsulfinyl)-2-methyl-2-phenylaziridine (R_s,*S*)-2e. R_f 0.36 (petroleum ether/Et_2O 1 : 1). Yellow crystals, yield 61% (+ 7% dr 87/13). $[\alpha]_D$ −296.9 (*c* 0.3, MeOH). Mp 58.5–58.8 °C. ee > 98%. ν_{max}/cm^{-1} 890, 1074, 2922, 2954, 2983. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.18 (9H, s), 1.66 (3H, s), 2.10 (1H, s), 3.05 (1H, s), 7.25–7.42 (5H, m). δ_C(75 MHz, $CDCl_3$) 22.7, 26.1, 31.8, 45.1, 57.1, 128.2, 128.3 (2C), 128.4 (2C), 138.3. MS (ES, pos. mode) *m*/*z* (%): 238 (M + H$^+$, 100). Anal. Calcd for $C_{13}H_{19}NOS$: C 65.78; H 8.07; N 5.90. Found: C 65.52; H 8.05; N 5.79%.

(R_s,*S*)-1-(*tert*-Butylsulfinyl)-2-allyl-2-phenylaziridine (R_s,*S*)-2f. Prepared with 2.5 equivalents of AllylMgCl. R_f 0.32 (petroleum ether/Et_2O 1 : 1). Yellow oil, yield 85%. $[\alpha]_D$ −281.4 (*c* 0.4, MeOH). ee > 98%. ν_{max}/cm^{-1} 698, 969, 1083, 1360, 1448, 2979. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.19 (9H, s), 2.10 (1H, s), 2.47 and 2.78 (2H, d × d, J = 14.3, 7.2 Hz), 3.06 (1H, s), 4.97–5.05 (2H, m), 5.63–5.76 (1H, m), 7.24–7.39 (5H, m). δ_C(75 MHz, $CDCl_3$) 22.8, 28.7, 44.0, 47.5, 57.2, 118.2, 128.3 (3C), 129.2 (2C), 133.3, 136.4. MS (ES, pos. mode) *m*/*z* (%): 264 (M + H$^+$, 100). Anal. Calcd for $C_{15}H_{21}NOS$: C 68.40; H 8.04; N 5.32. Found: C 68.12; H 7.93; N 5.19%.

Debromination of α-bromo ketimine 3 to (R_s)-*N*-(1-phenylethylidene)-*tert*-butanesulfinamide 4

In a flame-dried flask a 0.5 M solution of α-bromo *N*-*tert*-butanesulfinyl ketimine **3** (1 equiv, 1.00 g, 3.31 mmol) in dry CH_2Cl_2 under nitrogen atmosphere was prepared. The stirred solution was cooled to −78 °C before 2.0 equivalents of a 2 M solution of *i*PrMgCl (2.0 equiv, 3.31 mL, 6.62 mmol) in THF was added dropwise. The reaction was stirred for 1 h at −78 °C. The reaction was quenched at this temperature by addition of a saturated solution of NH_4Cl (3 mL) and diluted with saturated aqueous $NaHCO_3$ (15 mL) and EtOAc (15 mL) at room temperature. The aqueous layer was extracted with EtOAc (2 × 15 mL). The combined organic layers were dried ($MgSO_4$, containing a trace of K_2CO_3), filtered and evaporated *in vacuo*, leading to 0.74 g (3.31 mmol) of (R_s)-*N*-(1-phenylethylidene)-*tert*-butanesulfinamide **4** (quant.).

(R_s)-*N*-(1-Phenylethylidene)-*tert*-butanesulfinamide 4. Yellow oil, quantitative yield. $[\alpha]_D$ −2.4 (*c* 0.7, $CHCl_3$). ν_{max}/cm^{-1} 1070, 1578, 1596, 1610. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.33 (9H, s), 2.77 (3H, s), 7.26–7.45 (3H, m), 7.89 (2H, d, J = 7.4 Hz). δ_C(75 MHz, $CDCl_3$) 22.6, 24.2, 57.4, 127.3 (2C), 128.4 (2C), 131.7, 138.8, 176.4. MS (ES, pos. mode) *m*/*z* (%): 224 (M + H$^+$, 100). All spectroscopic data were in good agreement with reported data.[26]

Synthesis of chiral *N*-sulfonylaziridines 5 starting from *N*-sulfinylaziridines 2

The synthesis of (*S*)-1-(*tert*-butylsulfonyl)-2-methyl-2-phenylaziridine (*S*)-**5e** is representative. (R_s,*S*)-1-(*tert*-Butylsulfinyl)-2-methyl-2-phenylaziridine (R_s,*S*)-**2e** (0.10 g, 0.42 mmol) was dissolved in CH_2Cl_2 (2 mL) and the stirred solution was cooled to −78 °C. *m*-CPBA (1.5 equiv, 0.11 g, 0.63 mmol) was then added in one portion. The reaction mixture was allowed to warm up to 0 °C and stirred for 0.5 h at 0 °C. Subsequently the reaction mixture was poured into a saturated aqueous solution of $NaHCO_3$ (5 mL) and extracted with dichloromethane (3 × 5 mL). The combined organic phases were washed with a 2 N solution of NaOH (3 × 5 mL) and subsequently dried ($MgSO_4$), filtered and evaporated *in vacuo* to yield 0.09 g (0.37 mmol) of pure (*S*)-1-(*tert*-butylsulfonyl)-2-methyl-2-phenylaziridine (*S*)-**5e**.

(*S*)-1-(*tert*-Butylsulfonyl)-2-methyl-2-phenylaziridine (*S*)-5e. Colourless oil, yield 94%. $[\alpha]_D$ (*S*)-**5e** +136.6 (*c* 1.0, $CHCl_3$) *vs.* (*R*)-**5e** −142.5 (*c* 1.3, $CHCl_3$) in Lit.[6] ee > 98%. ν_{max}/cm^{-1} 1114, 1304, 2932, 2983. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.51 (9H, s), 2.00 (3H, s), 2.50 (1H, s), 2.93 (1H, s), 7.25–7.45 (5H, m). δ_C(75 MHz, $CDCl_3$) 20.9, 24.2, 43.5, 49.2, 60.9, 126.4 (2C), 127.6, 128.4 (2C), 141.6. MS (ES, neg. mode) *m*/*z* (%): 252 (M − H^+, 100). Anal. Calcd for $C_{13}H_{19}NO_2S$: C 61.63; H 7.56; N 5.53. Found: C 61.39; H 7.32; N 5.41%.

(*S*)-1-(*tert*-Butylsulfonyl)-2-allyl-2-phenylaziridine (*S*)-5f. Reaction performed at room temperature for 15 min. White crystals, yield 85%. $[\alpha]_D$ + 66.1 (*c* 0.5, $CHCl_3$). Mp 73.2–73.6 °C. ν_{max}/cm^{-1} 880, 978, 1110, 1298, 2932, 2978. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.49 (9H, s), 2.67 (1H, s), 2.88 (1H, s), 2.92 (1H, d × d, *J* = 14.9, 7.7 Hz), 3.11 (1H, d × d, *J* = 14.9, 6.6 Hz), 4.96–5.04 (2H, m), 5.68–5.81 (1H, m), 7.25–7.44 (5H, m). δ_C(75 MHz, $CDCl_3$) 24.1, 39.8, 41.3, 52.9, 61.0, 118.4, 127.9, 128.1 (2C), 128.2 (2C), 133.6, 139.0. MS (ES, pos. mode) *m*/*z* (%): 280 (M + H^+, 100). Anal. Calcd for $C_{15}H_{21}NO_2S$: C 64.48; H 7.58; N 5.01. Found: C 64.52; H 7.60; N 5.12%.

Synthesis of *N*-sulfonyl β-amino alcohols 6

The synthesis of *N*-(2-hydroxy-2-phenylpent-4-enyl)-*tert*-butanesulfonamide **6f** is representative. (R_s,*S*)-1-(*tert*-Butylsulfinyl)-2-allyl-2-phenylaziridine (R_s,*S*)-**2f** (0.10 g, 0.38 mmol) was dissolved in CH_2Cl_2 (2 mL) and *m*-CPBA (1.5 equiv, 98.4 mg, 0.57 mmol) was then added in one portion. The reaction mixture was stirred at room temperature for 15 min. Subsequently the reaction mixture was poured in a saturated aqueous solution of $NaHCO_3$ (5 mL) and extracted with dichloromethane (3 × 5 mL). The combined organic phases were washed with a 2 N solution of NaOH (3 × 5 mL) and subsequently dried ($MgSO_4$), filtered and evaporated *in vacuo*. In a second step, the resulting crude mixture was dissolved in water (2 mL) and stirred at reflux temperature for 4 h. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography to yield 90.2 mg (0.32 mmol) of pure *N*-(2-hydroxy-2-phenylpent-4-enyl)-*tert*-butanesulfonamide **6f**.

***N*-(2-Hydroxy-2-phenylbutyl)-*tert*-butanesulfonamide 6d.** R_f 0.20 (petroleum ether/Et_2O 1 : 1). White crystals, yield 88%. Mp 119.6–119.9 °C. ee = 4%. δ_H(300 MHz, $CDCl_3$; Me_4Si) 0.69 (3H, t, *J* = 7.2 Hz), 1.24 (9H, s), 1.84 (2H, q, *J* = 7.2 Hz), 2.66 (1H, br s), 3.33 (1H, d × d, *J* = 13.3, 4.7 Hz), 3.43 (1H, d × d, *J* = 13.3, 7.2 Hz), 4.19–4.28 (1H, m), 7.16–7.36 (5H, m). Anal. Calcd for $C_{14}H_{23}NO_3S$: C 58.92; H 8.12; N 4.91. Found: C 58.78; H 8.02; N 4.72%. All spectroscopic data were in good agreement with reported data.[21]

***N*-(2-Hydroxy-2-phenylpropyl)-*tert*-butanesulfonamide 6e.** Prepared in accordance with the reaction conditions as discussed in Table 3, entry 1. White crystals, yield 87%. Mp 98.6–99.0 °C. ν_{max}/cm^{-1} 1118, 1302, 3294, 3448. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.32 (9H, s), 1.62 (3H, s), 2.56 (1H, br s), 3.36 (1H, d × d, *J* = 14.0, 4.2 Hz), 3.45 (1H, d × d, *J* = 14.0, 7.7 Hz), 4.31 (1H, br s), 7.24–7.50 (5H, m). δ_C(75 MHz, $CDCl_3$) 24.3, 27.3, 55.6, 60.1, 74.2, 125.0 (2C), 127.4, 128.6 (2C), 145.0. MS (ES, neg. mode) *m*/*z* (%): 270 (M − H^+, 100). Anal. Calcd for $C_{13}H_{21}NO_3S$: C 57.54; H 7.80; N 5.16. Found: C 57.32; H 7.65; N 5.07%.

***N*-(Hydroxy-2-phenylpent-4-enyl)-*tert*-butanesulfonamide 6f.** R_f 0.18 (petroleum ether/Et_2O 1 : 1). White crystals, yield 71%. Mp 114.5–115.1 °C. ee = 8%. ^1H NMR (300 Mz, $CDCl_3$): δ 1.31 (9H, s), 2.61–2.69 (2H, m), 2.80 (1H, d × d, *J* = 13.8, 5.5 Hz), 3.37 (1H, d × d, *J* = 13.2, 4.4 Hz), 3.52 (1H, d × d, *J* = 13.2, 7.7 Hz), 4.23–4.32 (1H, m), 5.11–5.23 (2H, m), 5.47–5.61 (1H, m), 7.24–7.45 (5H, m). Anal. Calcd for $C_{15}H_{23}NO_3S$: C 60.58; H 7.79; N 4.71. Found: C 60.31; H 7.58; N 4.62%. All spectroscopic data were in good agreement with reported data.[21]

Synthesis of (R_s)-*N*-(2-chloro-1-propylidene)-*tert*-butanesulfinamide 7

(R_s)-*N*-(2-Chloro-1-propylidene)-*tert*-butanesulfinamide **7** was prepared according to a literature procedure.[17a,17f]

(R_s)-*N*-(2-Chloro-1-propylidene)-*tert*-butanesulfinamide 7. Yellow oil, yield 63%. *E*/*Z* = 85/15. $[\alpha]_D$ −128.6 (*c* 0.7, $CHCl_3$). ν_{max}/cm^{-1} 753, 1074, 1363, 1626, 2960. δ_H(300 MHz, $CDCl_3$; Me_4Si) *E*-isomer 1.27 (9 H, s), 2.46 (3 H, s), 4.10 (1 H, d, *J* = 15.1 Hz), 4.12 (1 H, d, *J* = 15.1 Hz); *Z*-isomer 1.27 (9 H, s), 2.33 (3 H, s), 4.57 (1 H, d, *J* = 12.7 Hz), 4.66 (1 H, d, *J* = 12.7 Hz). δ_C(75 MHz, $CDCl_3$) *E*-isomer 20.0, 22.4, 49.9, 57.6, 177.0; *Z*-isomer 17.6, 22.6, 41.1, 58.0, 175.9. MS (ES, pos. mode) *m*/*z* (%): 196/198 (M + H^+, 100). (R_s)-*N*-(2-Chloro-1-propylidene)-*tert*-butanesulfinamide **7** is a known compound in literature but no spectral data were available.[17f]

Synthesis of chiral *N*-sulfinyl 2-alkyl and 2-allyl-2-methylaziridines 8

N-Sulfinyl 2-alkyl and 2-allyl-2-methylaziridines **8** were prepared according to the synthesis of *N*-sulfinyl 2-alkyl and 2-allyl-2-arylaziridines **2**.

(R_s)-1-(*tert*-Butylsulfinyl)-2,2-dimethylaziridine (R_s)-8a. R_f 0.44 (petroleum ether/Et_2O 1 : 1). Colourless oil, yield 52%. $[\alpha]_D$ −210.8 (*c* 0.3, MeOH). ee > 98%. ν_{max}/cm^{-1} 1073, 1117, 1362, 1460, 2981. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.21 (9H, s), 1.28 (3H, s), 1.41 (3H, s), 1.74 and 2.44 (2H, 2 × s). δ_C(75 MHz, $CDCl_3$) 19.4, 22.6, 25.0, 32.0, 39.1, 57.1. MS (ES, pos. mode) *m*/*z* (%):

176 (M + H$^+$, 100). Anal. Calcd for $C_8H_{17}NOS$: C 54.81; H 9.78; N 7.99. Found: C 54.71; H 9.73; N 7.77%.

(R_s,*R*)-1-(*tert*-Butylsulfinyl)-2-ethyl-2-methylaziridine (R_s,*R*)-8b. R_f 0.56 (petroleum ether/Et_2O 1 : 1), colourless oil. The diastereomers **8b** could not be separated *via* flash chromatography resulting in **8b** (57%, dr 92/8). The spectral data of **(R_s,*R*)-8b** were obtained from the mixture of diastereomers **8b** (dr 92 : 8). $[\alpha]_D$ −193.7 (*c* 0.4, MeOH). ν_{max}/cm^{-1} 903, 1075, 1360, 1458, 2963. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.06 (3H, t, J = 7.2 Hz), 1.21 (9H, s), 1.27 (3H, s), 1.63–1.76 (2H, m), 1.74 and 2.41 (2H, 2 × s). δ_C(75 MHz, $CDCl_3$) 11.1, 22.1, 22.7, 26.7, 32.3, 43.4, 57.4. MS (ES, pos. mode) *m*/*z* (%): 190 (M + H$^+$, 100). Anal. Calcd for $C_9H_{19}NOS$: C 57.10; H 10.12; N 7.40. Found: C 56.91; H 10.01; N 7.21%.

(R_s,*R*)-1-(*tert*-Butylsulfinyl)-2-allyl-2-methylaziridine (R_s,*R*)-8c. R_f 0.66 (petroleum ether/Et_2O 1 : 1). Yellow oil, yield 59% (+7% dr 76/24). $[\alpha]_D$ −249.0 (*c* 0.4, MeOH). ee > 98%. ν_{max}/cm^{-1} 915, 1068, 1360, 1458, 2979. δ_H(300 MHz, $CDCl_3$; Me_4Si) 1.22 (9H, s), 1.27 (3H, s), 1.78 and 2.48 (2H, 2 × s), 2.44 (2H, d, J = 7.2 Hz), 5.09–5.19 (2H, m), 5.78–5.93 (1H, m). δ_C(75 MHz, $CDCl_3$) 22.6, 22.7, 31.8, 38.2, 41.8, 57.5,117.9, 134.5. MS (ES, pos. mode) *m*/*z* (%): 202 (M + H$^+$, 100). Anal. Calcd for $C_{10}H_{19}NOS$: C 59.66; H 9.51; N 6.96. Found: C 59.41; H 9.35; N 6.72%.

Scanned copies of the ^{1}H and ^{13}C NMR spectra of chiral *N*-sulfinyl 2-alkyl- and 2-allyl-2-arylaziridines **2**, *N*-sulfonylaziridines **5**, *N*-sulfonyl β-amino alcohols **6**, α-chloro ketimine **7** and *N*-sulfinyl 2-alkyl and 2-allyl-2-methylaziridines **8** are added in the supporting information.

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References

1 (*a*) X. E. Hu, *Tetrahedron*, 2004, **60**, 2701 and references therein; (*b*) J. B. Sweeney, *Chem. Soc. Rev.*, 2002, **31**, 247; (*c*) W. McCoull and F. A. Davis, *Synthesis*, 2000, 1347; (*d*) D. Tanner, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 599; (*e*) C. A. Olsen, H. Franzyk and J. W. Jaroszewski, *Eur. J. Org. Chem.*, 2007, 1717; (*f*) S. Minakata, Y. Okada, Y. Oderaotoshi and M. Komatsu, *Org. Lett.*, 2005, **7**, 3509; (*g*) Y. Fukuta, T. Mita, N. Fukuda, M. Kanai and M. Shibasaki, *J. Am. Chem. Soc.*, 2006, **128**, 6312.

2 (*a*) H. Wang, X. Zhao, Y. Li and L. Lu, *Org. Lett.*, 2006, **8**, 1379; (*b*) S. D. Kuduk, C. N. D. Marco, S. M. Pitzenberger and N. Tsou, *Tetrahedron Lett.*, 2006, **47**, 2377; (*c*) M. Crucianelli, F. De Angelis, F. Lazarro, L. Malpezzi, A. Volonterio and M. Zanda, *J. Fluorine. Chem.*, 2004, **125**, 573; (*d*) A. Asensio, P. Bravo, M. Crucianelli, A. Farina, S. Fustero, J. G. Soler, S. V. Meille, W. Panzeri, F. Viani, A. Volonterio and M. Zanda, *Eur. J. Org. Chem.*, 2001, 1449; (*e*) F. A. Davis, V. Srirajan and D. Titus, *J. Org. Chem.*, 1999, **64**, 6931; (*f*) P. Bravo, M. Crucianelli, B. Vergani and M. Zanda, *Tetrahedron Lett.*, 1998, **38**, 7771.

3 (*a*) H. Pellissier, *Tetrahedron*, 2010, **66**, 1509; (*b*) J. A. Halfen, *Curr. Org. Chem.*, 2005, **9**, 657; (*c*) P. Müller and C. Fruit, *Chem. Rev.*, 2003, **103**, 2905; (*d*) H. M. I. Osborn and J. B. Sweeney, *Tetrahedron: Asymmetry*, 1997, **8**, 1693; (*e*) D. Tanner, *Pure Appl. Chem.*, 1993, **65**, 1319; (*f*) *Aziridines and Epoxides in Organic Synthesis*, A. K. Yudin, Ed.; Wiley-VCH: Weinheim, 2006; (*g*) A. Padwa, In *Comprehensive Heterocyclic Chemistry III*, ed A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor, Elsevier: Oxford, 2008, Vol. 1, pp 1–104.

4 (*a*) Y. Sugi and S. Mitsui, *Bull. Chem. Soc. Jpn.*, 1970, **43**, 564; (*b*) P. Fu, M. L. Snapper and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2008, **130**, 5530.

5 A. Toshimitsu, H. Abe, C. Hirosawa and K. Tamao, *J. Chem. Soc., Perkin Trans. 1*, 1994, **1**, 3465.

6 B. Musio, G. J. Clarkson, M. Shipman, S. Florio and R. Luisi, *Org. Lett.*, 2009, **11**, 325.

7 (*a*) R. S. Atkinson, A. P. Ayscough, W. T. Gattrell and T. M. Raynham, *J. Chem. Soc., Perkin Trans. 1*, 1998, 2783; (*b*) V. Subbarayan, J. V. Ruppel, S. Zhu, J. A. Perman and X. P. Zhang, *Chem. Commun.*, 2009, 4266; (*c*) D. Ryan, P. McMorn, D. Bethell and G. Hutchings, *Org. Biomol. Chem.*, 2004, **2**, 3566.

8 D. Morton, D. Pearson, R. A. Field and R. A. Stockman, *Chem. Commun.*, 2006, 1833.

9 (*a*) S. Mangelinckx, N. Giubellina and N. De Kimpe, *Chem. Rev.*, 2004, **104**, 2353; (*b*) N. Giubellina, W. Aelterman and N. De Kimpe, *Pure Appl. Chem.*, 2003, **75**, 1433; (*c*) C. Stevens and N. De Kimpe, *Org. Prep. Proced. Int.*, 1990, **22**, 589.

10 (*a*) N. De Kimpe, R. Verhé, L. De Buyck and N. Schamp, *Synth. Commun.*, 1975, **5**, 269; (*b*) N. De Kimpe, N. Schamp and R. Verhé, *Synth. Commun.*, 1975, **5**, 403; (*c*) N. De Kimpe, R. Verhé, L. De Buyck and N. Schamp, *J. Org. Chem.*, 1980, **45**, 5319; (*d*) N. De Kimpe, P. Sulmon, R. Verhé, L. De Buyck and N. Schamp, *J. Org. Chem.*, 1983, **48**, 4320; (*e*) P. Sulmon, N. De Kimpe and N. Schamp, *Tetrahedron*, 1989, **45**, 3907; (*f*) C. Stevens and N. De Kimpe, *J. Org. Chem.*, 1993, **58**, 132; (*g*) N. De Kimpe and D. De Smaele, *Tetrahedron Lett.*, 1994, **35**, 8023; (*h*) J. M. Concellon, E. Riego, I. A. Rivero and A Ochoa, *J. Org. Chem.*, 2004, **69**, 6244.

11 (*a*) N. De Kimpe and N. Schamp, *Org. Prep. Proced. Int.*, 1979, **11**, 115; (*b*) N. De Kimpe and N. Schamp, *J. Org. Chem.*, 1975, **40**, 3749; (*c*) N. De Kimpe, R. Verhé, L. De Buyck, H. Hasma and N. Schamp, *Tetrahedron*, 1976, **32**, 2457; (*d*) N. De Kimpe, E. Stanoeva, R. Verhé and N. Schamp, *Synthesis*, 1988, 587; (*e*) N. De Kimpe, R. Verhé, L. De Buyck and N. Schamp, *Synth. Commun.*, 1975, **5**(4), 269.

12 (*a*) F. A. Davis, R. E. Reddy, J. M. Szewczyk, G. V. Reddy, P. S. Portonovo, H. Zhang, D. Fanelli, R. T. Reddy, P. Zhou and P. J. Carroll, *J. Org. Chem.*, 1997, **62**, 2555; (*b*) P. Zhou, B.-C. Chen and F. A. Davis, *Tetrahedron*, 2004, **60**, 8003 and references cited therein.

13 (*a*) D. A. Cogan, G. Lui and J. A. Ellman, *Tetrahedron*, 1999, **55**, 8883; (*b*) J. A. Ellman, T. D. Owens and T. P. Tang, *Acc. Chem. Res.*, 2002, **35**, 984; (*c*) J. A. Ellman, *Pure Appl. Chem.*, 2003, **75**, 39.

14 F. Ferreira, C. Botuha, F. Chemla and A. Pérez-Luna, *Chem. Soc. Rev.*, 2009, **38**, 1162 and references cited therein.

15 (*a*) H. Wang, X. Zhao, Y. Li and L. Lu, *Org. Lett.*, 2006, **8**, 1379; (*b*) S. D. Kuduk, C. N. D. Marco, S. M. Pitzenberger and N. Tsou, *Tetrahedron Lett.*, 2006, **47**, 2377; (*c*) M. Crucianelli, F. De Angelis, F. Lazarro, L. Malpezzi, A. Volonterio and M. Zanda, *J. Fluorine Chem.*, 2004, **125**, 573; (*d*) A. Asensio, P. Bravo, M. Crucianelli, A. Farina, S. Fustero, J. G. Soler, S. V. Meille, W. Panzeri, F. Viani, A. Volonterio and M. Zanda, *Eur. J. Org. Chem.*, 2001, 1449; (*e*) F. A. Davis, V. Srirajan and D. Titus, *J. Org. Chem.*, 1999, **64**, 6931; (*f*) P. Bravo, M. Crucianelli, B. Vergani and M. Zanda, *Tetrahedron Lett.*, 1998, **39**, 7771.

16 (*a*) F. A. Davis, K. R. Prasad, B. Nolt and Y. Wu, *Org. Lett.*, 2003, **5**, 925; (*b*) L. B. Schenkel and J. A. Ellman, *Org. Lett.*, 2003, **5**, 545; (*c*) F. A. Davis, M. B. Nolt, Y. Wu, K. R. Prasad, D. Li, B. Yang, K. Bowen, S. H. Lee and J. H. Eardley, *J. Org. Chem.*, 2005, **70**, 2184; (*d*) F. A. Davis, Y. Zhang, Y. Andemichael, T. Fang, D. L. Fanelli and H. Zhang, *J. Org. Chem.*, 1999, **64**, 1403.

17 (*a*) B. Denolf, E. Leemans and N. De Kimpe, *J. Org. Chem.*, 2007, **72**, 3211; (*b*) B. Denolf, E. Leemans and N. De Kimpe, *J. Org. Chem.*, 2008, **73**, 5662; (*c*) B. Denolf, S. Mangelinckx, K. W. Törnroos and N. De Kimpe, *Org. Lett.*, 2006, **8**, 3129; (*d*) B. Denolf, S. Mangelinckx, K. W. Törnroos and N. De Kimpe, *Org. Lett.*, 2007, **9**, 187; (*e*) D. M. Hodgson, J. Kloesges and B. Evans, *Org. Lett.*, 2008, **10**, 2781; (*f*) Q. Chen, J. Li and C. Yuan, *Synthesis*, 2008, 2986; (*g*) E. Leemans, S. Mangelinckx and N. De Kimpe, *Synlett*, 2009, **8**, 1265; (*h*) D. M. Hodgson, J. Kloesges and B. Evans, *Synthesis*, 2009, 1923.

18 R. Almansa, D. Guijarro and M. Yus, *Tetrahedron: Asymmetry*, 2008, **19**, 603.

19 F. Alonso, I. P. Beletskaya and M. Yus, *Chem. Rev.*, 2002, **102**, 4009.

20 W. H. Pirkle, D. L. Sikkenga and M. S. Pavlin, *J. Org. Chem.*, 1977, **42**, 384.
21 F. Schmidt, F. Keller, E. Vedrenne and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2009, **48**, 1149.
22 N. De Kimpe, P. Sulmon, L. Moëns, N. Schamp, J.-P. Declerq and M. Van Meerssche, *J. Org. Chem.*, 1986, **51**, 3839.
23 (*a*) F. A. Davis and W. McCoull, *J. Org. Chem.*, 1999, **64**, 3396; (*b*) T. P. Tang, S. K. Volkman and J. A. Ellman, *J. Org. Chem.*, 2001, **66**, 8772.
24 The synthesized α-chloro *N*-*tert*-butanesulfinyl imines **1** were obtained as single *E*-isomers: see reference 17a.
25 (*a*) T. Fujisawa, Y. Kooriyama and M. Shimizu, *Tetrahedron Lett.*, 1996, **37**, 3881; (*b*) S. D. Kuduk, R. M. DiPardo, R. K. Chang, C. Ng and M. G. Bock, *Tetrahedron Lett.*, 2004, **45**, 6641.
26 G. Liu, D. A. Cogan, T. D. Owens, T. P. Tang and J. A. Ellman, *J. Org. Chem.*, 1999, **64**, 1278.

