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Optically pure *trans*-2,3-disubstituted *N*-sulfinyl aziridines. Regio- and stereoselective opening mediated by the sulfinyl group

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Abstract—A new entry to optically pure *trans*-2,3-disubstituted *N*-sulfinyl aziridines starting from 1,2-aminosulfides, involving formation of a sulfonium salt intermediate followed by intramolecular nucleophilic attack by the sulfinamide nitrogen atom, is reported. The regio- and stereoselective opening of the aziridine ring can be achieved by anchimeric assistance of the sulfinyl group.
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1. Introduction

Optically active aziridines are versatile building blocks that have found widespread use in organic synthesis.[1] Additionally, the aziridine nucleus is also included in some natural and biologically active products, such as mitomycins and azinomycins,[2] and has been used as ligands and auxiliaries in asymmetric synthesis.[1a,f,3]

Asymmetric methods for aziridine synthesis are mainly based on nitrene transfer or equivalents to olefins and carbene/carbenoids transfer to imines.[4] Alkene aziridination has allowed high enantioselectivities with cinnamate esters, chromene derivatives, and styrene but simple alkenes resulted in low enantioselectivity.[4c,5] The addition of chiral metallocarbenes to imines has been less successful.[6] Best results have been achieved by addition of ethyl diazoacetate to imines in the presence of chiral boron Lewis acid catalysts to afford *cis*-aziridines (up to 99% ee).[7] Recently, enantiopure *trans*-2-ethenylaziridines have been synthesized from allenyl zinc species and chiral *N*-sulfinylimines.[8] The use of *S*-chiral sulfinylimines with achiral bromoenolates[9] and α-halomethyl phosphonates[10] has also been studied, but only in the first case high levels of stereocontrol are observed.

The addition of achiral sulfonium and sulfoxonium ylides to enantiopure sulfinylimines has been described but only moderate diastereoselectivities were achieved.[11] As alternative method, aziridination of *N*-sulfonylimines with chiral ylides derived from the camphor skeleton[12] and Eliel's oxathiane[13] to afford *cis*-alkynylaziridines in moderate enantioselectivity and cis/trans mixtures in up to 99.9% ee has also been reported. Aggarwal et al. have developed one of the best catalytic imine aziridination procedure in which ylides were generated in situ from diazocompounds or, more safely, from the corresponding tosyl hydrazone salts and a chiral sulfide.[14] The procedure afforded aziridines in high ee with diastereoselectivities depending on the activating group on nitrogen (cis/trans ratio of ca. 1:3 and 1:6 using *N*-SES[14a,b] and *N*-TcBoc aldimines,[14c] respectively). The asymmetric aziridination of imines via aza-Darzens reaction has also been reported. Thus, addition of a chiral bromoacylsultam to imines afforded *cis*- or *trans*-aziridines with a high levels of diastereoselectivity.[15]

As most of these methods are quite efficient to prepare *cis*-aziridines whereas the trans selective aziridination remains less settled, indirect routes involving preparation and cyclization of enantiomerically enriched 1,2-amino alcohols[16] or 1,2-aminosulfides[17] stand as the most viable alternatives to prepare these isomers.

Recently, we have reported a highly stereoselective one-step asymmetric synthesis of *anti*-1,2-disubstituted 1,2-aminosulfide derivatives[18] (Scheme 1). We now report an efficient method to prepare *trans*-2,3-disubstituted aziridines starting from these aminosulfides. Moreover, as the resulting aziridines have a sulfinyl group at the appropriated position to act as an anchimeric assistant in the opening reactions of the aziridine rings, we have studied the ability of this group

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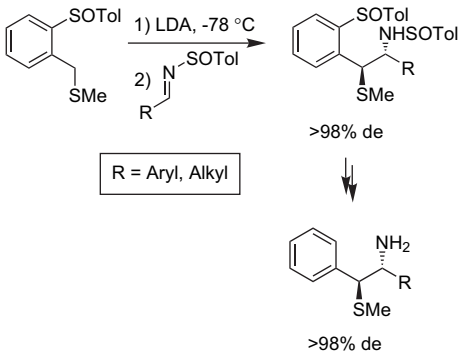


Scheme 1.

in controlling the regio- and stereoselectivity of these reactions. This anchimeric assistance has been reported in some reactions such as the hydrolysis of nitriles[19] and the addition of halogens to double bonds.[20]

2. Results and discussion

Aminosulfides **1a–e** and **1g** were synthesized as single diastereoisomers[18] by reaction of the lithium (*S*)-α-(methylthio)-2-(*p*-tolylsulfinyl)benzyl carbanion with (*S*)-*N*-*p*-tolylsulfinyl aldimines. For compound **1f**, a 96:4 mixture of two stereoisomers in 65% yield was achieved (see Section 4).

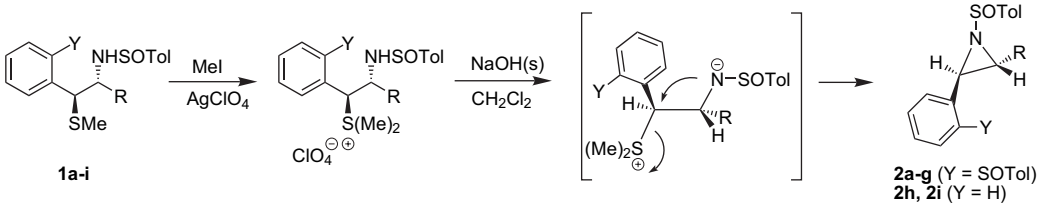
Aminosulfides **1a–g** were transformed into aziridines through a one pot procedure. This method involves the methylation at sulfenyl sulfur with MeI in the presence of $AgClO_4$. The resulting sulfonium salts were isolated simply by filtration of the crude reaction mixture through a pad of Celite followed by washing with CH_2Cl_2 and evaporate to dryness. Sulfonium salts were then transformed to the corresponding aziridines by cyclization with powered NaOH and quenching the reaction mixture with water. The overall process afforded analytically pure aziridines in moderate to high yield after one chromatographic purification. The scope of the aziridine synthesis is summarized in Table 1.

A range of 2,3-disubstituted aziridines bearing aromatic and heteroaromatic substituents of varying steric demand and electronic effects were accessed as single stereoisomers (de>98%; entries 1–6). No other isomer could be detected by NMR (300 MHz) from the reaction crudes. In addition, the synthesis of 2-alkyl-3-arylaziridine **2g** was carried out with analogous result (entry 7). The moderate yields obtained for **2b** and **2f** (entries 2 and 6) were due to the low solubility of the corresponding sulfonium salts in CH_2Cl_2. The use of more efficient solvents did not allow removing residual silver salts that partially inhibited the further cyclization step.

Hydrogenolysis of the Ar–SOTol bond can be made under mild conditions with organolithium compounds[21] and it was possible to remove the chiral auxiliary before cyclization step. It has been illustrated by C-desulfinylation of **1a** and **1g** with *t*-BuLi (1.8 equiv) followed by quenching with saturated NH_4Cl to afford the *N*-sulfinyl aminosulfides **1h** and **1i**, respectively, in nearly quantitative yield. Remarkably, the N-desulfinylation does not occur under these conditions. Subsequent intramolecular cyclization of the **1h** and **1i** takes place under the experimental conditions described above, affording 2,3-diphenyl and 2-butyl-3-phenyl *N*-sulfinyl aziridines, **2h** and **2i**, respectively, in good yields (entries 8 and 9). It suggests that the sulfinyl group at the aromatic ring has no significant role in the cyclization process.

Although S_N1 and S_N2 processes are possible from benzylsulfonium salts,[22] the isolation of only one diastereoisomer in all the substrates shown in Table 1 suggests that cyclization must occur with inversion of the configuration at C-2 according to an internal S_N2 process (see scheme in Table 1). The intramolecular attack of the sulfinamide anion to the benzyl carbon must be much faster than heterolytic cleavage of the C–S bond to generate the benzylic carbocation. This is expected for aminosulfides **1a–g**, bearing a sulfinyl group, but it is also the case for **1h** and **1i** lacking of deactivating group at the ring. Moreover, the complete stereoselectivity observed in these reactions indicates that no base catalyzed epimerization occurred and the intermediate did not revert back to the corresponding ylide and imine.

Table 1. Synthesis of *N*-sulfinyl aziridines **2a–i**

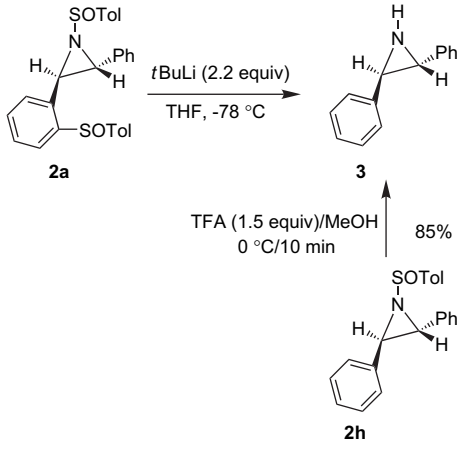


1a-i

2a-g (Y = SOTol)
2h, 2i (Y = H)

Entry	Substrate	Y	R	Aziridine (% isolated yield)	de (%)
1	**1a**	SOTol	Ph	(2*R*,3*R*)-(−)-**2a** (78)	>98
2	**1b**	SOTol	*o*-BrC_6H_4	(2*R*,3*R*)-(+)-**2b** (43)	>98
3	**1c**	SOTol	*p*-$MeOC_6H_4$	(2*R*,3*R*)-(−)-**2c** (65)	>98
4	**1d**	SOTol	*p*-CNC_6H_4	(2*R*,3*R*)-(−)-**2d** (65)	>98
5	**1e**	SOTol	2-Naphthyl	(2*R*,3*R*)-(−)-**2e** (76)	>98
6	**1f**	SOTol	2-Pyridyl	(2*R*,3*R*)-(−)-**2f** (45)	>98
7	**1g**	SOTol	*n*-Bu	(2*R*,3*R*)-(+)-**2g** (75)	>98
8	**1h**	H	Ph	(2*R*,3*R*)-(+)-**2h** (77)	>98
9	**1i**	H	*n*-Bu	(2*R*,3*R*)-(+)-**2i** (76)	>98

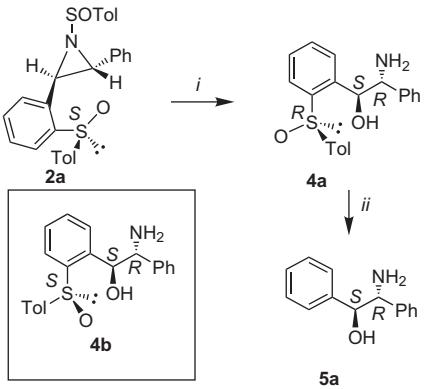
The trans-configuration for the aziridines **2a–i** was based on the reaction mechanism and clearly confirmed by the coupling constants of the vicinal hydrogens H-2 and H-3 of 4.1–4.7 Hz.[23] The absolute configuration was established for (2*R*,3*R*)-**2a** and for (2*R*,3*R*)-**2h** by chemical correlation with the known (+)-(*R*,*R*)-*trans*-2,3-diphenylaziridine **3**.[24] C-desulfinylation and N-desulfinylation of **2a**, in one pot reaction, take place in almost quantitative yield by reaction with *t*-BuLi (2.2 equiv). For **2h** the hydrolysis of the N–S bond was carried out by reaction with TFA (1.5 equiv)/MeOH without ring-opening (Scheme 2). The obtained aziridine **3** exhibited the same specific optical rotation as that reported in the literature,[24] so that it was considered to be enantiopure. These two reactions illustrate the way to obtain NH-aziridines from the *N*-sulfinyl aziridines **2a–i** shown in Table 1. It is remarkable that the cleavage of the N–S bond with *t*-BuLi is possible for **2a** but not for **1a**.[18] The similar behavior observed in all the cyclization reactions, all of them evolving in a completely stereoselective manner, suggests that the absolute configuration for compounds **2b–i** is identical to that determined for **2a**.



Scheme 2.

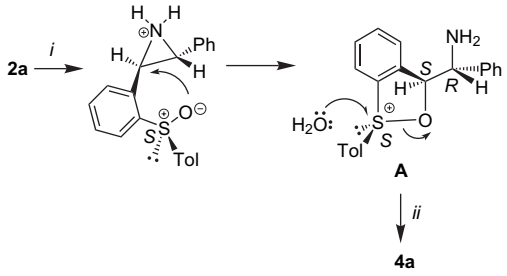
In order to study the influence of the sulfinyl group on the course of the opening ring we choose compound **2a**. According to the electronic effects of the aromatic rings, the nucleophilic processes evolving through unimolecular mechanisms (S_N1) should mainly take place on the benzyl carbon joined to the Ph group with epimerization. By contrast, reactions involving S_N2 mechanisms would be completely stereoselective but moderately regioselective. We first studied the reaction of **2a** with TFA in MeOH followed by reaction with aqueous HCl and neutralization. Only one aminoalcohol, **4a**, was formed under these conditions, which indicates that the opening of the aziridine ring of **2a** has occurred with a complete control of the regio- and stereoselectivity (Scheme 3).

The absolute configuration of the aliphatic chiral carbons at **4a** was established by chemical correlation with the (1*S*,2*R*)-2-amino-1,2-diphenylethane-1-ol **5a**.[25] This correlation was performed by reaction of **4a** with Ra–Ni.[26] The configuration at sulfur was established as *R* by comparison of the NMR data of **4a** with those of the **4b** (Scheme 3), previously obtained.[27] As they are different, both compounds should be diastereoisomers, which means that they differ in the configuration at sulfur.



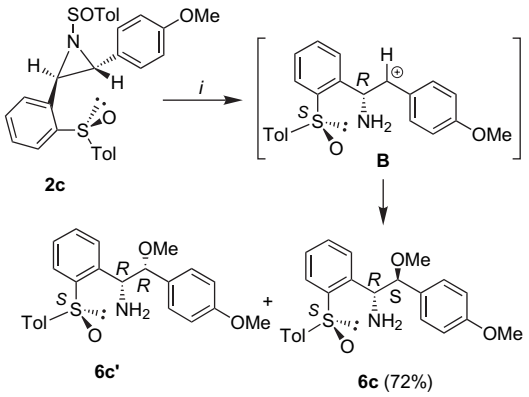
Scheme 3. Reagents and conditions: *i*. (1) TFA (1.5 equiv), MeOH, 0 °C, 15 min, (2) HCl(aq) 1 M followed by neutralization; *ii*. Ni–Ra, THF.

In order to explain these results, the anchimeric assistance of the sulfinyl group in the opening of the aziridine ring must be assumed. After the hydrolysis of the N–S bond by TFA, the protonation at aziridinic nitrogen must be followed by the intramolecular attack of the sulfinyl oxygen to form an oxysulfonium intermediate **A** (Scheme 4). The attack of the nucleophile (H_2O) to the sulfur of this intermediate, maybe catalyzed by the protonation at oxygen with HCl, would determine the formation of the sulfoxide **4a** with (*R*)-configuration at sulfur.



Scheme 4. Reagents and conditions: *i*. TFA (1.5 equiv), MeOH, 0 °C, 15 min; *ii*. HCl(aq) 1 M.

Finally we have studied the reaction of **2c** with TFA in methanol. In this case, a 80:20 mixture of two β-aminoethers, **6c** and **6′c**, was obtained (Scheme 5). They were purified by chromatography, but only the major one (**6c**) could be obtained in diastereomerically pure form. Regiochemistry as well as stereochemistry of **6c** have been determined by ^1H NMR. The major isomer (**6c**) exhibits a coupling constant in benzene (6.8 Hz), which increases in DMSO (8.0 Hz). It suggests that population of the conformation with and *anti* relationship between the coupled protons increases when intramolecular associations of the OH and NH_2 groups (hydrogen bonds) are minimized by the solvent. This behavior is only expected for the *erythro* isomer with the opposite configuration at the chiral carbons. Regiochemistry of **6c** was deduced from NOESY experiments performed in DMSO (Fig. 1) and benzene. It is remarkable that the proton joined to the oxygenated carbon exhibits a lower chemical shift than the one joined to the nitrogenated carbon, which can only be explained as a consequence of the anisotropic effect of the S–O bond, which reinforces the regiochemistry postulated for **6c**.



Scheme 5. Reagents and conditions: *i*. (1) TFA (1.5 equiv), MeOH, 0 °C, 15 min.

This is the typical result expected for S_N1 processes involving stable benzyl carbocations stabilized by the *p*-OMe group that can be attacked by the solvent, methanol, from any of its diastereotopic faces, affording **6c** and **6′c**. The low stability of the carbocations derived from **2a** determines that they cannot be spontaneously formed from the protonated species shown in Scheme 4. It is also remarkable that nucleophilic intramolecular attack of the sulfinyl oxygen to the carbocation **B** (it would yield the alcohol instead of the OMe derivative) is slower than the attack of the solvent. It suggests that the formation of a five-membered ring like **A** in Scheme 4 is much easier than the formation of a six-membered ring that must be formed from **B** of Scheme 5.

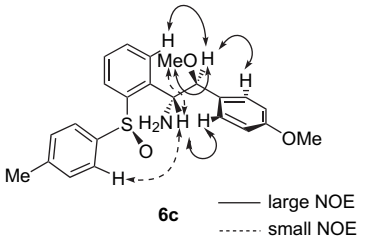


Figure 1. Effects of NOEs observed for NOESY experiments from **6c**.

3. Conclusion

In summary a new entry to enantiopure *trans-N*-sulfinyl aziridines starting from enantiopure 1,2-aminosulfides is reported. It involves their conversion into the corresponding 2-aminosulfonium salts followed by the completely stereoselective elimination of the sulfur moiety according to an internal S_N2 process. The anchimeric assistance of the sulfinyl group allows the complete regio- and stereocontrolled opening of some *ortho*-sulfinylphenyl aziridines in acidic medium.

4. Experimental

4.1. General

Dry solvents and liquid reagents were distilled under argon just prior to use. THF was distilled from sodium and benzophenone ketyl, CH_2Cl_2 was dried over P_2O_5, and diisopropylamine over KOH. *n*-BuLi (1.6 M solution in hexane) were purchased from Âcros. All reaction vessels, after being flame-dried, were kept under argon. Reactions were monitored by TLC on commercially available precoated plates (Merck silica gel 60 F_{254}). Column chromatography was performed by using Silica Gel Merck 60 (230–400 mesh) and *Varian* SCX column. Melting points were measured using a Gallemkamp apparatus in open capillary tubes and are uncorrected. Optical rotations were measured with a 141 Perkin–Elmer polarimeter. ^{1}H NMR spectra (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$) spectra were performed with a Bruker AC-300 spectrometer. Chemical shifts (δ) are given in parts per million, relative to TMS, coupling constants (J) in hertz. Mass spectra were measured by electron impact (EI, 70 eV) or FAB with a VG AutoSpec spectrometer.

4.2. Synthesis of [1*R*,2*S*,(*S*)*S*]-*N*-{1-pyridyl-2-[(*S*)-2-(*p*-toluenesulfinyl)phenyl]-2-(methylthio)ethyl}-*p*-toluene sulfinamide,[18] 1f

A solution of *n*-BuLi (0.60 mmol, 1.6 M in hexane, 1.2 equiv) was added over ^{i}Pr$_2$NH (0.89 mmol, 1.8 equiv) in THF (3 ml) at 0 °C. After 45 min stirring, the mixture was cooled at −78 °C and then a solution of (*S*)-α-methylthio-2-(*p*-tolylsulfinyl)toluene (138 mg, 0.50 mmol, 1.0 equiv) in THF (2 ml) was added. After 5 min stirring, *N*-(2-pyridinemethylidene)-*p*-toluene sulfinamide[28] (244 mg, 1.0 mmol, 2.0 equiv) dissolved in THF (4 ml) was added at −78 °C. When the reaction was completed (5 min), the mixture was hydrolyzed at that temperature with saturated aqueous NH_4Cl (2 ml) and extracted with CH_2Cl_2 (3×10 ml). The combined organic extracts were dried with $MgSO_4$ and the solvent was removed under reduced pressure to afford a mixture of epimers in C_1, in 96:4 ratio. The residue was purified by flash-column chromatography (AcOEt/hexane 4:1) to give pure aminosulfide **1f** (60%): $[\alpha]_D^{20}$ +18.4 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (dd, 1H, *J* 4.6, 1.5, H-arom.), 8.11 and 7.66 (2dd, 2H, *J* 7.2, 1.5, H-arom.), 7.69–7.57 (m, 3H, H-arom.), 7.33 (dd, 1H, *J* 7.7, 0.9, H-arom.), 7.26–7.22 (m, 1H, H-arom.), 7.60, 6.94, 6.87, and 6.50 (2 AA′BB′ systems, 8H, H-arom.), 4.90 (d, 1H, *J* 10.5, H-C2), 4.68 (t, 1H, *J* 10.5, H-C1), 4.39 (d, 1H, *J* 10.5, –NH), 2.34 and 2.11 (2s, 6H, 2CH_3C$_6$H$_4$–), 1.63 (s, 3H, CH_3S–); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.2, 144.5, 141.8, 141.4, 140.6 and 139.6 (C-arom.), 139.7, 136.5, 131.8, 129.6 (2C), 129.0 (2C), 128.9, 128.2, 126.1 (2C), 125.0 (2C), 124.5, 123.4 and 123.1 (CH-arom.), 65.1 and 49.7 (C-1 and C-2), 21.2 (2CH_3C$_6$H$_4$–), 14.8 (CH_3S–). HRMS calcd for $C_{28}H_{28}N_2O_2S_3$: 520.1313; found, 520.1307.

4.3. General procedure for the reactions of aziridination summarized in Table 1

To a solution of 1,2-aminosulfides [(**1a–i**), 0.1 mmol] in methyliodide (1 ml) was added silver perchlorate (20.8 mg, 0.1 mmol). The mixture was stirred for 3 h at room temperature and then filtered through a pad of Celite, the filtrate was washed with CH_2Cl_2. The solvent was evaporated to give the required salt, as a white solid, which was used without further purification. To a solution of the appropriate salt (1 mmol) in CH_2Cl_2 (5 ml) was added powered

KOH (4.1 mg, 0.062 mmol). The mixture was stirred for 1 h at room temperature. The reaction was hydrolyzed with 4 ml of water, and the mixture was extracted with CH_2Cl_2 (3×4 ml). The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash-column chromatography.

4.3.1. *trans*-(2*R*,3*R*)-2-Phenyl-3-[(*S*)-2-(*p*-toluenesulfinyl)-phenyl]-1-[(*S*)-(*p*-toluenesulfinyl)]aziridine, 2a. Eluent for chromatography: hexane/Et_2O 1:4. Yield: 78%; white syrup; $[\alpha]_D^{20}$ −23.6 (*c* 0.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.02 (dd, 1H, *J* 7.8, 0.9, H-arom.), 7.56–7.19 (m, 12H, H-arom.), 4.22 and 4.14 (2d, 2H, *J* 4.4, H-C2 and H-C3), 2.36 and 2.35 (2s, 6H, 2C$H_3C_6H_4$–); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.1, 142.6, 142.0, 141.6, 141.0, 133.8 and 132.7 (C-arom.), 130.9, 130.1, 129.4, 129.3, 128.5, 128.4, 128.3, 126.4, 124.8 and 124.5 (CH-arom.), (C-2 and C-3 are missing), 21.4 and 21.3 (2$CH_3C_6H_4$–). HRMS calcd for $C_{21}H_{18}NOS$ (M^+−SOTol): 332.1109; found, 332.1106.

4.3.2. *trans*-(2*R*,3*R*)-2-(*o*-Bromophenyl)-3-[(*S*)-2-(*p*-toluenesulfinyl)phenyl]-1-[(*S*)-(*p*-toluenesulfinyl)]aziridine, 2b. Eluent for chromatography: hexane/Et_2O 2:1. Yield: 43%; white syrup; $[\alpha]_D^{20}$ +48.3 (*c* 0.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.96 (d, 1H, *J* 7.7, H-arom.), 7.59, 7.58, 7.45, and 7.44 (2 AA′BB′ systems, 8H, H-arom.), 7.56–7.50 (m, 1H, H-arom.), 7.34–7.17 (m, 6H, H-arom.), 4.33 and 4.29 (2d, 2H, *J* 4.7, H-C2 and H-C3), 2.38 (s, 6H, C$H_3C_6H_4$–); ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.2, 151.8, 142.9, 142.2, 142.0, 141.6, 141.0 and 132.3 (C-arom.), 132.4, 131.1, 130.1 (2C), 129.9, 129.6, 129.4 (2C), 128.7, 127.4, 126.4 (2C), 124.8 and 124.6 (3C, CH-arom.), (C-2 and C-3 are missing), 21.4 (2$CH_3C_6H_4$–). HRMS calcd for $C_{21}H_{17}BrNOS$ (M^+−SOTol): 410.0214; found, 410.0219.

4.3.3. *trans*-(2*R*,3*R*)-2-(*p*-Methoxyphenyl)-3-[(*S*)-2-(*p*-toluenesulfinyl)phenyl]-1-[(*S*)-(*p*-toluenesulfinyl)]aziridine, 2c. Eluent for chromatography: hexane/Et_2O 1:2. Yield: 65%; yellow syrup; $[\alpha]_D^{20}$ −44.1 (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.98 (d, 1H, *J* 7.8, H-arom.), 7.45 (dd, 4H, *J* 8.0, 6.1, H-arom.), 7.34 (dd, 4H, *J* 6.4, 2.5, H-arom.), 7.23–7.13 (m, 5H, H-arom.), 6.92 (d, part of AA′BB′ system, 2H, H-arom.), 4.27 and 4.00 (2d, 2H, *J* 4.1, H-C2 and H-C3), 3.83 (s, 3H, CH_3O–C_6H_4–), 2.36 and 2.35 (2s, 6H, 2C$H_3C_6H_4$–). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.7, 144.8, 142.0, 141.6, 141.5, 141.2, 141.0 and 133.4 (C-arom.), 132.0, 131.0, 130.8 (2C), 130.5, 130.2 (2C), 129.4 (2C), 128.0, 126.2 (2C), 124.8 (2C) and 114.3 (2C, CH-arom.), 55.2 ($CH_3OC_6H_4$–), (C2 and C3 are missing), 21.4 (2$CH_3C_6H_4$–). HRMS calcd for $C_{22}H_{20}NO_2S$ (M^+−SOTol): 362.1215; found, 362.1225.

4.3.4. *trans*-(2*R*,3*R*)-2-(*p*-Cyanophenyl)-3-[(*S*)-2-(*p*-toluenesulfinyl)phenyl]-1-[(*S*)-(*p*-toluenesulfinyl)]aziridine, 2d. Eluent for chromatography: hexane/Et_2O 1:2. Yield: 65%; white syrup; $[\alpha]_D^{20}$ −27.0 (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.97 (d, 1H, *J* 7.8, H-arom.), 7.65 (d, part of AA′BB′ system, 2H, H-arom.), 7.59–7.29 (m, 5H, H-arom.), 7.44, 7.43, 7.23, and 7.22 (2 AA′BB′ systems, 8H, H-arom.), 4.21 and 4.17 (2d, 2H, *J* 4.1, H-C2 and H-C3), 2.37 and 2.36 (2s, 6H, C$H_3C_6H_4$–); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.2, 142.3, 142.1, 142.0, 140.6, 140.0, 133.8 and 133.2 (C-arom.), 132.3, 131.1, 130.1, 129.7, 129.6, 128.9, 128.6, 126.4, 124.7 and 124.5 (CH-arom.), 59.9 and 41.9 (C-2 and C-3), 21.4 and 21.2 (2$CH_3C_6H_4$–). HRMS calcd for $C_{22}H_{17}N_2OS$: (M^+−SOTol): 357.1062; found, 357.1054.

4.3.5. *trans*-(2*R*,3*R*)-2-(2-Naphthyl)-3-[(*S*)-2-(*p*-toluenesulfinyl)phenyl]-1-[(*S*)-(*p*-toluenesulfinyl)]aziridine, 2e. Eluent for chromatography: hexane/AcOEt 1:1. Yield: 76%; white syrup; $[\alpha]_D^{20}$ −91.5 (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.04 (dd, 1H, *J* 7.8, 1.0, H-arom.), 7.85, 7.19, and 7.20 (part of AA′BB′ system, 4H, H-arom.), 7.56–7.30 (m, 15H, H-arom.), 4.32 and 4.30 (2d, 2H, *J* 4.3, H-C2 and H-C3), 2.35 and 2.34 (2s, 6H, 2C$H_3C_6H_4$–); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.1, 142.7, 142.1, 141.6, 141.0, 133.2, 133.0, 132.7 and 131.4 (C-arom.), 131.0, 130.1, 129.5, 129.4, 128.7, 128.3, 128.1, 128.0, 127.7, 126.5, 126.4, 125.3, 124.8 and 124.6 (CH-arom.), (C-2 and C-3 are missing), 21.4 (2$CH_3C_6H_4$–). HRMS calcd for $C_{25}H_{20}$ NOS (M^+−SOTol): 382.1266; found, 382.1252.

4.3.6. *trans*-(2*R*,3*R*)-2-(Pyridyl)-3-[(*S*)-2-(*p*-toluenesulfinyl)phenyl]-1-[(*S*)-(*p*-toluenesulfinyl)]aziridine, 2f. Eluent for chromatography: hexane/Et_2O 1:2. Yield: 45%; white syrup; $[\alpha]_D^{20}$ −46.3 (*c* 0.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.97 (d, 1H, *J* 7.9, H-arom.), 7.71 (dd, 1H, *J* 7.9, 1.7, H-arom.), 7.50–7.29 (m, 5H, H-arom.), 7.48, 7.45, 7.20, and 7.19 (2 AA′BB′ systems, 8H, H-arom.), 4.48 and 4.19 (2d, 2H, *J* 4.1, H-C2 and H-C3), 2.35 (s, 6H, C$H_3C_6H_4$–); ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.9, 144.9, 142.5, 141.9, 141.6, 140.9 and 132.7 (C-arom.), 139.5, 136.7, 131.0 (3C), 130.1, 129.4 (2C), 128.6, 126.2 (2C), 124.8 (2C), 124.3, 123.4 and 123.2 (CH-arom.), (C2 and C3 are missing), 21.4 (2$CH_3C_6H_4$–).

4.3.7. *trans*-(2*R*,3*R*)-2-Butyl-3-[(*S*)-2-(*p*-toluenesulfinyl)-phenyl]-1-[(*S*)-(*p*-toluenesulfinyl)]aziridine, 2g. Eluent for chromatography: hexane/Et_2O 1:3. Yield: 75%; colorless oil; $[\alpha]_D^{20}$ +27.2 (*c* 0.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.87 (dd, 1H, *J* 7.7, 1.1, H-arom.), 7.49, 7.45, 7.25, and 7.18 (2 AA′BB′ systems, 8H, H-arom.), 7.36 (dt, 1H, *J* 7.7, 1.1, H-arom.), 7.25 and 6.75 (2d, 2H, *J* 7.7, H-arom.), 3.81 (d, 1H, *J* 4.1, H-C3), 2.74 (dt, 1H, *J* 6.4, 4.1, H-C2), 2.38 and 2.35 (2s, 6H, 2C$H_3C_6H_4$–), 2.07–1.38 (3m, 6H, $CH_3(CH_2)_3$–), 0.96 (t, 1H, *J* 7.2, C$H_3(CH_2)_3$–); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.4, 142.8, 141.7, 141.4, 141.3 and 134.8 (C-arom.), 130.9, 130.1, 129.3, 128.5, 126.7, 125.8, 124.7 and 124.0 (CH-arom.), 49.8 and 33.9 (C-2 and C-3), 30.3, 28.2 and 22.4 ($CH_3(CH_2)_3$–), 21.4 and 21.3 (2$CH_3C_6H_4$–), 13.9 ($CH_3(CH_2)_3$). HRMS calcd for $C_{19}H_{22}NOS$ (M^+−SOTol): 312.1422; found, 312.1420.

4.3.8. *trans*-[2*R*,3*R*,(*S*)*S*]-2,3-Diphenyl-1-(*p*-toluenesulfinyl)aziridine, 2h. Eluent for chromatography: hexane/Et_2O 4:1. Yield: 77%; white syrup; $[\alpha]_D^{20}$ +117.9 (*c* 0.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.60 (d, 1H, *J* 8.2, H-arom.), 7.45–7.32 (m, 8H, H-arom.), 7.23 (d, 1H, *J* 8.2, H-arom.), 4.17 (s, 2H, H-C2 and H-C3), 2.36 (s, 3H, C$H_3C_6H_4$–); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.0, 141.3 and 134.7 (C-arom.), 129.4 (2C), 128.4 (3C), 128.1 (3C) and 124.9 (2C, CH-arom.), 43.7 (C2 and C3), 21.3 ($CH_3C_6H_4$–).

4.3.9. *trans*-[2*R*,3*R*,(*S*)*S*]-2-Butyl-3-phenyl-1-(*p*-toluenesulfinyl)aziridine, 2i. Eluent for chromatography: hexane/Et_2O 4:1. Yield: 76%; colorless oil; $[\alpha]_D^{20}$ +16.0 (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.61 and 7.22 (AA′BB′ system, 4H, H-arom.), 7.26–7.16 (m, 3H, H-arom.), 7.12 (dd, 2H, *J* 7.7, 2.2, H-arom.), 3.67 (d, 1H, *J* 4.1, H-C3), 2.75–2.70 (m, 1H, H-C2), 2.10–1.21 (2m, 6H, $-(CH_2)_3CH_3$), 0.95 (t, 3H, *J* 7.1, $-(CH_2)_3CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.2, 141.2 and 137.1 (C-arom.), 129.4 (2C), 128.2 (2C), 127.3, 126.8 (2C) and 125.0 (2C, CH-arom.), 49.2 and 37.5 (C2 and C3), 30.4, 28.2 and 22.3 ($-CH_2)_3CH_3$), 21.3 ($CH_3C_6H_4$–), 14.0 ($-(CH_2)_3CH_3$).

4.4. Representative procedure for C–S desulfinylation

To a stirred solution of **1a** and **1h** (0.12 mmol) in THF (2 ml) was added *t*-BuLi (0.15 ml, 0.22 mmol, 1.5 M in hexane, 1.8 equiv). When the reaction was completed (5 min), the mixture was hydrolyzed with saturated aqueous NH_4Cl (1 ml) and extracted with CH_2Cl_2 (3×3 ml). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash-column chromatography.

4.4.1. [1*R*,2*S*,(*S*)*S*]-*N*-[1,2-(Diphenyl)-2-(methylthio)ethyl]-*p*-toluene sulfinamide, 1h. This product was obtained from **1a**. Eluent for chromatography: hexane/Et_2O 1:1; quantitative yield; colorless syrup; spectroscopic and optical rotation data of compound **1h** are coincident with those previously reported: $[\alpha]_D^{20}$ +155.0 (*c* 0.7, $CHCl_3$) [lit.[18]=+155.8 (*c* 0.5, $CHCl_3$)]; ^1H NMR (300 MHz, $CDCl_3$): δ 7.33–7.21 (m, 7H, H-arom.), 7.20–7.15 (m, 3H, H-arom.), 7.00–6.98 (m, 2H, H-arom.), 4.76 (dd, 1H, *J* 6.1, 6.5, H-C1), 4.75 (br s, 1H, –NH), 4.21 (d, 1H, *J* 6.5, H-C2), 2.31 (s, 3H, $CH_3C_6H_4$–), 1.84 (s, 3H, CH_3S–).

4.4.2. [1*R*,2*S*,(*S*)*S*]-*N*-[1-Butyl-2-phenyl-2-(methylthio)ethyl]-*p*-toluene sulfinamide, 1i. This product was obtained from **1g**. Eluent for chromatography: hexane/Et_2O 4:1; quantitative yield; colorless oil; $[\alpha]_D^{20}$ +180.6 (*c* 0.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.53 and 7.40 (AA′BB′ system, 4H, H-arom.), 7.34–7.23 (m, 5H, H-arom.), 4.26 (d, 1H, *J* 9.4, H-C2), 4.18 (d, 1H, *J* 5.0, –NH), 3.65–3.56 (m, 1H, H-C1), 2.39 (s, 3H, $CH_3C_6H_4$–), 1.96 (s, 3H, CH_3S–), 1.51–0.92 (m, 6H, $CH_3(CH_2)_3$–), 0.78 (t, 1H, *J* 7.0, $CH_3(CH_2)_3$–); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.0, 141.0 and 139.2 (C-arom.), 129.2 (2C), 128.9 (2C), 128.3 (2C), 127.2 and 125.7 (2C, CH-arom.), 59.4 and 59.3 (C-1 and C-2), 32.1, 27.8 and 22.1 ($CH_3(CH_2)_3$–), 21.4 and 21.2 ($2CH_3C_6H_4$–), 15.0 and 13.8 (CH_3S– and $CH_3(CH_2)_3$). HRMS calcd for $C_{19}H_{22}NOS$: 312.1422; found, 312.1421.

4.4.3. (+)-(2*R*,3*R*)-2,3-Diphenylaziridine, 3. This product was obtained from **2a** following the procedure described above but using 2.2 equiv of *t*-BuLi. The product was purified by SCX column chromatography. Yield: 75%; colorless syrup; $[\alpha]_D^{20}$ +320 (*c* 0.5, $CHCl_3$) [lit.[24]=328.8 (*c* 1.25, $CHCl_3$)]; spectroscopic data of compound **3** are coincident with those previously reported:[24] ^1H NMR (300 MHz, $CDCl_3$): δ 7.29–7.40 (m, 10H, H-arom.), 3.12 (s, 2H, H-C2 and H-C3), 1.70 (br s, 1H, –NH).

4.5. Representative procedure N–S desulfinylation

Method A: To a stirred solution of aziridine **2a** (0.05 mmol) in methanol (1 ml) was added TFA (6.3 μl, 0.08 mmol, 1.5 equiv). After the mixture was stirred for 15 min at 0 °C, the solvent was evaporated, and the residue was filtered through SCX column chromatography. The reaction mixture was diluted in methanol (1 ml) and then HCl (0.5 ml, 1 N) was added. After 1 h, concentrated NH_3 was added until the solution was brought to pH 10. The solvent was evaporated, and the residue was purified by SCX column chromatography to afford the corresponding aminoalcohol.

4.5.1. (1*R*,2*S*)-2-Amine-2-phenyl-1-[(*R*)-(2-*p*-toluenesulfinyl)phenyl]-ethanol, 4a. Eluent for chromatography: NH_3/methanol (7 M). Yield: 70%; colorless oil; $[\alpha]_D^{20}$ +40 (*c* 0.3, EtOH); ^1H NMR (300 MHz, $CDCl_3$): δ 7.84 (d, 1H, *J* 7.4, H-arom.), 7.77 (d, 1H, *J* 6.7, H-arom.), 7.60 (dd, 1H, *J* 7.4, 6.7, H-arom.), 7.48–7.32 (m, 6H, H-arom.), 7.26–7.17 (m, 4H, H-arom.), 4.93 (br s, 1H, HO-C1), 4.84 and 4.44 (2d, 2H, *J* 8.3, H-C1 and H-C2), 2.36 (s, 3H, $CH_3C_6H_4$–). HRMS calcd for $C_{21}H_{22}NO_2S$ (M^++1): 352.1365; found, 352.1341.

Method B: To a stirred solution of aziridine **2c** (0.05 mmol) in methanol (1 ml) was added TFA (6.3 μl, 0.08 mmol, 1.5 equiv). After the mixture was stirred for 15 min at 0 °C, the solvent was evaporated, and the residue was purified by flash-column chromatography (CH_2Cl_2/MeOH 95:5) to give a mixture of amines **6c** and **6′c** in a 80:20 ratio (yield 90%). Only the major product could be isolated as pure compound.

4.5.2. (1*R*,2*S*)-2-Methoxy-2-(*p*-methoxyphenyl)-1-[(*S*)-(2-*p*-toluenesulfinyl)phenyl]-ethylamine, 6c. White syrup; $[\alpha]_D^{20}$ −127.1 (*c* 0.7, $CHCl_3$); ^1H NMR (300 MHz, DMSO-d_6): δ 7.56 (m, 2H, H-arom.), 7.43–7.32 (m, 2H, H-arom.), 7.48 and 7.28 (AA′BB′ system, 4H, $CH_3C_6H_4$–), 7.01 and 6.75 (AA′BB′ system, 4H, H-arom.), 4.46 (d, 1H, *J* 7.98, H-C1), 4.19 (d, 1H, *J* 7.98, H-C2), 3.67 (s, 3H, CH_3O–C_6H_4–), 3.12 (s, 3H, CH_3O-C2), 2.29 (s, 3H, $CH_3C_6H_4$–); ^{13}C NMR (75 MHz, DMSO-d_6): δ 158.8, 144.0, 143.2, 141.0 and 140.3 (C-arom.), 130.7 (CH-arom.), 130.4 (C-arom.), 130.1 and 128.8 (2C, CH-arom.), 128.4 and 128.3 (2C, CH-arom.), 125.1 (2C), 123.2 and 113.5 (2C, CH-arom.), 87.6 (C-2), 56.5 and 56.4 (C-1 and CH_3O-C-2), 55.1 ($CH_3OC_6H_4$–), 21.0 ($CH_3C_6H_4$–). ^1H NMR (300 MHz, C_6D_6): δ 8.21 (m, 1H, H-arom.), 7.66 (m, 3H, H-arom.), 7.24–7.09 (m, 4H, H-arom.), 6.85 (m, 4H, H-arom.), 4.89 (br s, 1H, H-C1), 4.30 (d, 1H, *J* 6.80, H-C2), 3.35 (s, 3H, CH_3O–C_6H_4–), 3.20 (s, 3H, CH_3O-C2), 1.97 (s, 3H, $CH_3C_6H_4$–). HRMS calcd for $C_{23}H_{26}NO_3S$ (M^++1): 396.1627; found, 396.1616.

4.5.3. (1*R*,2*R*)-2-Methoxy-2-(*p*-methoxyphenyl)-1-[(*S*)-(2-*p*-toluenesulfinyl)phenyl]-ethylamine, 6′c. White syrup; ^1H NMR (300 MHz, $CDCl_3$), described from a mixture of compounds **6c** and **6′c**: δ 7.96 and 7.60 (2dd, 2H, *J* 7.5, 1.7, H-arom.), 7.55–7.37 (m, 2H, H-arom.), 7.48, 7.22, 7.11, and 6.86 (2 AA′BB′ systems, 8H, H-arom.), 4.58 and

4.30 (2d, 2H, *J* 6.3, H-C1 and H-C2), 3.81 (s, 3H, CH_3O–C_6H_4–), 3.13 (s, 3H, CH_3O-C2), 2.34 (s, 3H, C$H_3C_6H_4$–).

4.6. Representative procedure for C–S desulfinylation with Ni–Ra

A solution of compound **4a** (0.05 mmol) in THF (1 ml) was added to a suspension of activated Raney nickel (350 mg) in THF (1 ml). The mixture was stirred for 2 h, and the crude was purified by SCX column to afford the aminoalcohol **5a**.

4.6.1. (1*S*,2*R*)-2-Amino-1,2-diphenylethanol, 5a. Yield: 68%; $[\alpha]_D^{20}$ +6.9 (*c* 0.5, EtOH) [lit.[25]=+7.0 (*c* 0.6, EtOH)]; spectroscopic data of compound **5a** are coincident with those previously reported:[25] ^{1}H NMR (300 MHz, CD_3OD): δ 7.30–7.19 (m, 10H, H-arom.), 4.81 and 4.04 (2d, 2H, *J* 6.1, H-C1 and H-C2).

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