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PAPER

Enantiomerically pure 2-aryl(alkyl)-2-trifluoromethylaziridines: synthesis and ring opening with selected *O*- and *N*-nucleophiles†‡

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We report herein the synthesis of enantiomerically pure 2-phenyl- and 2-ethyl-2-trifluoromethylaziridines by Mitsunobu-type cyclisation of the corresponding *N*-protected amino alcohols, and our results regarding their ring opening with selected nucleophiles. Under basic conditions, *N*-tosyl aziridines have been regioselectively opened at the less hindered carbon. Under acidic conditions, the regioselectivity of the attack depends on the nature of the substituent at C-2 and on the nitrogen protecting group.

Introduction

Trifluoromethylated compounds have found a wide range of applications as pharmaceuticals, agrochemicals or materials due to the specific properties introduced by the fluorine atoms.[1] Nitrogen-containing derivatives in particular are of great interest,[1,2] however the synthesis of enantiopure molecules with a quaternary trifluoromethyl group adjacent to the nitrogen atom is still challenging.[1]

Aziridines,[3] and chiral ones in particular, are recognized as important intermediates for the synthesis of a wide array of nitrogen-containing compounds by way of ring-opening reactions,[4] the regioselectivity of these reactions being strongly dependent on the nature of the substituents and the reaction conditions.[4b,e]

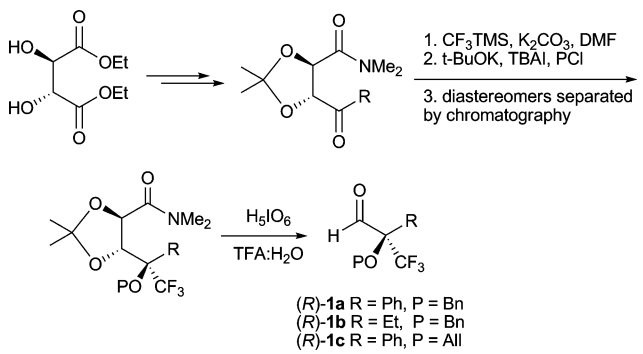
However, despite their great synthetic interest, only a few optically active aziridines bearing a trifluoromethyl moiety have been reported.[5] Amongst them, only one derivative belonging to the class of 2-aryl(alkyl)-2-trifluoromethylaziridines has been described. Its synthesis involved the stereospecific alkylation of a trifluoromethylated aziridinyl anion with benzylbromide, albeit in low yield which prevent further studies.[5e–g]

Studies on the ring opening of variously *N*-substituted trifluoromethyl aziridines[5e–g,6] have shown that: (i) the activating electron withdrawing sulfonyl group facilitates their reaction with nucleophiles; (ii) the reaction is always totally regioselective, with the nucleophile attacking on the carbon not bearing the trifluoromethyl group, due to the electrostatic repulsion of this substituent towards nucleophiles.

In this context, we planned the synthesis of the enantiopure *N*-tosyl 2-phenyl- and 2-ethyl-2-trifluoromethylaziridines from the corresponding enantiopure α-trifluoromethyl-α-alkoxyaldehydes. These aziridines, one containing an aryl group and the other one an alkyl group, allowed us to study the influence of the substituent geminal to the trifluoromethyl group on the regioselectivity of the ring opening with selected nucleophiles. The observed results led us to assess the influence of the substituent at nitrogen, thus to synthesize also the *N*-benzyl-2-phenyl-2-trifluoromethylaziridine.

Results and discussion

We recently reported the diastereoselective synthesis of the starting alkoxyaldehydes (*R*)-**1** from (L)-tartaric acid derived ketoamide (Scheme 1).[7,8]



Scheme 1 Preparation of alkoxyaldehydes (*R*)-**1**.[7]

The reaction of the alkoxyaldehyde (*R*)-**1a** with *p*-toluenesulfonamide in the presence of $TiCl_4$ and triethylamine[9] afforded the corresponding imine (*R*)-**2a** in 75% yield (Scheme 2). The *N*-tosylimine function then needed to be reduced into sulfonamide. The treatment of (*R*)-**2a** with sodium borohydride in methanol afforded only the stable hemiaminal derivative **3a** in 63% yield. To overcome this drawback, the imine was reduced using either

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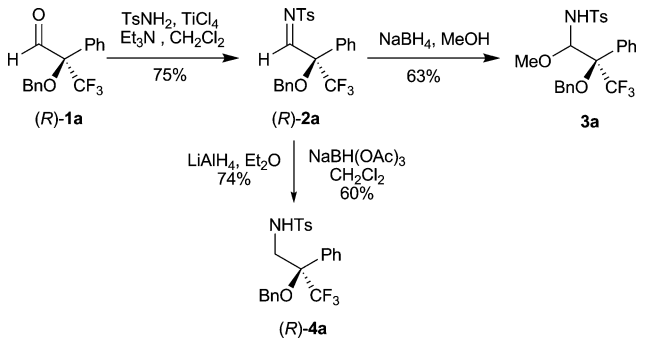
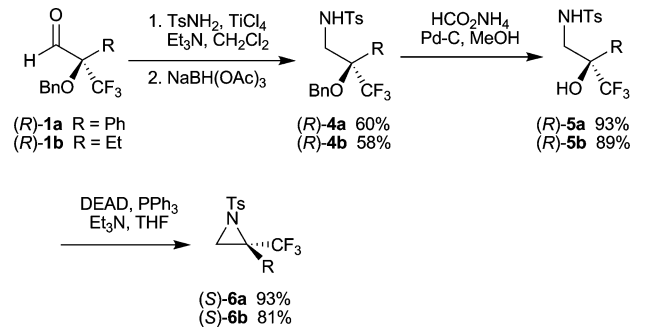
‡ Electronic supplementary information (ESI) available: Preparation of racemic samples, copies of NMR spectra (^{19}F, ^{1}H and ^{13}C) for all new compounds and chromatograms. CCDC reference number 779933. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0ob00690d



Scheme 2 First attempts for the preparation of the alkoxysulfonamide (*R*)-**4a**.

$LiAlH_4$ in diethylether or $NaBH(OAc)_3$ in dichloromethane to give the alkoxysulfonamide (*R*)-**4a** in respectively 74 and 60% yield.

After optimisation of the reaction conditions, we were able to perform a "sequential one-pot" reductive amination of (*R*)-**1a**,**b** which afforded directly the β-alkoxysulfonamides (*R*)-**4a**,**b** in quite good yields (respectively 58% and 60%) (Scheme 3). Subsequent cleavage of the *O*-benzyl protecting group of (*R*)-**4a**,**b** led to the β-hydroxysulfonamides (*R*)-**5a**,**b** in excellent yields (93 and 89%). (*R*)-**5a**,**b** which contain a tertiary-alcohol function bearing a trifluoromethyl group were then subjected to the Mitsunobu conditions.[10,11] Their treatment with diethyl azodicarboxylate and triphenylphosphine in the presence of triethylamine in THF afforded cleanly the aziridines (*S*)-**6a**,**b** which were isolated in excellent yields after chromatography on silica gel (respectively 93 and 81% yields) (Scheme 3).



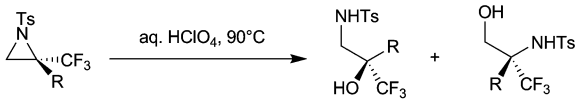
Scheme 3 Preparation of the activated aziridines (*S*)-**6a**,**b**.

The enantiomeric purity of the aziridine (*S*)-**6a** (ee = 100%) was confirmed by chiral HPLC, and the clean inversion of configuration at the tertiary-alcohol stereocenter[11] was confirmed by X-ray diffraction (*vide infra*).

Having found a convenient access to disubstituted aziridines (*S*)-**6a**,**b**, we evaluated their reactivity toward the synthesis of the β-hydroxysulfonamides **7**,[12] regioisomers of **5**.

The aziridine (*S*)-**6a** proved to be inert under neutral conditions. Under acidic conditions ($HClO_4$, H_2O, 90 °C)[4b] the *N*-tosyl-2-phenyl-2-trifluoromethylaziridine (*S*)-**6a** was opened with complete regioselectivity, leading to the β-hydroxysulfonamide (*R*)-**5a** (83% yield) (Table 1, entry 1). The protected β-amino alcohol (*R*)-**5a**, which is unfortunately the precursor of (*S*)-**6a**, results from water attacking at the benzylic position, on the carbon bearing the trifluoromethyl group. (*R*)-**5a** was isolated in good yield albeit with partial racemization of the quaternary stereocenter (ee = 88%). This high ee suggests that the acid hydrolysis of the *N*-tosyl-2-phenyl-2-trifluoromethylaziridine (*S*)-**6a** proceeds mainly *via* an S_N2 pathway at the more electrophilic position, whereas the slight racemisation might result from the formation of an incipient α-trifluoromethylated carbenium ion stabilized by the phenyl group.[13,14]

Table 1 Acidic hydrolysis of the *N*-tosylaziridines (*S*)-**6a**,**b**

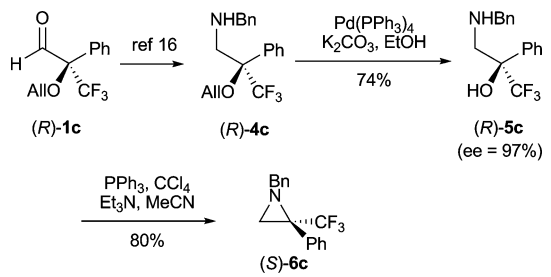


entry	aziridine	R	time	ratio[a] (*R*)-**5** : (*S*)-**7**	isolated product	yield
1	(*S*)-**6a**	Ph	1 h 30	100 : 0	(*R*)-**5a** (ee = 88%)[b]	83%
2	(*S*)-**6b**	Et	20 h	7 : 93	(*S*)-**7b**	69%

[a] determined by ^{19}F NMR on the crude mixture. [b] determined by chiral HPLC, see ESI.‡

As the presence of the phenyl group[4e,15] should explain this unusual reactivity of a trifluoromethylated aziridine, we performed the same reaction on the 2-ethyl analogue (*S*)-**6b**. The treatment of *N*-tosyl-2-ethyl-2-trifluoromethylaziridine (*S*)-**6b** under the same conditions led indeed predominantly to the β-hydroxysulfonamide (*S*)-**7b** which was isolated in 69% yield, but surprisingly, a small amount of the regioisomer (*R*)-**5b** was also detected by ^{19}F NMR in the crude mixture (Table 1, entry 2). Owing to this unusual nucleophilic attack on the CF_3-bearing carbon, we were keen to investigate the influence of the activating tosyl group on the regioselectivity of the acid hydrolysis.

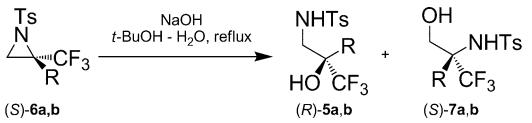
As *N*-benzyl-2-trifluoromethylaziridine is known to react with various nucleophiles under acidic conditions,[6b] we prepared the *N*-benzyl-2-phenyl-2-trifluoromethylaziridine (*S*)-**6c**, a non activated analogue of aziridine (*S*)-**6a**. The palladium catalysed deallylation of the known *N*-benzyl amino ether (*R*)-**4c**[16] afforded the *N*-benzyl amino alcohol (*R*)-**5c** in 74% yield (Scheme 4). We first attempted to cyclize the *N*-benzyl β-amino alcohol (*R*)-**5c** (ee = 97%)[17] under Mitsunobu conditions (DEAD, PPh_3, Et_3N, THF) but not surprisingly[10b] the aziridine (*S*)-**6c** was isolated in low yield (39%) due to the formation of many byproducts. (*R*)-**5c** was thus cyclised into the aziridine (*S*)-**6c** using an alternative method.[18,19]



Scheme 4 Preparation of the non-activated aziridine (*S*)-**6c**.

Under the previous acidic hydrolysis conditions, the nucleophile attacked preferentially the non-activated aziridine (*S*)-**6c** at C-3 leading to the β-amino alcohol (*S*)-**7c** as the major product (78%

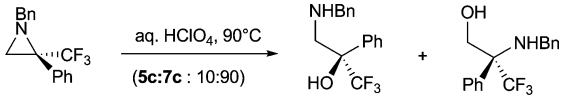
Table 2 Basic hydrolysis of *N*-tosylaziridines (*S*)-**6a**,**b**



(*S*)-**6a**,**b** (*R*)-**5a**,**b** (*S*)-**7a**,**b**

entry	aziridine	R	time	ratio[a] (*R*)-**5** : (*S*)-**7**	isolated product	yield
1	(*S*)-**6a**	Ph	26 h	3 : 97	(*S*)-**7a**	84%
2	(*S*)-**6b**	Et	21 h	0 : 100	(*S*)-**7b**	93%

[a] determined by ^{19}F NMR on the crude mixture.



(*S*)-**6c** (*R*)-**5c** 3% (ee = 92%) (*S*)-**7c** 78% (ee = 97%)

Scheme 5 Acidic hydrolysis of *N*-benzylaziridine (*S*)-**6c**.

yield), along with a small amount of (*R*)-**5c** (3% yield, ee = 92%) (Scheme 5).

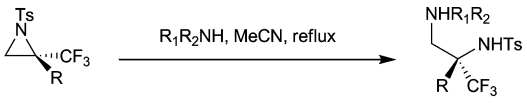
The above results highlighted that the nucleophilic ring opening of the 2-phenyl substituted aziridine (*S*)-**6a** at the CF_3-bearing carbon C-2, under acidic conditions, is due to the presence of both the aryl group geminal to CF_3 and the sulfonyl group of the nitrogen which enhances the electrophilicity of the adjacent carbons.

Despite scarce reports on the ring opening of aziridines with hydroxide ion,[4b] we finally attempted reactions under basic conditions with the aim of favouring the ring opening at C-3 for both aziridines (*S*)-**6a** and (*S*)-**6b** (Table 2).[20] Aziridine (*S*)-**6a** was treated with sodium hydroxide in a mixture of *tert*-butanol and water at reflux. The hydroxide attack was highly regioselective at C-3, giving the β-hydroxysulfonamide (*S*)-**7a** in excellent yield (84%) (entry 1). Only traces of its regioisomer (*R*)-**5a** could be observed by ^{19}F NMR of the crude product. The ring opening of the aziridine (*S*)-**6b** under these conditions afforded only the β-hydroxysulfonamide (*S*)-**7b** which was isolated in 93% yield (entry 2).

The ring opening of aziridines (*S*)-**6a** and (*S*)-**6b** was also examined with various amines in refluxing acetonitrile (Table 3).[20] In all cases, the ring opening proceeded solely at C-3, the less hindered carbon (Table 3). Treatment with primary and secondary amines afforded the corresponding β-aminosulfonamides[12] (*S*)-**8a**,**b**, (*S*)-**9a**,**b** and (*S*)-**10a**,**b** in excellent yields (from 90 to 97%) (entries 1–6). Not surprisingly, the reaction with the less nucleophilic aniline was more sluggish (entries 7–8).[21] Aziridines (*S*)-**6a**,**b** also reacted with paratoluenesulfonamide in the presence of potassium carbonate (entries 9,10).

Recrystallization of β-diamine (*S*)-**9a** from ether–petroleum ether gave colorless needles, which were subjected to X-ray diffraction analysis.‡ The absolute configuration of the quaternary carbon bearing the trifluoromethyl group was found to be *S*, thus confirming the inversion of its configuration during the cyclisation reaction (Mitsunobu reaction)[11] of the β-hydroxysulfonamide (*R*)-**5a** leading to the aziridine (*S*)-**6a** (Fig. 1).

Table 3 Reactions of *N*-tosylaziridines (*S*)-**6a**,**b** with *N*-nucleophiles



(*S*)-**6a** R = Ph (*S*)-**6b** R = Et (*S*)-**8-12a**,**b**

entry	aziridine	R_1R_2NH	time	isolated product	yield
1	(*S*)-**6a**	$BnNH_2$	20 h	(*S*)-**8a**	90%
2	(*S*)-**6b**	$BnNH_2$	22 h	(*S*)-**8b**	96%
3	(*S*)-**6a**	(*R*)-α-Me-$BnNH_2$	24 h	(*S*)-**9a**	95%
4	(*S*)-**6b**	(*R*)- α-Me-$BnNH_2$	24 h	(*S*)-**9b**	98%
5	(*S*)-**6a**	morpholine	22 h	(*S*)-**10a**	93%
6	(*S*)-**6b**	morpholine	15 h	(*S*)-**10b**	97%
7	(*S*)-**6a**	aniline[a]	48 h	(*S*)-**11a**	99%
8	(*S*)-**6b**	aniline[a]	40 h	(*S*)-**11b**	98%
9	(*S*)-**6a**	$TsNH_2$[b]	22 h	(*S*)-**12a**	85%
10	(*S*)-**6b**	$TsNH_2$[b]	22 h	(*S*)-**12b**	76%

[a] 2 equiv of aniline were used. [b] K_2CO_3 (1.2 equiv) was added.

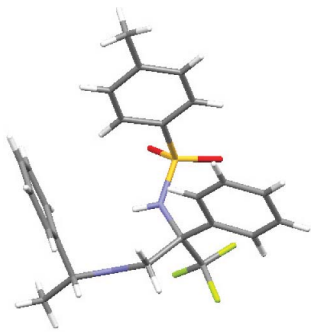


Fig. 1 Structure of compound (*S*)-**9a** from single crystal X-ray data.

Conclusion

In conclusion we have reported the synthesis of enantiomerically pure or enriched *N*-tosyl and *N*-benzyl 2-phenyl- and *N*-tosyl-2-ethyl-2-trifluoromethylaziridines by cyclisation of the corresponding *N*-protected amino alcohols, and their reaction with selected nucleophiles. Under acidic conditions the attack depends on the nature of the substituent at C-2 and on the nitrogen protecting group. Remarkably, attack on the carbon bearing the trifluoromethyl group has been observed for the first time. The ring opening of *N*-tosyl 2,2-disubstituted trifluoromethylated aziridines with hydroxide or amines is highly regioselective, at the less hindered carbon.

Experimental section

General experimental

THF and ether were distilled from sodium–benzophenone. CH_2Cl_2 was distilled from CaH_2. Others reagents and solvents were obtained from common commercial sources and used as received. Thin-layer chromatography using precoated aluminium backed plates (Merck Kieselgel 60F254) were visualized by UV light and an aqueous solution of potassium permanganate. Silicagel (Macherey–Nagel GmbH & Co KG – (40–63 μm, ASTM for column chromatography) was used for flash chromatography. Melting points (mp) were determined on a Stuart apparatus SMP3

and were uncorrected. Optical rotations were measured on a Perkin Elmer precisely model 341 polarimeter at room temperature (*c.a.* 20 °C). NMR spectra were recorded on a Bruker advance 250. Coupling constants (*J*) are reported in Hz. In the ^{13}C NMR data, reported signal multiplicities are related to C–F coupling. HRMS were recorded on a Micromass ESI-Q–TOF mass spectrometer using an electrospray source in positive mode (ESI^+). Analytical HPLC were performed either on an Agilent 1100 series LC or a Shimadzu LC10AS system equipped with a tunable UV detector. Crystallographic data were recorded on a Brüker Kappa Apex II equipped with an Oxford Cryosystem 700 cryostat. The structures were solved by direct methods with additional light atoms found by Fourier methods. Hydrogen atoms were added at calculated positions and refined using a riding model. Anisotropic displacement parameters were used for all non H-atoms; H-atoms were given isotropic displacement parameters equal to 1.2 or 1.5 times the equivalent isotropic displacement parameter of the atom to which the H-atom is attached. Aldehydes (*R*)-**1a**,**b**[7] and *N*-benzylamino alcohol (*R*)-**4c**[16] were prepared according to reported procedures.

(*R*)-2-Benzyloxy-3,3,3-trifluoro-2-phenyl-*N*-tosylpropylamine (*R*)-2a

To a solution of aldehyde (*R*)-**1a** (428 mg, 1.46 mmol), *p*-toluenesulfonamide (249 mg, 1.46 mmol, 1 equiv) and triethylamine distilled over KOH (608 µL, 4.37 mmol, 3 equiv) in CH_2Cl_2 (10 mL) was added, at 0 °C and under Ar, a solution of $TiCl_4$ (120 µL, 1.09 mmol, 0.75 equiv) in CH_2Cl_2 (3 mL). The reaction mixture was stirred for 5 min at 0 °C and at rt for 3 h. The reaction mixture was then filtered through celite and the filtrate was concentrated under reduced pressure. The residue was triturated with Et_2O (dried over $MgSO_4$), the suspension was heated at reflux for 10 min, filtered and the filtrate was concentrated under reduced pressure to give the aldimine (*R*)-**2a** (491 mg, 75%) as a yellow–brownish oil which was used in the next step without further purification. δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) −73.0 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.46 (s, 3 H), 4.56 (d, *J* 11.5, 1 H), 4.70 (d, *J* 11.5, 1 H), 7.30–7.45 (m, 12 H), 7.80 (d, *J* 8.0, 2 H), 8.76 (d, *J* 1.5, 1 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 21.7, 68.7, 82.8 (q, *J* 28.5), 123.2 (q, *J* 288.0), 127.3, 128.0, 128.3, 128.6, 128.8, 130.0, 133.5, 136.9, 145.8, 169.7.

(2*R*)-2-Benzyloxy-3,3,3-trifluoro-1-methoxy-2-phenyl-*N*-tosylpropylamine 3a

A solution of imine (*R*)-**2a** (134 mg, 0,30 mmol) and $NaBH_4$ (11 mg, 0,30 mmol, 1 equiv) in MeOH (2 mL) was stirred at rt and under Ar for 18 h. The reaction mixture was then concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and was washed with HCl 20%. The organic layer was extracted, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue (mixture of 2 diastereomers 51 : 49 according to the ^{19}F NMR) on silica gel (PE : EtOAc 6 : 1) afforded the hemiaminal **3a** (91 mg, 63%) as a colorless oil (Found: $[M+Na]^+$, 502.1166. $C_{24}H_{24}F_3NNaO_4S$ requires 502.1276); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) −65.2 and −68.4 (s, 3 F); δ_H NMR (250 MHz; $CDCl_3$; Me_4Si) 2.26 and 2.29 (2 s, 3 H), 3.09 and 3.32 (2 s, 3 H), 4.55 (m, 2 H), 4.87 and 5.11 (2 d, *J* 10.0, 1 H), 5.26 (m, 1 H), 6.85–7.70 (m, 14 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 21.4 and 21.5, 56.9 and 57.7, 67.7 and 68.0, 84.2 (q, *J* 25.5) and 85.3 (q, *J* 24.0), 86.5 and 88.8, 126.4, 126.8, 126.9, 127.2, 127.5, 127.8, 127.9, 128.1, 128.3, 128.4, 128.5, 128.7, 129.1, 129.4, 129.5 (q, *J* 314.0) and 129.8 (q, *J* 312.0), 137.8 and 138.3, 142.9 and 143.4.

General procedure for the synthesis of β-benzyloxysulfonamides (*R*)-4a,b by reductive amination of (*R*)-1a,b

To a solution of aldehyde (*R*)-**1a**,**b**, *p*-toluenesulfonamide (1 equiv) and triethylamine (distilled over KOH, 3 equiv) in CH_2Cl_2 was added, at 0 °C and under Ar, a solution of $TiCl_4$ (0.75 equiv) in CH_2Cl_2. The reaction mixture was stirred 5 min at 0 °C and at rt until the completion of the conversion of the aldehyde (*R*)-**1a**,**b** into tosylimine (*R*)-**2a**,**b** (reaction monitored by ^{19}F NMR). The reaction mixture was then filtered through celite and $NaBH(OAc)_3$ (2.5 equiv) was added to the filtrate. The reaction mixture was stirred for 15 supplementary hours. The reaction mixture was then washed with a sat. aq. sol. of Na_2CO_3 and brine. The organic layer was extracted, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue on silica gel afforded the β-benzyloxysulfonamide (*R*)-**4a**,**b**.

(+)-(*R*)-2-Benzyloxy-3,3,3-trifluoro-2-phenyl-*N*-tosypropylamine (*R*)-4a

Following the general procedure, a solution of $TiCl_4$ (292 µL, 2.66 mmol, 0.75 equiv) in CH_2Cl_2 (5 mL) was added to a solution of aldehyde (*R*)-**1a** (1.04 g, 3.55 mmol), *p*-toluenesulfonamide (608 mg, 3.55 mmol, 1 equiv) and Et_3N (1.48 mL, 10.65 mmol, 3 equiv) in CH_2Cl_2 (30 mL). After 4 h of reaction the reaction was filtered on celite and $NaBH(OAc)_3$ (1.88 g, 8.88 mmol, 2.5 equiv) was added. Chromatography (PE : EtOAc 6 : 1) afforded the β-benzyloxysulfonamide (*R*)-**4a** (955 mg, 60%) as a white solid (Found: $[M+Na]^+$, 472.1168. $C_{23}H_{22}F_3NNaO_3S$ requires 472.1170); mp 86 °C (from EtOAc–PE); $[\alpha]_D^{20}$ +21 (*c* 1.05 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) −72.1 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.41 (s, 3 H), 3.54 (dd, *J* 5.0 and 13.0, 1 H), 3.77 (dd, *J* 6.5 and 13.0, 1 H), 4.50 (s, 2 H), 4.72 (br s, 1 H), 7.26 (d, *J* 8.0, 2 H), 7.33–7.40 (m, 10 H), 7.65 (d, *J* 8.0, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 21.3, 45.6, 66.6, 80.8 (q, *J* 27.0), 124.6 (q, *J* 295.5), 126.99, 127.04, 127.4, 128.4, 128.7, 129.3, 129.7, 132.8, 136.0, 136.7, 143.6.

(–)-(*R*)-2-Benzyloxy-*N*-tosyl-2-trifluoromethylbutylamine (*R*)-4b

Following the general procedure for the reductive amination, a solution of $TiCl_4$ (69 µL, 0.62 mmol, 0.75 equiv) in CH_2Cl_2 (1 mL) was added to a solution of aldehyde (*R*)-**1b** (204 mg, 0.83 mmol), *p*-toluene sulfonamide (142 mg, 0.835 mmol, 1 equiv) and Et_3N (347 µL, 2.49 mmol, 3 equiv) in CH_2Cl_2 (4 mL). After 5 h of reaction the reaction was filtered on celite and $NaBH(OAc)_3$ (439 mg, 2.07 mmol, 2.5 equiv) was added. Chromatography (PE : CH_2Cl_2 1 : 6) afforded the β-benzyloxysulfonamide (*R*)-**4b** (193 mg, 58%) as a white solid (Found: $[M+Na]^+$, 424.1182. $C_{19}H_{22}F_3NNaO_3S$ requires 424.1170); mp 59 °C (from CH_2Cl_2–PE); $[\alpha]_D^{20}$ −32 (*c* 0.99 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) −73.3 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 1.01 (t, *J* 7.5, 3 H), 1.98 (q, *J* 7.5, 2 H), 2.39 (s, 3 H), 3.16 (dd, *J* 6.0 and 13.0, 1 H),

3.28 (dd, *J* 7.0 and 13.0, 1 H), 4.51 (d, *J* 11.5, 1 H), 4.55 (d, *J* 11.0, 1 H), 4.91 (t, *J* 6.5, 1 H), 7.24–7.34 (m, 7 H), 7.70 (d, *J* 8.0, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 7.0, 21.3, 21.7, 43.8, 66.1, 79.1 (q, *J* 25.5), 125.5 (q, *J* 291.0), 127.0, 127.6, 127.9, 128.4, 129.7, 136.2, 137.0, 143.6.

General procedure for the synthesis of β-hydroxysulfonamides (*R*)-5a,b

A suspension of benzyloxysulfonamide (*R*)-**4a**,**b**, ammonium formate (3.0 equiv) and Pd/C (10%, 0.05 equiv) in methanol was heated at reflux. After the complete disappearance of the amino-ether (*R*)-**4a**,**b**, the reaction mixture was cooled to rt, filtered through celite and the filtrate was concentrated under reduced pressure. Purification by chromatography on silica gel or recrystallisation afforded the β-hydroxysulfonamide (*R*)-**5a**,**b**.

(+)-(*R*)-1,1,1-Trifluoro-2-phenyl-3-tosylaminopropan-2-ol (*R*)-5a

According to the general procedure, the benzyloxysulfonamide (*R*)-**4a** (900 mg, 2.0 mmol) was reacted with ammonium formate (378 mg, 6.0 mmol, 3.0 equiv) and Pd/C (10%, 107 mg, 0.1 mmol, 0.05 equiv) in methanol (10 mL) for 2 h. Recrystallization (PE–Et_2O) yielded the β-hydroxysulfonamide (*R*)-**5a** (660 mg, 93%) as a white solid (Found: $[M+Na]^+$, 382.0712. $C_{16}H_{16}F_3NNaO_3S$ requires 382.0701); mp 139 °C (from Et_2O–PE); $[\alpha]_D^{20}$ +42 (*c* 0.97 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) −78.4 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) δ 2.43 (s, 3 H), 3.51 (dd, *J* 6.0 and 14.0, 1 H), 3.59 (dd, *J* 7.5 and 14.0, 1 H), 3.98 (br s, 1 H), 4.96 (t, *J* 7.0, 1 H), 7.25–7.38 (m, 5 H), 7.49 (m, 2 H), 7.66 (d, *J* 8.0, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si): 21.4, 47.3, 75.7 (q, *J* 28.5), 124.7 (q, *J* 286.5), 126.4, 127.0, 128.6, 129.0, 129.9, 134.8, 135.7, 144.2. 100% ee determined by chiral HPLC (chiralcel OD-H column, hexane : isopropanol 95 : 5, flow rate 1 mL min^{-1}): *t* = 17.4 min (*rac.* *t* = 17.4 and 23.8 min).

(+)-(*R*)-1-Tosylamino-2-trifluoromethylbutan-2-ol (*R*)-5b

According to the general procedure, the benzyloxysulfonamide (*R*)-**4b** (250 mg, 0.62 mmol) was reacted with ammonium formate (117 mg, 1.86 mmol, 3.0 equiv) and Pd/C (10%, 33 mg, 0.03 mmol, 0.05 equiv) in methanol (4 mL) for 2 h. Chromatography on silica gel (PE : Et_2O 2 : 1) yielded the β-hydroxysulfonamide (*R*)-**5b** (169 mg, 89%) as a white solid (Found: $[M+Na]^+$, 334.0702. $C_{12}H_{16}F_3NNaO_3S$ requires 334.0701); mp 62–63 °C (from Et_2O–PE); $[\alpha]_D^{20}$ +31 (*c* 0.99 in $CHCl_3$); δ_F NMR (235.3 MHz; $CDCl_3$; $CFCl_3$) −79.1 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 0.95 (t, *J* 7.5, 3 H), 1.77 (m, 2 H), 2.43 (s, 3 H), 3.09 (dd, *J* 6.0 and 14.0, 1 H), 3.17 (dd, *J* 9.0 and 14.0, 1 H), 3.38 (br s, 1 H), 5.38 (dd, *J* 6.0 and 7.5, 1 H), 7.32 (d, *J* 8.0, 2 H), 7.75 (d, *J* 8.0, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 6.9, 21.4, 25.4, 44.6, 74.3 (q, *J* 27.0), 125.7 (q, *J* 287.0), 127.0, 129.9, 135.9, 144.1.

(−)-(*R*)-3-Benzylamino-1,1,1-trifluoro-2-phenylpropan-2-ol (*R*)-5c

A suspension of amino ether (*R*)-**4c** (436 mg, 1.30 mmol), tetrakis(triphenylphosphine)palladium(0) (75 mg, 0.065 mmol, 0.05 equiv) and potassium carbonate (539 mg, 3.90 mmol, 3 equiv) in absolute ethanol (10 mL) was heated at reflux, under Ar, for 40 min. The reaction mixture was cooled to rt and filtered through celite (Et_2O). The filtrate was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the residue by chromatography on silica gel (PE : Et_2O 3 : 1) afforded the β-amino alcohol (*R*)-**5c** (284 mg, 74%) as a colorless oil (Found: $[M+H]^+$, 296.1267. $C_{16}H_{17}F_3NO$ requires 296.1262); $[\alpha]_D^{20}$ −14 (*c* 0.96 in $CHCl_3$), (*R*)-**5c**·HCl $[\alpha]_D^{20}$ −16 (*c* 0.66 in MeOH) [lit.[8d] enantiomer *S*·HCl $[\alpha]_D^{23}$ +1.5 (*c* 0.92 in MeOH)]; δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) −78.6 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.98 (dd, *J* 1.0 and 13.0, 1 H), 3.43 (d, *J* 13.0, 1 H), 3.72 (s, 2 H), 7.15–7.40 (m, 7 H), 7.56 (dd, *J* 1.0 and 7.5 Hz, 2 H), OH and NH not detected; δ_C NMR (62.9 MHz; $CDCl_3$; Me_4Si) 52.4, 53.8, 73.7 (q, *J* 28.0), 125.5 (q, *J* 285.5), 126.1, 127.4, 128.0, 128.3, 128.5, 128.6, 137.6, 138.9. 97% ee determined by chiral HPLC (chiralpak IC column, hexane : isopropanol 90 : 10, flow rate 0.5 mL min^{-1}): t_{minor} = 9.5 min, t_{major} = 10.3 min.

General procedure for the synthesis of aziridines (*S*)-6a,b

A solution of β-hydroxysulfonamide (*R*)-**5a**,**b**, diethylazodicarboxylate (1.5 equiv), triphenylphosphine (1.5 equiv) and triethylamine (2.5 equiv) in THF was stirred at rt and under Ar. After the complete disappearance of the β-hydroxysulfonamide (*R*)-**5a**,**b**, the reaction was concentrated under reduced pressure and was purified by chromatography on silica gel to give the aziridine (*S*)-**6a**,**b**.

(−)-(*S*)-2-Phenyl-*N*-tosyl-2-trifluoromethylaziridine (*S*)-6a

According to the general procedure, a solution of β-hydroxysulfonamide (*R*)-**5a** (1.10 g, 3.07 mmol) was reacted with DEAD (724 μL, 4.60 mmol, 1.5 equiv), PPh_3 (1.21 g, 4.60 mmol, 1.5 equiv) and triethylamine (1.07 mL, 7.68 mmol, 2.5 equiv) in THF (30 mL) for 5 h. Purification by chromatography on silica gel (PE : EtOAc 4 : 1) afforded the aziridine (*S*)-**6a** (978 mg, 93%) as a white solid (Found: $[M+Na]^+$, 364.0609. $C_{16}H_{14}F_3NNaO_2S$ requires 364.0595); mp 135–136 °C (from EtOAc–PE); $[\alpha]_D^{20}$ −96 (*c* 1.11 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) −74.0 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.41 (s, 3 H), 2.84 (s, 1 H), 3.20 (d, *J* 1.0, 1 H), 7.28 (d, *J* 8.0, 2 H), 7.41 (m, 3 H), 7.60 (d, *J* 7.0, 2 H), 7.71 (d, *J* 8.0, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 21.5, 34.2 (d, *J* 2.5), 51.9 (q, *J* 36.5), 122.6 (q, *J* 278.0), 126.7, 128.0, 128.3, 129.6, 130.4, 131.2, 135.4, 144.9. 100% ee determined by chiral HPLC (chiralcel OD-H column, hexane : isopropanol 90 : 10, flow rate 1 mL min^{-1}): *t* = 11.2 min (*rac.* *t* = 11.2 and 17.0 min).

(−)-(*S*)-2-Ethyl-*N*-tosyl-2-trifluoromethylaziridine (*S*)-6b

According to the general procedure, a solution of β-hydroxysulfonamide (*R*)-**5b** (146 mg, 0.47 mmol) was reacted with DEAD (112 μL, 0.71 mmol, 1.5 equiv), PPh_3 (185 mg, 0.71 mmol, 1.5 equiv) and triethylamine (164 μL, 1.18 mmol, 2.5 equiv) in THF (3 mL) for 3 h 30. Purification by chromatography on silica gel (PE : Et_2O 3 : 1) afforded the aziridine (*S*)-**6b** (110 mg, 81%) as a white solid (Found: $[M+Na]^+$, 316.0597. $C_{12}H_{14}F_3NNaO_2S$ requires 316.0595). mp 44–45 °C (from Et_2O–PE); $[\alpha]_D^{20}$ −19 (*c* 0.99 in $CHCl_3$); δ_F NMR (235.3 MHz; $CDCl_3$; $CFCl_3$) −73.7 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 1.25 (td, *J* 1.5 and 7.5, 3 H), 2.35 (q, *J* 7.5, 2 H), 2.45 (s, 3 H), 2.55 (s, 1 H), 2.73 (d, *J* 1.5, 1 H), 7.35 (d, *J* 8.0, 2 H), 7.85 (d, *J* 8.0, 2 H); δ_C (62.9 MHz; $CDCl_3$;

Me_4Si) 11.2, 20.2, 21.6, 35.1 (d, *J* 2.0), 50.4 (q, *J* 35.0), 123.2 (q, *J* 279.0), 127.6, 129.7, 136.5, 144.8.

(–)-(*S*)-*N*-Benzyl-2-phenyl-2-trifluoromethylaziridine (*S*)-6c

A solution of triphenylphosphine (759 mg, 2.89 mmol, 4 equiv) and carbon tetrachloride (698 μL, 7.23 mmol, 10 equiv) in acetonitrile (2 mL) was stirred at rt and under Ar for 1 h. A solution of β-amino alcohol (*R*)-**5c** (213 mg, 0.72 mmol) in acetonitrile (3 mL) was then added to the reaction mixture followed by the addition of triethylamine (504 μL, 3.62 mmol, 5 equiv). The reaction mixture was stirred for additional 4 h and was then concentrated under reduced pressure. Purification of the residue by chromatography on silica gel (PE : Et_2O 7 : 1, solid deposit) afforded the aziridine (*S*)-**6c** (171 mg, 80%) as a colorless oil (Found: [M+Na]+, 300.0982. $C_{16}H_{14}F_3NNa$ requires 300.0976); $[\alpha]_D^{20}$ –19 (*c* 0.92 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) –72.9 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.00 (s, 1 H), 2.62 (s, 1 H), 3.00 (d, *J* 14.0, 1 H), 3.57 (d, *J* 14.0, 1 H), 7.28 (m, 5 H), 7.38 (m, 5 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 35.2, 48.1 (q, *J* 35.0), 57.8, 124.5 (q, *J* 276.0), 127.1, 127.6, 128.3, 128.4, 129.1, 129.5, 131.7, 138.4.

General procedure for the preparation of β-amino alcohol (*S*)-7a,b by ring opening of *N*-tosylaziridines (*S*)-6a,b with hydroxyl anion

A solution of aziridine (*S*)-**6a**,**b** and NaOH (5.5 equiv) in a mixture of *t*-BuOH–H_2O (1 : 5) was heated at reflux. After the complete disappearance of aziridine, the reaction mixture was cooled to rt, acidified with HCl 10% and extracted with CH_2Cl_2. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the residue by recrystallisation or by chromatography on silica gel afforded the β-amino alcohol (*S*)-**7a**,**b**.

(+)-(*S*)-3,3,3-Trifluoro-2-phenyl-2-tosylaminopropan-1-ol (*S*)-7a

According to the general procedure, aziridine (*S*)-**6a** (125 mg, 0.37 mmol) was reacted with NaOH (80 mg, 2.03 mmol, 5.5 equiv) in a mixture of *t*-BuOH (3 mL) and H_2O (15 mL) for 26 h to give the β-amino alcohols (*R*)-**5a** : (*S*)-**7a** as a 3 : 97 mixture (determined by ^{19}F NMR). Recrystallisation from CH_2Cl_2–PE afforded the β-amino alcohol (*S*)-**7a** (110 mg, 84%) as a white solid (Found: $[M+Na]^+$, 382.0694. $C_{16}H_{16}F_3NNaO_3S$ requires 382.0701); mp 155 °C (from CH_2Cl_2–PE); $[\alpha]_D^{20}$ +28 (*c* 0.94 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) –73.6 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.43 (s, 3 H), 2.97 (m, 1 H), 4.26 (br d, *J* 13.0, 1 H), 4.47 (br d, *J* 13.0, 1 H), 5.46 (br s, 1 H), 7.22–7.41 (m, 7 H), 7.66 (d, *J* 8.0, 2 H); δ_C NMR (62.9 MHz; CD_2Cl_2; Me_4Si) 21.6, 63.1 (d, *J* 8.0), 68.4 (q, *J* 25.5), 125.1 (q, *J* 287.0), 127.5, 127.9, 128.7, 129.4, 129.9, 133.0, 138.2, 144.7. 100% ee determined by chiral HPLC (chiralpak IC column, hexane : isopropanol 90 : 10, flow rate 1 mL min^{-1}): *t* = 24.3 min (*rac.* *t* = 24.3 and 26.0 min)

(–)-(*S*)-2-Tosylamino-2-trifluoromethylbutan-1-ol (*S*)-7b

According to the general procedure, aziridine (*S*)-**6b** (81 mg, 0.28 mmol) was reacted with NaOH (61 mg, 1.54 mmol, 5.5 equiv.) in a mixture of *t*-BuOH (2 mL) and H_2O (10 mL) for 21 h. Chromatography (PE : EtOAc 2 : 1) afforded the β-amino alcohol (*S*)-**7b** (80 mg, 93%) as a white solid (Found: $[M+Na]^+$, 334.0694. $C_{12}H_{16}F_3NNaO_3S$ requires 334.0701); mp 140 °C (from EtOAc–PE); $[\alpha]_D^{20}$ –1 (*c* 0.91 in $CHCl_3$); δ_F NMR (235.3 MHz; $CDCl_3$; $CFCl_3$) δ –74.0 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 0.88 (t, *J* 7.5, 3 H), 1.82 (m, 2 H), 2.36 (s, 3 H), 2.80 (m, 1 H), 3.67 (dd, *J* 6.0 and 12.5, 1 H), 3.95 (d, *J* 12.5, 1 H), 5.44 (s, 3 H), 7.23 (d, *J* 8.0, 2 H), 7.71 (d, *J* 8.0, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 7.4, 21.5, 24.4, 61.4, 65.2 (q, *J* 25.0), 125.3 (q, *J* 288.0), 126.9, 129.6, 138.3, 143.8.

(–)-(*S*)-2-Benzylamino-3,3,3-trifluoro-2-phenylpropan-1-ol (*S*)-7c

A suspension of aziridine (*S*)-**6c** (123 mg, 0.44 mmol) in a mixture of $HClO_4$–H_2O (0.75 mL/2 mL) was heated at 90 °C for 1 h 30. The reaction mixture was then cooled to rt, diluted with Et_2O and hydrolyzed with a sat. aq. sol. of Na_2CO_3. The organic layer was extracted, washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to give the β-amino alcohols (*R*)-**5c** and (*S*)-**7c** as a 10 : 90 mixture (determined by ^{19}F NMR). Chromatography (PE : EtOAc 15 : 1) afforded first the minor β-amino alcohol (*R*)-**5c** (4 mg, 3%, 92% ee determined by chiral HPLC, chiralpak IC column, hexane : isopropanol 90 : 10, flow rate 0.5 mL min^{-1}: t_{minor} = 9.5 min, t_{major} = 10.3 min) as a colorless oil, and then the major β-amino alcohol (*S*)-**7c** (102 mg, 78%) as a white solid (Found: $[M+Na]^+$, 318.1079. $C_{16}H_{16}F_3NNaO$ requires 318.1082); mp 73 °C (from EtOAc–PE); $[\alpha]_D^{20}$ –8 (*c* 0.77 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) –68.7 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.38 (br s, 2 H), 3.71 (s, 2 H), 3.80 (dd, *J* 1.5 and 12.0, 1 H), 4.16 (d, *J* 12.0, 1 H), 7.26–7.44 (m, 8 H), 7.63 (d, *J* 7.0, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 46.7, 65.6, 67.2 (q, *J* 23.5), 126.8 (q, *J* 291.0), 127.2, 127.5, 127.9, 128.5, 128.7, 134.5, 139.8. 97% ee determined by chiral HPLC (chiralpak IC column, hexane : isopropanol 90 : 10, flow rate 0.5 mL min^{-1}): t_{minor} = 11.9 min, t_{major} = 13.5 min.

General procedure for the ring opening of *N*-tosylaziridines *S*)-6a,b with amines

A solution of aziridine (*S*)-**6a**,**b** and amine (1.2 or 2.0 equiv) in acetonitrile was heated at reflux. After the complete disappearance of aziridine (*S*)-**6a**,**b**, the reaction mixture was cooled to rt and concentrated under reduced pressure. Purification by chromatography on silica gel or recrystallisation afforded the β-diamines (*S*)-**8a**,**b**, (*S*)-**9a**,**b**, (*S*)-**10a**,**b** or (*S*)-**11a**,**b**.

(+)-(*S*)-*N*-Benzyl-3,3,3-trifluoro-2-phenyl-2-tosylaminopropylamine (*S*)-8a

According to the general procedure, aziridine (*S*)-**6a** (102 mg, 0.30 mmol) was reacted with benzylamine (39 μL, 0.36 mmol, 1.2 equiv) in MeCN (3 mL) for 20 h. Chromatography (PE : EtOAc 5 : 1) afforded the β-diamine (*S*)-**8a** (120 mg, 90%) as a white solid (Found $[M+H]^+$, 449.1511. $C_{23}H_{24}F_3N_2O_2S$ requires 449.1511); mp 122 °C (from EtOAc–PE); $[\alpha]_D^{20}$ +61 (*c* 1.02 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) –69.3 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.39 (s, 3 H), 3.03 (d, *J* 13.0, 1 H), 3.34 (d, *J* 13.0, 1 H), 3.78 (s, 2 H), 7.16–7.41 (m, 12 H), 7.54 (d, *J* 8.0, 2 H), 2 NH not detected; δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 21.5, 53.8, 54.1, 66.3 (q, *J* 26.5), 125.2 (q, *J* 288.0), 127.0, 127.4, 128.1, 128.2, 128.5, 128.6, 129.1, 134.1, 139.0, 139.2, 143.1. 100% ee determined by chiral HPLC

(chiralpak IC column, hexane : isopropanol 90 : 10, flow rate 1 mL min^{-1}): t = 18.6 min (*rac.* t = 16.4 and 18.6 min)

(+)-(*S*)-*N*-Benzyl-2-tosylamino-2-trifluoromethylbutylamine (*S*)-8b

According to the general procedure, aziridine (*S*)-**6b** (77 mg, 0.26 mmol) was reacted with benzylamine (34 μL, 0.31 mmol, 1.2 equiv) in MeCN (3 mL) for 22 h. Chromatography (PE : EtOAc 5 : 1) afforded the β-diamine (*S*)-**8b** (101 mg, 96%) as a colorless oil (Found: $[M+H]^+$, 401.1502. $C_{19}H_{24}F_3N_2O_2S$ requires 401.1511); $[\alpha]_D^{20}$ +12 (*c* 1.02 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) –73.4 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 0.90 (t, *J* 7.5, 3 H), 1.74 (sext, *J* 7.5, 1 H), 2.12 (sext, *J* 7.5, 1 H), 2.39 (s, 3 H), 2.58 (br d, *J* 13.5, 1 H), 3.03 (d, *J* 13.5, 1 H), 3.75 (d, *J* 13.5, 1 H), 3.81 (d, *J* 13.5, 1 H), 7.20–7.35 (m, 7 H), 7.68 (d, *J* 8.0, 2 H), 2 NH not detected; δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 7.3, 21.4, 23.1, 50.0, 53.9, 62.7 (q, *J* 25.5), 125.9 (q, *J* 288.5), 126.7, 127.4, 128.2, 128.6, 129.2, 139.1, 139.3, 143.0.

(+)-(1*S*,1′*R*)-*N*-[(1′-Phenyl)ethyl]-3,3,3-trifluoro-2-phenyl-2-tosylaminopropylamine (*S*)-9a

According to the general procedure, aziridine (*S*)-**6a** (59 mg, 0.173 mmol) was reacted with (*R*)-(+)-α-methylbenzylamine (27 μL, 0.207 mmol, 1.2 equiv) in MeCN (3 mL) for 24 h. Recrystallisation (PE : AcOEt) afforded the β-diamine (*S*)-**9a** (76 mg, 95%) as a white solid (Found: $[M+H]^+$, 463.1650. $C_{24}H_{26}F_3N_2O_2S$ requires 463.1667); mp 150 °C (from Et_2O–PE); $[\alpha]_D^{20}$ +40 (*c* 1.0 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) –68.9 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 1.38 (d, *J* 6.5, 3 H), 2.40 (s, 3 H), 2.79 (d, *J* 13.5, 1 H), 3.24 (d, *J* 13.5, 1 H), 3.74 (q, *J* 6.5, 1 H), 7.12–7.39 (m, 12 H), 7.48 (d, *J* 8.0, 2 H), 2 NH not detected; δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 21.5, 24.0, 53.0, 58.2, 65.9 (q, *J* 26.5), 125.3 (q, *J* 288.5), 126.7, 127.0, 127.3, 127.4, 128.1, 128.4, 128.7, 129.0, 139.1, 143.0, 143.9. An analytical sample of (*S*)-**9a** was crystallized in Et_2O–PE. Selected crystallographic data: $C_{24}H_{25}F_3N_2O_2S$, FW = 462.52, T = 100(2) K, λ = 0.71073 Å, Orthorhombic, $P2_1\,2_1\,2_1$, a = 9.6263(13) Å, b = 14.1765(14) Å, c = 16.473(2) Å, V = 2248.1(5) $Å^3$, Z = 4, crystal size = 0.4 × 0.1 × 0.1 mm^3, reflections collected = 6529, independent reflections = 5364, R (int) = 0.0452, parameters = 291, R_1 [$I > 2\sigma(I)$] = 0.0420, wR_2 [$I > 2\sigma(I)$] = 0.0978, R_1 (all data) = 0.0566, wR_2 (all data) = 0.1031. Full crystallographic data for this compound have been deposited with the CCDC, reference number 779933.‡

(+)-(1*S*,1′*R*)-*N*-[(1′-Phenyl)ethyl]-2-tosylamino-2-trifluoromethylbutylamine (*S*)-9b

According to the general procedure, aziridine (*S*)-**6b** (62 mg, 0.213 mmol) was reacted with (*R*)-(+)-α-methylbenzylamine (33 μL, 0.256 mmol, 1.2 equiv) in MeCN (3 mL) for 24 h. Chromatography (PE : Et_2O 3 : 1) afforded the β-diamine (*S*)-**9b** (87 mg, 98%) as a white solid (Found: $[M+H]^+$, 415.1680. $C_{20}H_{26}F_3N_2O_2S$ requires 415.1667); mp 91 °C (from Et_2O–PE); $[\alpha]_D^{20}$ +18 (*c* 0.84 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) –73.4 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 0.70 (t, *J* 7.5, 3 H), 1.39 (d, *J* 6.5, 3 H), 1.50 (br s, 1 H), 1.73 (sext, *J* 7.5, 1 H), 1.92 (sext, *J* 7.5, 1 H), 2.37 (d, *J* 13.0, 1 H), 2.40 (s, 3 H), 2.97 (d, *J* 13.0, 1 H), 3.75 (q, *J* 6.5, 1 H), 6.38 (br s, 1 H), 7.21 (d, *J* 8.0, 2 H), 7.22–7.36 (m, 5 H), 7.62 (d, *J* 8.0, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 7.2, 21.4, 23.0, 24.2, 48.4, 58.3, 62.4 (q, *J* 25.5), 125.6 (q, *J* 288.5), 126.7, 126.9, 127.5, 128.7, 129.2, 139.5, 142.9, 143.8.

(+)-(*S*)-1,1,1-Trifluoro-3-morpholin-4-yl-2-phenyl-*N*-tosylpropan-2-amine (*S*)-10a

According to the general procedure, aziridine (*S*)-**6a** (102 mg, 0.30 mmol) was reacted with morpholine (32 μL, 0.36 mmol, 1.2 equiv.) in MeCN (3 mL) for 22 h. Chromatography (PE : EtOAc 4 : 1) afforded the β-diamine (*S*)-**10a** (119 mg, 93%) as a white solid (Found: $[M+H]^+$, 429.1465. $C_{20}H_{24}F_3N_2O_3S$ requires 429.1460); mp 114 °C (from EtOAc–PE); $[\alpha]_D^{20}$ +38 (*c* 1.04 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) δ –69.9 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.32 (s, 3 H), 2.48 (m, 4 H), 2.95 (d, *J* 14.5, 1 H), 3.07 (d, *J* 14.5, 1 H), 3.58 (m, 4 H), 6.40 (br s, 1 H), 7.13–7.21 (m, 5 H), 7.32 (d, *J* 7.0, 2 H), 7.51 (d, *J* 8.0, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 21.4, 55.0, 64.3, 65.8 (q, *J* 26.0), 67.0, 125.0 (q, *J* 287.5), 127.0, 127.5, 128.0, 128.5, 129.1, 134.2, 139.1, 143.2.

(+)-(*S*)-1-Morpholin-4-yl-*N*-tosyl-2-trifluoromethylbutan-2-amine (*S*)-10b

According to the general procedure, aziridine (*S*)-**6b** (78 mg, 0.27 mmol) was reacted with morpholine (28 μL, 0.32 mmol, 1.2 equiv) in MeCN (3 mL) for 15 h. Chromatography (PE : EtOAc 2 : 1) afforded the β-diamine (*S*)-**10b** (99 mg, 97%) as a white solid (Found: $[M+H]^+$, 381.1464. $C_{16}H_{24}F_3N_2O_3S$ requires 381.1460); mp 112 °C (from EtOAc–PE); $[\alpha]_D^{20}$ +34 (*c* 1.04 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) –73.4 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 0.94 (t, *J* 7.5, 3 H), 1.77 (sext, *J* 7.5, 1 H), 2.12 (sext, *J* 7.5, 1 H), 2.42 (s, 3 H), 2.54 (br d, *J* 15.0, 1 H), 2.64 (m, 4 H), 2.82 (d, *J* 15.0, 1 H), 3.71 (m, 4 H), 6.29 (br s, 1 H), 7.29 (d, *J* 8.0, 2 H), 7.75 (d, *J* 8.0, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 7.4, 21.4, 23.4, 54.8, 59.9, 62.1 (q, *J* 25.5), 67.2, 125.6 (q, *J* 288.0), 126.8, 129.3, 139.1, 143.2.

(–)-(*S*)-3,3,3-Trifluoro-*N*,2-diphenyl-2-tosylaminopropylamine (*S*)-11a

According to the general procedure, aziridine (*S*)-**6a** (127 mg, 0.37 mmol) was reacted with aniline (68 μL, 0.75 mmol, 2.0 equiv) in MeCN (2 mL) for 48 h. Chromatography (PE : Et_2O 3 : 1) afforded the β-diamine (*S*)-**11a** (156 mg, 99%) as a colorless oil (Found: $[M+H]^+$, 435.1336. $C_{22}H_{22}F_3N_2O_2S$ requires 435.1354); $[\alpha]_D^{20}$ –20 (*c* 0.3 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) –72.4 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.38 (s, 3 H), 3.68 (br s, 1 H), 3.90 (d, *J* 14.0, 1 H), 4.03 (d, *J* 14.0, 1 H), 5.79 (s, 1 H), 6.49 (d, *J* 8.0, 2 H), 6.74 (t, *J* 7.5, 1 H), 7.09–7.18 (m, 4 H), 7.23–7.35 (m, 3 H), 7.49 (d, *J* 7.0, 2 H), 7.59 (d, *J* 8.5, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 21.5, 47.6, 67.3 (q, *J* 26.5), 113.5, 118.7, 124.9 (q, *J* 287.5), 127.0, 127.5, 128.5, 129.2, 129.3, 133.2, 138.5, 143.5, 146.8.

(–)-(*S*)-1-Phenyl-2-tosylamino-2-trifluoromethylbutylamine (*S*)-11b

According to the general procedure, aziridine (*S*)-**6b** (99 mg, 0.34 mmol) was reacted with aniline (61 μL, 0.67 mmol, 2.0 equiv) in MeCN (2 mL) for 40 h. Chromatography (PE : Et_2O 3 : 1) afforded the β-diamine (*S*)-**11b** (128 mg, 98%) as a colorless oil

(Found: $[M+H]^+$, 387.1339. $C_{18}H_{22}F_3N_2O_2S$ requires 387.1354); $[\alpha]_D^{20}$ −47 (*c* 0.1 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) −73.9 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 1.00 (t, *J* 7.5, 3 H), 1.89 (sext, *J* 7.5, 1 H), 2.14 (sext, *J* 7.5, 1 H), 2.41 (s, 3 H), 3.45 (d, *J* 14.0, 1 H), 3.54 (d, *J* 14.0, 1 H), 3.80 (br s, 1 H), 5.56 (s, 1 H), 6.63 (d, *J* 7.5, 2 H), 6.79 (t, *J* 7.5, 1 H), 7.19 (dd, *J* 7.5 and 8.5, 2 H), 7.27 (d, *J* 8.0, 2 H), 7.75 (d, *J* 8.5, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 7.6, 21.5, 23.7, 46.0, 64.2 (q, *J* 25.5), 113.8, 118.8, 125.7 (q, *J* 288.5), 126.9, 129.3, 129.5, 138.7, 143.6, 147.3.

General procedure for the ring opening of *N*-tosylaziridines (*S*)-6a,b with sulfonamide

A suspension of aziridine (*S*)-**6a**,**b**, *p*-toluenesulfonamide (1.2 equiv) and potassium carbonate (1.2 equiv) in acetonitrile was heated at reflux. After the complete disappearance of aziridine (*S*)-**6a**,**b**, the reaction mixture was cooled to rt, diluted with CH_2Cl_2 and washed with water. The organic layer was extracted, dried ($MgSO_4$) and concentrated under reduced pressure. Purification by chromatography on silica gel (PE : EtOAc) afforded the β-diamine (*S*)-**12a**,**b**.

(−)-(*S*)-3,3,3-Trifluoro-2-phenyl-2-tosylamino-*N*-tosylpropylamine (*S*)-12a

According to the general procedure, aziridine (*S*)-**6a** (102 mg, 0.30 mmol) was reacted with *p*-toluenesulfonamide (61 mg, 0.36 mmol, 1.2 equiv) and potassium carbonate (49 mg, 0.36 mmol, 1.2 equiv) in MeCN (3 mL) for 22 h. Chromatography (PE : EtOAc 3 : 2) afforded the β-diamine (*S*)-**12a** (130 mg, 85%) as a white solid (Found: $[M+Na]^+$, 535.0952. $C_{23}H_{23}F_3N_2NaO_4S_2$ requires 535.0949); mp 149 °C (from EtOAc–PE); $[\alpha]_D^{20}$ −25 (*c* 0.95 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) −72.6 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 2.42 (s, 3 H), 2.45 (s, 3 H), 3.77 (d, *J* 7.5, 2 H), 5.28 (t, *J* 7.5, 1 H), 5.58 (s, 1 H), 7.19–7.39 (m, 9 H), 7.56 (d, *J* 8.5, 2 H), 7.71 (d, *J* 8.5, 2 H); δ_C (62.9 MHz; $CDCl_3$; Me_4Si) 21.4, 45.3, 66.7 (q, *J* 27.0), 124.2 (q, *J* 288.0), 127.0, 127.3, 128.4, 129.1, 129.4, 129.8, 132.2, 136.3, 137.8, 143.7, 143.8. 100% ee determined by chiral HPLC (chiralpak IC column, hexane : isopropanol 75 : 25, flow rate 1 mL min^{-1}): *t* = 28.7 min (*rac.* *t* = 28.7 and 36.0 min)

(−)-(*S*)-2-Tosylamino-*N*-tosyl-2-trifluoromethylbutylamine (*S*)-12b

According to the general procedure, aziridine (*S*)-**6b** (92 mg, 0.31 mmol) was reacted with *p*-toluenesulfonamide (64 mg, 0.38 mmol, 1.2 equiv) and potassium carbonate (52 mg, 0.38 mmol, 1.2 equiv) in MeCN (3 mL) for 22 h. Chromatography (PE : EtOAc 2 : 1) afforded the β-diamine (*S*)-**12b** (110 mg, 76%) as a white solid (Found: $[M+Na]^+$, 487.0957. $C_{19}H_{23}F_3N_2NaO_4S_2$ requires 487.0949); mp 169 °C (from EtOAc–PE); $[\alpha]_D^{20}$ −71 (*c* 0.94 in $CHCl_3$); δ_F (235.3 MHz; $CDCl_3$; $CFCl_3$) −73.5 (s, 3 F); δ_H (250 MHz; $CDCl_3$; Me_4Si) 1.00 (t, *J* 7.0, 3 H), 1.99 (m, 2 H), 2.42 (s, 3 H), 2.45 (s, 3 H), 3.25 (dd, *J* 10.0 and 14.0, 1 H), 3.40 (dd, *J* 5.5 and 14.0, 1 H), 5.36 (s, 1 H), 5.53 (dd, *J* 5.5 and 10.0, 1 H), 7.26 (d, *J* 8.0, 2 H), 7.35 (d, *J* 8.0, 2 H), 7.67 (d, *J* 8.0, 2 H), 7.78 (d, *J* 8.0, 2 H); δ_C NMR (62.9 MHz; $CDCl_3$; Me_4Si) 7.2, 21.5, 26.1, 43.0, 64.2 (q, *J* 26.0), 124.9 (q, *J* 288.5), 126.7, 126.9, 129.3, 129.9, 136.6, 138.4, 143.4, 143.7.

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