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Stereoselective synthesis of heterosubstituted aziridines and their functionalization

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Abstract—Lithiated (α-chloroalkyl)heterocycles, generated by deprotonation with LDA at −78 °C in THF, add to various enantiopure imines affording 'one pot' chiral heterosubstituted aziridines in a diastereoselective manner. Lithiated heterosubstituted aziridines, obtained by deprotonation of the corresponding aziridines with *n*-BuLi at −78 °C in THF, were trapped by electrophiles (D_2O or CH_3I) with high stereoselectivity.

1. Introduction

Aziridines are useful chiral building blocks for the synthesis of modified amino acids[1] and nitrogen-containing functional compounds via ring opening and ring expansion reactions.[2–4] Chiral aziridines form an attractive class of compounds, since they are available in highly enantioenriched form by a variety of procedures and can be used for asymmetric synthesis in a number of different ways.[5]

Studies on the chemistry of aziridinyl anions, which are a particular kind of carbanions, have previously appeared.[6] For example, the alkylation of 2-phenylsulfonylaziridines, via aziridinyllithium formation and trapping with alkyl halides, was reported.[7] Generation of aziridinyllithiums of phenyl aziridine thioesters and trapping with electrophiles seemed to proceed with retention of configuration or moderate diastereoselectivities according to the starting isomer.[8]

We reported, some time ago, a simple diastereoselective synthesis of various heterosubstituted aziridines based on a Darzens reaction of lithiated (α-chloroalkyl)heterocycles with imines.[9] The option of freeing the masked acyl group of some heteroaryl moieties,[10] makes these aziridine derivatives susceptible to further functionalization.[11] Concerning the generation of aziridinyl anions as synthetic intermediates, we found recently, in our laboratories, that some *N*-sulfonyloxazolinylaziridines can easily be lithiated and then captured by electrophiles in a configurationally stable manner.[12]

In this paper we describe the synthesis of chiral heterosubstituted aziridines by the coupling reaction of lithiated (α-chloroalkyl)heterocycles with various enantiopure imines. Some of the chiral aziridines obtained were then lithiated and captured by electrophiles; the stereochemistry of these reactions has been also investigated.

2. Results and discussion

The required (α-chloroalkyl)heterocycles **1a**–**h**, prepared as described in Section 4, and stoichiometric amount of the enantiopure (*R*)-imine **2a** were added to a stirred solution of lithium diisopropylamide (LDA) in THF at −78 °C to produce diastereoselectively the chiral aziridines **3a**–**h**, in satisfactory yields (30–90%), as reported in Table 1.

The substituted aziridines, containing new stereocentres, were isolated as the only reaction products. A *cis* arrangement (the heterocycle and the phenyl group both on the same side) was noticed for compounds (+)-**3a**, (+)-**3b**, (−)-**3c**, (+)-**3e**, (+)-**3g** and (+)-**3h** while the aziridines (−)-**3d**, and (−)-**3f** showed a *trans* arrangement (the heterocycle and the phenyl group on opposite sides).

Keywords: Heterosubstituted aziridines; Aziridinyl anion; Nucleophilic addition.
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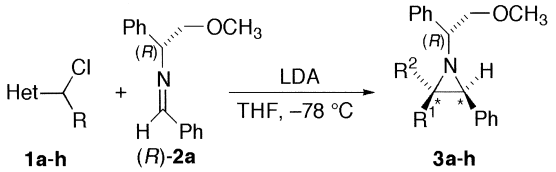
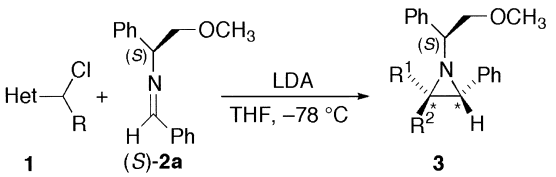
Table 1. Synthesis of chiral nonracemic heterosubstituted aziridines from (α-chloroalkyl)heterocycles and the enantiopure (*R*)-imine **2a**



Compound	R^1	R^2	Product **3** (yield %)[a]	dr[b]	Relative configuration[c]	$[\alpha]_D^{22}$[d]
1a	4-Methylthiazol-2-yl	H	(+)-**3a** (48)	>98:2	$2'R^*,3'R^*$	+12.9
1b	4-Methylthiazol-2-yl	CH_3	(+)-**3b** (90)	>98:2	$1'R,2'S,3'S$[e,f]	+23.1
1c	2-Benzothiazolyl	H	(−)-**3c** (90)	>98:2	$2'R^*,3'R^*$	−61.7
1d	CH_3	2-Benzothiazolyl	(−)-**3d** (60)	>98:2	$2'R^*,3'S^*$	−199.4
1e	4,4-Dimethyl-2-oxazolin-2-yl	H	(+)-**3e** (45)	>98:2	$1'S,2'S,3'S$[e]	+28.1
1f	CH_3	4,4-Dimethyl-2-oxazolin-2-yl	(−)-**3f** (35)	>98:2	$1'S,2'R,3'S$[e,f]	−43.6
1g	2-Pyridyl	H	(+)-**3g** (60)	>98:2	$2'R^*,3'R^*$	+22.4
1h	4-Pyridyl	H	(+)-**3h** (30)	>98:2	$2'R^*,3'R^*$	+40.0

[a] Isolated yield.
[b] Diastereomeric ratio determined by ^{1}H NMR spectroscopy; only one diastereomer in the ^{1}H NMR spectrum of the crude product.
[c] Denoted by configurational descriptors R^*,R^* and R^*,S^*; by convention, when the absolute configuration is not known the first center is always assigned to be R^*.
[d] *c* 0.01–0.07, $CHCl_3$ (see Section 4 for details).
[e] Absolute configuration ascertained as described (see text).
[f] See also Ref. 18.

Table 2. Synthesis of chiral nonracemic heterosubstituted aziridines from (α-chloroalkyl)heterocycles and the enantiopure (*S*)-imine **2a**



Compound	R^1	R^2	Product **3** (yield %)[a]	dr[b]	Relative configuration	$[\alpha]_D^{22}$[c]
1a	4-Methylthiazol-2-yl	H	(−)-**3a** (45)	>98:2	$2'R^*,3'R^*$	−12.6
1e	4,4-Dimethyl-2-oxazolin-2-yl	H	(−)-**3e** (52)	>98:2	$1'R,2'R,3'R$[d]	−29.3
1f	CH_3	4,4-Dimethyl-2-oxazolin-2-yl	(+)-**3f** (31)	>98:2	$1'R,2'S,3'R$[d]	+43.1

[a] Isolated yield.
[b] Diastereomeric ratio determined by ^{1}H NMR spectroscopy; only one diastereomer in the ^{1}H NMR spectrum of the crude product.
[c] *c* 0.01–0.07, $CHCl_3$ (see Section 4 for details).
[d] Presumed absolute configuration on the basis of data of Table 1.

Analogous reactions were performed using the substrates **1a**, **1e**, and **1f** and the enantiopure (*S*)-imine **2a**. The obtained results are reported in Table 2. The chiral heterosubstituted aziridines (−)-**3a**, (−)-**3e**, and (+)-**3f** were isolated in satisfactory yields (31–52%). As expected, these products showed similar optical rotation values of those measured for compounds (+)-**3a**, (+)-**3e**, and (−)-**3f** (Table 1) but with opposite sign.

An attempt was made to react the substrates **1a** and **1f** with different enantiopure imines (*S*)-**2b** and (*R*)-**2b** (Chart 1), following the same reaction procedure reported above.

The reactions proceed in a highly stereoselective manner,

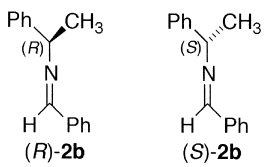


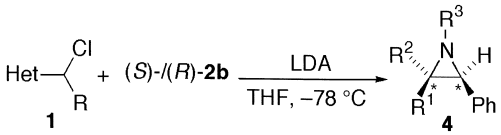
Chart 1.

affording (+)-**4a**, (+)-**4f**, and (−)-**4a**, (−)-**4f**, respectively, in satisfactory yields (50–55%). The results are reported in Table 3. (+)- and (−)-**4a** were isolated as an inseparable mixture of two diastereomers of $(2'R^*,3'R^*)$ configuration in a ratio of 4:1. (+)- and (−)-**4f** were instead a mixture of two separable diastereomers (petroleum ether/Et_2O 7/3) obtained in a 2:1 ratio both having a $(2'R^*,3'S^*)$ configuration. The ratios were evaluated from the ^{1}H NMR spectra of the crude products.

The higher diastereoselectivity observed using the chiral imines (*R*)- and (*S*)-**2a**, rather than the chiral imines (*R*)- and (*S*)-**2b** could be due to the different steric hindrance of the alkyl group linked to the nitrogen atom. Moreover, we suppose that the oxygen atom of 2-methoxy-1-phenylethyl substituent of **2a** can participate to the internal coordination[6d] during the process that leads to the aziridinic ring closure, affording the products in a more stereoselective manner.

The lithiation of aziridines (+)-**3a**, and (+)-**4a** with *n*-butillithium (*n*-BuLi) at −78 °C in THF, followed by the

Table 3. Synthesis of chiral nonracemic heterosubstituted aziridines from (α-chloroalkyl)heterocycles and the enantiopure (*S*)- and (*R*)-imines **2b**



Compound	Imine	R^1	R^2	R^3	Product (yield %)[a]	dr[b]
1a	(*S*)-**2b**	4-Methylthiazol-2-yl	H	(*S*)-PhCHCH$_3$	(+)-**4a** (50)	$2'R^*,3'R^*/2'R^*,3'R^*$=4/1[c,d]
1a	(*R*)-**2b**	4-Methylthiazol-2-yl	H	(*R*)-PhCHCH$_3$	(−)-**4a** (53)	$2'R^*,3'R^*/2'R^*,3'R^*$=4/1[c,d]
1f	(*S*)-**2b**	CH_3	4,4-Dimethyl-2-oxazolin-2-yl	(*S*)-PhCHCH$_3$	(+)-**4f** (55)	$2'R^*,3'S^*/2'R^*,3'S^*$=2/1[d,e]
1f	(*R*)-**2b**	CH_3	4,4-Dimethyl-2-oxazolin-2-yl	(*R*)-PhCHCH$_3$	(−)-**4f** (52)	$2'R^*,3'S^*/2'R^*,3'S^*$=2/1[d,e]

[a] Overall isolated yields in both diastereomers.
[b] Diastereomeric ratio determined by ^{1}H NMR spectroscopy on the crude product; relative configuration.
[c] An inseparable mixture of two *cis*-configurated diastereomeric aziridines formed. (+)-**4a**: $[\alpha]_D^{22}$=+14.1; (−)-**4a**: $[\alpha]_D^{22}$=−13.5.
[d] *c* 0.03–0.08, $CHCl_3$ (see Section 4 for details).
[e] A diastereomeric mixture of two ($2'R^*,3'S^*$)-configurated aziridines separable by column chromatography (silica gel, petroleum ether/Et_2O 7/3) formed. (+)-**4f**: (major diastereomer) $[\alpha]_D^{22}$=+36.0; (minor diastereomer) $[\alpha]_D^{22}$=+24.3; (−)-**4f**: (major diastereomer) $[\alpha]_D^{22}$=−35.3; (minor diastereomer) $[\alpha]_D^{22}$=−25.9.

addition of deuterium oxide (D_2O) or methyl iodide (CH_3I) after 1 h gave the 2-deuterated thiazolylaziridines **5** (90%D) and **6** (95%D) and the 2-methylated thiazolylaziridine (+)-**3b**, retaining the configuration of the starting aziridines (Chart 2).

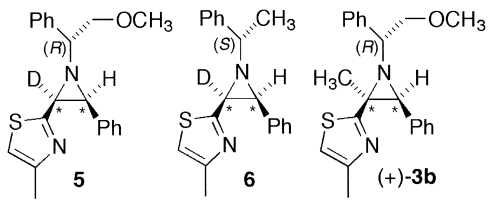


Chart 2.

The structures of the 2-deuterated aziridines **5** and **6** were established by ^{1}H NMR data: the doublet of the aziridinic α-hydrogen, substituted by a deuterium atom, almost disappears, while the doublet of the aziridine β-hydrogen becomes a singlet. No chemical shift displacements were observed for the deuterated compounds **5** and **6** which then retain the configurations of the starting aziridines (+)-**3a**, and (+)-**4a**.

The stereochemistry of aziridines (+)- and (−)-**3a**, (−)-**3c**, (+)- and (−)-**3e**, (+)-**3g**, (+)-**3h**, (+)- and (−)-**4a** was assigned on the basis of the ^{1}H NMR coupling constants between the two aziridinyl hydrogens ($J_{cis}>J_{trans}$);[13] the configurations of aziridines (+)-**3b**, (−)-**3d**, (+)- and (−)-**3f**, (+)- and (−)-**4f** were established on the basis of an upfield shift of the CH_3 group in the case of a *cis* relationship with the Ph group. Indeed, it has been reported that an high field displacement occurs when a CH_3 group is on the same side of a Ph group, while a smaller upfield shift is observed when the Me group and H are on the same side.[14] The configuration assignment was also confirmed, for these latter aziridines by ^{13}C NMR spectroscopy on the basis of the very small long-range $^3J_{CH}$ coupling constant ($^3J_{CH3-H}\approx$0 Hz) between the aziridine β-hydrogen and the carbon of the α-methyl group when these groups are on opposite sides, as reported.[15] The good crystalline form of compound (+)-**3b** allowed us to perform X-ray measurements (Fig. 1) and to assign in this case the absolute configuration.[16] The aziridine asymmetric carbons have 2′*S* and 3′*S* configuration; while the nitrogen has 1′*R* configuration. These latter results also confirm the assigned *cis* relative configuration (the heterocycle and the CH_3 group both on the same side).

Moreover, it was possible to assign the absolute configuration to oxazolinylaziridines (+)-**3e** and (−)-**3f** by NMR spectroscopy, as follows. Oxazolinylaziridine (+)-**3e** was assigned the *cis* relative configuration with the nitrogen lone pair *trans* to the vicinal aziridine ring protons (H_a and H_b) on the basis of the value ($^3J_{H-H}$=6.9 Hz) of their coupling constant.[17] After complete attribution of all the protons (^{1}H, ^{13}C, selective homonuclear decoupling experiments, HETCOR and HMBC) the absolute configuration was deduced from 2D-NOESY correlations. Between the two possible diastereomers **3e**-**A** and **3e**-**B** (Fig. 2), both having the same relative configuration, strong NOE interactions between H_c and H_a/H_b together with a weak one between CH_3O and H_b (at δ=2.90) were diagnostic of a 1′*S*,2′*S*,3′*S* absolute configuration for the aziridine ring. Relative[18] and absolute configuration (1′*S*,2′*R*,3′*S*) of the oxazolinylaziridine (−)-**3f** was similarly established using 2D-NOESY Phase-Sensitive experiments showing in this case, in particular, significant NOEs interactions either between

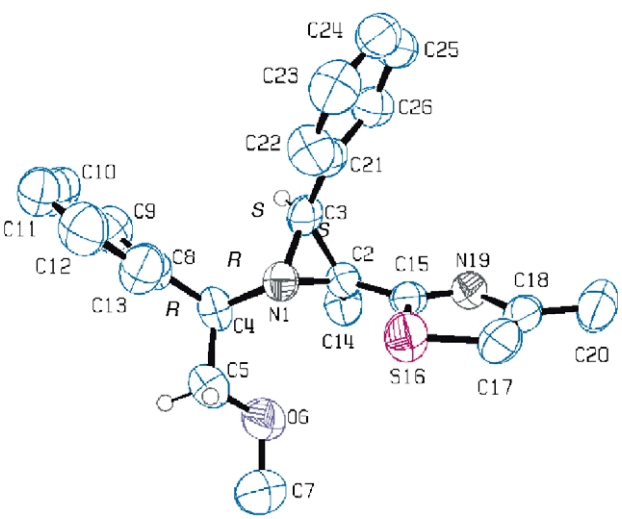


Figure 1. ORTEP view of compound (+)-**3b**.

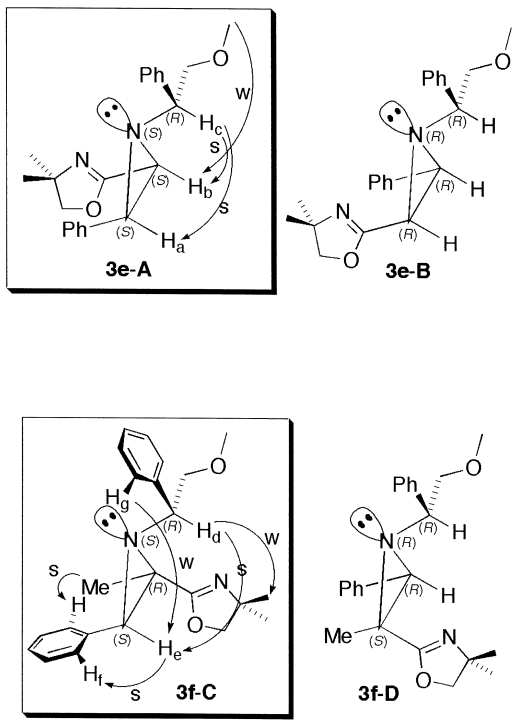


Figure 2. Oxazolinylaziridines **3e** (diastereomers **3e**-**A** and **3e**-**B**) and **3f** (diastereomers **3f**-**C** and **3f**-**D**). Selected NOEs interactions; s=strong, w=weak.

the benzylic proton H_d and the aziridine proton H_e or the latter with both the *ortho* aromatic ring protons H_f and H_g, as depicted in Figure 2 in the case of diastereomer **3f**-**C** compared to diastereomer **3f**-**D** having the same relative configuration. These close proximity relationships between the above-cited protons for the two diastereomers **3e**-**A** and **3f**-**C**, and consequently, the relative conformations of the two side chains linked at the nitrogen atoms, were also confirmed by means of calculations. To this end, preliminarily, equilibrium geometries were calculated for each diastereomer having the same relative and absolute configuration of **3e**-**A**,**B** and **3f**-**C**,**D** starting with a systematic conformer distribution analysis. Conformers were grouped into families on the basis of relevant torsion angle values. The best representative of each family was submitted to a PM3 semi-empirical geometry optimization and, in order to introduce electron correlation in the computation of the energetics, we performed, on the best conformer of each analogue, single-point calculations using the density functional theory (DFT) at the B3LYP/6-31+G*//PM3 level of theory.[19] The resulting diastereomers, the best representatives in terms of energy and geometry of **3e**-**A**,**B** and **3f**-**C**,**D** (Fig. 3), were found to have the same local conformations of those depicted in Figure 2, so supporting the NOESY conclusions.

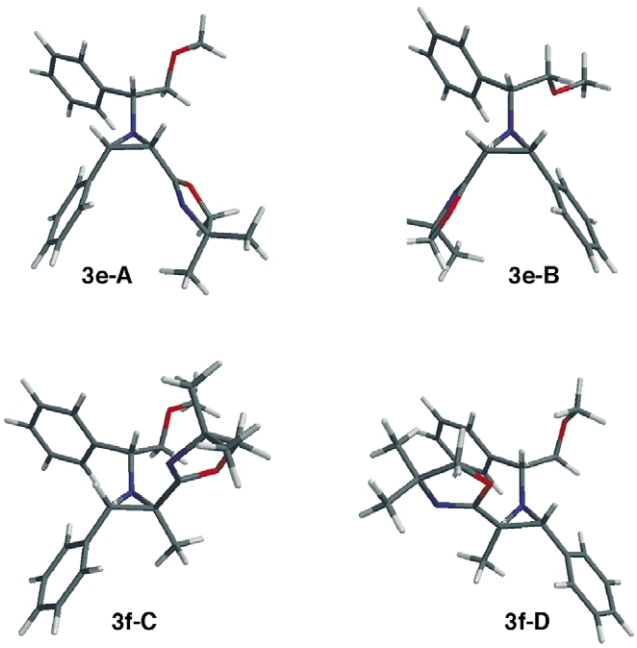


Figure 3. PM3-optimized geometries of the four diastereomers (1′*S*,2′*S*,3′*S*)-**3e**-**A**, (1′*R*,2′*R*,3′*R*)-**3e**-**B**, (1′*S*,2′*R*,3′*S*)-**3f**-**C**, (1′*R*,2′*S*,3′*R*)-**3f**-**D**.

3. Conclusion

In conclusion, chiral heterosubstituted aziridines can be prepared in a diastereoselective manner, by the 'one pot' addition of lithiated (α-chloroalkyl)heterocycles to various enantiopure imines. The different steric hindrance and coordination power of the alkyl group, linked to the iminic nitrogen atom, could influence the aziridine ring closure process and, consequently, the diastereoselectivity. Aziridines synthesized from chiral imines (*R*)- and (*S*)-**2a** form in a higher diastereoselectivity than those from the chiral imines (*R*)- and (*S*)-**2b**. Moreover, aziridines (+)-**3a** and (+)-**4a** can be lithiated and trapped by deuterium oxide or methyl iodide to give more functionalized aziridines with retention of configuration.

4. Experimental

n-BuLi was a commercial solution in hexanes (Aldrich) and was titrated with *N*-pivaloyl-*o*-toluidine prior to use.[20] THF, lithium diisopropylamide (LDA), deuterium oxide, methyl iodide, (*R*)-(−)-2-amino-2-phenylethanol, (*S*)-(+)-2-amino-2-phenylethanol, (*R*)-(+)-1-phenylethylamine, (*S*)-(−)-1-phenylethylamine, 4-methylthiazole, 2-aminothiophenol, glycolic acid, lactic acid, 2,4,4-trimethyl-2-oxazoline, 2-ethyl-4,4-dimethyl-2-oxazoline, 2-(chloromethyl)pyridine hydrochloride, 4-(chloromethyl)pyridine hydrochloride, were of commercial grade (Aldrich), and were used without further purification. Acetaldehyde and benzaldehyde of commercial grade (Aldrich), were purified by distillation prior to use. Petroleum ether refers to the 40–60 °C boiling fraction. The ^{1}H and the ^{13}C NMR spectra were recorded on a Bruker Avance 400 apparatus (400.13 and 100.62 MHz, for ^{1}H and ^{13}C, respectively) with $CDCl_3$ as solvent and TMS as internal standard (δ_H=7.24 for ^{1}H spectra; δ_H=77.0 for ^{13}C spectra). The IR spectra were recorded on a Perkin–Elmer spectrometer Model 283. GC–MS analyses were performed with Hewlett–Packard HP-5890 series II gas chromatograph (5% diphenyl/95% dimethylpolysiloxane capillary column, 30 m, 0.25 mm i.d.), equipped with an HP 5971 mass-selective detector operating at 70 eV (EI). The electrospray ionization (HR-ESI-MS) experiments were

carried out in a hybrid Q*q*TOF mass spectrometer (PE SCIEX-QSTAR) equipped with an ion spray ionization source. MS(+) spectra were acquired by direct infusion (5 μL/min) of a solution containing the appropriate sample (10 pmol/μL), dissolved in solution 0.1% acetic acid, methanol/water 50/50 at the optimum ion voltage of 4800 V. The nitrogen gas flow was set at 30 psi (pounds per square inch) and the potentials of the orifice, the focusing ring and the skimmer were kept at 30, 50, and 25 V relative to ground, respectively. Polarimetric measurements were performed by a Jasco P-1020 polarimeter. Melting points were determined using an electrothermal melting point apparatus and are uncorrected. TLC were performed on Merck silica gel plates with F-254 indicator; viewing was by UV light (254 nm). Column chromatographies were performed on silica gel (63–200 μm) using petroleum ether/diethyl ether (Et_2O) mixtures as eluents. All reactions involving air-sensitive reagents were performed under nitrogen, in oven-dried glassware using syringe/septum cap techniques.

4.1. General procedures for the preparation of the substrates (1a–h) and imines (2a–b)

Compound **1a** was prepared by formylation of 4-methylthiazole, reduction of the so obtained 2-thiazolylaldehyde and subsequent halogenation, following reported synthetic protocols.[9d] Compound **1b** was obtained by the coupling reaction of 2-(4-methyl)thiazolyllithium with acetaldehyde and subsequent halogenation.[9d] Substrates **1c**, **1d** were obtained by reaction of 2-aminothiophenol with glycolic or lactic acid and subsequent halogenation.[21] 2-(α-Chloroalkyl)oxazolines **1e**, **1f** were prepared by halogenation of the commercially available 2-methyl and 2-ethyl derivatives according to reported procedures.[22] 2-(α-Choroalkyl)-piridines **1g**, **1h** were obtained by treatment of the commercially available hydrochlorides with a 5% NaOH solution.[22] Chiral imines **2a**,**2b** were prepared by the coupling of chiral 2-methoxy-1-phenylethylamine (*R* or *S*) or chiral 1-phenylethylamine (*R* or *S*) with benzaldehyde according to the reported protocols.[23] 2-Methoxy-1-phenylethylamine (*R* or *S*) was prepared by methylation[24] of the commercial enantiopure 2-amino-2-phenylethanol (*R* or *S*).

4.2. General procedure for the preparation of heterosubstituted aziridines (3a–h)

To a stirred solution of LDA (2.0 M in hexanes, 1 mL, 2.0 mmol), in THF (30 mL) at −78 °C under nitrogen, a mixture of 1 mmol of **1a–h**, and 1 mmol of imine **2a** in 10 mL of THF was added dropwise. After 20 min the resulting mixture was slowly allowed to warm to room temperature and then, after 3 h, quenched with sat. aq. NH_4Cl. The aqueous layer was extracted with Et_2O (3×20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude products were purified by column chromatography [silica gel, petroleum ether/Et_2O, 1:1 for (+)-**3a**, (+)-**3b**, (−)-**3c**, (+)-**3e**, (+)-**3g**, 7:3 for (+)-**3h**, 9:1 for (−)-**3f** and (−)-**3d**] to afford the pure heterosubstituted aziridines, yields: 30–90%. The substituted aziridines (−)-**3a**, (−)-**3e**, (+)-**3f**, (+)- and (−)-**4a**, (+)- and (−)-**4f** were prepared with this same procedure.

4.2.1. 2-[1-(2-Methoxy-1-phenylethyl)-3-phenylaziridin-2-yl]-4-methylthiazole (+)-3a. Yield: 168 mg, (48%), yellow solid, mp 95–97 °C (*n*-hexane). ^{1}H NMR (400.13 MHz): δ 2.31 (s, 3H), 3.12 (d, 1H, *J*=6.4 Hz), 3.21 (dd, 1H, *J*=5.0, 7.2 Hz), 3.28 (s, 3H), 3.62 (d, 1H, *J*=6.4 Hz), 3.70 (dd, 1H, *J*=5.0, 9.7 Hz), 3.85 (dd, 1H, *J*=7.2, 9.7 Hz), 6.58 (s, 1H), 7.05–7.27 (m, 6H), 7.33 (t, 2H, *J*=7.6 Hz), 7.50 (d, 2H, *J*=7.2 Hz). ^{13}C NMR (100.62 MHz): δ 16.8, 47.4, 47.7, 50.9, 73.4, 77.7, 113.0, 126.7, 127.4, 127.6, 127.7, 127.9, 128.2, 134.8, 139.5, 152.1, 167.6. GC–MS (70 eV) *m*/*z* (rel. int.): 350 (7, M^+), 305 (5), 347 (7), 215 (100), 188 (53). IR (film): 3080, 3020, 2910, 2860, 1600, 1590, 1450, 1300, 1230, 1100, 750, 690 cm^{-1}. $[\alpha]_D^{22}$=+12.9 ($CHCl_3$, *c* 0.07). HR-ESI-MS: *m*/*z* calcd for $C_{21}H_{23}N_2OS$: 351.1531, $[M+H]^+$; found 351.1528.

4.2.2. 2-[1-(2-Methoxy-1-phenylethyl)-2-methyl-3-phenylaziridin-2-yl]-4-methylthiazole (+)-3b. Yield: 327.6 mg (90%), yellow solid, mp 82–84 °C (*n*-hexane). ^{1}H NMR (400.13 MHz): δ 2.06 (s, 3H), 2.31 (d, 3H, *J*=0.8 Hz), 3.01 (s, 1H), 3.35 (s, 3H), 3.76–3.87 (m, 3H), 6.60 (q, 1H, *J*=0.8 Hz), 7.05–7.55 (m, 10H). ^{13}C NMR (100.62 MHz): δ 17.7, 17.8, 50.9, 54.1, 59.6, 65.3, 78.5, 113.6, 126.9, 127.7, 128.1, 128.2, 128.6, 128.8, 136.4, 140.5, 142.9, 173.5. GC–MS (70 eV) *m*/*z* (rel. int.): 364 (1, M^+), 238 (61), 229 (100), 207 (28), 91 (44). IR (film): 3030, 2920, 2860, 1450, 1300, 1120, 750, 700 cm^{-1}. $[\alpha]_D^{22}$=+23.1 ($CHCl_3$, *c* 0.06). HR-ESI-MS: *m*/*z* calcd for $C_{22}H_{25}N_2OS$: 365.5126, $[M+H]^+$; found 365.5120.

4.2.3. 2-[1-(2-Methoxy-1-phenylethyl)-3-phenylaziridin-2-yl]benzothiazole (−)-3c. Yield: 347.4 mg (90%), yellow solid, mp 60–62 °C (petroleum ether). ^{1}H NMR (400.13 MHz): δ 3.23 (d, 1H, *J*=6.2 Hz), 3.27–3.29 (m, 4H), 3.72 (dd, 1H, *J*=4.6, 9.0 Hz), 3.77 (d, 1H, *J*=6.2 Hz), 3.91 (t, 1H, *J*=9.0 Hz), 7.05–7.50 (m, 12H), 7.74 (d, 1H, *J*=8.0 Hz), 7.90 (d, 1H, *J*=8.0 Hz). ^{13}C NMR (100.62 MHz): δ 43.1, 44.2, 59.0, 60.7, 78.7, 126.6, 126.8, 127.3, 127.4, 127.5, 127.6, 127.9, 128.0, 128.2, 128.3, 135.3, 139.3, 151.5, 166.2. GC–MS (70 eV) *m*/*z* (rel. int.): 386 (5, M^+), 355 (8), 327 (10), 251 (100). IR ($CHCl_3$): 3060, 3020, 2950, 1600, 1590, 1490, 1440, 1375, 1100, 750, 690 cm^{-1}. $[\alpha]_D^{22}$=−61.7 ($CHCl_3$, *c* 0.01). HR-ESI-MS: *m*/*z* calcd for $C_{24}H_{23}N_2OS$: 387.1531, $[M+H]^+$; found 387.1530.

4.2.4. 2-[1-(2-Methoxy-1-phenylethyl)-2-methyl-3-phenylaziridin-2-yl]benzothiazole (−)-3d. Yield: 240 mg (60%), yellow solid, mp 131–133 °C (petroleum ether). ^{1}H NMR (400.13 MHz): δ 1.53 (s, 3H), 2.99 (s, 3H), 3.48–3.63 (m, 2H), 3.93 (t, 1H, *J*=6.4 Hz), 4.10 (s, 1H), 7.15–7.50 (m, 12H), 7.87 (d, 1H, *J*=7.8 Hz), 8.10 (d, 1H, *J*=8.0 Hz). ^{13}C NMR (100.62 MHz): δ 19.9, 48.9, 50.8, 58.7, 62.8, 77.1, 121.4, 123.3, 125.0, 126.1, 126.8, 127.5, 127.7, 127.8, 128.2, 128.3, 135.2, 136.8, 140.5, 152.7, 170.3. IR (film): 3060, 3020, 2950, 1600, 1490, 1440, 1375, 1100, 750, 690 cm^{-1}. $[\alpha]_D^{22}$=−199.4 ($CHCl_3$, *c* 0.02). HR-ESI-MS: *m*/*z* calcd for $C_{25}H_{25}N_2OS$: 401.1690, $[M+H]^+$; found 401.1703.

4.2.5. 2-[1-(2-Methoxy-1-phenylethyl)-3-phenylaziridin-2-yl]-4,4-dimethyl-4,5-dihydrooxazole (+)-3e. Yield:

157.5 mg (45%), white solid, mp 71–72 °C (*n*-hexane). ^{1}H NMR (400.13 MHz): δ 1.00 (s, 3H), 1.08 (s, 3H), 2.86 (d, 1H, J=6.8 Hz), 2.90 (d, 1H, J=6.8 Hz), 3.03 (t, 1H, J=5.5 Hz), 3.37 (s, 3H), 3.58 (d, 1H, J=8.0 Hz), 3.66–3.75 (m, 2H), 3.90 (dd, 1H, J=8.0, 9.7 Hz), 7.13–7.30 (m, 9H), 7.48 (d, 1H, J=7.2 Hz). ^{13}C NMR (100.62 MHz): δ 27.9, 28.0, 43.4, 44.2, 59.1, 66.9, 73.9, 76.6, 78.7, 126.8, 127.4, 127.5, 127.6, 127.7, 128.2, 132.0, 139.4, 162.0. GC–MS (70 eV) *m*/*z* (rel. int.): 350 (8, M^+), 319 (7), 238 (20), 215 (100), 91 (60). IR (film): 3050, 2910, 1650, 1450, 1370, 1100 cm^{-1}. $[\alpha]_D^{22}$=+28.1 ($CHCl_3$, *c* 0.01). HR-ESI-MS: *m*/*z* calcd for $C_{22}H_{27}N_2O_2$: 351.2072, $[M+H]^+$; found 351.2073.

4.2.6. 2-[1-(2-Methoxy-1-phenylethyl)-2-methyl-3-phenylaziridin-2-yl]-4,4-dimethyl-4,5-dihydrooxazole (−)-3f. Yield: 127.4 mg (35%), white solid, mp 66–68 °C (*n*-hexane). ^{1}H NMR (400.13 MHz): δ 1.20 (s, 3H), 1.38 (s, 6H), 3.27 (s, 3H), 3.55 (s, 1H), 3.67–3.78 (m, 3H), 4.04 (s, 2H), 7.14–7.31 (m, 8H), 7.45–7.50 (m, 2H). ^{13}C NMR (100.62 MHz): δ 17.0, 28.0, 28.3, 43.9, 48.6, 58.9, 64.8, 67.2, 77.0, 78.6, 126.4, 127.2, 127.4, 127.5, 127.9, 128.2, 136.4, 140.6, 163.4. GC–MS (70 eV) *m*/*z* (rel. int.): 364 (4, M^+), 332 (6), 317 (8), 238 (43), 91 (100). IR (film): 3030, 2960, 2910, 2880, 1645, 1450, 1310, 1130, 750, 700 cm^{-1}. $[\alpha]_D^{22}$=−43.6 ($CHCl_3$, *c* 0.05). HR-ESI-MS: *m*/*z* calcd for $C_{23}H_{29}N_2O_2$: 365.2229, $[M+H]^+$; found 365.2221.

4.2.7. 2-[1-(2-Methoxy-1-phenylethyl)-3-phenylaziridin-2-yl]pyridine (+)-3g. Yield: mg 198.0 (60%), white solid, mp 110–111 °C (petroleum ether). ^{1}H NMR (400.13 MHz): δ 3.07 (d, 1H, J=6.8 Hz), 3.22 (dd, 1H, J=5.5, 6.9 Hz), 3.28 (s, 3H), 3.46 (d, 1H, J=6.8 Hz), 3.73 (dd, 1H, J=5.5, 9.7 Hz), 3.86 (dd, 1H, J=6.9, 9.7 Hz), 6.97–7.54 (m, 13H), 8.39 (d, 1H, J=4.8 Hz). ^{13}C NMR (100.62 MHz): δ 46.9, 51.3, 59.2, 73.7, 78.0, 121.5, 122.3, 126.4, 127.5, 127.7, 127.9, 128.0, 128.4, 135.5, 135.9, 140.3, 148.7, 157.0. GC–MS (70 eV) *m*/*z* (rel. int.): 330 (1, M^+), 285 (9), 207 (26), 195 (100), 182 (24), 180 (20), 92 (53). IR ($CHCl_3$): 3060, 2950, 1590, 1460, 1100 cm^{-1}. $[\alpha]_D^{22}$=+22.4 ($CHCl_3$, *c* 0.02). HR-ESI-MS: *m*/*z* calcd for $C_{22}H_{23}N_2O$: 331.1810, $[M+H]^+$; found 331.1805.

4.2.8. 4-[1-(2-Methoxy-1-phenylethyl)-3-phenylaziridin-2-yl]pyridine (+)-3h. Yield: 99 mg (30%), white solid, mp 72–74 °C (*n*-hexane). ^{1}H NMR (400.13 MHz): δ 3.01 (d, 1H, J=6.7 Hz), 3.20 (dd, 1H, J=4.7, 7.7 Hz), 3.26 (d, 1H, J=6.7 Hz), 3.29 (s, 3H), 3.70 (dd, 1H, J=4.7, 9.5 Hz), 3.83 (dd, 1H, J=7.7, 9.5 Hz), 7.05 (s, 5H), 7.16 (d, 2H, J=3.8 Hz), 7.26 (d, 1H, J=8.0 Hz), 7.32 (t, 2H, J=7.3 Hz), 7.50 (d, 2H, J=7.3 Hz), 8.37 (s, 2H). ^{13}C NMR (100.62 MHz): δ 46.7 49.0, 59.2, 73.9, 78.3, 123.2, 126.7, 127.5, 127.6, 127.7, 127.8, 128.4, 129.8, 135.4, 139.8, 148.9. GC–MS (70 eV) *m*/*z* (rel. int.): 330 (1, M^+), 195 (100), 167 (10), 91 (7). IR ($CHCl_3$): 3060, 3020, 2910, 2880, 1600, 1490, 1450, 1420, 1190, 1120, 900, 730, 700 cm^{-1}. $[\alpha]_D^{22}$=+40.0 ($CHCl_3$, *c* 0.07). HR-ESI-MS: *m*/*z* calcd for $C_{22}H_{23}N_2O$: 331.1810, $[M+H]^+$; found 331.1806.

4.2.9. 2-[1-(2-Methoxy-1-phenylethyl)-3-phenylaziridin-2-yl]-4-methyl-thiazole (−)-3a. Yield: 157.5 mg (45%), yellow solid, mp, spectroscopic data, GC–MS and HR-ESI-MS data are the same of those reported for the enantiomer (+)-**3a**. $[\alpha]_D^{22}$=−12.6 ($CHCl_3$, *c* 0.06).

4.2.10. 2-[1-(2-Methoxy-1-phenylethyl)-3-phenylaziridin-2-yl]-4,4-dimethyl-4,5-dihydrooxazole (−)-3e. Yield: 182 mg (52%), white solid, mp, spectroscopic data, GC–MS and HR-ESI-MS data are the same of those reported for the enantiomer (+)-**3e**. $[\alpha]_D^{22}$=−29.3 ($CHCl_3$, *c* 0.01).

4.2.11. 2-[1-(2-Methoxy-1-phenylethyl)-2-methyl-3-phenylaziridin-2-yl]-4,4-dimethyl-4,5-dihydrooxazole (+)-3f. Yield: 112.84 mg (31%), white solid, mp, spectroscopic data, GC–MS and HR-ESI-MS data are the same of those reported for the enantiomer (−)-**3f**. $[\alpha]_D^{22}$=+43.1 ($CHCl_3$, *c* 0.04).

4.2.12. 2-[3-Phenyl-1-(1-phenylethyl)-aziridin-2-yl]-4-methylthiazole (+)-4a. Overall yield: 160 mg (50%), yellow oil. Inseparable mixture of two *cis*-configurated diastereomeric aziridines (dr=4/1 by ^{1}H NMR of the crude product). $[\alpha]_D^{22}$=+14.1 ($CHCl_3$, *c* 0.07).

Major diastereomer. ^{1}H NMR (400.13 MHz): δ 1.55 (d, 3H, J=6.5 Hz), 2.32 (s, 3H), 3.05 (q, 1H, J=6.5 Hz), 3.19 (d, 1H, J=6.4 Hz), 3.39 (d, 1H, J=6.4 Hz), 6.59 (s, 1H), 7.07–7.25 (m, 6H), 7.34 (t, 2H, J=7.6 Hz), 7.50 (d, 2H, J=7.3 Hz). ^{13}C NMR (100.62 MHz): δ 16.9, 23.0, 46.6, 50.0, 70.0, 113.3, 126.9, 127.0, 127.3, 127.6, 128.3, 128.4, 135.0, 143.6, 152.3, 168.0. GC–MS (70 eV) *m*/*z* (rel. int.): 320 (1, M^+), 215 (100), 200 (4), 188 (9), 112 (25). HR-ESI-MS: *m*/*z* calcd for $C_{20}H_{21}N_2S$: 321.1425, $[M+H]^+$; found 321.1428. IR (film): 3060, 3020, 2910, 2840, 1720, 1600, 1440, 740, 700 cm^{-1}.

Minor diastereomer. ^{1}H NMR (400.13 MHz): δ 1.55 (d, 3H, J=6.5 Hz), 2.32 (s, 3H), 3.05 (q, 1H, J=6.5 Hz), 3.26 (d, 1H, J=6.4 Hz), 3.31 (d, 1H, J=6.4 Hz), 6.46 (s, 1H), 7.07–7.25 (m, 6H), 7.34 (t, 2H, J=7.6 Hz), 7.44 (d, 2H, J=7.3 Hz). ^{13}C NMR (100.62 MHz): δ 17.0, 22.7, 46.6, 50.0, 70.0, 113.2, 126.9, 127.1, 127.3, 127.5, 128.2, 128.4, 135.1, 143.6, 152.2, 167.9. For IR, GC–MS and HR-ESI-MS see Major diastereomer.

4.2.13. 2-[2-Methyl-3-phenyl-1-(1-phenylethyl)-aziridin-2-yl]-4,4-dimethyl-4,5-dihydrooxazole (+)-4f. Overall yield: 183.7 mg (55%), colorless oil. A diastereomeric mixture of two (2′*R* *,3′*S* *)-configurated aziridines separable by column chromatography (silica gel, petroleum ether/Et_2O 7/3) formed; dr 2/1.

Major diastereomer. 119.0 mg, oil. ^{1}H NMR (400.13 MHz): δ 0.95 (s, 3H), 1.05 (s, 3H), 1.55 (d, 3H, J=6.4 Hz), 1.80 (s, 3H), 2.71 (s, 1H), 3.49 (q, 1H, J=6.4 Hz), 3.54 (d, 1H, J=7.0 Hz), 3.63 (d, 1H, J=7.0 Hz), 7.1–7.5 (m, 10H). ^{13}C NMR (100.62 MHz): δ 14.3, 24.2, 28.0, 28.1, 45.4, 51.9, 61.8, 66.9, 78.7, 126.6, 127.0, 127.2, 127.3, 127.4, 128.2, 136.8, 144.4, 164.5. GC–MS (70 eV) *m*/*z* (rel. int.): 334 (1, M^+), 229 (100), 174 (40), 104 (54). IR ($CHCl_3$): 3060, 2940, 2850, 1640, 1450, 1360 cm^{-1}. $[\alpha]_D^{22}$=+36.0 ($CHCl_3$, *c* 0.03). HR-ESI-MS: *m*/*z* calcd for $C_{22}H_{27}N_2O$: 335.2123, $[M+H]^+$; found 335.2119.

Minor diastereomer. 64.3 mg, oil. ^{1}H NMR (400.13 MHz):

δ 0.91 (s, 3H), 0.94 (s, 3H), 1.44 (s, 3H), 1.52 (d, 3H, J=6.4 Hz), 2.88 (s, 1H), 3.46 (d, 1H, J=7.9 Hz), 3.51 (q, 1H, J=6.4 Hz), 3.63 (d, 1H, J=7.9 Hz), 7.2–7.3 (m, 8H), 7.45 (d, 1H, J=7.5 Hz), 7.57 (d, 1H, J=7.5 Hz). ^{13}C NMR (100.62 MHz): δ 14.3, 25.0, 27.9, 28.0, 29.7, 45.0, 52.8, 66.9, 78.6, 126.4, 126.5, 126.7, 126.9, 127.7, 128.2, 137.0, 145.2, 164.4. $[\alpha]_D^{22}$=+24.3 ($CHCl_3$, c 0.02). For IR, GC–MS and HR-ESI-MS see Major diastereomer.

4.2.14. 2-[3-Phenyl-1-(1-phenylethyl)-aziridin-2-yl]-4-methylthiazole (−)-4a. Inseparable mixture of two *cis*-configurated diastereomeric aziridines (dr=4/1 by ^{1}H NMR of the crude product). Overall yield: 169.6 mg (53%), yellow oil. $[\alpha]_D^{22}$=−13.5 ($CHCl_3$, c 0.08). Spectroscopic data, GC–MS and HR-ESI-MS data are the same of those reported for the mixture of the corresponding enantiomers (+)-**4a**.

4.2.15. 2-[2-Methyl-3-phenyl-1-(1-phenylethyl)-aziridin-2-yl]-4,4-dimethyl-4,5-dihydrooxazole (−)-4f. A diastereomeric mixture of two ($2'R^*$,$3'S^*$)-configurated aziridines separable by column chromatography (silica gel, petroleum ether/Et_2O 7/3) formed; dr 2/1. Overall yield: 173.7 mg (52%), colorless oil. Spectroscopic data, GC–MS and HR-ESI-MS data are the same of those reported for the two corresponding enantiomers (+)-**4f**.

Major diastereomer. $[\alpha]_D^{22}$=−35.3 ($CHCl_3$, c 0.03).

Minor diastereomer. $[\alpha]_D^{22}$=−25.9 ($CHCl_3$, c 0.02).

4.3. General procedure for the preparation of deuterated and methylated thiazolyl aziridines [5, 6, and (+)-3b]

To a stirred solution of 1 mmol of (+)-**3a**, or (+)-**4a** in THF (30 mL) at −78 °C, *n*-BuLi (2.5 M in hexanes, 1 mL, 2.5 mmol) was added dropwise under nitrogen. The resulting mixture was stirred at −78 °C for 1 h, and then 1.5 mmol of D_2O or CH_3I was added and the reaction was warmed up to room temperature and quenched with sat. aq. NH_4Cl. The aqueous layer was extracted with Et_2O (3×20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude products were purified by column chromatography (silica gel, petroleum ether/Et_2O, 1:1) to afford the pure deuterated or methylated aziridines **5**, **6**, and (+)-**3b**; yields: 50–90%.

4.3.1. 2-[2-Deutero-1-(2-methoxy-1-phenylethyl)-3-phenyl-aziridin-2-yl]-4-methylthiazole (5). Yield: 315.9 mg (90%), (90%D), yellow oil. The IR and ^{13}C NMR data are the same of compound (+)-**3a**. In the ^{1}H NMR spectrum the doublet at 3.12 ppm becomes a singlet, while the doublet at 3.62 ppm almost disappears. GC–MS (70 eV) m/z (rel. int.): 351 (1, M^+), 216 (100), 189 (7), 113 (17). HR-ESI-MS: m/z calcd for $C_{21}H_{22}DN_2OS$: 352.1594, $[M+H]^+$; found 352.1589. $[\alpha]_D^{22}$=+13.3 ($CHCl_3$, c 0.07).

4.3.2. 2-[2-Deutero-3-phenyl-1-(1-phenylethyl)-aziridin-2-yl]-4-methylthiazole (6). Inseparable mixture of two *cis*-configurated diastereomeric aziridines (dr=4/1) both 95%D. Overall yield: mg 288.9 (90%), yellow oil. IR and ^{13}C NMR data are the same of compound (+)-**4a**.

Major diastereomer. In the ^{1}H NMR spectrum the doublet at 3.19 ppm becomes a singlet, while the doublet at 3.39 ppm disappears. GC–MS (70 eV) m/z (rel. int.): 321 (0, M^+), 216 (100), 201 (11), 113 (15). HR-ESI-MS: m/z calcd for $C_{20}H_{20}DN_2S$: 322.1488, $[M+H]^+$; found 322.1481.

Minor diastereomer. In the ^{1}H NMR spectrum the doublet at 3.26 ppm becomes a singlet, while the doublet at 3.31 ppm disappears. For GC–MS and HR-ESI-MS see Major diastereomer.

4.3.3. 2-[1-(2-Methoxy-1-phenylethyl)-2-methyl-3-phenylaziridin-2-yl]-4-methylthiazole (+)-3b. Yield: 182 mg (50%), yellow solid, mp, spectroscopic data, GC–MS and HR-ESI-MS data are the same of those above-reported for this compound. $[\alpha]_D^{22}$=+23.9 ($CHCl_3$, c 0.06).

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References and notes

1. Baldwin, J. E.; Farthing, C. N.; Russel, A. T.; Schofield, C. J.; Spivey, A. C. *Tetrahedron Lett.* **1996**, *37*, 3761–3764.
2. Garner, P.; Dogan, O.; Pillai, S. *Tetrahedron* **1994**, *35*, 1653–1656.
3. (a) Deyrup, J. A. *The chemistry of heterocyclic compounds*; Hassner, A., Ed.; Wiley: New York, 1983; Vol. 42, pp 1–124. (b) Pearson, W. H.; Lion, B. W.; Bergmeier, S. C. *Comprehensive heterocyclic chemistry II*; Padwa, A., Ed.; Pergamon: Oxford, 1996; Vol. 1A, pp 1–60. (c) Rai, K. M. L.; Hassner, A. *Comprehensive heterocyclic chemistry II*; Padwa, A., Ed.; Pergamon: Oxford, 1996; Vol. 1A, pp 61–96.
4. Contrill, A. A.; Osborn, H. M. I.; Sweeney, J. B. *Tetrahedron* **1998**, *54*, 2181–2208.
5. (a) Tanner, D. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 599–619. (b) Osborn, H. M. I.; Sweeney, J. B. *Tetrahedron: Asymmetry* **1997**, *8*(11), 1693–1715. (c) Mc Coull, W.; Davis, F. A. *Synthesis* **2000**(10), 1347–1365.
6. (a) Satoh, T. *Chem. Rev.* **1996**, *96*, 3303–3325. (b) Vedejs, E.; Moss, W. O. *J. Am. Chem. Soc.* **1993**, *115*, 1607–1608. (c) Vedejs, E.; Kendall, J. T. *J. Am. Chem. Soc.* **1997**, *119*, 6941–6942. (d) Alezra, V.; Bonin, M.; Micouin, L.; Policar, C.; Husson, H.-P. *Eur. J. Org. Chem.* **2001**, 2589–2594.
7. Reutrakul, V.; Prapansiri, V.; Panyachotipun, C. *Tetrahedron Lett.* **1984**, *25*, 1949.

8. (a) Seebach, D.; Haner, R. *Chem. Lett.* **1987**, 49. (b) Haner, R.; Olano, B.; Seebach, D. *Helv. Chim. Acta* **1987**, *70*, 1676.
9. (a) Florio, S.; Troisi, L.; Capriati, V. *J. Org. Chem.* **1995**, *60*, 2279–2282. (b) Florio, S.; Troisi, L.; Capriati, V. *Tetrahedron Lett.* **1998**, *39*, 7951–7954. (c) Florio, S.; Troisi, L.; Capriati, V.; Ingrosso, G. *Tetrahedron Lett.* **1999**, *40*, 6101–6104. (d) Bona, F.; De Vitis, L.; Florio, S.; Ronzini, L.; Troisi, L. *Tetrahedron* **2003**, *59*, 1381–1387, and ref. therein.
10. (a) Corey, E. J.; Boger, D. L. *Tetrahedron Lett.* **1978**, *1*, 13–16. (b) Florio, S.; Capriati, V.; Luisi, R. *Tetrahedron Lett.* **1996**, *37*, 4781–4784. (c) Dondoni, A. In *Modern synthetic methods*; Scheffold, R., Ed.; Helvetica Chimica Acta: Basel, Switzerland, 1992; pp 377–473.
11. Dondoni, A.; Perrone, D. *Aldrichim. Acta* **1997**, *30*, 35–46.
12. Luisi, R.; Capriati, V.; Florio, S.; Ranaldo, R. *Tetrahedron Lett.* **2003**, *44*, 2677–2681.
13. Wartski, L. *Bull. Soc. Chim. Fr.* **1975**, 1663.
14. Alvernhe, G.; Laurent, A. *Bull. Soc. Chim. Fr.* **1970**, *8-9*, 3003–3010.
15. Kingsbury, C. A.; Durham, D. L.; Hutton, R. *J. Org. Chem.* **1978**, *43*, 4696–4700.
16. CCDC 212745 contain the supplementary crystallographic data (excluding structure factors) for compound (+)-**3b**. These data can be obtained free of charge via www.ccdc.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336-033; or deposit@ccdc.cam.ac.uk).
17. Yonezawa, T.; Morishima, I. *J. Mol. Spectry* **1968**, *27*, 210.
18. The observed $^{1}J_{CH}$ value of 167.2 Hz found for the aziridine C–H bond also testified a trans relationship between this bond and the nitrogen lone pair as described in Ref. 17. This same orientation of the nitrogen lone pair was also spectroscopically confirmed ($^{1}J_{CH}$=162.7 Hz) in the case of compound (+)-**3b**.
19. All calculations and graphical representations were performed by SPARTAN, Version 02, Wavefunction, Inc., Irvine, CA, USA, 2002.
20. Suffert, J. *J. Org. Chem.* **1989**, *54*, 509–512.
21. (a) Chikashita, H.; Ikegami, S.; Okumura, T.; Itoh, K. *Synthesis* **1986**, *5*, 375–377. (b) Zubarovskii, V. M. *Zhr. Obsch. Khim.* **1954**, *24*, 1664. *Chem Abstr.* **1955**, *49*, 13223. (c) Altamura, M.; Perrotta, E. *J. Org. Chem.* **1993**, *58*, 272–274. (d) Florio, S.; Granito, C.; Ingrosso, G.; Troisi, L. *Eur. J. Org. Chem.* **2000**, 3465–3472, and ref. therein.
22. Capriati, V.; Florio, S.; Ingrosso, G.; Granito, C.; Troisi, L. *Eur. J. Org. Chem.* **2000**, 478–484, and references therein cited.
23. (a) Taguchi, K.; Westheimer, F. H. *J. Org. Chem.* **1971**, *36*, 1570–1572. (b) De Kimpe, N.; De Cock, W.; Stevens, C. *Tetrahedron* **1992**, *48*, 2739–2760.
24. Smith, A. B.; Yager, K. M.; Taylor, C. M. *J. Am. Chem. Soc.* **1995**, *117*, 10879–10888.