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# On the effect of ring substituents in the carbonylation of aziridines

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**Abstract**—The effect of ring substituents on the cobalt carbonyl-catalyzed carbonylation of functionalized aziridines to β-lactams has been investigated. A variety of aziridines with different substituents and stereochemistry has been synthesized and subjected to carbonylation. The ring expansion to β-lactam takes place in the absence of an electron-withdrawing substituent and higher yields are always obtained for *cis*-aziridines. Moreover, the regioselectivity of the reaction is affected by the nature of substituents at ring carbon atoms. © 2001 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

Cobalt carbonyl-catalyzed carbonylative ring expansion of aziridines has proved to be a versatile reaction for the stereospecific synthesis of β-lactams in excellent yields.[1,2] The reaction proceeds through nucleophilic ring opening of the aziridine by the in situ-generated tetracarbonylcobaltate anion $[Co(CO)_4]^-$, followed by CO insertion and final ring closure to β-lactam. The reaction is reported to proceed via a $S_N2$-like mechanism with inversion of configuration at the stereocenter which undergoes CO insertion and shows stereospecificity and high regioselectivity: from *cis*-aziridines *trans*-β-lactams are obtained, whereas *cis*-β-lactams are isolated from *trans*-aziridines.[1,2]

Previous results have shown that substituents at the aziridine ring carbon atoms, as well as at nitrogen, have a strong effect on the Co-catalyzed carbonylation reaction.[2] More recently, with the aim of obtaining appropriate functionalized β-lactams, we applied this procedure to 2-alkoxycarbonyl-aziridines and 2-hydroxymethylaziridines, obtaining the corresponding β-lactams only from the latter.[1]

These results prompted us to investigate in greater detail the effect of ring substituents on the Co-catalyzed carbonylation of functionalized aziridines: for this purpose a range of aziridines bearing appropriate substituents on the ring carbon atoms as well as on the ring nitrogen atom were synthesized and subjected to carbonylation.

## 2. Results and discussion

### 2.1. Synthesis of aziridines

Aziridines **3a–e**, **4b,d**, **5d** and **6d** were synthesized from the parent *N*-benzyl-2-alkoxycarbonylaziridines **1a–e** following the procedure already described for **1b** and reported in Scheme 1.[1] Aziridines **1a–e** were obtained by benzylamine aminative cyclization of the dibromoderivatives prepared by bromine addition to the appropriate commercially available α,β-unsaturated esters. Aziridines **1b–d** were obtained as a mixture of *cis*/*trans* isomers and aziridine **1e** as the only *trans* isomer. Reduction of **1a–e** with lithium aluminium hydride afforded the corresponding hydroxymethyl derivatives **2a–e**, which were protected as TBDMS-ethers **3a–e** or as acetyl esters *cis*-**4b,d** by treatment with *tert*-butyldimethylsilylchloride (TBDMSCl) or by esterification with acetic acid in the presence of dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (DMAP), respectively. Amidation of *cis*-**1d** with aqueous ammonia, followed by reduction with lithium aluminium hydride in THF, afforded the corresponding 2-aminomethyl derivative *cis*-**5d**. Reduction of aziridine *cis*-**1d** with DIBAL-H at −78°C yielded the corresponding 2-formylderivative *cis*-**6d**.

*N*-Benzyl-2-acetyl-3-phenylaziridine **7d** was synthesized in analogy with aziridine **1d**, by bromination of commercially available 4-phenyl-3-buten-2-one, followed by aminative cyclization.

Symmetric *N*-benzyl-2,3-bis-(*tert*-butyldimethylsilyloxy)-methylaziridine (*cis*-**3f**) was obtained by treating the corresponding *N*-H aziridine **8**, synthesized as described in the literature,[3] with benzyl bromide and potassium carbonate in refluxing acetonitrile (Scheme 2).

*Keywords*: aziridines; β-lactams; carbonylation; cobalt.

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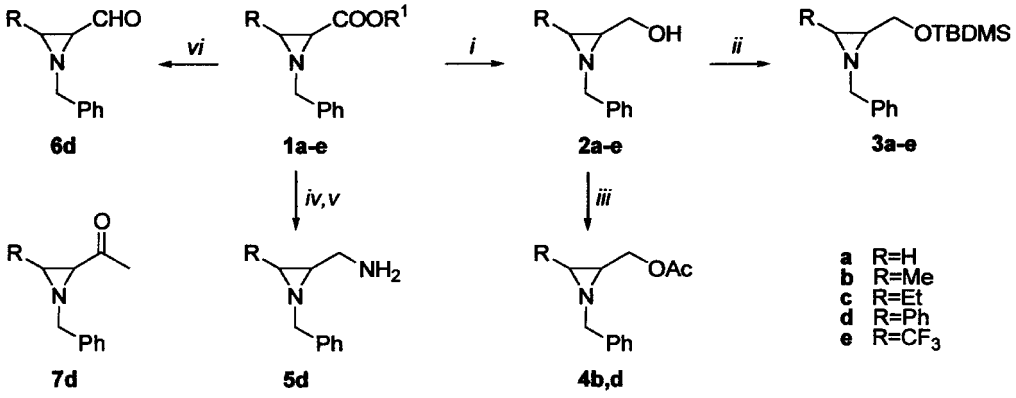
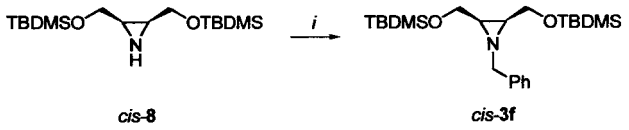



**Scheme 1.** (i) $LiAlH_4$, THF; (ii) TBDMSCl, DMAP, $CH_2Cl_2$; (iii) HOAc, DCC, DMAP, $CH_2Cl_2$; (iv) aq $NH_3$; (v) $LiAlH_4$, THF; (vi) DIBAL-H, $CH_2Cl_2$.




**Scheme 2.** (i) $PhCH_2Br$, $K_2CO_3$, $CH_3CN$ (81%).

2-(*tert*-Butyldimethylsilyloxy)methyl-3-phenylaziridine[4] (*cis*-**11**) was synthesized starting from 2-methoxycarbonyl-3-phenylaziridine (*cis*-**9**), prepared by aminative cyclization of methyl 2,3-dibromo-3-phenylpropanoate with ammonia. Reduction of *cis*-**9** with $LiAlH_4$ gave aziridine **10** which was protected as TBDMS-ether **11** by treatment with *tert*-butyldimethylsilylchloride. *N*-Acetyl derivative *cis*-**12** was obtained by reaction of **11** with acetyl chloride and triethylamine. Treatment of *N*-H aziridine **11** with ethyl bromoacetate afforded aziridine *cis*-**13** (Scheme 3).

Spectroscopic data of compounds **1**–**13** were in close agreement with the structures. The relative *cis*/*trans* stereochemistry was assigned on the basis of $^1H$ NMR spectral analysis ($^3J_{H,Hcis} > {}^3J_{H,Htrans}$).[5] Moreover, $^1H$ NMR spectra of *trans*-aziridines **1**(**b**–**d**)–**3**(**b**–**d**), in particular, showed the presence of two invertomers at nitrogen, due to slow nitrogen inversion on the NMR scale.[6]

## 2.2. Carbonylation of aziridines

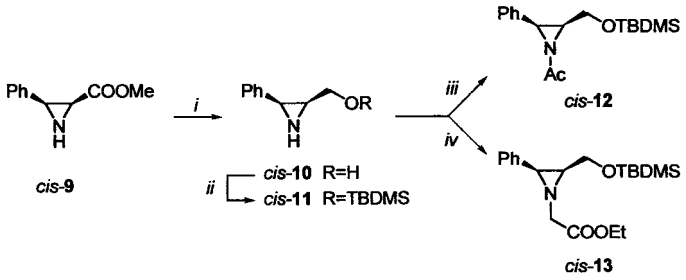
Following a well-established protocol,[1] aziridines were dissolved in freshly distilled and oxygen-free anhydrous 1,2-dimethoxyethane (DME) and treated with carbon monoxide (500 psi) and $Co_2(CO)_8$ for 14 h at 100°C in a stainless steel pressure vessel, using a 12:1 ratio of aziridine/catalyst. After removal of the catalyst by filtration on silica gel, the crude residue was purified by column chromatography. When the carbonyl insertion occurred into both the two ring carbon–nitrogen bonds, two regioisomers were isolated.

Carbonyl insertion was confirmed by $^{13}C$ NMR spectroscopy, with the carbonyl carbon occurring at 168–171 ppm. The relative stereochemistry of β-lactam regioisomers was determined by $^1H$ NMR spectroscopy ($^3J_{H,Hcis} > {}^3J_{H,Htrans}$) and the ring substitution pattern was assigned according to the *cross-cleavage* MS fragmentation.[1] The spectroscopic data of compounds **14**–**23** were in close agreement with the structures.

## 2.3. Carbonylation of aziridines 3a–f: effect of substituent at $C_3$ ring carbon atom

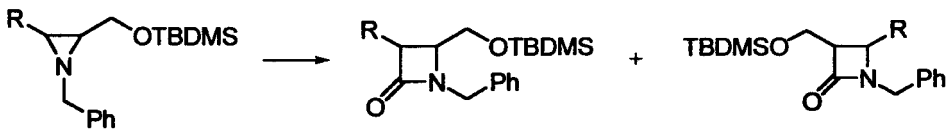
Carbonylation of *N*-benzyl-2-(*tert*-butyldimethylsilyloxy)-methylaziridine **3a** and 3-phenyl substituted aziridine **3d** afforded solely one β-lactam, **14a** and **14d**, respectively, while carbonylation of 3-alkyl substituted aziridines **3b**,**c** gave two β-lactam regioisomers **14b**,**c** and **15b**,**c**, the former being significantly predominant. All attempts at carbonylation of *trans*-**3e** failed, whereas aziridine *cis*-**3f**, which does not present any problem in terms of regiospecificity, afforded stereospecifically β-lactam *trans*-**14f**. The results are shown in Table 1.

As already observed for **3b**,[1] the carbonylation reaction on




**Scheme 3.** (i) $LiAlH_4$, THF (68%); (ii) TBDMSCl, DMAP, THF (97%); (iii) AcCl, $NEt_3$, $CH_2Cl_2$ (85%); (iv) $BrCH_2COOEt$, $K_2CO_3$, $CH_3CN$ (52%).

**Table 1.** Carbonylation of aziridines **3a–f**




**3a-f** **14 (major)** **15 (minor)**

| Aziridines | | R | β-Lactams | | | | |
|---|---|---|---|---|---|---|---|
| No. | Stereochemistry | | No. | | Stereochemistry | Relative ratio **14/15** | Yield (%) |
| **3a** | | H | **14a** | | – | 100 | 40 |
| **3b**[a] | *cis* | $CH_3$ | **14b** | **15b** | *trans* | 92:8 | 99.8[a] |
| **3b**[a] | *trans* | $CH_3$ | **14b** | **15b** | *cis* | 88:12 | 63[a] |
| **3c** | *cis* | $C_2H_5$ | **14c** | **15c** | *trans* | 83:17 | 98 |
| **3c** | *trans* | $C_2H_5$ | **14c** | **15c** | *cis* | 73:27 | 60 |
| **3d** | *cis* | Ph | **14d** | | *trans* | 100 | 95 |
| **3d** | *trans* | Ph | **14d** | | *cis* | 100 | 40 |
| **3e** | *trans* | $CF_3$ | – | | – | – | – |
| **3f** | *cis* | $CH_2OTBDMS$ | **14f** | | *trans* | 100 | 90 |

[a] From Ref. 1.

aziridines **3a–f** is stereospecific: from *cis* aziridines *trans* β-lactams are obtained, whereas *cis* β-lactams are isolated from *trans* aziridines.

Moreover, carbonylation reactions show regioselectivity regardless of the relative stereochemistry of the aziridine ring: (i) for aziridines **3a** and **3d**, CO insertion occurs exclusively into the ring $C_3$ carbon–nitrogen bond, affording only one β-lactam regioisomer, **14a** and **14d**, respectively; (ii) for aziridines **3b** and **3c** on the other hand two β-lactam regioisomers are obtained, namely **14b**,**c** and **15b**,**c**. Their relative ratio shows, yet again, the preferential carbonyl insertion into the alkyl-bearing ring $C_3$ carbon–nitrogen bond (regioisomer **14**) rather than into the *O*-protected hydroxymethyl-bearing ring $C_2$ carbon–nitrogen bond (regioisomer **15**). These results indicate that the regioselectivity of carbonylation is driven by electronic and steric effects: CO insertion occurs preferentially on the ring carbon atom displaying the higher electrophilic character or the lower steric hindrance. For aziridines **3a**,**d**, bearing a primary or a benzylic ring $C_2$ atom, respectively, the electronic effects seem to predominate and only one β-lactam regioisomer is obtained. In the case of aziridines **3b**,**c**, having both ring-C atoms as secondary carbons, CO insertion occurs on both nitrogen–carbon ring bonds, with preferential insertion on the less sterically hindered N–$C_3$ bond. In particular, higher regioselectivity (Me>Et) is observed in relation to a lesser steric hindrance of the substituent. Nevertheless, sterically hindered symmetric aziridine *cis*-**3f** gives carbonylation in very high yield.

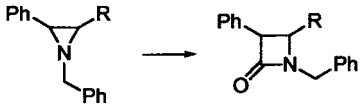
With regard to the relative ring stereochemistry, the carbonylation of *cis*-aziridines **3b**,**c** displays higher regioselectivity and affords remarkably higher yields by comparison with the corresponding *trans* derivatives.

## 2.4. Carbonylation of aziridines 2b–4b and 1d–7d: effect of substituent at $C_2$ ring carbon atom

Previous results showed that aziridine **1b**, characterized by the presence of an alkoxycarbonyl group on the ring, gave preferential elimination to an α,β-unsaturated system instead of CO insertion, while aziridine **3b**, bearing a silylated 2-hydroxymethyl group, was successfully carbonylated.[1] These results led us to investigate more thoroughly the compatibility of the carbonylation reaction with the nature of substituents at $C_2$ ring carbon atom for *N*-benzyl-3-phenylaziridines, taking into account the high regio- and stereospecificity observed in the case of aziridines **3d** (Table 1). Functional groups at $C_2$, such as a carboxylate group (**1d**), a formyl (**6d**), an acetyl (**7d**) or an aminomethyl (**5d**) as well as a free or protected hydroxymethyl group (**2d–4d**) were chosen. The results of carbonylation reactions for 3-phenylderivatives **1d–7d** are reported in Table 2 and compared with derivative **3d**.

As already observed for aziridine *cis*-**1b**,[1] the presence of a carboxylate or a carbonyl group directly linked to the aziridine ring $C_2$ carbon atom in compounds **1d**, **6d** and **7d** is detrimental for carbonylation and no β-lactams are recovered from the reaction mixture.

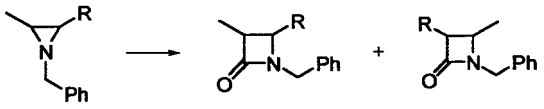
**Table 2.** Carbonylation of aziridines **1d–7d**




**1d-7d** **14d, 16-18**

| Aziridines | | R | β-Lactams | | |
|---|---|---|---|---|---|
| No. | Stereochemistry | | No. | Stereochemistry | Yield (%) |
| **1d** | *cis* | $COOCH_3$ | – | – | – |
| **7d** | *cis* | $COCH_3$ | – | – | – |
| **6d** | *cis* | CHO | – | – | – |
| **2d** | *cis* | $CH_2OH$ | **16** | *trans* | 79 |
| **3d** | *cis* | $CH_2OTBDMS$ | **14d** | *trans* | 96 |
| **4d** | *cis* | $CH_2OAc$ | **17** | *trans* | 86 |
| **5d** | *cis* | $CH_2NH_2$ | **18** | *trans* | 68 |
| **2d** | *trans* | $CH_2OH$ | – | – | – |
| **3d** | *trans* | $CH_2OTBDMS$ | **14d** | *cis* | 40 |

**Table 3.** Carbonylation of aziridines **2b–4b**




**2b-4b** **14b, 19, 20** **15b, 21**

| Aziridines | | R | β-Lactams | | | | |
|---|---|---|---|---|---|---|---|
| No. | Stereochemistry | | No. | | Stereochemistry | Relative ratio[a] | Yield (%) |
| **2b** | *cis* | $CH_2OH$ | **19** | | *trans* | 100 | 84 |
| **3b**[b] | *cis* | $CH_2OTBDMS$ | **14b** | **15b** | *trans* | 92:8 | 99.8[b] |
| **4b** | *cis* | $CH_2OAc$ | **20** | **21** | *trans* | 86:14 | 82 |
| **2b** | *trans* | $CH_2OH$ | –[c] | | –[c] | –[c] | –[c] |
| **3b**[b] | *trans* | $CH_2OTBDMS$ | **14b** | **15b** | *cis* | 88:12 | 63[b] |

[a] Relative ratio between the regioisomers (**14b/15b** or **20/21**).
[b] From Ref. 1.
[c] The product of the carbonylation reaction is the *trans* lactone 4-benzylamino-3-methyltetrahydrofuran-2-one (**22**) in 64% yield.

Carbonylation of unprotected hydroxymethylaziridine *cis*-**2d** as well as its acetate ester *cis*-**4d** proceeded stereo- and regiospecifically, affording only one β-lactam, *trans*-**16** and *trans*-**17**, respectively, in high yields: CO insertion occurs exclusively on the $C_3$–N bond as observed for the O–TBDMS analogue *cis*-**3d**. Carbonylation of *cis*-**4d**, affording β-lactam **17**, underlines the compatibility of a carbonyl group as substituent when isolated from the ring system.

Furthermore, *N*-benzyl-2-aminomethyl-3-phenylaziridine (*cis*-**5d**) gave regio- and stereospecific carbonylation, yielding *trans*-β-lactam **18** in good yield.

Surprisingly, when moving to *trans*-hydroxymethylaziridines, carbonylation of free aziridine *trans*-**2d** did not occur, whereas the corresponding protected *trans*-**3d** was carbonylated albeit in low yield.

The influence of the hydroxymethyl group protection was evaluated also for the 3-methyl analogues **2b–4b**. The results of carbonylation reactions are collected in Table 3.

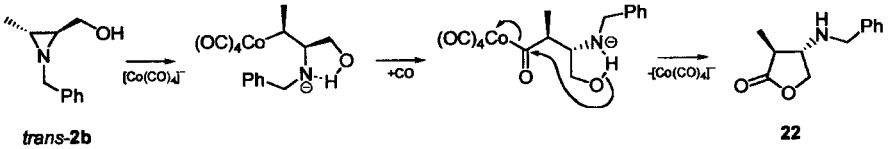
Aziridine *cis*-**2b**, bearing a free hydroxymethyl group on the $C_2$ ring carbon atom, and its acetate ester *cis*-**4b** were successfully and stereospecifically carbonylated to β-lactams, as already observed for the corresponding O–TBDMS derivative **3b** (Table 3). Carbonylation of acetyl derivative *cis*-**4b** affords two β-lactam regioisomers *trans*-**20** and *trans*-**21** in good yield and without affecting regioselectivity, when compared with the OTBDMS analogue *cis*-**3b**.

Interestingly, unlike derivatives *cis*-**3b** and **4b**, carbonylation of unprotected hydroxymethyl aziridine *cis*-**2b** is regiospecific, yielding only one β-lactam *trans*-**19**, indicative of CO insertion exclusively on the $C_3$–N bond. This result seems to suggest the presence of an intramolecular hydrogen bond between the hydroxy group and the nitrogen, favouring for CO insertion and thus for regiospecificity. Carbonylation of the *trans* isomer **2b** on the other hand, proceeds to the stereo- and regioselective formation of *trans*-lactone 4-benzylamino-3-methyltetrahydrofuran-2-one (**22**) in good yield. The structure and *trans* stereochemistry of lactone **22** was confirmed by NOESY and COSY NMR spectroscopy. By assuming the same mechanism reported for carbonylation to β-lactams,[1] lactone formation could be explained through the initial $[Co(CO)_4]^-$ nucleophilic opening of the aziridine ring followed by CO insertion into the Co–$C_3$ bond. The cyclization to the five-membered lactone **22** indicates the nucleophilic attack of alcoholic oxygen on the carbonyl through a proton migration from O to N, promoted by an intramolecular hydrogen bond (Scheme 4).

## 2.5. Carbonylation of aziridines *cis*-11–13: effect of substituent at the ring nitrogen atom

Since *cis*-*N*-benzyl-2-(*tert*-butyldimethylsilyloxy)methyl-3-phenylaziridine **3d** gave the best results in terms of regio- and stereoselectivity, as reported above, *N*-H, *N*-acetyl and *N*-(ethoxycarbonyl)methyl aziridines, *cis*-**11–13**, respectively, were chosen and subjected to the carbonylation conditions in order to investigate the influence of substituents at the ring nitrogen atom. The results are reported in Table 4 and compared with derivative *cis*-**3d**.

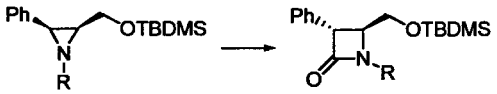
The nature of the substituent on ring nitrogen is significant for carbonylation. *N*-unsubstituted aziridine *cis*-**11**, as well as *N*-acetylaziridine *cis*-**12**, did not show any reactivity: no β-lactams were recovered, only the unreacted aziridines. In the case of *cis*-**12**, the presence of an acetyl group on nitrogen, which is known to increase the reactivity towards




*trans*-**2b** **22**

**Scheme 4.**

**Table 4.** Carbonylation of *cis* aziridines **3d**, **11**–**13**




**3d, 11-13** **14d, 23**

| Aziridines | | R | β-Lactams | | |
|---|---|---|---|---|---|
| No. | Stereochemistry | | No. | Stereochemistry | Yield (%) |
| **11** | *cis* | H | – | – | – |
| **3d** | *cis* | Bn | **14d** | *trans* | 95 |
| **12** | *cis* | $COCH_3$ | – | – | – |
| **13** | *cis* | $CH_2COOEt$ | **23** | *trans* | 63 |

nucleophiles,[7] decreases the basicity with respect to *cis*-**3d**: the basicity of the ring nitrogen atom is reported to play an important role in the formation of the $[Co(CO)_4]^-$ anion, as well as in the ring closure of the nucleophilic ring-opening intermediate to β-lactam.[2]

More interesting is the carbonylation of aziridine *cis*-**13**: *trans*-β-lactam **23**, bearing a carboxymethyl group on nitrogen, a typical substituent in the framework of several β-lactam antibiotics,[8] was regio- and stereospecifically obtained in good chemical yield.

## 3. Conclusions

These results broaden the range of aziridines that can be used as substrates for the cobalt carbonyl-catalyzed carbonylation, thus making available a variety of functionalized β-lactams that might be used as suitable precursors of antibiotic drugs.

Even though the presence of electron-withdrawing substituents on ring carbon atoms, such as a trifluoromethyl or an alkoxycarbonyl group, proved incompatible with carbonylation, a hydroxymethyl (protected or unprotected) and an aminomethyl group as ring carbon substituents, as well as an alkoxycarbonylmethyl group on the ring nitrogen allowed us to perform the carbonylative ring-expansion to β-lactams, whilst at the same time retaining the possibility of a further reactivity on the ring substituents.

## 4. Experimental

### 4.1. General procedure

$^1H$ and $^{13}C$ NMR spectra were recorded in $CDCl_3$ solution on a Bruker DPX-200 MHz and a Bruker AMQ 400 MHz spectrometers; chemical shifts are reported in $\delta$ values from TMS as internal standard; coupling constants (*J*) are given in Hz. For mass spectral determinations a Finnigan MAT SSQ A mass spectrometer was used (EI, 70 eV). Elemental analyses were performed with a Carlo Erba Elemental Analyzer 1110. All organic solvents were dried and distilled by standard methods prior to use and all reactions were carried out using oven-dried glassware. Chromatographic purification of compounds was performed on silica gel (particle size 0.05–0.20 mm). The metal catalyst $Co_2(CO)_8$ was purchased from Merck.

The syntheses of compounds *cis*- and *trans*-**1b**–**3b**, *cis*- and *trans*-**9b**, **10b** are described elsewhere.[1] Trifluorinated aziridine *trans*-**1e** was prepared from the corresponding dibromo derivative as reported in the literature.[9] Compound **8** was synthesized following the procedure already described.[3]

**4.1.1. 1-Benzyl-2-methoxycarbonylaziridine (1a).**[10] A solution of commercial methyl 2,3-dibromopropanoate (2.6 mL, 20.48 mmol) in methanol (50 mL) was slowly added dropwise at 0°C to a stirred solution of benzylamine (7.83 mL, 71.68 mmol) in methanol (100 mL) and left to warm to rt overnight. The reaction mixture was rotary evaporated, diluted with ether (100 mL), washed with water (200 mL) and the aqueous phase extracted with ethyl ether (3×50 mL). The combined organic phases were dried ($MgSO_4$), concentrated in vacuo and chromatographed (ethyl ether/light petroleum 60:40) to afford **1a** as a pale yellow liquid (3.30 g, 84% yield), which was used without further purification. $^1H$ NMR (200 MHz): $\delta$ 1.74 (1H, dd, $J$=1.0, 6.5 Hz, C$H_2$), 2.20 (1H, dd, $J$=3.0, 6.5 Hz, C$H_2$), 2.26 (1H, dd, $J$=1.0, 3.0 Hz, C*H*COOMe), 3.54 (2H, s, C$H_2$Ph), 3.71 (3H, s, COOC$H_3$), 7.20–7.40 (5H, m, aromatic). MS, *m*/*z*: 191 (2, $M^+$), 190 (18), 176 (20), 132 (50), 104 (26), 91 (100), 65 (21%).

**4.1.2. *cis*- and *trans*-1-Benzyl-3-ethyl-2-methoxycarbonylaziridine (1c).** Methyl 2,3-dibromopentanoate (7.65 g, 27.94 mmol), prepared by bromination of methyl *trans*-2-pentenoate[11] in $CCl_4$ at rt, was dissolved in methanol (70 mL) and slowly added at 0°C to a stirred solution of benzylamine (12.6 mL, 115.35 mmol) in methanol (200 mL). The reaction mixture was stirred overnight, leaving to warm to rt. After rotary evaporation of the solvent, the residue was dissolved in ethyl ether (180 mL), washed with water (360 mL) and the aqueous phase extracted with ethyl ether (3×90 mL). The combined organic phases were dried ($MgSO_4$) and concentrated to give a crude brown-yellowish oil which was chromatographed on $SiO_2$ (light petroleum/ethyl ether 80:20 and then 60:40) to afford aziridine *cis*-**1c** (4.02 g) and aziridine *trans*-**1c** (1.81 g), both as yellowish oils, in a 69:31 ratio and in 95% total yield. Aziridine *cis*-**1c** was further purified by in vacuo distillation on a Vigreux column: colourless oil, bp 102°C (0.6 mm Hg). $^1H$ NMR spectroscopy showed compound *trans*-**1c** as a 72:28 mixture of two invertomers at nitrogen, due to slow nitrogen inversion on the NMR scale.

*cis*-**1c.** $^1H$ NMR (200 MHz): $\delta$ 0.88 (3H, t, $J$=7.5 Hz, C$H_3$CH$_2$), 1.39–1.77 (2H, m, CH$_3$C$H_2$), 1.87 (1H, q, $J$=6.5 Hz, CH$_3$CH$_2$C*H*), 2.26 (1H, d, $J$=6.5 Hz, C*H*COOCH$_3$), 3.53 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.62 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.72 (3H, s, COOC$H_3$), 7.22–7.36 (5H, m, aromatic). MS, *m*/*z*: 219 (6, $M^+$), 204 (1), 190 (1), 160 (21), 146 (3), 131 (3), 128 (2), 91 (100), 68 (8), 65 (13%). Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.02; H, 7.98; N, 6.45.

*trans*-**1c.** $^1H$ NMR (400 MHz): major invertomer: $\delta$ 0.87 (3H, t, $J$=7.5 Hz, C$H_3$CH$_2$), 1.38–1.59 (2H, m, CH$_3$C$H_2$), 2.27 (1H, dt, $J$=2.5, 6.0 Hz, CH$_3$CH$_2$C*H*), 2.51 (1H, d, $J$=2.5 Hz, C*H*COOCH$_3$), 3.69 (3H, s, COOC$H_3$), 3.91 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.99 (1H, d, $J$=13.5 Hz,

C$H_2$Ph), 7.29–7.41 (5H, m, aromatic); minor invertomer: $\delta$ 1.09 (3H, t, $J$=7.5 Hz, C$H_3$CH$_2$), 1.59–1.83 (2H, m, CH$_3$C$H_2$), 2.05 (1H, m, CH$_3$CH$_2$C$H$), 2.49 (1H, m, C$H$COOCH$_3$), 3.72 (3H, s, COOC$H_3$), 3.65 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 3.92 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 7.22–7.29 (5H, m, aromatic). MS, *m/z*: 219 (6, M$^+$), 204 (1), 190 (1), 160 (21), 146 (3), 131 (3), 128 (2), 91 (100), 68 (8), 65 (13%). Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 70.97; H, 8.05; N, 6.55.

**4.1.3. *cis*- and *trans*-1-Benzyl-2-methoxycarbonyl-3-phenylaziridine (1d).** Benzylamine (3.56 mL, 32.59 mmol) was added dropwise at 0°C to a stirred solution of methyl 2,3-dibromo-3-phenylpropanoate[12] (3 g, 9.32 mmol) in methanol (120 mL). After 9 days the reaction mixture was rotary evaporated, the residue dissolved in water (110 mL) and extracted with ethyl ether (3×50 mL). The combined organic phases were dried ($MgSO_4$), concentrated in vacuo and chromatographed on $SiO_2$ (light petroleum/ethyl ether 80:20 and finally 50:50) to afford aziridine *cis*-**1d** (white solid, 1.70 g) and aziridine *trans*-**1d** (light yellow viscous liquid, 493 mg) in a 78:22 ratio and in 88% total yield. By crystallization from $CH_2Cl_2$/*n*-pentane, aziridine *cis*-**1d** was obtained as white crystals, mp 64–68°C. $^1$H NMR spectroscopy showed broad and poorly resolved signals for aziridine *trans*-**1d**, indicating the presence of two invertomers at nitrogen.

*cis*-**1d**. $^1$H NMR (200 MHz): $\delta$ 2.69 (1H, d, $J$=7.0 Hz, C$H$COOMe), 3.11 (1H, d, $J$=7.0 Hz, PhC$H$), 3.52 (3H, s, COOC$H_3$), 3.71 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.97 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 7.20–7.51 (10H, m, aromatic). MS, *m/z*: 267 (2, M$^+$), 266 (4), 236 (3), 208 (3), 176 (75), 144 (18), 117 (42), 116 (100), 91 (51), 77 (15), 65 (16%). Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.21; H, 6.32; N, 5.15.

*trans*-**1d**. $^1$H NMR (200 MHz): $\delta$ 2.87 (1H, br d, $J$=2.0 Hz, C$H$COOMe), 3.41 (1H, br s, PhC$H$), 3.77 (3H, br s, COOC$H_3$), 4.17 (1H, br d, $J$=14.0 Hz, C$H_2$Ph), 4.34 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 7.29–7.47 (10H, m, aromatic). MS, *m/z*: 267 (2, M$^+$), 266 (5), 236 (3), 208 (2), 176 (75), 144 (18), 116 (100), 91 (56), 77 (15), 65 (17%). Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.02; H, 6.67; N, 5.09.

### 4.2. Synthesis of hydroxymethyl aziridines 2a,c–e. General procedure

A 1.0 M $LiAlH_4$ solution in THF (2 mmol) was slowly added dropwise through a dropping funnel to a stirred solution of aziridines **1a**,**c**–**e** (1 mmol) in freshly distilled anhydrous THF (5 mL) at room temperature, under nitrogen flow (for aziridine **1a** the reaction was carried out at −40°C to avoid ring opening). When TLC analysis showed total disappearance of the starting material, the reaction mixture was cooled to 0°C and carefully quenched by dropwise addition of water (100 μL), followed by an aqueous 0.15N NaOH solution (100 μL). The white inorganic precipitate was filtered off and washed with abundant ethyl ether: the filtrate was dried ($MgSO_4$) and the solvent evaporated under reduced pressure to give a residue which was subjected to column chromatography on $SiO_2$.

**4.2.1. 1-Benzyl-2-hydroxymethylaziridine (2a).** Column chromatography (ethyl ether/light petroleum 90:10) afforded **2a** as a white solid (70% yield), mp 64–66°C (lit.,[13] 84–85°C, optically pure). $^1$H NMR (200 MHz): $\delta$ 1.53 (1H, m, C$H$CH$_2$OH), 1.81–1.91 (2H, m, NC$H_2$CH), 2.25 (1H, br, CH$_2$O$H$), 3.44 (1H, dd, $J$=5.0, 11.5 Hz, C$H_2$OH), 3.46 (1H, d, $J$=13.0 Hz, C$H_2$Ph), 3.56 (1H, d, $J$=13.0 Hz, C$H_2$Ph), 3.81 (1H, dd, $J$=3.0, 11.5 Hz, C$H_2$OH), 7.25–7.39 (5H, m, aromatic). MS, *m/z*: 164 (8, [M+1]$^+$), 163 (7), 162 (7), 132 (6), 91 (100), 72 (75), 65 (32%).

**4.2.2. *cis*-1-Benzyl-3-ethyl-2-hydroxymethylaziridine (*cis*-2c).** After chromatography (ethyl ether/light petroleum 80:20 and finally pure ethyl ether) *cis*-**2c** was obtained as a light pink sticky oil (86% yield). $^1$H NMR (200 MHz): $\delta$ 0.88 (3H, t, $J$=7.5 Hz, C$H_3$CH$_2$), 1.42 (2H, m, CH$_3$C$H_2$), 1.62 (1H, q, $J$=6.5 Hz, CH$_3$CH$_2$C$H$), 1.84 (1H, dt, $J$=5.0, 6.5 Hz, C$H$CH$_2$OH), 2.38 (1H, br, CH$_2$O$H$), 3.45 (1H, d, $J$=13.0 Hz, C$H_2$Ph), 3.48 (1H, dd, $J$=11.5, 7.0 Hz, C$H_2$OH), 3.55 (1H, d, $J$=13.0 Hz, C$H_2$Ph), 3.71 (1H, dd, $J$=11.5, 5.0 Hz, C$H_2$OH), 7.22–7.36 (5H, m, aromatic). MS, *m/z*: 190 (1, [M−1]$^+$), 160 (1), 146 (1), 117 (1), 100 (16), 91 (39), 72 (100), 65 (59%). Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.19; H, 9.07; N, 7.46.

**4.2.3. *trans*-1-Benzyl-3-ethyl-2-hydroxymethylaziridine (*trans*-2c).** Column chromatography (ethyl ether/light petroleum 90:10 and finally pure ethyl ether) afforded *trans*-**2c** (68% yield; light yellow sticky oil) as a 77:23 mixture of two invertomers at nitrogen, due to slow nitrogen inversion on the NMR scale. $^1$H NMR (400 MHz): major invertomer: $\delta$ 1.09 (3H, t, $J$=7.5 Hz, C$H_3$CH$_2$), 1.56–1.82 (3H, m, CH$_3$C$H_2$ and EtC$H$), 2.05 (1H, ddd, $J$=7.5, 6.0, 3.5 Hz, C$H$CH$_2$O), 2.62 (1H, br, CH$_2$O$H$), 3.42 (1H, dd, $J$=11.0, 4.5 Hz, C$H_2$OH), 3.58 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.74 (1H, br d, $J$=11.0 Hz, C$H_2$OH), 3.87 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 7.33–7.45 (5H, m, aromatic); minor invertomer: $\delta$ 0.87 (3H, t, $J$=7.5 Hz, C$H_3$CH$_2$), 1.43–1.53 (3H, m, CH$_3$C$H_2$ and EtC$H$), 2.12 (1H, dt, $J$=8.5, 3.5 Hz, C$H$CH$_2$O), 2.40 (1H, br, CH$_2$O$H$), 3.65 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 3.80 (1H, m, C$H_2$OH), 3.88 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 3.94 (1H, m, C$H_2$OH), 7.26–7.32 (5H, m, aromatic). MS, *m/z*: 190 (1, [M−1]$^+$), 160 (2), 146 (1), 130 (2), 100 (19), 91 (40), 77 (6), 72 (100), 65 (55%). Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.09; H, 8.82; N, 7.51.

**4.2.4. *cis*-1-Benzyl-2-hydroxymethyl-3-phenylaziridine (*cis*-2d).** Chromatography (ethyl ether/light petroleum 50:50) afforded *cis*-**2d** as a light yellow sticky oil (99% yield). $^1$H NMR (200 MHz): $\delta$ 1.69 (1H, br, CH$_2$O$H$), 2.22 (1H, dt, $J$=6.0, 6.5 Hz, C$H$CH$_2$OH), 2.94 (1H, d, $J$=6.5 Hz, PhC$H$), 3.34 (1H, dd, $J$=7.0, 11.5 Hz, CHC$H_2$OH), 3.50 (1H, dd, $J$=6.0, 11.5 Hz, CHC$H_2$OH), 3.70 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.80 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 7.20–7.50 (10H, m, aromatic). MS, *m/z*: 239 (5, M$^+$), 238 (19), 208 (2), 162 (100), 148 (53), 118 (13), 105 (8), 91 (24), 77 (12%). Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.23; H, 7.34; N, 5.91.

**4.2.5. *trans*-1-Benzyl-2-hydroxymethyl-3-phenylaziridine (*trans*-2d).** Chromatography (ethyl ether/light petroleum

80:20) gave *trans*-**2d** as pale yellow viscous liquid (83% yield). $^1$H NMR spectroscopy showed compound *trans*-**2d** as a 79:21 mixture of two invertomers at nitrogen. $^1$H NMR (400 MHz): major invertomer: $\delta$ 2.43–2.49 (1H, m, C*H*$CH_2$OH), 2.83 (1H, br, $CH_2$O*H*), 3.19 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.34 (1H, d, $J$=3.5 Hz, PhC*H*), 3.46 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.55–3.65 (1H, m, CHC$H_2$OH), 3.83–3.90 (1H, m, CHC$H_2$OH), 7.20–7.60 (10H, m, aromatic); minor invertomer: $\delta$ 2.11 (1H, br, $CH_2$O*H*), 2.53 (1H, d, $J$=3.5 Hz, PhC*H*), 2.56–2.62 (1H, m, C*H*$CH_2$OH), 3.90–3.98 (2H, m, C$H_2$OH and C$H_2$Ph), 4.01–4.10 (2H, m, C$H_2$OH and C$H_2$Ph), 7.20–7.60 (10H, m, aromatic). MS, *m*/*z*: 239 (3, $M^+$), 238 (9), 208 (2), 162 (39), 148 (17), 118 (6), 105 (6), 91 (100), 77 (12%). Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.15; H, 7.28; N, 6.02.

**4.2.6. *trans*-1-Benzyl-2-hydroxymethyl-3-trifluoromethylaziridine (*trans*-2e).** The crude residue was chromatographed (ethyl ether/light petroleum 60:40), to provide *trans*-**2e** as a pale yellow sticky liquid (92% yield). $^1$H NMR spectroscopy showed broad and poorly resolved signals, indicating the presence of two invertomers at nitrogen. $^1$H NMR (200 MHz): $\delta$ 1.60 (1H, br, O*H*), 2.10–2.90 (2H, br m, $CF_3$C*H* and C*H*$CH_2$OH), 3.89 (4H, m, CHC$H_2$OH and C$H_2$Ph), 7.23–7.40 (5H, m, aromatic). MS, *m*/*z*: 231 (5, $M^+$), 213 (2), 200 (10), 181 (2), 160 (1), 140 (33), 112 (30), 104 (10), 91 (100), 77 (12), 65 (18%). Anal. Calcd for $C_{11}H_{12}F_3NO$: C, 57.14; H, 5.23; N, 6.06. Found: C, 57.28; H, 5.38; N, 6.23.

### 4.3. Synthesis of protected hydroxymethyl aziridines 3a,c–e. General procedure

The hydroxymethylaziridine (1 mmol) was dissolved in anhydrous dichloromethane (6 mL): DMAP (2.5 mmol) and TBDMSCl (1.2 mmol) were added at rt under magnetic strirring and nitrogen flow (for the synthesis of aziridine **3a**, the parent hydroxymethylaziridine **2a** was cooled to −20°C, in order to avoid the easy opening of the aziridine ring). After disappearance of the starting material, the reaction mixture was then diluted with $CH_2Cl_2$ (12 mL), washed with water (2×20 mL) and brine (20 mL), dried over $MgSO_4$ and rotary evaporated. The residue was then chromatographed to afford the desired TBDMS-derivative in pure form.

**4.3.1. 1-Benzyl-2-(*tert*-butyldimethylsilyloxymethyl)-aziridine (3a).** Chromatography (light petroleum/ethyl ether 80:20) afforded **3a** as a pale yellow liquid (98% yield). $^1$H NMR (200 MHz): $\delta$ 0.11 (6H, s, $^t$Bu*Me*$_2$Si), 0.94 (9H, s, $^t$*Bu*Me$_2$Si), 2.97 (1H, quintet, $J$=5.5 Hz, C*H*$CH_2$O), 3.62–3.80 (4H, m, NC$H_2$CH and CHC$H_2$O), 3.85 (1H, d, $J$=13.0 Hz, C$H_2$Ph), 3.94 (1H, d, $J$=13.0 Hz, C$H_2$Ph), 7.26–7.39 (5H, m, aromatic). MS, *m*/*z*: 277 (1, $M^+$), 262 (3), 220 (100), 146 (4), 91 (88), 73 (27%). Anal. Calcd for $C_{16}H_{27}NOSi$: C, 69.26; H, 9.81; N, 5.05. Found: C, 69.03; H, 9.98; N, 5.20.

**4.3.2. *cis*-1-Benzyl-2-(*tert*-butyldimethylsilyloxymethyl)-3-ethylaziridine (*cis*-3c).** After chromatography (light petroleum/ethyl ether 90:10) *cis*-**3c** was obtained as a light yellow oil (91% yield). $^1$H NMR (200 MHz): $\delta$ 0.09 (6H, s, $^t$Bu*Me*$_2$Si), 0.94 (9H, s, $^t$*Bu*Me$_2$Si), 0.96 (3H, t, $J$=7.0 Hz, C$H_3$$CH_2$), 1.29–1.63 (3H, m, $CH_3$C$H_2$ and $CH_3CH_2$C*H*), 1.81 (1H, q, $J$=6.0 Hz, C*H*$CH_2$O), 3.48 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.59 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.62 (1H, dd, $J$=6.5, 11.0 Hz, C$H_2$O), 3.81 (1H, dd, $J$=6.0, 11.0 Hz, C$H_2$O), 7.24–7.42 (5H, m, aromatic). MS, *m*/*z*: 305 (5, $M^+$), 290 (3), 276 (8), 248 (53), 214 (23), 206 (13), 174 (3), 160 (8), 158 (16), 91 (100), 75 (19), 73 (87%). Anal. Calcd for $C_{18}H_{31}NOSi$: C, 70.76; H, 10.23; N, 4.58. Found: C, 70.67; H, 10.31; N, 4.49.

**4.3.3. *trans*-1-Benzyl-2-(*tert*-butyldimethylsilyloxymethyl)-3-ethylaziridine (*trans*-3c).** Aziridine *trans*-**3c** was prepared in close analogy with the *cis* analogue (78% yield; pale yellow oil). $^1$H NMR spectroscopy showed *trans*-**3c** as a 53:47 mixture of two invertomers at nitrogen. $^1$H NMR (400 MHz): major invertomer: $\delta$ 0.058 (3H, s, $^t$Bu*Me*$_2$Si), 0.063 (3H, s, $^t$Bu*Me*$_2$Si), 0.92 (9H, s, $^t$*Bu*Me$_2$Si), 1.11 (3H, t, $J$=7.5 Hz, C$H_3$$CH_2$), 1.40–1.85 (3H, m, $CH_3$C$H_2$ and C*H*$CH_2$O), 1.90 (1H, ddd, $J$=7.5, 6.0, 3.5 Hz, $CH_3CH_2$C*H*), 3.55 (1H, dd, $J$=6.0, 11.0 Hz, C$H_2$O), 3.57 (1H, d, $J$=13.0 Hz, C$H_2$Ph), 3.68 (1H, dd, $J$=6.0, 11.0 Hz, C$H_2$O), 4.03 (1H, d, $J$=13.0 Hz, C$H_2$Ph), 7.30–7.40 (5H, m, aromatic); minor invertomer: $\delta$ 0.11 (3H, s, $^t$Bu*Me*$_2$Si), 0.12 (3H, s, $^t$Bu*Me*$_2$Si), 0.86 (3H, t, $J$=7.5 Hz, C$H_3$$CH_2$), 0.95 (9H, s, $^t$*Bu*Me$_2$Si), 1.40–1.85 (3H, m, $CH_3$C$H_2$ and $CH_3CH_2$C*H*), 2.14 (1H, dt, $J$=7.5, 3.5 Hz, C*H*$CH_2$O), 3.50 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 3.86 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 3.92 (1H, dd, $J$=7.5, 12.0 Hz, C$H_2$O), 4.04 (1H, dd, $J$=3.5, 12.0 Hz, C$H_2$O), 7.30–7.40 (5H, m, aromatic). MS, *m*/*z*: 305 (3, $M^+$), 290 (1), 248 (50), 214 (26), 174 (2), 144 (2), 129 (2), 91 (100), 83 (6), 75 (20%). Anal. Calcd for $C_{18}H_{31}NOSi$: C, 70.76; H, 10.23; N, 4.58. Found: C, 70.51; H, 10.39; N, 4.42.

**4.3.4. *cis*-1-Benzyl-2-(*tert*-butyldimethylsilyloxymethyl)-3-phenylaziridine (*cis*-3d).** The residue was chromatographed (light petroleum/ethyl ether 90:10) to afford *cis*-**3d** as a light yellow oil (86% yield). $^1$H NMR (200 MHz): $\delta$ −0.12 (3H, s, $^t$Bu*Me*$_2$Si), −0.10 (3H, s, $^t$Bu*Me*$_2$Si), 0.84 (9H, s, $^t$*Bu*Me$_2$Si), 2.16 (1H, dt, $J$=5.5, 6.5 Hz, C*H*$CH_2$O), 2.85 (1H, d, $J$=6.5 Hz, PhC*H*), 3.32 (1H, dd, $J$=6.5, 11.0 Hz, CHC$H_2$O), 3.62 (1H, dd, $J$=5.5, 11.0 Hz, CHC$H_2$O), 3.64 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.85 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 7.20–7.49 (10H, m, aromatic). MS, *m*/*z*: 353 (36, $M^+$), 338 (4), 296 (38), 262 (100), 206 (25), 130 (11), 115 (12), 91 (58), 73 (79%). Anal. Calcd for $C_{22}H_{31}NOSi$: C, 74.73; H, 8.84; N, 3.96. Found: C, 74.66; H, 8.99; N, 4.07.

**4.3.5. *trans*-1-Benzyl-2-(*tert*-butyldimethylsilyloxymethyl)-3-phenylaziridine (*trans*-3d).** After purification by chromatography (light petroleum/ethyl ether 80:20), *trans*-**3d** was obtained as a light yellow oil (90% yield). $^1$H NMR spectroscopy showed *trans*-**3d** as a 57:43 mixture of two invertomers at nitrogen. $^1$H NMR (400 MHz): major invertomer: $\delta$ 0.17 (6H, s, $^t$Bu*Me*$_2$Si), 1.01 (9H, s, $^t$*Bu*Me$_2$Si), 2.50–2.52 (1H, m, C*H*$CH_2$O), 2.70 (1H, d, $J$=2.5 Hz, PhC*H*), 3.79–3.85 (2H, m, CHC$H_2$O), 3.87 (1H, d, $J$=14.5 Hz, C$H_2$Ph), 4.25 (1H, d, $J$=14.5 Hz, C$H_2$Ph), 7.20–7.50 (10H, m, aromatic); minor invertomer: $\delta$ 0.14 (6H, s, $^t$Bu*Me*$_2$Si), 0.98 (9H, s, $^t$*Bu*Me$_2$Si), 2.50–2.52 (1H, m, C*H*$CH_2$O), 3.19 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 3.24 (1H, d,

$J$=3.0 Hz, PhC$H$), 3.49 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 4.16 (1H, dd, $J$=3.0, 12.0 Hz, CHC$H_2$O), 4.21 (1H, dd, $J$=7.0, 12.0 Hz, CHC$H_2$O), 7.20–7.50 (10 H, m, aromatic). MS, *m/z*: 353 (2, $M^+$), 296 (5), 262 (42), 206 (9), 130 (10), 115 (13), 91 (63), 73 (100%). Anal. Calcd for $C_{22}H_{31}NOSi$: C, 74.73; H, 8.84; N, 3.96. Found: C, 74.53; H, 9.06; N, 4.13.

**4.3.6. *trans*-1-Benzyl-2-(*tert*-butyldimethylsilyloxymethyl)-3-trifluoromethylaziridine (*trans*-3e).** Column chromatography (light petroleum/ethyl ether 95:5) gave *trans* **3e** as a pale reddish liquid (88% yield). As for *trans* **2e**, $^1$H NMR spectroscopy showed broad and poorly resolved signals, indicating the presence of two invertomers at nitrogen. $^1$H NMR (200 MHz): $\delta$ 0.07 (6H, s, $^t$Bu$Me_2$Si), 0.90 (9H, s, $^t$*Bu*Me$_2$Si), 2.40 (1H, m, *ring* H), 2.58 (1H, br m, *ring* H), 3.72 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 3.97 (2H, s, C$H_2$O), 4.01 (1H, d, $J$=14.0 Hz, C$H_2$Ph), 7.22–7.39 (5H, m, aromatic). MS, *m/z*: 345 (1, $M^+$), 330 (1), 288 (33), 276 (1), 241 (1), 200 (2), 168 (1), 144 (4), 91 (100), 77 (12), 65 (6%). Anal. Calcd for $C_{17}H_{26}F_3NOSi$: C, 59.10; H, 7.59; N, 4.05. Found: C, 59.23; H, 7.81; N, 4.23.

**4.3.7. *cis*-1-Benzyl-2,3-bis-(*tert*-butyldimethylsilyloxymethyl)aziridine (*cis*-3f).** Aziridine *cis*-**8**[3] (886 mg, 2.67 mmol) was dissolved in anhydrous acetonitrile (22 mL). Potassium carbonate (1.11 g, 8.01 mmol) and benzyl bromide (318 μL, 2.67 mmol) were added at rt to the stirred solution and the mixture was refluxed for 1 h. After addition of water (50 mL) and extraction with ethyl ether (3×30 mL), the combined phases were dried ($MgSO_4$) and concentrated in vacuo. Chromatography on silica gel (light petroleum/diisopropyl ether 95:5) gave *N*-benzylaziridine *cis*-**3f** as a light yellow oil (912 mg, 81% yield). $^1$H NMR (200 MHz): $\delta$ 0.08 (2×6H, s, $^t$Bu$Me_2$Si), 0.93 (2×9H, s, *Bu*$^t$Me$_2$Si), 1.83–1.93 (2×1H, m, C$H$CH$_2$O), 3.57 (2H, s, PhC$H_2$), 3.66–3.76 (2×2H, m, C$H_2$O), 7.26–7.44 (5H, m, aromatic). MS, *m/z*: 421 (7, $M^+$), 364 (51), 276 (30), 206 (99), 147 (13), 115 (11), 91 (100), 73 (62%). Anal. Calcd for $C_{23}H_{43}NO_2Si_2$: C, 65.50; H, 10.28; N, 3.32. Found: C, 65.71; H, 10.40; N, 3.18.

**4.3.8. *cis*-2-Acetoxymethyl-1-benzyl-3-methylaziridine (*cis*-4b).** Aziridine *cis*-**2b** (200 mg, 1.13 mmol) was dissolved in anhydrous dichloromethane (20 mL) and DCC (279 mg, 1.35 mmol), acetic acid (71 μL, 1.2 mmol) and few crystals of DMAP were added and the mixture was stirred at rt for 3 h. DCU was removed by filtration, the filtrate was concentrated under reduced pressure and purified by chromatography (ethyl ether/light petroleum 70:30) to give *cis*-**4b** as a pale yellow oil (232 mg, 94% yield). $^1$H NMR (200 MHz): $\delta$ 1.25 (3H, d, $J$=5.5 Hz, C$H_3$CH), 1.69–1.82 (1H, m, CH$_3$C$H$), 1.83–1.91 (1H, m, C$H$CH$_2$OAc), 2.01 (3H, s, OCOC$H_3$), 3.45 (1H, d, $J$=13.5 Hz, NC$H_2$Ph), 3.65 (1H, d, $J$=13.5 Hz, NC$H_2$Ph), 4.07 (1H, dd, $J$=11.5, 7.0 Hz, C$H_2$OAc), 4.18 (1H, dd, $J$=11.5, 5.5 Hz, C$H_2$OAc), 7.27–7.38 (5H, m, aromatic). MS, *m/z*: 218 (2, $[M-1]^+$), 160 (12), 128 (13), 91 (65), 86 (100), 77 (3), 65 (14%). Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.05; H, 7.93; N, 6.58.

**4.3.9. *cis*-2-Acetoxymethyl-1-benzyl-3-phenylaziridine (*cis*-4d).** DCC (160 mg, 0.78 mmol), acetic acid (40 μL, 0.70 mmol) and few crystals of DMAP were added to a solution of aziridine *cis*-**2d** (154 mg, 0.64 mmol) in anhydrous dichloromethane (11 mL) and the mixture was stirred at rt for 3 h. DCU was filtered off, the filtrate was concentrated in vacuo and purified by chromatography (ethyl ether/light petroleum 70:30) to give *cis*-**4d** as a pale yellow oil (179 mg, 99% yield). $^1$H NMR (200 MHz): $\delta$ 1.95 (3H, s, COC$H_3$), 2.26 (1H, ddd, $J$=7.5, 6.5, 5.0 Hz, C$H$CH$_2$OAc), 2.93 (1H, d, $J$=6.5 Hz, PhC$H$), 3.69 (1H, d, $J$=13.5 Hz, NC$H_2$Ph), 3.77 (1H, dd, $J$=12.0, 7.5 Hz, C$H_2$OAc), 3.80 (1H, d, $J$=13.5 Hz, NC$H_2$Ph), 3.96 (1H, dd, $J$=12.0, 5.0 Hz, C$H_2$OAc), 7.22–7.49 (10H, m, aromatic). MS, *m/z*: 222 (2, $[M-59]^+$), 190 (66), 148 (92), 130 (13), 120 (23), 91 (100), 77 (11), 65 (19), 43 (57%). Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.69; H, 6.96; N, 5.11.

**4.3.10. *cis*-2-Aminomethyl-1-benzyl-3-phenylaziridine (*cis*-5d).** A stirred solution of aziridine *cis*-**1d** (400 mg, 1.50 mmol) in aqueous ammonia (40 mL) was refluxed for 6 h. After removal of the solvent, the crude residue was chromatographed (ethyl acetate/ethyl ether 80:20) affording *cis*-1-benzyl-2-carbamoyl-3-phenylaziridine as a white solid (176 mg, 47% yield). By close analogy with reduction of aziridine[6] **1**, the amide was reduced with $LiAlH_4$ in THF at −10°C to the corresponding amino derivative. After chromatography (ethyl acetate/ethyl ether 80:20), *cis*-**5d** was recovered as a sticky yellow liquid in 49% yield.

***cis*-1-Benzyl-2-carbamoyl-3-phenylaziridine.** $^1$H NMR (200 MHz): $\delta$ 2.63 (1H, d, $J$=7.0 Hz, C$H$CO), 3.20 (1H, d, $J$=7.0 Hz, PhC$H$), 4.43 (1H, d, $J$=13.0 Hz, NC$H_2$Ph), 4.51 (1H, d, $J$=13.0 Hz, NC$H_2$Ph), 5.14 (1H, br, CON$H_2$), 6.09 (1H, br, CON$H_2$), 7.20–7.45 (10H, m, aromatic). MS, *m/z*: 252 (2, $M^+$), 251 (6), 208 (1), 207 (1), 175 (45), 161 (32), 120 (8), 118 (9), 106 (6), 104 (10), 91 (100), 77 (9), 65 (12), 51 (7%).

*cis*-**5d.** $^1$H NMR (200 MHz): $\delta$ 1.62 (2H, br, CH$_2$N$H_2$), 2.23 (1H, m, C$H$CH$_2$), 2.94 (1H, d, $J$=6.5 Hz, PhC$H$), 3.34 (1H, dd, $J$=7.0, 11.5 Hz, CHC$H_2$NH$_2$), 3.50 (1H, dd, $J$=6.0, 11.5 Hz, CHC$H_2$NH$_2$), 3.70 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 3.80 (1H, d, $J$=13.5 Hz, C$H_2$Ph), 7.23–7.47 (10H, m, aromatic). MS, *m/z*: 239 (1, $[M+1]^+$), 161 (100), 147 (14), 105 (43), 91 (96), 77 (8%). Anal. Calcd for $C_{16}H_{18}N_2$: C, 80.63; H, 7.61; N, 11.75. Found: C, 80.33; H, 7.86; N, 11.48.

**4.3.11. *cis*-1-Benzyl-2-formyl-3-phenylaziridine (*cis*-6d).** A 20% DIBAL-H solution in hexane (1.4 mL, 1.97 mmol) was slowly added dropwise through a dropping funnel to a stirred solution of aziridine *cis*-**1d** (250 mg, 0.94 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at −78°C, under nitrogen flow. After 15 min, NaF (0.83 g, 19.7 mmol) and $H_2O$ (0.6 mL) were added and the reaction mixture allowed to reach rt. The white inorganic precipitate was filtered off and washed with ethyl ether. The filtrate was dried ($MgSO_4$) and the solvent evaporated under reduced pressure. The crude residue was chromatographed on $SiO_2$ (light petroleum/ethyl ether 90:10) to afford *cis*-**6d** as a pale yellow liquid in 52% yield, as well as *cis*-**2d** in trace amounts.

*cis*-**6d.** $^1$H NMR (200 MHz): $\delta$ 2.49 (1H, t, $J$=6.5 Hz, C$H$CHO), 3.28 (1H, d, $J$=6.5 Hz, PhC$H$), 3.74 (1H, d,

$J$=13.5 Hz, NC$H_2$), 3.94 (1H, d, $J$=13.5 Hz, NC$H_2$), 7.27–7.48 (10H, m, aromatic), 8.97 (1H, d, $J$=6.5 Hz, C$H$O). MS, $m/z$: 195 (27, $[M-42]^+$), 194 (27), 178 (1), 152 (2), 139 (1), 117 (10), 104 (5), 91 (100), 77 (9), 65 (21%). Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.83; H, 6.51; N, 5.75.

**4.3.12. *cis*- and *trans*-2-Acetyl-1-benzyl-3-phenylaziridine (7d).** 3,4-Dibromo-4-phenylbutan-2-one (5 g, 16.3 mmol), obtained by bromination of commercially available 4-phenyl-3-buten-2-one in $CCl_4$ at rt, was dissolved in DMF (35 mL) and slowly added at 0°C to a stirred solution of benzylamine (6.25 mL, 53.1 mmol) in DMF (15 mL). The reaction mixture was stirred for 30 min, leaving to warm to rt. After rotary evaporation of the solvent, the residue was diluted with water (125 mL) and extracted with petroleum ether (5×50 mL). The combined organic phases were dried ($MgSO_4$) and concentrated to give a crude oil which was chromatographed on $SiO_2$ (light petroleum/ethyl ether 80:20) to afford aziridine *cis*-**7d** (1.11 g, reddish-yellow oil) and aziridine *trans*-**7d** (1.33 g, dark yellow oil) in 61% total yield. For *trans*-**7d** $^1$H NMR spectroscopy showed broad and poorly resolved signals, indicating the presence of two invertomers at nitrogen.

*cis*-**7d.** $^1$H NMR (200 MHz): $\delta$ 1.75 (3H, s, COC$H_3$), 2.67 (1H, d, $J$=7.0 Hz, C$H$COMe), 3.42 (1H, d, $J$=7.0 Hz, PhC$H$), 3.74 (1H, d, $J$=13.5 Hz, NC$H_2$Ph), 3.84 (1H, d, $J$=13.5 Hz, NC$H_2$Ph), 7.22-7.49 (10H, m, aromatic). MS, $m/z$: 251 (5, $M^+$), 223 (18), 208 (1), 174 (1), 160 (1), 132 (1), 118 (5), 104 (100), 91 (53), 78 (5), 65 (9%). Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.48; H, 6.95; N, 5.36.

*trans*-**7d.** $^1$H NMR (200 MHz): $\delta$ 2.25 (3H, s, COC$H_3$), 3.01 (1H, br, C$H$COMe), 3.42 (1H, br, PhC$H$), 3.99 (1H, br d, $J$=13.5 Hz, NC$H_2$Ph), 4.28 (1H, br d, $J$=13.5 Hz, NC$H_2$Ph), 7.25–7.35 (10H, m, aromatic). MS, $m/z$: 251 (6, $M^+$), 223 (26), 118 (5), 104 (100), 91 (61), 78 (8), 65 (9%). Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.51; H, 7.03; N, 5.29.

**4.3.13. *cis*-2-Methoxycarbonyl-3-phenylaziridine (*cis*-9)[4].** Gaseous ammonia (3.52 g, 207 mmol) was bubbled into anhydrous acetonitrile (150 mL) cooled at −10°C in a four-necked round bottom flask, until the desired weight was reached. A solution of methyl 2,3-dibromo-3-phenylpropanoate (7.5 g, 24 mmol) in $CH_3CN$ (45 mL) was then added dropwise under vigorous magnetic stirring, keeping the temperature at −10°C. The mixture was then left to react in the dark at rt and after 14 days triethylamine (3.25 mL, 1 mol) was added. After a further 6 days the precipitate was removed by filtration and the filtrate concentrated in vacuo. The crude residue was purified by chromatography on silica gel (light petroleum/ethyl ether 60:40) to afford *trans*-2-methoxycarbonyl-3-phenylaziridine **9** (1.949 g), as a light yellow oil, and *cis*-**9** (0.890 g) as white crystals (mp 71–73°C), in 70% overall yield.

*cis*-**9.** $^1$H NMR (200 MHz) $\delta$ 1.48 (1H, br, N$H$), 3.06 (1H, d, $J$=6.5 Hz, C$H$COOMe), 3.52 (1H, d, $J$=6.5 Hz, PhC$H$), 3.55 (3H, s, COOC$H_3$), 7.25–7.45 (5H, m, aromatic). MS, $m/z$: 177 (3, $M^+$), 176 (2) 162 (9), 146 (19), 117 (100), 104 (3), 90 (36), 77 (5), 65 (6%). Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.51; H, 6.45; N, 7.78.

*trans*-**9.** $^1$H NMR (200 MHz) $\delta$ 1.96 (1H, br, N$H$), 2.63 (1H, d, $J$=2.0 Hz, C$H$COOMe), 3.30 (1H, d, $J$=2.0 Hz, PhC$H$), 3.83 (3H, s, COOC$H_3$), 7.25–7.46 (5H, m, aromatic). MS, $m/z$: 177 (1, $M^+$), 176 (2), 162 (46), 118 (71), 117 (9), 104 (13), 91 (100), 77 (6). 74 (18), 65 (8%). Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.92; H, 6.47; N, 8.08.

**4.3.14. *cis*-2-Hydroxymethyl-3-phenylaziridine (*cis*-10).** Following the general procedure described for aziridines **2**, reduction of *cis*-**9** at −10°C gave *cis*-**10** (ethyl acetate/light petroleum 70:30) as a white solid, mp 92–94°C (68% yield); $^1$H NMR (200 MHz): $\delta$ 1.74 (2H, br s, O$H$ and N$H$), 2.69 (1H, m, C$H$CH$_2$OH), 3.29 (1H, dd, $J$=7.0, 12.0 Hz, C$H_2$OH), 3.47 (1H, d, $J$=6.5 Hz, PhC$H$), 3.49 (1H, dd, $J$=5.5, 12.0 Hz, C$H_2$OH), 7.24–7.43 (5H, m, aromatic). MS, $m/z$: 149 (3, $[M+1]^+$), 148 (13), 130 (60), 118 (44), 105 (56), 104 (100), 91 (42), 77 (35), 65 (17%). Anal. Calcd for $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.30; H, 7.49; N, 9.43.

**4.3.15. *cis*-2-(*tert*-Butyldimethylsilyloxymethyl)-3-phenylaziridine (*cis*-11).** Following the above described protocol for aziridines **3**, protection of hydroxymethylaziridine **10** gave *cis*-**11** (ethyl acetate/light petroleum 50:50) as a pale yellow liquid (97% yield); $^1$H NMR (200 MHz): $\delta$ −0.11 (3H, s, $^t$Bu$Me_2$Si), −0.09 (3H, s, $^t$Bu$Me_2$Si), 0.84 (9H, s, $^t$*Bu*Me$_2$Si), 2.58–2.63 (1H, q, $J$=6.5 Hz, C$H$CH$_2$O), 3.25 (1H, dd, $J$=6.5, 10.5 Hz, C$H_2$O) 3.39 (1H, d, $J$=6.5 Hz, PhC$H$), 3.57 (1H, dd, $J$=5.5, 10.5 Hz, C$H_2$O), 7.21–7.43 (5H, m, aromatic). MS, $m/z$: 263 (1, $M^+$), 248 (2), 206 (62), 176 (33), 131 (69), 104 (100), 91 (18), 75 (23%). Anal. Calcd for $C_{15}H_{25}NOSi$: C, 68.38; H, 9.56; N, 5.32. Found: C, 68.25; H, 9.67; N, 5.44.

**4.3.16. *cis*-1-Acetyl-2-(*tert*-butyldimethylsilyloxymethyl)-3-phenylaziridine (*cis*-12).** Triethylamine (1.22 mL, 8.8 mmol) and a solution of acetyl chloride (46 μL, 0.65 mmol) in $CH_2Cl_2$ (10 mL) were added sequentially to a solution of aziridine *cis*-**11** (150 mg, 0.57 mmol) in $CH_2Cl_2$ (10 mL) cooled at −10°C. After 30 min at rt, the reaction mixture was diluted with $CH_2Cl_2$, washed with water (2×25 mL) and aqueous $NaHCO_3$ (2×25 mL). The organic phase was dried ($MgSO_4$) and rotary evaporated. After chromatography (light petroleum/ethyl ether 70:30) *cis*-**12** was obtained as a pale yellow liquid (150 mg, 85% yield). $^1$H NMR (200 MHz): $\delta$ −0.07 (3H, s, $^t$Bu$Me_2$Si), −0.11 (3H, s, $^t$Bu$Me_2$Si), 0.85 (9H, s, $^t$*Bu*Me$_2$Si), 2.26 (3H, s, COC$H_3$), 2.97 (1H, q, $J$=6.0 Hz, C$H$CH$_2$O), 3.34 (1H, dd, $J$=6.0, 11.0 Hz, C$H_2$O), 3.60 (1H, dd, $J$=6.0, 11.0 Hz, C$H_2$O), 3.77 (1H, d, $J$=6.0 Hz, PhC$H$), 7.29–7.38 (5H, m, aromatic). MS, $m/z$: 305 (1, $M^+$), 262 (24), 248 (76), 218 (72), 206 (100), 177 (14), 144 (42), 131 (49), 115 (26), 104 (41), 91 (42), 75 (34), 73 (98%). Anal. Calcd for $C_{17}H_{27}NO_2Si$: C, 66.84; H, 8.91; N, 4.59. Found: C, 66.71; H, 9.05; N, 4.72.

**4.3.17. *cis*-2-(*tert*-Butyldimethylsilyloxymethyl)-1-ethoxycarbonylmethyl-3-phenylaziridine (*cis*-13).** Aziridine *cis*-**11** (250 mg, 0.95 mmol) and ethyl bromoacetate

(164 μL, 1.42 mmol) were dissolved in anhydrous acetonitrile (15.2 mL) and potassium carbonate (394 mg, 2.85 mmol) was added. The mixture was refluxed for 7 h, cooled to rt and diluted with water (50 mL). The solution was extracted with ethyl ether (3×50 mL) and the combined organic phases were dried ($MgSO_4$) and rotary evaporated. After chromatography (light petroleum/ethyl ether 90:10) *cis*-**13** was obtained as a pale yellow liquid (174 mg, 52% yield). $^1$H NMR (200 MHz): δ −0.14 (3H, s, $^t$Bu*Me*$_2$Si), −0.11 (3H, s, $^t$Bu*Me*$_2$Si), 0.83 (9H, s, $^t$*Bu*Me$_2$Si), 1.29 (3H, t, *J*=7.0 Hz, COOCH$_2$C*H*$_3$), 2.09 (1H, m, C*H*CH$_2$O), 2.83 (1H, d, *J*=6.5 Hz, PhC*H*), 3.22 (1H, dd, *J*=7.5, 11.0 Hz, CHC*H*$_2$O), 3.24 (1H, d, *J*=16.0 Hz, C*H*$_2$COOEt), 3.49 (1H, d, *J*=16.0 Hz, C*H*$_2$COOEt), 3.75 (1H, dd, *J*=5.0, 11.0 Hz, CHC*H*$_2$O), 4.24 (2H, q, *J*=7.0 Hz, COOC*H*$_2$CH$_3$), 7.24–7.46 (5H, m, aromatic). MS, *m*/*z*: 349 (51, $M^+$), 292 (62), 276 (68), 262 (100), 234 (50), 206 (57), 204 (97), 144 (48), 115 (31), 101 (41), 91 (56), 73 (92%). Anal. Calcd for $C_{19}H_{31}NO_3Si$: C, 65.29; H, 8.94; N, 4.01. Found: C, 65.20; H, 9.10; N, 4.13.

### 4.4. General procedure for the dicobalt octacarbonyl-catalyzed carbonylation of aziridines

The aziridine (1 mmol) was dissolved in freshly distilled and oxygen-free anhydrous DME (10 mL) in a stainless steel autoclave, equipped with a glass liner and a stirring bar, and the metal catalyst $Co_2(CO)_8$ (1/12 mmol) was added. After purging with CO, the autoclave was charged with 500 psi of carbon monoxide and placed in an oil bath at 100°C for 14 h. The work-up of the reaction mixture was carried out as previously reported,[1] giving a crude residue which was purified by chromatography on silica gel, using the eluent indicated below [in square brackets].

**4.4.1. 1-Benzyl-4-(*tert*-butyldimethylsilyloxymethyl)-azetidin-2-one (14a).** From aziridine **3a**, β-lactam **14a** [light petroleum/ethyl ether 50:50] was obtained in 40% yield as a dark yellow liquid; $^1$H NMR (200 MHz): δ 0.07 (6H, s, $^t$Bu*Me*$_2$Si), 0.92 (9H, s, $^t$*Bu*Me$_2$Si), 2.73 (1H, dd, *J*=1.5, 14.5 Hz, ring CH$_2$), 2.94 (1H, dd, *J*=5.0, 14.5 Hz, ring CH$_2$), 3.58–3.79 (3H, m, C*H*CH$_2$O and CHC*H*$_2$O), 4.18 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 4.71 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 7.26–7.42 (5H, m, aromatic). MS, *m*/*z*: 305 (1, $M^+$), 304 (1), 290 (1), 262 (1), 249 (1), 248 (4), 207 (17), 206 (100), 132 (2), 115 (3), 91 (53), 73 (7), 59 (6%). Anal. Calcd for $C_{17}H_{27}NO_2Si$: C, 66.84; H, 8.91; N, 4.59. Found: C, 67.13; H, 9.12; N, 4.67.

**4.4.2. *trans*-1-Benzyl-4-(*tert*-butyldimethylsilyloxymethyl)-3-ethylazetidin-2-one (*trans*-14c) and *trans*-1-benzyl-3-(*tert*-butyldimethylsilyloxymethyl)-4-ethylazetidin-2-one (*trans*-15c).** From aziridine *cis*-**3c**, β-lactams *trans*-**14c** and *trans*-**15c** (83:17) were isolated [light petroleum/ethyl ether 70:30] in 98% overall yield, both as a light yellow oil.

*trans*-**14c.** $^1$H NMR (400 MHz): δ 0.04 (6H, s, $^t$Bu*Me*$_2$Si), 0.89 (9H, s, $^t$*Bu*Me$_2$Si), 0.97 (3H, t, *J*=7.5 Hz, C*H*$_3$CH$_2$), 1.60 (1H, ddq, *J*=9.0, 14.0, 7.5 Hz, CH$_3$C*H*$_2$), 1.79 (1H, ddq, *J*=5.5, 14.0, 7.5 Hz, CH$_3$C*H*$_2$), 2.84 (1H, dddd, *J*=0.5, 2.0, 5.5, 9.0 Hz, CH$_3$CH$_2$C*H*), 3.24 (1H, ddd, *J*=2.0, 4.5, 5.5 Hz, C*H*CH$_2$O), 3.65 (1H, dd, *J*=5.5, 11.0 Hz, C*H*$_2$O), 3.69 (1H, dd, *J*=4.5, 11.0 Hz, C*H*$_2$O), 4.09 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 4.70 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 7.25–7.36 (5H, m, aromatic). $^{13}$C NMR: δ −4.86 ($^t$Bu*Me*$_2$Si), −4.84 ($^t$Bu*Me*$_2$Si), 12.3 (*C*H$_3$CH$_2$), 18.9 (Me$_3$*C*Me$_2$Si), 21.9 (CH$_3$*C*H$_2$), 26.5 (*Me*$_3$CMe$_2$Si), 45.5 (*C*H$_2$Ph), 54.5 (CH$_3$CH$_2$*C*H), 58.8 (*C*HCH$_2$O), 64.4 (*C*H$_2$O), 128.2, 128.9, 129.3, 137.2, 170.8 (carbonyl). MS, *m*/*z*: 333 (1, $M^+$), 332 (1), 318 (1), 305 (1), 288 (1), 276 (3), 248 (2), 207 (15), 206 (100), 188 (1), 143 (17), 91 (46), 75 (18), 73 (8%). Anal. Calcd for $C_{19}H_{31}NO_2Si$: C, 68.42; H, 9.37; N, 4.20. Found: C, 68.36; H, 9.44; N, 4.31.

*trans*-**15c.** $^1$H NMR (400 MHz): δ 0.06 (6H, s, $^t$Bu*Me*$_2$Si), 0.87 (3H, t, *J*=7.5 Hz, CH$_2$C*H*$_3$), 0.88 (9H, s, $^t$*Bu*Me$_2$Si), 1.34–1.46 (1H, m, C*H*$_2$CH$_3$), 1.66–1.84 (1H, m, C*H*$_2$CH$_3$), 2.92 (1H, dddd, *J*=0.5, 2.0, 3.5, 6.0 Hz, OCH$_2$C*H*), 3.42 (1H, ddd, *J*=2.0, 4.0, 9.0 Hz, C*H*CH$_2$CH$_3$), 3.87 (1H, dd, *J*=3.5, 11.0 Hz, OC*H*$_2$), 3.91 (1H, dd, *J*=6.0, 11.0 Hz, OC*H*$_2$), 4.10 (1H, d, *J*=15.5 Hz, C*H*$_2$Ph), 4.65 (1H, d, *J*=15.5 Hz, C*H*$_2$Ph), 7.25–7.35 (5H, m, aromatic). $^{13}$C NMR: δ −4.8 ($^t$Bu*Me*$_2$Si), −4.7 ($^t$Bu*Me*$_2$Si), 10.3 (CH$_2$*C*H$_3$), 19.0 (Me$_3$*C*Me$_2$Si), 25.7 (*C*H$_2$CH$_3$), 26.5 (*Me*$_3$CMe$_2$Si), 44.4 (*C*H$_2$Ph), 57.2 (*C*HCH$_2$CH$_3$), 58.5 (OCH$_2$*C*H), 60.6 (O*C*H$_2$), 128.2, 128.8, 129.3, 136.8, 168.4 (carbonyl). MS, *m*/*z*: 334 (1, $[M+1]^+$), 333 (1), 332 (1), 318 (3), 304 (1), 277 (19), 276 (100), 246 (3), 219 (1), 184 (4), 143 (5), 129 (1), 91 (38), 75 (13), 73 (4%). Anal. Calcd for $C_{19}H_{31}NO_2Si$: C, 68.42; H, 9.37; N, 4.20. Found: C, 68.21; H, 9.63; N, 3.94.

**4.4.3. *cis*-1-Benzyl-4-(*tert*-butyldimethylsilyloxymethyl)-3-ethylazetidin-2-one (*cis*-14c) and *cis*-1-benzyl-3-(*tert*-butyldimethylsilyloxymethyl)-4-ethylazetidin-2-one (*cis*-15c).** From aziridine *trans*-**3c**, β-lactams *cis*-**14c** and *cis*-**15c** (73:27) were isolated [light petroleum/ethyl ether 70:30] as yellow oils in 60% overall yield.

*cis*-**14c.** $^1$H NMR (200 MHz): δ 0.054 (3H, s, $^t$Bu*Me*$_2$Si), 0.056 (3H, s, $^t$Bu*Me*$_2$Si), 0.91 (9H, s, $^t$*Bu*Me$_2$Si), 1.09 (3H, t, *J*=7.5 Hz, C*H*$_3$CH$_2$), 1.57–1.89 (2H, m, CH$_3$C*H*$_2$), 3.11 (1H, dt, *J*=5.0, 8.0 Hz, CH$_3$CH$_2$C*H*), 3.63 (1H, dt, *J*=5.0, 5.5 Hz, C*H*CH$_2$O), 3.73 (1H, dd, *J*=5.5, 10.5 Hz, CHC*H*$_2$O), 3.79 (1H, dd, *J*=5.5, 10.5 Hz, CHC*H*$_2$O), 4.19 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 4.70 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 7.25–7.39 (5H, m, aromatic). MS, *m*/*z*: 333 (1, $M^+$), 248 (4), 206 (100), 143 (17), 91 (67), 75 (31%). Anal. Calcd for $C_{19}H_{31}NO_2Si$: C, 68.42; H, 9.37; N, 4.20. Found: C, 68.26; H, 9.58; N, 4.02.

*cis*-**15c.** $^1$H NMR (400 MHz): δ 0.06 (6H, s, $^t$Bu*Me*$_2$Si), 0.87 (3H, t, *J*=7.5 Hz, CH$_2$C*H*$_3$), 0.89 (9H, s, $^t$*Bu*Me$_2$Si), 1.32–1.43 (1H, m, C*H*$_2$CH$_3$), 1.68–1.83 (1H, m, C*H*$_2$CH$_3$), 2.94 (1H, dt, *J*=3.5, 5.5 Hz, OCH$_2$C*H*), 3.40 (1H, ddd, *J*=4.0, 5.5, 9.0 Hz, C*H*CH$_2$CH$_3$), 3.85 (1H, dd, *J*=3.5, 11.0 Hz, OC*H*$_2$), 3.90 (1H, dd, *J*=5.5, 11.0 Hz, OC*H*$_2$), 4.11 (1H, d, *J*=15.5 Hz, C*H*$_2$Ph), 4.63 (1H, d, *J*=15.5 Hz, C*H*$_2$Ph), 7.22–7.40 (5H, m, aromatic). MS, *m*/*z*: 318 (3, $[M-15]^+$), 276 (100), 246 (3), 184 (7), 143 (7), 129 (3), 91 (98), 75 (40%). Anal. Calcd for $C_{19}H_{31}NO_2Si$: C, 68.42; H, 9.37; N, 4.20. Found: C, 68.20; H, 9.61; N, 3.95.

**4.4.4. *trans*-1-Benzyl-4-(*tert*-butyldimethylsilyloxymethyl)-3-phenylazetidin-2-one (*trans*-14d).** From aziridine *cis*-**3d**, β-lactam *trans*-**14d** [light petroleum/ethyl ether 80:20] was

obtained as a clear yellow liquid in 95% yield; $^1$H NMR (200 MHz): $\delta$ 0.11 (6H, s, $^t$Bu*Me*$_2$Si), 0.95 (9H, s, $^t$*Bu*Me$_2$Si), 3.63 (1H, dt, *J*=2.5, 4.5 Hz, C*H*CH$_2$O), 3.81 (1H, dd, *J*=4.5, 11.0 Hz, CHC*H*$_2$O), 3.88 (1H, dd, *J*=4.0, 11.0 Hz, CHC*H*$_2$O), 4.18 (1H, d, *J*=2.5 Hz, PhC*H*), 4.23 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 4.84 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 7.24–7.39 (10H, m, aromatic). $^{13}$C NMR: $\delta$ −4.81 ($^t$Bu*Me*$_2$Si), −4.76 ($^t$Bu*Me*$_2$Si), 18.9 (Me$_3$*C*Me$_2$Si), 26.5 (*Me*$_3$CMe$_2$Si), 45.8 (*C*H$_2$Ph), 57.4 (Ph*C*H), 61.6 (*C*HCH$_2$O), 63.4 (CH*C*H$_2$O), 128.1, 128.2, 128.4, 129.0 129.5, 136.1, 136.9, 168.7 (carbonyl). MS, *m*/*z*: 381 (5, M$^+$), 366 (1), 324 (6), 248 (28), 206 (23), 191 (100), 117 (43), 91 (40), 73 (12), 59 (3%). Anal. Calcd for $C_{23}H_{31}NO_2Si$: C, 72.39; H, 8.19; N, 3.67. Found: C, 72.16; H, 8.31; N, 3.85.

**4.4.5. *cis*-1-Benzyl-4-(*tert*-butyldimethylsilyloxymethyl)-3-phenylazetidin-2-one (*cis*-14d).** From aziridine *trans*-**3d**, β-lactam *cis*-**14d** [light petroleum/ethyl ether 80:20] was obtained as yellow sticky liquid in 40% yield; $^1$H NMR (200 MHz): $\delta$ 0.09 (6H, s, $^t$Bu*Me*$_2$Si), 0.91 (9H, s, $^t$*Bu*Me$_2$Si), 3.59 (1H, dt, *J*=5.5, 4.0 Hz, C*H*CH$_2$O), 3.83 (1H, dd, *J*=4.5, 11.0 Hz, CHC*H*$_2$O), 3.86 (1H, dd, *J*=4.0, 11.0 Hz, CHC*H*$_2$O), 4.21 (1H, d, *J*=5.5 Hz, PhC*H*), 4.23 (1H, d, *J*=15.5 Hz, C*H*$_2$Ph), 4.84 (1H, d, *J*=15.5 Hz, C*H*$_2$Ph), 7.25–7.45 (10H, m, aromatic). MS, *m*/*z*: 324 (50, [M−57]$^+$), 248 (9), 191 (100), 135 (33), 117 (20), 91 (56), 73 (29), 59 (10%). Anal. Calcd for $C_{23}H_{31}NO_2Si$: C, 72.39; H, 8.19; N, 3.67. Found: C, 72.11; H, 8.36; N, 3.90.

**4.4.6. *trans*-1-Benzyl-3,4-bis-(*tert*-butyldimethylsilyloxymethyl)azetidin-2-one (*trans*-14f).** From aziridine *cis*-**3f**, β-lactam *trans*-**14f** was obtained [light petroleum/ethyl ether 70:30] as a pale yellow oil in 90% yield; $^1$H NMR (200 MHz): $\delta$ 0.06 (2×3H, s, $^t$Bu*Me*$_2$Si), 0.08 (2×3H, s, $^t$Bu*Me*$_2$Si), 0.89 (9H, s, $^t$*Bu*Me$_2$Si), 0.91 (9H, s, $^t$*Bu*Me$_2$Si), 3.06–3.19 (1H, m, C*H*CHCH$_2$O), 3.62–3.81 (2H, m, CHC*H*$_2$O), 3.69 (1H, ddd, *J*=6.5, 5.0, 2.0 Hz, CHC*H*CH$_2$O), 3.86 (1H, dd, *J*=11.0, 3.5 Hz, CHC*H*$_2$O), 3.97 (1H, dd, *J*=11.0, 5.0 Hz, CHC*H*$_2$O), 4.15 (1H, d, *J*=15.5 Hz, C*H*$_2$Ph), 4.74 (1H, d, *J*=15.5 Hz, C*H*$_2$Ph), 7.27–7.34 (5H, m, aromatic). MS, *m*/*z*: 448 (1, [M−1]$^+$), 434 (3), 392 (100), 362 (1), 336 (1), 304 (1), 264 (1), 260 (4), 248 (3), 206 (57), 149 (2), 147 (16), 133 (3), 91 (46), 73 (19%). Anal. Calcd for $C_{24}H_{43}NO_3Si_2$: C, 64.09; H, 9.64; N, 3.11. Found: C, 63.88; H, 9.90; N, 3.38.

**4.4.7. *trans*-1-Benzyl-4-hydroxymethyl-3-phenylazetidin-2-one (16).** From aziridine *cis*-**2d**, β-lactam *trans*-**16** was obtained [ethyl ether 100%] as a white solid, mp 92–94°C, in 79% yield; $^1$H NMR (200 MHz): $\delta$ 1.62 (1H, br, O*H*), 3.67 (1H, dt, *J*=4.0, 2.5 Hz, C*H*CH$_2$OH), 3.80 (2H, m, C*H*$_2$OH), 4.26 (1H, d, *J*=2.5 Hz, PhC*H*), 4.49 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 4.62 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 7.20–7.45 (10H, m, aromatic); $^{13}$C NMR: $\delta$ 45.5, 56.5, 61.4, 61.9, 127.8, 127.9, 128.4, 128.8, 129.3, 129.4, 135.5, 136.5, 169.1. MS, *m*/*z*: 268 (100, [M+1]$^+$), 240 (2), 134 (67), 115 (9), 105 (20), 91 (88), 78 (17), 65 (14%). Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.22; H, 6.29; N, 5.12.

**4.4.8. *trans*-4-Acetoxymethyl-1-benzyl-3-phenylazetidin-2-one (17).** From aziridine *cis*-**4d**, β-lactam *trans*-**17** was obtained [ethyl ether/light petroleum 60:40] as a sticky yellow liquid in 86% yield; $^1$H NMR (200 MHz): $\delta$ 2.07 (3H, s, OCOC*H*$_3$), 3.73 (1H, ddd, *J*=5.0, 3.5, 2.5 Hz, C*H*CH$_2$O), 4.15 (1H, dd, *J*=12.0, 5.0 Hz, CHC*H*$_2$O), 4.20 (1H, d, *J*=2.5 Hz, PhC*H*), 4.28 (1H, d, *J*=5.0 Hz, C*H*$_2$Ph), 4.45 (1H, dd, *J*=12.0, 3.5 Hz, CHC*H*$_2$O), 4.77 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 7.23–7.45 (10H, m, aromatic); $^{13}$C NMR: $\delta$ 21.0, 45.6, 57.7, 58.6, 63.4, 127.7, 128.1, 128.3, 128.7, 129.29, 129.33, 134.9, 136.2, 167.9, 170.8. MS, *m*/*z*: 310 (1, [M+1]$^+$), 267 (1), 206 (1), 176 (100), 134 (65), 133 (50), 116 (38), 91 (76%). Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.56; H, 6.26; N, 4.46.

**4.4.9. *trans*-4-Aminomethyl-1-benzyl-3-phenylazetidin-2-one (18).** From aziridine *cis*-**5d**, β-lactam *trans*-**18** was obtained [ethyl acetate/light petroleum 60:40] as a pale yellow solid in 68% yield; $^1$H NMR (200 MHz): $\delta$ 1.96 (2H, br, CH$_2$N*H*$_2$), 3.65 (1H, dt, *J*=2.5, 3.5 Hz, C*H*CH$_2$), 3.74 (1H, dd, *J*=4.0, 12.0 Hz, C*H*$_2$NH$_2$), 3.84 (1H, dd, *J*=3.5, 12.0 Hz, C*H*$_2$NH$_2$), 4.27 (1H, d, *J*=2.5 Hz, PhC*H*), 4.44 (1H, d, *J*=15.0 Hz, NC*H*$_2$Ph), 4.65 (1H, d, *J*=15.0 Hz, NC*H*$_2$Ph), 7.24–7.46 (10H, m, aromatic). MS, *m*/*z*: 267 (1, [M+1]$^+$), 236 (5), 133 (22), 105 (13), 91 (100%). Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.38; H, 7.02; N, 10.78.

**4.4.10. *trans*-1-Benzyl-4-hydroxymethyl-3-methylazetidin-2-one (19).** From aziridine *cis*-**2b**, β-lactam *trans*-**19** was obtained [ethyl acetate 100%] as a sticky yellow liquid solidifying at 4°C in 84% yield; $^1$H NMR (200 MHz): $\delta$ 1.30 (3H, d, *J*=7.5 Hz, C*H*$_3$CH), 1.73 (1H, br, O*H*), 3.06 (1H, dq, *J*=2.0, 7.5 Hz, CH$_3$C*H*), 3.26 (1H, ddd, *J*=4.5, 3.5, 2.0 Hz, C*H*CH$_2$OH), 3.62 (1H, dd, *J*=12.0, 4.5 Hz, CHC*H*$_2$OH), 3.72 (1H, dd, *J*=12.0, 3.5 Hz, CHC*H*$_2$OH), 4.38 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 4.51 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 7.28–7.44 (5H, m, aromatic); $^{13}$C NMR: $\delta$ 13.0, 45.3, 46.7, 61.1, 62.0, 128.1, 128.6, 129.1, 129.2, 136.7, 171.6. MS, *m*/*z*: 205 (2, M$^+$), 133 (18), 132 (33), 118 (6), 105 (13), 91 (100), 72 (21), 65 (15), 57 (35%). Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.02; H, 7.28; N, 6.94.

**4.4.11. *trans*-4-Acetoxymethyl-1-benzyl-3-methylazetidin-2-one (20) and *trans*-3-acetoxymethyl-1-benzyl-4-methylazetidin-2-one (21).** From aziridine *cis*-**4b**, β-lactams *trans*-**20** and *trans*-**21** (86:14) were obtained [ethyl ether 100%] as a yellowish oily unresolvable mixture in 82% yield.

*trans*-**20.** $^1$H NMR (400 MHz): $\delta$ 1.31 (3H, d, *J*=7.5 Hz, C*H*$_3$CH), 2.02 (3H, s, OCOC*H*$_3$), 3.02 (1H, dq, *J*=2.0, 7.5 Hz, CH$_3$C*H*), 3.31 (1H, ddd, *J*=5.5, 3.5, 2.0 Hz, C*H*CH$_2$O), 4.00 (1H, dd, *J*=12.0, 5.5 Hz, CHC*H*$_2$O), 4.18 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 4.30 (1H, dd, *J*=12.0, 3.5 Hz, CHC*H*$_2$O), 4.63 (1H, d, *J*=15.0 Hz, C*H*$_2$Ph), 7.26–7.43 (5H, m, aromatic). MS, *m*/*z*: 219 (6, [M−28]$^+$), 205 (3), 192 (1), 187 (1), 174 (1), 160 (12), 133 (8), 132 (18), 114 (27), 105 (13), 104 (13), 91 (100), 72 (40%). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.72; H, 7.26; N, 5.85.

*trans*-**21.** $^1$H NMR (400 MHz): $\delta$ 1.31 (3H, d, *J*=7.5 Hz, CHC*H*$_3$), 2.02 (3H, s, OCOC*H*$_3$), 3.02 (1H, dq, *J*=2.0,

7.5 Hz, C*H*$CH_3$), 3.31 (1H, ddd, *J*=6.0, 3.5, 2.0 Hz, $OCH_2CH$), 4.03 (1H, d, *J*=15.0 Hz, C$H_2$Ph), 4.31 (1H, dd, *J*=12.0, 6.0 Hz, $OCH_2CH$), 4.39 (1H, dd, *J*=12.0, 3.5 Hz, $OCH_2CH$), 4.74 (1H, d, *J*=15.0 Hz, C$H_2$Ph), 7.26–7.43 (5H, m, aromatic). MS, *m*/*z*: 219 (1, $[M-28]^+$), 205 (1), 192 (1), 187 (1), 174 (1), 160 (10), 133 (10), 132 (25), 114 (88), 105 (15), 104 (14), 91 (100), 72 (62%). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.23; H, 6.81; N, 5.89.

**4.4.12. *trans*-4-Benzylamino-3-methyltetrahydrofuran-2-one (22).** From *trans*-aziridine **2b**, *trans*-lactone **22** was obtained [ethyl ether/ethyl acetate 50:50] as an amber sticky oil in 82% yield. $^1$H NMR (200 MHz): δ 1.33 (3H, d, *J*=7.0 Hz, $CH_3CH$), 1.61 (1H, br, N*H*$CH_2$), 2.47 (1H, quintet, *J*=7.5 Hz, $CH_3CH$), 3.31 (1H, dt, *J*=8.0, 7.0 Hz, C*H*NH), 3.86 (2H, d, *J*=2.5 Hz, $NHCH_2$), 3.90 (1H, dd, *J*=9.0, 7.0 Hz, $OCH_2$), 4.39 (1H, dd, *J*=9.0, 6.5 Hz, $OCH_2$), 7.26–7.43 (5H, m, aromatic). MS, *m*/*z*: 205 (25, $M^+$), 190 (1), 149 (24), 132 (11), 120 (17), 118 (4), 91 (100), 77 (4), 65 (13%). Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.11; H, 7.43; N, 6.90.

**4.4.13. *trans*-4-(*tert*-Butyldimethylsilyloxymethyl)-1-ethoxycarbonylmethyl-3-phenylazetidin-2-one (23).** From aziridine *cis*-**13**, β-lactam *trans*-**23** was obtained [light petroleum/ethyl ether 70:30] as a yellow sticky oil in 63% yield; $^1$H NMR (400 MHz): δ 0.10 (3H, s, $^t$Bu*Me*$_2$Si), 0.12 (3H, s, $^t$Bu*Me*$_2$Si), 0.93 (9H, s, $^t$*Bu*Me$_2$Si), 1.33 (3H, t, *J*=7.0 Hz, $COOCH_2CH_3$), 3.88 (1H, dd, *J*=11.5, 7.5 Hz, C$H_2$O), 3.92 (1H, d, *J*=18.0 Hz, C$H_2$COOEt), 3.97–4.03 (2H, m, C*H*$CH_2$O and $CHCH_2O$), 4.05 (1H, d, *J*=2.5 Hz, PhC*H*), 4.26 (2H, q, *J*=7.0 Hz, $COOCH_2CH_3$), 4.42 (1H, d, *J*=18.0 Hz, C$H_2$COOEt), 7.30–7.41 (5H, m, aromatic). $^{13}$C NMR: δ −5.1, 14.6, 18.5, 26.1, 30.1, 30.7, 42.9, 57.6, 61.9, 62.5, 64.1, 128.0, 128.2, 129.2, 135.2, 168.7, 168.8. MS, *m*/*z*: 377 (2, $M^+$), 320 (6), 304 (4), 248 (19), 244 (6), 202 (58), 191 (100), 117 (59), 115 (14), 75 (12), 73 (14%). Anal. Calcd for $C_{20}H_{31}NO_4Si$: C, 63.62; H, 8.28; N, 3.71. Found: C, 63.48; H, 8.07; N, 3.56.

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