The Origin of Chemical and Configurational Stability of Chiral Nonracemic *tert*-Butyl Aziridinecarboxylate Anions

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Professor Jean Normant on the occasion of his 65th birthday

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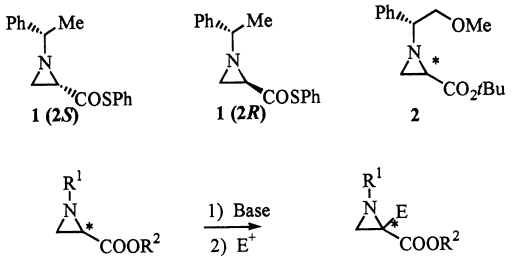
The origin of good chemical and configurational stability of aziridine ester anions derived from (*R*)-(–)-phenylglycinol has been investigated. Kinetic acidity seems to play an important role in the deprotonation step and chemical stability of the anionic species. Spectroscopic investigations showed that the good overall retention of configuration was governed by the directing effect of the nitrogen atom, which acts as a stereogenic centre in the alkylation step of the enolate intermediate.

Introduction

The preparation of chemically and configurationally stable three-membered ring anionic species is of particular interest for the efficient asymmetric elaboration of synthetically useful starting materials.[1] Since the pioneering works of Walborsky[2,3] and Boche[4] in the field of cyclopropane chemistry, it is known that cyclopropyl anions with an electron-withdrawing group can react as C−Li or delocalised carbanions. These two reactive species have been characterised by X-ray crystallography for cyclopropane anions with stabilising functional groups, and this shows that the nature of the functional groups can dramatically influence the geometry of the relative anionic species.[5] For cyclopropane ester anions, both C−Li,[6] planar[7] or pyramidal[8] enolate intermediates have been proposed to explain their reactivity.

The chemistry of aziridinyl ester anions was first investigated by Seebach and co-workers,[9,10] who reported that all attempts to generate such species led only to degradation and/or self-condensation. However, when the ester group was replaced with a thiol ester function, deprotonation and functionalisation of several aziridine thiol esters at very low temperature (−100 °C) could be obtained. Interestingly, retention of configuration was observed for compound **1(2*S*)**, and moderate *d.s.* (33−60%) was obtained when starting from its diastereomer **1(2*R*)** (Scheme 1).



Scheme 1

The authors first explained this apparent memory of chirality by the formation of a pyramidal enolate as a reactive species.[10] Another explanation was furnished several years later by Seebach in his review on the SRS principle (Self-Regeneration of Stereocenters), based on the chirality of the aziridine nitrogen atom.[11] We recently reported that aziridine esters **2** could be deprotonated and functionalised under milder conditions, with overall good to excellent retention of configuration.[12] In this article we disclose our full results in this field and our investigations on the origin of improved chemical and configurational stability of such species.

Results and Discussion

Aziridines **2**−**4** were prepared as 1:1 diastereomeric mixtures according to a reported procedure,[13] and each diastereomer could be separated by column chromatography (Scheme 2, Table 1).

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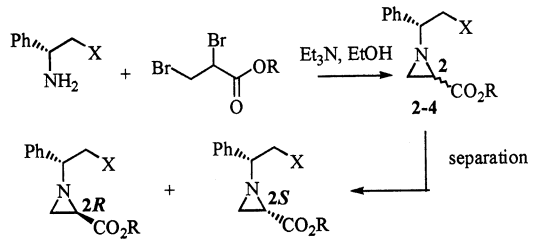


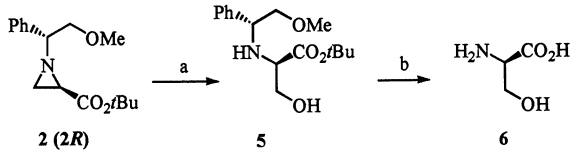
Scheme 2

Table 1. Preparation of Aziridines **2**–**4**

Compound	X	R	Yield [%][a]
2	OMe	*t*Bu	80
3	OMe	Et	94
4	H	*t*Bu	52

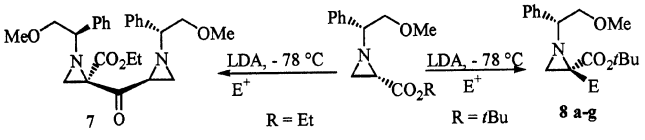
[a] Combined yield of diastereomers after chromatographic separation.

Absolute configuration of the newly created asymmetric centre was established by chemical correlation of compound **2(2*R*)** with D-serine (**6**) (Scheme 3) and assigned for other aziridines by comparison of NMR spectra.



Scheme 3. Reagents and conditions: a) 20% aq. $HClO_4$, 80 °C, 15 h, 48%; b) H_2, $Pd(OH)_2$, EtOH/H_2O (1:1), 100%

At first, deprotonation of compound **3(2*S*)** with LDA led only to self-condensation product **7**, as already observed in the cyclopropane series.[14] However, the *tert*-butyl ester **2(2*S*)** could be deprotonated by LDA in THF and reacted with various electrophiles at −78 °C, with or without DMPU (Scheme 4).



Scheme 4

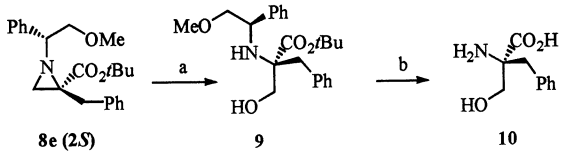
The use of other bases led only to starting material (NaH, LiHMDS), epimerised aziridine **2** (with KHMDS, *dr* = 80:20) or addition of the base to the carboxylic function (*t*BuLi) without deprotonation. Under optimised conditions (LDA, THF, −78 °C), functionalisation of aziridine **2(2*S*)** occurred with complete retention of configuration at the reactive centre (with benzaldehyde as electrophile, control of the second asymmetric centre was fairly poor) (Table 2).

Table 2. Functionalisation of Aziridine **2(2*S*)**

Compound	E^+	Yield [%][a] [no DMPU]	Yield [%][a] [with DMPU]	*dr* [%][b]
8a(2*R*)	$(CH_3)_3SiCl$	41	37	> 98:2
8b(2*S*)	CH_3I	47	59	> 98:2
8c(2*S*)	$CH_2{=}CHCH_2Br$	44	64	> 98:2
8d(2*S*)	$BrCH_2CO_2tBu$	–	54	> 98:2
8e(2*S*)	$ClCH_2Ph$	–	28	> 98:2
8f(2*R*)	cyclohexanone	21	–	> 98:2
8g(2*R*)	PhCHO	35	–	61:39

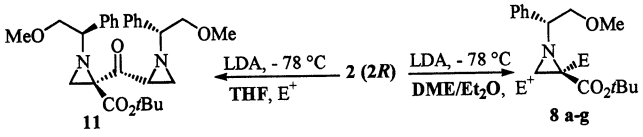
[a] Yield of isolated product. – [b] Determined by ^1H NMR spectroscopy of the crude reaction mixture.

The absolute configuration was established for compound **8e(2*S*)** by chemical correlation with (*S*)-α-benzylserine (**10**)[15] and assigned for other aziridines by comparison of ^1H and ^{13}C NMR spectra (Scheme 5).



Scheme 5. Reagents and conditions: a) 20% aq. $HClO_4$, 80 °C, 3 h, 31%; b) H_2, $Pd(OH)_2$, EtOH/H_2O (1:1), 100%

When performed on aziridine **2(2*R*)**, the same deprotonation conditions led only to self-condensation product **11**.[16] In contrast, in a 5:1 mixture of DME/Et_2O, this aziridine could be deprotonated and functionalised in a moderate yield (competitive self-condensation could not be completely avoided) but with good to excellent retention of configuration (Scheme 6 and Table 3).



Scheme 6

Table 3. Functionalisation of Aziridine **2(2*R*)**

Compound	E^+	Yield [%][a]	*dr* [%][b]
8a(2*S*)	$(CH_3)_3SiCl$	38[c]	89:11
8b(2*R*)	CH_3I	48	98:2
8c(2*R*)	$CH_2{=}CHCH_2Br$	49	94:6
8d(2*R*)	$BrCH_2CO_2tBu$	30	95:5

[a] Yield of isolated product. – [b] Determined by ^1H NMR spectroscopy of the crude reaction mixture. – [c] Diastereomers were not separated.

In the case of aziridine thiol esters **1**, Seebach and coworkers explained the excellent overall retention of configuration by the formation of a transient pyramidal enolate.[10] However, the hypothesis of a configurationally stable

C-lithiated intermediate, which has been characterised by Vedejs and co-workers for "non-stabilised" metallated aziridines,[17] cannot be ruled out, especially if one considers that aziridine ester anions bearing a potential chelating group (MeO) proved to be more stable than anions of compounds **1**.[18] We therefore decided to investigate the mechanism responsible for the good configurational and chemical stability in our system.

We first studied the role of the nitrogen lone pair. ^{1}H NMR spectra of compounds **2(2*S*)** and **2(2*R*)** showed the presence of a small amount (8%) of invertomers in [D$_6$]THF and this proportion remained unchanged at low temperature [−70 °C for **2(2*S*)** and −100 °C for **2(2*R*)**]. On the other hand, coalescence could be observed in [D$_6$]DMSO for both diastereomers around 333 K, and the free energy of inversion was calculated (about 16 kcal mol^{-1}). These results indicate that the nitrogen atom can be considered as a stereogenic centre, because of this high inversion energy barrier. The absolute configuration of the nitrogen atom for the major invertomers of both diastereomers was determined with $^1J_{H\text{-}C}$ coupling constants (Figure 1).[19] It appears that in both cases, the nitrogen lone pair is *anti* to the acidic proton.

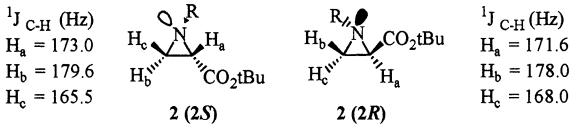


Figure 1. Relative configuration of the nitrogen atom

We then tried to characterise the reactive species. Low-temperature ^{1}H NMR experiments did not give significant results. However, low-temperature infrared experiments could be performed on deprotonated **2(2*S*)** (−65 °C, THF, same concentration as for alkylations). The IR spectra showed complete disappearance of the CO band ($\tilde{\nu}$ = 1739 cm^{-1}), and appearance of a new less intense band at 1710 cm^{-1}, this can be attributed to C=C vibration of an enolate.[20,21] Disappearance of a band at 1408 cm^{-1} (CH bending of the acidic proton) was also noticed. Similar results were obtained with compound **2(2*R*)** in a mixture of DME/Et$_2$O at −65 °C. All these results seem to indicate that the reactive species are enolates. The retention of configuration can be explained by an approach of electrophiles *anti* to the nitrogen lone pair.

We then investigated the origin of the improved chemical stability of the aziridine anions. Standard deprotonation conditions (LDA, THF, −78 °C) used with compound **4(2*S*)**, resulted in mainly starting material. This surprising result showed that the chelating methoxy group improves the kinetic acidity of aziridines, and therefore slows down the self-condensation rate.[22] A similar kinetic effect has already been observed by Vedejs and co-workers in the preparation of nonstabilised aziridine anions by a tin−lithium exchange.[18] For steric reasons, stabilisation of the transition state in the deprotonation step does not occur for diastereomer **2(2*R*)**, and an intermolecular stabilisation by DME is required. Finally, the difference in the chemical and configurational stability of the reactive species in the two diastereomeric series can be explained by the difference of stability between the diastereomeric enolates **12a** and **12b** (Figure 2).

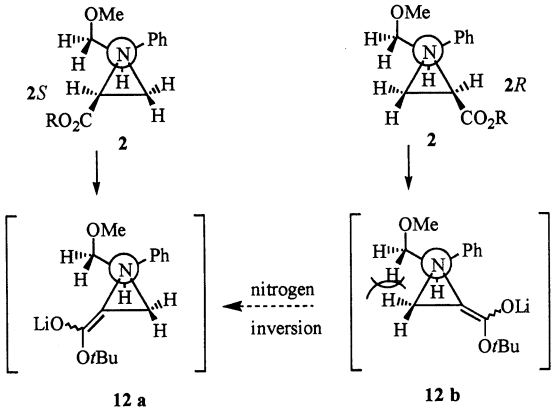


Figure 2. Relative stabilities of the enolates **12a** and **12b**

Steric hindrance between aziridines protons and methylenic protons of the chiral moiety probably destabilises enolate **12b**, and leads to an enhanced self-condensation rate (chemical instability) and epimerisation through nitrogen inversion (configurational instability).

Conclusion

We have shown that it is possible to generate and functionalise chemically and configurationally stable aziridine ester anions. The deprotonation rate is highly dependent on the kinetic acidity of the substrate, and this can be improved by the presence of a chelating group on the molecule or by the use of DME as a solvent. Several spectroscopic investigations proved that the reactive species is an enolate, and that the overall good retention of configuration was governed by the directing effect of the nitrogen atom, which acts as a stereogenic centre in the alkylation step.

Experimental Section

General Procedures: All reactions involving air-sensitive materials were carried out under argon. Sensitive liquids were transferred by a syringe. Product purification was performed by flash chromatography on silica gel (Merck, 230−400 mesh). THF was successively distilled from sodium benzophenone and LAH. DME was distilled from sodium benzophenone. − Routine infrared spectra (IR) were recorded neat with a Perkin−Elmer 1600 spectrophotometer. Low-temperature IR spectra were recorded with an FTIR Bruker IFS66 spectrometer driven by an Opus 2.2 program. A fluorine cell was mounted on a cryogenic device Graseby Specac equipped with a temperature reader (P/N 20120). Low temperature (−65 °C) was obtained with EtOH/dry ice in the cold finger. The main chamber of the Graseby Specac device was maintained under argon. − Optical rotations of $CHCl_3$ or H_2O solutions were measured at 20 °C with a Perkin−Elmer 141 automatic polarimeter. − ^{1}H NMR and

^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, with a Bruker AC 300 spectrometer. − Mass spectra were recorded in the chemical ionisation mode (NH_3) with an AEI MS-9 spectrometer. High-resolution mass spectra were obtained with a Kratos MS 80RF spectrometer.

General Procedure for the Preparation of Aziridines. − Preparation of Aziridines 2(2*R*) and 2(2*S*) is Typical: To a solution of *tert*-butyl 2,3-dibromopropionate (1.60 g, 5.56 mmol) in ethanol (100 mL) was added (*R*)-methoxyphenylglycinol (0.84 g, 5.56 mmol) at −20 °C. After stirring for 5 min, triethylamine (2.32 mL, 16.7 mmol) was added and the reaction mixture was stirred for 48 h. The solvent was then removed (evaporator), and the resulting mixture was diluted with diethyl ether. The solid triethylamine salts were filtered off and washed twice with ether. After removal of the solvent, the residue was purified by flash chromatography on silica gel (95:5 CH_2Cl_2/cyclohexane eluent) to give 1.22 g (80%) of **2** as a colourless oil [402 mg of diastereomer **(2*S*)**, 378 mg of mixture and 443 mg of diastereomer **(2*R*)**]. − $C_{16}H_{23}NO_3$ (277.4): calcd. C 69.29, H 8.36, N 5.05; found C 68.92, H 8.35, N 4.93.

Aziridine 2(2*S*): Analytical TLC on silica gel, 95:5 CH_2Cl_2/cyclohexane, R_f = 0.25. − $[\alpha]_D$ = −65 (c = 0.7, $CHCl_3$). − IR (neat): 2979, 2929 and 1738 cm^{-1}. − MS: 278 [M + 1]. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45−7.25 (m, 5 H), 3.70 (dd, J = 9.8, 7.7 Hz, 1 H), 3.61 (dd, J = 9.8, 4.8 Hz, 1 H), 3.37 (s, 3 H), 2.69 (dd, J = 7.7, 4.8 Hz, 1 H), 2.38 (dd, J = 6.3, 3.4 Hz, 1 H), 2.01 (dd, J = 3.4, 1.0 Hz, 1 H), 1.50 (s, 9 H), 1.42 (dd, J = 6.3, 1.0 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.9, 139.6, 128.1, 127.5, 80.8, 77.8, 73.3, 59.0, 40.0, 31.1, 27.9.

Aziridine 2(2*R*): Analytical TLC on silica gel, 95:5 CH_2Cl_2/cyclohexane, R_f = 0.20. − $[\alpha]_D$ = +15 (c = 1.1, $CHCl_3$). − IR (neat): 2979, 2929 and 1738 cm^{-1}. − MS: 278 [M + 1]. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42−7.23 (m, 5 H), 3.72 (dd, J = 9.8, 7.9 Hz, 1 H), 3.54 (dd, J = 9.8, 4.5 Hz, 1 H), 3.34 (s, 3 H), 2.75 (dd, J = 7.9, 4.5 Hz, 1 H), 2.39 (dd, J = 3.3, 1.0 Hz, 1 H), 1.98 (dd, J = 6.4, 1.0 Hz, 1 H), 1.87 (dd, J = 6.4, 3.3 Hz, 1 H), 1.40 (s, 9 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.7, 139.8, 128.0, 127.2, 127.1, 80.6, 78.0, 73.1, 58.8, 35.6, 35.5, 27.7.

Aziridine 3(2*S*): Analytical TLC on silica gel, 95:5 CH_2Cl_2/cyclohexane, R_f = 0.48. − $[\alpha]_D$ = −79 (c = 0.98, CH_2Cl_2). − IR (neat): 2983 and 1740 cm^{-1}. − MS: 250 [M + 1]. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27−7.45 (m, 5 H), 4.13−4.31 (m, 2 H), 3.75 (dd, J = 9.8, 7.7 Hz, 1 H), 3.60 (dd, J = 9.8, 4.8 Hz, 1 H), 3.36 (s, 3 H), 2.74 (dd, J = 7.7, 4.8 Hz, 1 H), 2.49 (dd, J = 6.5, 3.3 Hz, 1 H), 2.08 (d, J = 3.3 Hz, 1 H), 1.52 (d, J = 6.5 Hz, 1 H), 1.32 (t, J = 7.2 Hz, 3 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.0, 139.7, 128.5, 127.8, 77.9, 73.7, 61.1, 59.3, 39.5, 31.7, 14.4. − HRMS calcd. for $C_{14}H_{20}NO_3$: 250.1443, found 250.1441.

Aziridine 3(2*R*): Analytical TLC on silica gel, 95:5 CH_2Cl_2/cyclohexane, R_f = 0.42. − $[\alpha]_D$ = +22 (c = 0.95, CH_2Cl_2). − IR (neat): 2981 and 1743 cm^{-1}. − MS: 250 [M + 1]. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24−7.43 (m, 5 H), 4.16 (q, J = 7.3 Hz, 2 H), 3.76 (dd, J = 9.8, 8.0 Hz, 1 H), 3.56 (dd, J = 9.8, 4.4 Hz, 1 H), 3.37 (s, 3 H), 2.77 (dd, J = 8.0, 4.4 Hz, 1 H), 2.44 (d, J = 3.2 Hz, 1 H), 2.07 (d, J = 6.6 Hz, 1 H), 1.99 (dd, J = 6.6, 3.2 Hz, 1 H), 1.22 (t, J = 7.3 Hz, 3 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.0, 139.8, 128.5, 127.7, 127.4, 78.2, 73.6, 61.1, 59.2, 36.5, 35.1, 14.3.

Aziridine 4(2*S*): Analytical TLC on silica gel, 95:5 CH_2Cl_2/cyclohexane, R_f = 0.40. − $[\alpha]_D$ = −90 (c = 1.42, $CHCl_3$). − IR (neat): 2978 and 1738 cm^{-1}. − MS: 248 [M + 1]. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24−7.45 (m, 5 H), 2.50 (q, J = 6.5 Hz, 1 H), 2.09 (dd, J = 6.4, 3.2 Hz, 1 H), 2.05 (dd, J = 2.2, 1.1 Hz, 1 H), 1.66 (dd, J = 6.4, 1.1 Hz, 1 H), 1.49 (s, 9 H), 1.46 (d, J = 6.5 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.1, 143.7, 128.3, 127.2, 127.0, 81.3, 69.9, 38.9, 33.8, 28.1, 23.4. − HRMS calcd. for $C_{15}H_{22}NO_2$: 248.1651, found 248.1646

Self-Condensation Product 7(2*R*,2′*S*): Analytical TLC on silica gel, 20:80 AcOEt/cyclohexane, R_f = 0.20. − IR (neat): 2927, 1722, 1603 cm^{-1}. − MS: 453 [M + 1]. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17−7.40 (m, 10 H), 3.56−3.95 (m, 6 H), 3.52 (dd, J = 9.6, 4.7 Hz, 1 H), 3.40 (s, 3 H), 3.35 (s, 3 H), 2.97 (dd, J = 6.7, 2.9 Hz, 1 H), 2.81 (s, 1 H), 2.77 (dd, J = 7.9, 4.7 Hz, 1 H), 2.70 (s, 1 H), 1.97 (s, 1 H), 1.50 (d, J = 6.7 Hz, 1 H), 0.85 (m, 3 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.3, 166.0, 140.0, 139.6, 128.4, 127.8, 78.6, 78.1, 73.6, 65.9, 61.7, 59.2, 59.1, 49.4, 42.4, 39.9, 34.2, 13.6.

General Procedure for the Alkylation of Compound 2(2S). − With DMPU: To a solution of aziridine **2(2*S*)** (150 mg, 0.54 mmol) in dry THF (10 mL) at −78 °C under argon was added LDA (1.5 M in cyclohexane, 722 μL, 1.08 mmol). After 1 h, the electrophile (1.62 mmol) and the DMPU (196 μL, 1.62 mmol) were consecutively added. The reaction mixture was maintained at −78 °C for 7 h and then quenched with saturated aqueous NH_4Cl solution (5 mL). The cooling bath was removed, the solution was allowed to warm to room temperature and diluted with ether (5 mL). The aqueous layer was separated and extracted with two 10-mL portions of CH_2Cl_2, and the combined organic phases were dried with $MgSO_4$, filtered and concentrated. The crude reaction product was purified by flash chromatography on silica gel to give the pure alkylated aziridines as colourless oils. − **Without DMPU:** To a solution of aziridine **2(2*S*)** (140 mg, 0.50 mmol) in dry THF (10 mL) at −78 °C under argon was added LDA (1.5 M in cyclohexane, 674 μL, 1.01 mmol). After 1 h, the electrophile (1.52 mmol) was added. The reaction mixture was maintained at −78 °C for 7 h and then quenched with saturated aqueous Na_2CO_3 solution (5 mL). The cooling bath was removed, the solution was allowed to warm to room temperature and diluted with EtOAc (5 mL). The aqueous layer was separated and extracted with two 10-mL portions of CH_2Cl_2, and the combined organic phases were dried with $MgSO_4$, filtered and concentrated. The crude reaction product was purified by flash chromatography on silica gel to give the pure alkylated aziridines as colourless oils.

General Procedure for Alkylation of Compound 2(2*R*): To a solution of aziridine **2(2*R*)** (140 mg, 0.50 mmol) in a mixture of dry DME (5 mL) and Et_2O (1 mL) at −78 °C under argon was added LDA (1.5 M in cyclohexane, 674 μL, 1.01 mmol). After stirring for 15 min, the electrophile (1.52 mmol) was added. The reaction mixture was maintained at −78 °C for 2 h and then quenched with saturated aqueous Na_2CO_3 solution (5 mL). The cooling bath was removed, the solution was allowed to warm to room temperature and diluted with EtOAc (5 mL). The aqueous layer was separated and extracted with two 10-mL portions of CH_2Cl_2, and the combined organic phases were dried with Na_2SO_4, filtered and concentrated. The crude reaction product was purified by flash chromatography on silica gel to give the pure alkylated aziridines as colourless oils and about 15−20% of self-condensation product.

Aziridine 8a(2*R*): Analytical TLC on silica gel, 90:10 CH_2Cl_2/cyclohexane, R_f = 0.43. − $[\alpha]_D$ = −100 (c = 1.0, $CHCl_3$). − IR (neat): 2976, 2927 and 1712 cm^{-1}. − MS: 350 [M + 1]. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35−7.20 (m, 5 H), 3.87 (dd, J = 7.5, 4.7 Hz, 1 H), 3.72 (dd, J = 9.8, 7.5 Hz, 1 H), 3.52 (dd, J = 9.8, 4.7 Hz, 1 H), 3.36 (s, 3 H), 2.35 (d, J = 1.4 Hz, 1 H), 2.12 (d, J = 1.4 Hz, 1 H), 1.23 (s, 9 H), −0.04 (s, 9 H). − ^{13}C NMR (75 MHz,

$CDCl_3$): δ = 170.4, 141.2, 128.3, 127.9, 127.3, 81.1, 79.0, 64.3, 59.1, 38.6, 33.3, 28.0, −1.5. − HRMS calcd. for $C_{19}H_{32}NO_3Si$: 350.2151, found 350.2158.

Aziridine 8b(2*S*): Analytical TLC on silica gel, 95:5 CH_2Cl_2/cyclohexane, R_f = 0.24. − $[\alpha]_D$ = −111 (*c* = 1.0, $CHCl_3$). − IR (neat): 2977, 2930 and 1717 cm^{-1}. − MS: 292 [M + 1]. − ^1H NMR (300 MHz, $CDCl_3$): δ = 7.38−7.17 (m, 5 H), 3.83 (dd, *J* = 7.5, 4.5 Hz, 1 H), 3.64 (dd, *J* = 9.8, 7.5 Hz, 1 H), 3.54 (dd, *J* = 9.8, 4.5 Hz, 1 H), 3.35 (s, 3 H), 2.41 (s, 1 H), 2.08 (s, 1 H), 1.40 (s, 3 H), 1.10 (s, 9 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.5, 141.0, 128.1, 127.6, 127.1, 81.0, 79.1, 64.9, 59.2, 42.2, 39.3, 27.6, 20.9. − HRMS calcd. for $C_{17}H_{26}NO_3$: 292.1913, found 292.1932.

Aziridine 8c(2*S*): Analytical TLC on silica gel, CH_2Cl_2, R_f = 0.31. − $[\alpha]_D$ = −86 (*c* = 1.0, $CHCl_3$). − IR (neat): 2979, 2929, and 1718 cm^{-1}. − MS: 318 [M + 1]. − ^1H NMR (300 MHz, $CDCl_3$): δ = 7.38−7.18 (m, 5 H), 5.83−5.70 (m, 1 H), 5.06 (dd, *J* = 19.0, 1.4 Hz, 1 H), 5.02 (d, *J* = 10.6 Hz, 1 H), 3.75 (dd, *J* = 7.2, 4.3 Hz, 1 H), 3.63 (dd, *J* = 9.7, 7.2 Hz, 1 H), 3.53 (dd, *J* = 9.7, 4.3 Hz, 1 H), 3.45 (s, 3 H), 2.91 (dd, *J* = 14.6, 7.1 Hz, 1 H), 2.41 (s, 1 H), 2.12 (s, 1 H), 2.08 (dd, *J* = 14.6, 6.3 Hz, 1 H), 1.10 (s, 9 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.5, 140.7, 134.6, 128.0, 127.7, 127.2, 117.0, 81.3, 79.0, 64.8, 59.2, 43.0, 39.9, 39.2, 27.6. − HRMS calcd. for $C_{19}H_{28}NO_3$: 318.2069, found 318.2066.

Aziridine 8d(2*S*): Analytical TLC on silica gel, 80:20 cyclohexane/EtOAc, R_f = 0.38. − $[\alpha]_D$ = −54 (*c* = 1.1, $CHCl_3$). − IR (neat): 2978, 2929 and 1732 cm^{-1}. − MS: 392 [M + 1]. − ^1H NMR (300 MHz, $CDCl_3$): δ = 7.38−7.17 (m, 5 H), 3.84 (dd, *J* = 7.3, 4.4 Hz, 1 H), 3.63 (dd, *J* = 9.8, 7.3 Hz, 1 H), 3.54 (dd, *J* = 9.8, 4.4 Hz, 1 H), 3.36 (s, 3 H), 3.27 (d, *J* = 17.0, 1 H), 2.58 (s, 1 H), 2.24 (s, 1 H), 2.12 (d, *J* = 17.0, 1 H), 1.44 (s, 9 H), 1.08 (s, 9 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4, 167.8, 140.6, 128.1, 127.6, 127.2, 81.5, 80.6, 78.8, 64.5, 59.2, 41.4, 40.9, 40.3, 28.2, 27.5. − HRMS calcd. for $C_{22}H_{34}NO_5$: 392.2437, found 392.2430.

Aziridine 8e(2*S*): Analytical TLC on silica gel, 90:10 cyclohexane/EtOAc, R_f = 0.26. − $[\alpha]_D$ = −117 (*c* = 0.8, $CHCl_3$). − IR (neat): 2979, 2930, and 1718 cm^{-1}. − MS: 368 [M + 1]. − ^1H NMR (300 MHz, $CDCl_3$): δ = 7.42−7.12 (m, 10 H), 3.73−3.53 (m, 4 H), 3.37 (s, 3 H), 2.61 (d, *J* = 14.8 Hz, 1 H), 2.55 (s, 1 H), 2.34 (s, 1 H), 0.93 (s, 9 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.1, 140.7, 138.7, 129.0, 128.1, 127.7, 127.2, 126.3, 81.4, 79.0, 65.1, 59.2, 44.5, 40.6, 40.5, 27.4. − HRMS calcd. for $C_{23}H_{30}NO_3$: 368.2226, found 368.2224. − For compounds from the functionalisation of aziridine **2(2R)**, the NMR spectra show two invertomers in different ratios depending on which electrophile is used. Both invertomers are described (NMR in $CDCl_3$) and their ^1H NMR spectra are given at 110 °C in deuterated DMSO (at this temperature, only one series of signals is observed).

Aziridine 8a(2*S*): For this compound, diastereomers could not be separated. Analytical TLC on silica gel, 90:10 cyclohexane/EtOAc, R_f = 0.55. − IR (neat): 2977, 2929, and 1715 cm^{-1}. − MS: 350 [M + 1]. − Ratio of invertomers: 7:1; only major diastereomer is described. − ^1H NMR (300 MHz, $CDCl_3$): δ = 7.47−7.20 (m, 5 H), 3.74 (t, *J* = 6.3 Hz, 1 H), 3.54−3.44 (m, 2 H), 3.31 (s, 3H*m*), 3.23 (s, 3 H), 1.92 (s, 1 H), 1.76 (s, 1 H), 1.53 (s, 9 H), 1.47 (s, 9H*m*), 0.12 (s, 9 H), −0.14 (s, 9H*m*). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.5, 142.0, 128.3, 128.1, 127.4, 81.3, 78.1, 63.6, 58.9, 37.3, 35.6, 28.3, −1.3. − ^1H NMR (300 MHz, [D_6] DMSO, 110 °C): δ = 7.40−7.20 (m, 5 H), 3.65−3.45 (m, 3 H), 3.19 (s, 3 H), 1.94 (s, 1 H), 1.83 (s, 1 H), 1.51 (s, 9 H), 0.09 (s, 9 H). − HRMS calcd. for $C_{19}H_{32}NO_3Si$: 350.2151, found 350.2148.

Aziridine 8b(2*R*): Analytical TLC on silica gel, 90:10 cyclohexane/EtOAc, R_f = 0.24. − $[\alpha]_D$ = +1.5 (*c* = 0.8, $CHCl_3$). − IR (neat): 2978, 2930, and 1720 cm^{-1}. − MS: 292 [M + 1]. Ratio of invertomers: 1:1. − ^1H NMR (300 MHz, $CDCl_3$): δ = 7.48−7.20 (m, 10 H), 3.84 (t, *J* = 6.3 Hz, 1 H), 3.73 (dd, *J* = 9.3, 7.7 Hz, 1 H), 3.60−3.46 (m, 3 H), 3.35 (s, 3 H), 3.34−3.30 (m, 1 H), 3.29 (s, 3 H), 2.53 (s, 1 H), 1.98 (s, 1 H), 1.72 (s, 1 H), 1.69 (s, 1 H), 1.53 (s, 9 H), 1.44 (s, 12 H), 1.18 (s, 3 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.9, 169.9, 141.2, 141.1, 128.3, 128.2, 128.0, 127.4, 127.2, 81.3, 80.7, 79.1, 77.8, 66.6, 63.1, 59.1, 42.8, 40.4, 38.8, 28.2, 28.0, 21.3, 12.3. − ^1H NMR (300 MHz, [D_6]DMSO, 110 °C) δ = 7.42−7.20 (m, 5 H), 3.60−3.40 (m, 3 H), 3.25 (s, 3 H), 2.12 (s, 1 H), 1.70 (s, 1 H), 1.45 (s, 9 H), 1.23 (s, 3 H). − HRMS calcd. for $C_{17}H_{26}NO_3$: 292.1913, found 292.1896.

Aziridine 8c(2*R*): Analytical TLC on silica gel, CH_2Cl_2, R_f = 0.30. − $[\alpha]_D$ = −41 (*c* = 0.8, $CHCl_3$). − IR (neat): 2978, 2926, and 1720 cm^{-1}. − MS: 318 [M + 1]. Ratio of invertomers: 4:1 (*M* for major and *m* for minor). − ^1H NMR (300 MHz, $CDCl_3$): δ = 7.45−7.22 (m, 5H*M* + 5H*m*), 5.98−5.83 (m, 1H*M*), 5.58−5.53 (m, 1H*m*), 5.10 (bd, *J* = 17.8 Hz, 1H*M*), 5.04 (bd, *J* = 10.8 Hz, 1H*M*), 4.98 (bd, *J* = 16.1 Hz, 1H*m*), 4.93 (bd, *J* = 9.3 Hz, 1H*m*), 3.75 (dd, *J* = 8.1, 6.4 Hz, 1H*M*), 3.70 (m, 1H*m*), 3.55−3.50 (m, 2H*M* + 1H*m*), 3.35 (m, 4H*m*), 3.28 (s, 3H*M*), 2.72 (dd, *J* = 14.6, 7.3 Hz, 1H*M*), 2.70 (s, 1H*m*), 2.47 (dd, *J* = 13.8, 7.4 Hz, 1H*m*), 2.23 (dd, *J* = 14.6, 6.4 Hz, 1H*M*), 2.00 (m, 1H*m*), 1.98 (s, 1H*M*), 1.75 (s, 1H*m*), 1.73 (s, 1H*M*), 1.52 (s, 9H*M*), 1.52 (s, 9H*m*). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1, 141.2 (*M*), 140.7 (*m*), 134.9 (*M*), 134.6 (*m*), 128.4, 128.1, 127.5, 117.0 (*m*), 116.7 (*M*), 81.6 (*M*), 80.9 (*m*), 79.1 (*m*), 77.9 (*M*), 66.9 (*m*), 63.3 (*M*), 59.1, 46.2, 39.5 (*M*), 38.5, 37.2 (*M*), 31.2 (*m*), 29.8 (*m*), 28.2 (*M*), 28.0 (*m*). − ^1H NMR (300 MHz, [D_6]DMSO, 110 °C): δ = 7.40−7.22 (m, 5 H), 5.79 (ddt, *J* = 17.2, 10.3, 6.7 Hz, 1 H), 5.08 (ddd, *J* = 17.3, 3.5, 1.5 Hz, 1 H), 5.01 (ddd, *J* = 10.3, 3.5, 1.5 Hz, 1 H), 3.60 (t, *J* = 5.7 Hz, 1 H), 3.52 (dd, *J* = 9.1, 5.8 Hz, 1 H), 3.50 (dd, *J* = 9.1, 5.6 Hz, 1 H), 3.23 (s, 3 H), 2.54 (dd, *J* = 14.7, 7.0 Hz, 1 H), 2.22 (ddt, *J* = 14.7, 6.7, 1.5 Hz, 1 H), 2.06 (s, 1 H), 1.76 (s, 1 H), 1.49 (s, 9 H). − HRMS calcd. for $C_{19}H_{28}NO_3$:318.2069, found 318.2070.

Aziridine 8d(2*R*): Analytical TLC on silica gel, 80:20 cyclohexane/EtOAc, R_f = 0.50. − $[\alpha]_D$ = −38 (*c* = 1.65, $CHCl_3$). − IR (neat): 1727 cm^{-1}. − MS: 392 [M + 1]. − Only one invertomer in $CDCl_3$. − ^1H NMR (300 MHz, $CDCl_3$): δ = 7.43−7.20 (m, 5 H), 3.84 (dd, *J* = 6.9, 5.7 Hz, 1 H), 3.56−3.46 (m, 1 H), 3.38−3.34 (m, 1 H), 3.29 (s, 3 H), 3.22 (d, *J* = 16.9 Hz, 1 H), 2.20 (d, *J* = 16.9 Hz, 1 H), 2.15 (s, 1 H), 1.87 (s, 1 H), 1.52 (s, 9 H), 1.46 (s, 9 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.5, 168.5, 140.8, 128.4, 128.0, 127.5, 81.7, 80.5, 77.8, 62.6, 59.1, 43.4, 41.9, 37.5, 28.2, 28.1. − Two invertomers in [D_6]DMSO at room temp. − ^1H NMR (300 MHz, [D_6]DMSO, 110 °C): δ = 7.40−7.22 (m, 5 H), 3.63 (t, *J* = 6.0 Hz, 1 H), 3.56 (dd, *J* = 9.6, 6.1 Hz, 1 H), 3.49 (dd, *J* = 9.6, 5.8 Hz, 1 H), 3.25 (s, 3 H), 2.78 (d, *J* = 16.5 Hz, 1 H), 2.28 (d, *J* = 16.5 Hz, 1 H), 2.17 (s, 1 H), 1.87 (s, 1 H), 1.48 (s, 9 H), 1.42 (s, 9 H). − HRMS calcd. for $C_{22}H_{34}NO_5$:392.2437, found 392.2430.

Self-Condensation Product 11(2*S*,2′*R*): Analytical TLC on silica gel, 95:5 CH_2Cl_2/cyclohexane, R_f = 0.22. − $[\alpha]_D$ = −20 (*c* = 1.0, $CHCl_3$). − IR (neat): 2927, 1732, and 1720 cm^{-1}. − MS: 481 [M + 1]. − ^1H NMR (300 MHz, $CDCl_3$): δ = 7.42−7.24 (m, 8 H), 7.09 (dd, *J* = 5.8, 2.1 Hz, 2 H), 3.95 (dd, *J* = 9.3, 3.3 Hz, 1 H), 3.77 (dd, *J* = 9.6, 8.1 Hz, 1 H), 3.57 (dd, *J* = 9.6, 4.4 Hz, 1 H), 3.37 (s, 3 H), 3.15 (s, 3 H), 3.13 (dd, *J* = 9.5, 3.3 Hz, 1 H), 2.94 (dd, *J* = 6.5, 3.3 Hz, 1 H), 2.91−2.80 (m, 2 H), 2.52 (d, *J* = 3.3 Hz, 1 H), 2.16 (d, *J* = 6.5 Hz, 1 H), 2.07 (d, *J* = 1.0 Hz, 1 H), 1.94 (d, *J* = 1.0 Hz, 1 H), 1.48 (s, 9 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ =

200.8, 165.8, 139.9, 139.5, 128.4, 128.2, 127.9, 127.5, 82.8, 78.4, 77.7, 74.4, 62.0, 59.1, 58.3, 51.8, 40.1, 38.8, 36.6, 28.0.

(*S*)-α-Benzylserine (10): $[\alpha]_D = -16$ ($c = 1.1$, H_2O). − MS: 196 [M + 1]. − ^{1}H NMR (300 MHz, D_2O): δ = 7.26−7.17 (m, 3 H), 7.11−7.05 (m, 2 H), 3.86 (d, $J = 12.1$ Hz, 1 H), 3.60 (d, $J = 12.1$ Hz, 1 H), 3.07 (d, $J = 14.2$ Hz, 1 H), 2.79 (d, $J = 14.2$ Hz, 1 H). − ^{13}C NMR (75 MHz, D_2O): δ = 173.5, 133.5, 129.9, 129.0, 127.9, 66.9, 64.0, 37.8. − HRMS calcd. for $C_{10}H_{13}NO_3$: 196.0974, found 196.0961.

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