Intramolecular Carbolithiation Reactions of Chiral α-Amino-organolithium Species

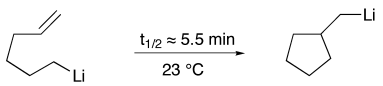
Neil J. Ashweek, Iain Coldham,* David J. Snowden, and Graham P. Vennall[a]

Abstract: Enantiomerically enriched α-amino-organolithium species, in which the lithium atom is attached to a stereogenic carbon centre, have been found to be chemically stable at room temperature in a solvent of very low polarity and undergo intramolecular carbolithiation onto an unactivated alkene. The configurational stability of the chiral organolithium species, bearing a variety of *N*-alkenyl substituents, was probed by studying the enantiomeric purity of the cyclization products. With *N*-but-3-enyl-2-lithiopyrrolidine, cyclization to the five-membered ring is more rapid than racemization and a high yield of the pyrrolizidine alkaloid (+)-pseudoheliotridane was obtained with no loss of optical purity. In contrast, with *N*-pent-4-enyl-2-lithiopyrrolidine, cyclization to the six-membered ring was found to occur with significant loss of optical purity. The cyclization to the six-membered ring was determined to occur with a half-life, $t_{1/2} \approx 90$ min at 23 °C. The epimerization of this organolithium species in hexane/Et_2O 4:1 was calculated to have a half-life, $t_{1/2} \approx 30$ min at 23 °C. Enhanced levels of enantioselectivity for the formation of the indolizidine ring system were obtained using an alkene bearing a terminal phenylthio substituent. With *N*-[(3-phenylthio)-prop-2-enyl]-2-lithiopyrrolidine, cyclization to the four-membered ring occurs with poor enantioselectivity at low temperature in THF but is highly enantioselective at room temperature in a solvent of very low polarity.

Keywords: alkaloids · cyclization · kinetics · lithium · tin

Introduction

Inter- and intramolecular carbometallation reactions of alkenes and alkynes are finding increasing use for regio- and stereocontrolled carbon–carbon bond formation in organic chemistry.[1, 2] Considerable efforts, particularly by Bailey and co-workers, have shown that intramolecular carbolithiation (anionic cyclization) reactions allow ready access to substituted cyclopentanes and other carbocyclic ring systems.[3] The core, unsubstituted substrate, 5-hexenyllithium, can be prepared by iodine–lithium exchange with *tert*-butyllithium, and undergoes cyclization with a half-life, $t_{1/2} \approx 5.5$ min at 23 °C (Scheme 1).[4, 5]



Scheme 1. Rate of anionic cyclization to cyclopentane ring in pentane/Et_2O.[5]

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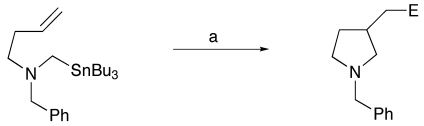
Our own work has made use of the ability to form an organolithium species by tin–lithium exchange from an aminoalkylstannane.[6, 7] This led to a new route to substituted pyrrolidines (Scheme 2).



Scheme 2. Anionic cyclizations to 3-substituted pyrrolidines.[6, 7] a) *n*BuLi, hexane/Et_2O 10:1, RT, 2 h, then E^+, 44–90%.

In this work, excellent results were obtained using the very low polarity solvent system hexane/Et_2O ($\approx$10:1) at room temperature. Under these conditions transmetallation of the α-amino-organostannane is slow, and complete tin–lithium exchange requires approximately 30 min. Other research groups have also studied the formation of heterocyclic compounds using an intramolecular carbometallation reaction.[2a,b, 8] Access to chiral α-hetero-organolithium species, for example by tin–lithium exchange[9] or proton abstraction,[10] opens up the possibility to determine the extent of intramolecular carbolithiation by retention or inversion of configuration at the carbanion centre, a study that is not feasible using iodine–lithium exchange with chiral secondary iodides.

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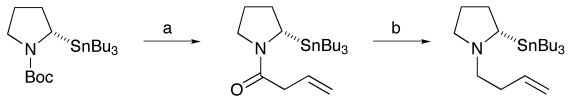
Chiral organolithium species are known to react intermolecularly with electrophiles with retention, inversion or racemization of configuration, depending on the substrate and electrophile.[10, 11] However, the stereoselectivity on intramolecular quench (anionic cyclization) was unknown at the outset of this work. This paper describes in full our results on the use of enantiomerically enriched organolithium species for the formation of cyclic amines and gives valuable information on how the extent of racemization depends on the *N*-alkenyl substituent. In addition to our own work,[7, 12] the number of reports on the use of chiral organolithium species for the formation of carbocyclic and heterocyclic ring systems has been growing.[13]

Results and Discussion

We required a route to enantiomerically enriched aminoalkylstannanes and hence (on transmetallation) α-amino-organolithium species, in which the nitrogen atom is tethered to an alkenyl group to allow intramolecular carbolithiation. A popular and convenient method to introduce a trialkyltin group α to a heteroatom makes use of chemistry developed by Hoppe and Beak, in which proton abstraction in the presence of (−)-sparteine induces asymmetry.[10] With the substrate *N*-*tert*-butoxycarbonyl (Boc) pyrrolidine, the 2-tributyltin derivative **1** (Scheme 3) was prepared with high optical purity.[14] Removal of the *N*-Boc group was problematic using a protic



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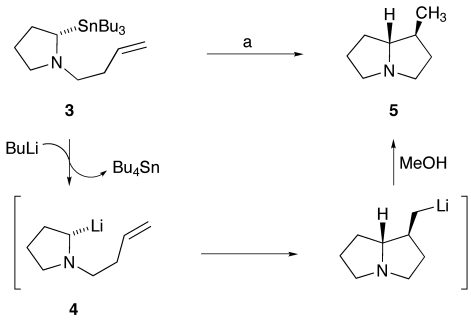
Scheme 3. Preparation of *N*-(but-3-enyl)-2-(tributylstannyl)pyrrolidine. a) *B*-bromocatecholborane, CH_2Cl_2, RT, 30 min, then CH_2=$CHCH_2COCl$, 65%; b) AlH_3, Et_2O, 0 °C, 2 h, 89%.

acid such as trifluoroacetic acid, but the use of the Lewis acid *B*-bromocatechol borane[15] gave the unstable free amine, which was treated immediately with 3-butenoyl chloride to give the amide **2**. Reduction of the amide with $LiAlH_4$ or alane (AlH_3) gave the desired substrate **3**. This amine had a high specific rotation, $[\alpha]_D^{23} = +107.0$ ($c = 2.6$, EtOH), although we were not able to verify at this stage that no loss in optical purity had occurred in the deprotection, acylation or reduction steps.

Transmetallation of chiral α-amino-organostannanes is often carried out at low temperature (typically −78 °C), in order to avoid racemization of the chiral organolithium species.[10a, 11a] We were somewhat disappointed to find, therefore, that treatment of the stannane **3** with *n*BuLi in THF at −78 °C, followed by gradual warming to room temperature, gave predominantly the protodestannylated product *N*-but-3-enylpyrrolidine. Alternative conditions, using the much less polar hexane/Et_2O (10:1) solvent system, require temperatures above 0 °C to effect transmetallation. Gratifyingly, these conditions resulted in a high yield of a single diastereomer (as determined by NMR) of the cyclized product **5**, after quenching with methanol (Scheme 4). The stereochemistry was confirmed by NOE experiments and by correlation with the known pseudoheliotridane **5**.[16] The enantiomeric excess (*ee*) of the product was determined by measuring the



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Scheme 4. Anionic cyclization to (+)-pseudoheliotridane. a) *n*BuLi, hexane/Et_2O 10:1, RT, 2 h, then MeOH, 90%.

peak area of the methyl doublet in the ^1H NMR spectrum in the presence of the chiral solvating agent (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.[17] Despite the ambient temperature of the reaction, the product was determined to have 94% *ee*, which indicates a completely enantiospecific cyclization, with no loss of optical purity. This result was verified from the specific rotation $[\alpha]_D^{23} = +6.8$ ($c = 0.5$, EtOH), which compared well with the literature value $[\alpha]_D^{23} = +7.0$ ($c = 0.5$, EtOH).[16] By the sign of rotation, we assign the product with absolute configuration as illustrated, such that the cyclization has occurred with complete retention of configuration at the carbanion centre. This result suggests that the lithium atom in the intermediate **4** (drawn as a monomer but note that the corresponding *N*-methyl compound has been found to be dimeric in THF)[18] coordinates to the alkene and that the transition state adopts a conformation (Figure 1) with a chair-like arrangement in which the lone pair on the nitrogen atom is pseudo-axial and could interact with the lithium atom.[18, 19] This postulate is in agreement with calculated[3] and experimental data.[20] This chemistry allows a very short, enantiospecific synthesis of the pyrrolizidine alkaloid (+)-pseudoheliotridane.

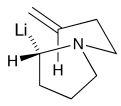

Figure 1. Conformation of the organolithium species **4** leading to pyrrolizidine **5**.

In addition, the result indicates that intramolecular carbolithiation reactions onto an alkene occur with complete retention of configuration at the carbanion centre. The anionic cyclization contrasts sharply with the related radical cyclization, which occurs to give predominantly the other diastereomer, heliotridane, as a racemic mixture.[21]

We were intrigued as to the origin of the remarkable configurational stability of the organolithium species **4**. Cyclization of the organolithium species **4** appears to proceed at a rate that is comparable with (or faster than) 5-hexenyllithium, as the cyclization of **4** is complete within the same time scale as the tin–lithium exchange (approximately 30 min at room temperature in a solvent of very low polarity). The organolithium species **4** is different from 5-hexenyllithium (it

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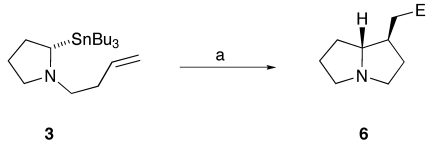
is likely to have nitrogen–lithium coordination[18, 19] and is a cyclic, secondary organolithium species), however, if it does cyclize at the same rate as 5-hexenyllithium, then it is possible to calculate that the half-life for epimerization of **4** must be at least 5 h, in order that essentially no loss of optical purity would result.

Intramolecular carbolithiation of the organolithium species **4** gives a new organolithium species which can be trapped with a protic source to give (+)-pseudoheliotridane **5**. Trapping with other electrophiles led to a selection of different substituted pyrrolizidines **6a–e** (Scheme 5, Table 1). In each case the products **6** were optically active, although it was no longer possible to verify the enantiomeric excess by NMR. As the cyclization occurs enantiospecifically, setting up both chiral centres in the product before electrophilic quench, then it is anticipated that there would be no loss in the optical purity of these products.



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Scheme 5. Anionic cyclizations to 1-substituted pyrrolizidines. a) *n*BuLi, hexane/Et_2O 10:1, RT, 2 h, then E^+, 41–63%.

Table 1. Preparation of 1-substituted pyrrolizidines **6**.

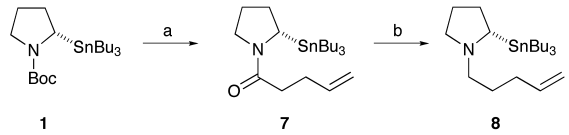
E^+	E	Product	Yield [%]
CD_3OD	D	**6a**	58
$Ph_2C{=}O$	$C(OH)Ph_2$	**6b**	62
Me_3SiCl	$SiMe_3$	**6c**	62
Me_3SnCl	$SnMe_3$	**6d**	68
PhCHO	CH(OH)Ph	**6e**	41[a]

[a] **6e** was a mixture (1:1) at the alcohol center.

Transmetallation of the organostannane **3** at −78 °C in the solvent THF gave, after warming to room temperature, *N*-but-3-enylpyrrolidine together with a small amount (≈19%) of pseudoheliotridane **5**. This product was determined (^{1}H NMR spectrum as above) to have been formed with 94% *ee* and had therefore proceeded with no loss of optical purity. The product pseudoheliotridane was also formed in 94% *ee* and in good yield using hexane/Et_2O as solvent in the presence of the additives *N*,*N*,*N*′,*N*′-tetramethylethylene diamine (TMEDA) or lithium iodide. Attempts to effect cyclization of the racemic organolithium species **4** in the presence of (−)-sparteine resulted in the formation of only *N*-but-3-enylpyrrolidine.

The observation that the intramolecular carbolithiation reaction to the pyrrolizidine **5** occurs with complete retention of configuration at the chiral carbanion centre is in agreement with recent results on the cyclization of other chiral organolithium species.[13] These cyclization reactions are restricted to the formation of five-membered rings, and must occur at rates that are significantly greater than the rate of racemization. The next logical investigation is to determine the effect of ring size on the stereochemical integrity of the chiral organolithium species. We therefore selected to investigate first the cyclization to the corresponding six-membered ring.

Removal of the *N*-Boc protecting group from the chiral stannane (*S*)-**1** (94% *ee*), followed immediately by *N*-acylation of the resulting 2-(tributylstannyl)pyrrolidine with 4-pentenoyl chloride gave the carboxylic amide **7** (Scheme 6). Reduction with $LiAlH_4$ gave the amine **8**. Alternatively, the amine **8** could be prepared directly from the stannane **1** by deprotection and immediate reductive amination with 4-pentenal.[22]



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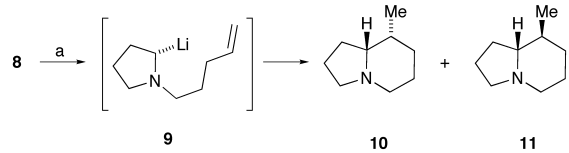
Scheme 6. Preparation of *N*-(pent-4-enyl)-2-(tributylstannyl)pyrrolidine. a) *B*-bromocatecholborane, CH_2Cl_2, RT, 30 min, then $CH_2{=}CHCH_2CH_2COCl$, 65%; b) $LiAlH_4$, Et_2O, 0 °C, 20 min, 90%.

The amine **8** in hexane/Et_2O (4:1) was treated with *n*BuLi (3 molar equivalents in hexanes) at room temperature to give the desired enantiomerically enriched organolithium species **9** (Scheme 7). Complete transmetallation required approximately 30 min and complete cyclization of this substrate required approximately 6 h at room temperature. Quenching



9 10 11

Scheme 7. Anionic cyclization to 1-methylindolizidine. a) *n*BuLi, hexane/Et_2O 4:1, RT, 6 h, then MeOH, 80% (**10**:**11** 95:5); or *n*BuLi, hexane/Et_2O/TMEDA 4:1:1, RT, 6 h, then MeOH, 76% (**10**:**11** 10:90).

with MeOH resulted in the formation of the diastereomeric indolizidines **10** and **11** in high yield (80–87%) and high diastereoselectivity (95:5, **10**:**11**), together with small amounts of the protodestannylated product *N*-pent-4-enylpyrrolidine. The relative stereochemistry of the major diastereomer **10** was determined by NOE experiments. Using NMR spectroscopy in the presence of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol,[17] the indolizidine **10** was determined to have 13% *ee*. The absolute configuration of the major enantiomer of the indolizidine **10** is unknown but is drawn as if cyclization occurs with retention of configuration, as determined for the corresponding cyclization to the five-membered ring.

An experiment in which aliquots were taken at different reaction times was carried out and the data is illustrated in Figure 2. After approximately 30 min, to allow for complete transmetallation, the product indolizidines **10** and **11** (95:5) could be isolated in low yield (22%) but enhanced enantiomeric excess (**10**, 62% *ee*). Longer reaction times gave increasing yields of the indolizidine products, but at the expense of enantiomeric purity. However, the enantiomeric excess did not drop off to zero on long reaction times, which suggests that the cyclization is irreversible. By plotting the log of the yield of product over time or the log of the amount of organolithium **9** (as determined by the amount of its proto-

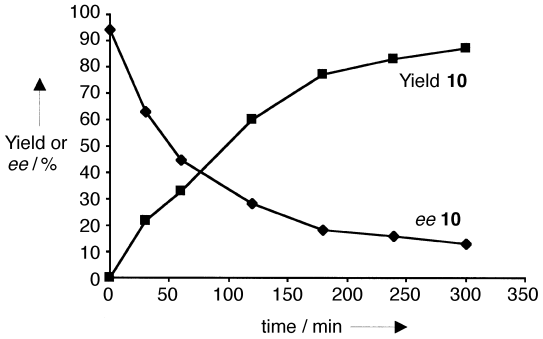


Figure 2. Yield [%] and enantiomeric excess [%] of **10** over time.

nated derivative) over time (Figure 3), the cyclization best fits first order kinetics, with a rate constant, $k_c \approx 1.2 \times 10^{-4}\,s^{-1}$, corresponding to a half-life for cyclization, $t_{1/2} \approx 90$ min at 23 °C. This is significantly slower than the rate of cyclization to the corresponding five-membered ring.

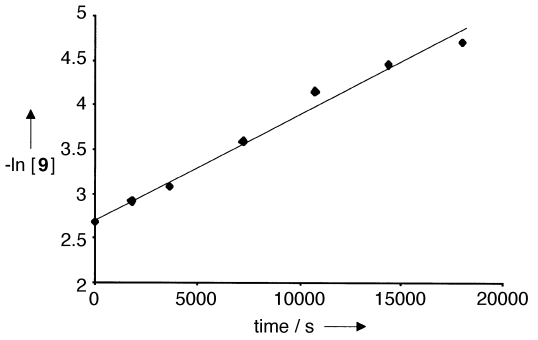
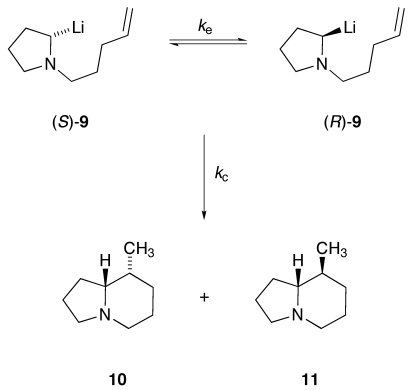


Figure 3. Determination of first order rate constant for cyclization of **9**.

Once the rate of cyclization is known, then the rate of epimerization of the organolithium species **9** can be determined (Scheme 8). The experimental data points and the simulated kinetics for the epimerization and cyclization are given in Figure 4. This graph illustrates the gradual formation of the two enantiomeric indolizidine products **10** (13% *ee* after 6 h) at the determined rate ($1.2 \times 10^{-4}\,s^{-1}$) starting from organolithium species of 94% *ee* [97:3 ratio of (*S*)-**9** to (*R*)-**9**, assuming transmetallation is rapid]. Using this data, it is clear that epimerization of the organolithium species **9** is faster than



Scheme 8. Epimerization and cyclization of intermediate organolithium species.

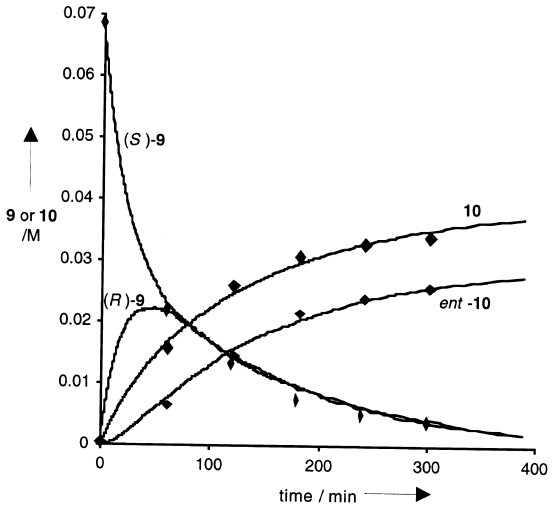


Figure 4. Kinetics simulation and plotted experimental data for cyclization to **10**.

cyclization and indeed that the organolithium species is racemic within 60 min. From the data, the calculated rate of epimerization of the organolithium species **9**, $k_e \approx 3.4 \times 10^{-4}\,s^{-1}$, corresponds to a half-life for epimerization, $t_{1/2} \approx 30$ min at 23 °C in hexane/Et_2O (4:1). This data is approximate as tin–lithium exchange requires 30 min, although it does indicate that the formation of the indolizidines **10** and **11** beyond 60 min results from racemic organolithium species and that the enantiomeric excess (13% *ee*) stems from cyclization occurring within 60 min, prior to racemization. The picture may be complicated further, if the organolithium species **9** exists preferentially as a heterochiral dimer (although NMR spectroscopy indicates that *N*-methyl-2-lithiopyrrolidine is a homochiral dimer[18]). The heterochiral dimer, if it forms, would be produced during racemization and may have different kinetics from the monomer or homochiral dimer for epimerization and cyclization.

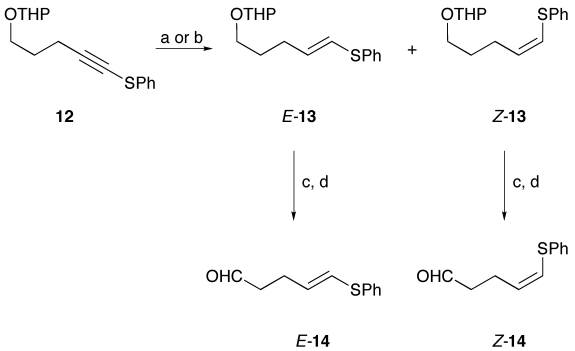
As far as we are aware, this is the first determination of the rate of epimerization of a chiral, cyclic α-amino-organolithium species. An acyclic benzylic α-amino-organolithium species has been reported to epimerize rapidly ($\Delta G^{\neq} = 9.0$ kcal mol^{-1} at 190 K).[23] With a half-life for epimerization of the organolithium species **9** of approximately only 30 min, racemization is (not surprizingly) slow in comparison with a benzylic organolithium species, but still competes with cyclization to a six-membered ring. This is in stark contrast to the completely enantiospecific cyclization of organolithium species **4**. If the organolithium species **4** epimerizes with a half-life that is similar to that of **9** (approximately 30 min at room temperature), then the rate of cyclization to the five-membered ring must be extremely rapid (the half-life for cyclization would have to be less than 30 s), in order that essentially no loss of optical purity (within expected error limits) in the formation of **5** occurs. Unfortunately, the slow transmetallation and rapid cyclization of the organolithium species **4** preclude the determination of kinetic data. If cyclization (to the five-membered ring) occurs at a rate that is similar to that determined by Bailey (Scheme 1), then the organolithium species **4** must racemize considerably more

0947-6539/02/0801-0198 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 1

slowly than **9** and this would have to be due to the greater ease with which the alkene (with a shorter tether) could coordinate to the lithium atom. We are currently investigating the relative ease of epimerization of different *N*-substituted 2-lithio-pyrrolidines.

The cyclization of the organolithium species **9** was sensitive to the solvent. When the stannane **8** was treated with *n*BuLi in THF or in hexane/Et_2O/(−)-sparteine, transmetallation took place, but no cyclization occurred and only *N*-pent-4-enyl-pyrrolidine could be isolated. However, the solvent system hexane/Et_2O/TMEDA (4:1:1, equating to 15 molar equivalents of TMEDA) allowed transmetallation and cyclization to give predominantly the indolizidine **11** (10:90, **10**:**11**; 76%). This represents a complete reversal of the diastereoselectivity in comparison with the reaction in the absence of TMEDA. Unfortunately, under these conditions the products **10** and **11** were both found to be racemic. The rate of transmetallation and cyclization in the presence of TMEDA was not determined but was not significantly different from that in the absence of TMEDA. The addition of TMEDA therefore appears to increase the rate of racemization of the organolithium species, presumably via coordination of TMEDA to the lithium atom.[24] This coordination must also influence the diastereoselectivity of the cyclization, to favour the product **11**.

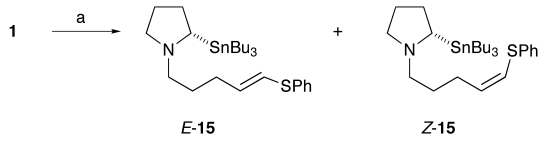
In order to improve the optical purity of the indolizidine products, it is necessary to increase the rate of cyclization and/or to slow the rate of racemization of the organolithium species. Alkenes substituted with an anion stabilising group have been shown to increase the rate of anionic cyclization reactions.[25, 26] We chose to investigate the phenylthio-substituted alkene, as the product sulfide after cyclization would be amenable to reductive cleavage to give the same indolizidines **10** and **11**. The required vinyl sulfides were prepared from the aldehydes *E*- and *Z*-**14**, which were prepared according to a modified literature procedure (Scheme 9).[26]



Scheme 9. Preparation of *E*- and *Z*-5-(phenylthio)pent-4-enal. a) $LiAlH_4$, THF, 40 °C, 3 h, 93% (*E*-:*Z*-**13** 100:0); b) DIBAL, hexane, −18 °C to RT, 7 h, 99% (*E*-:*Z*-**13** 0:100); c) TsOH, MeOH, H_2O, RT, 16 h, 100%; d) $(COCl)_2$, DMSO, CH_2Cl_2, −60 °C then Et_3N, *E*-**14** 69%, *Z*-**14** 64%.

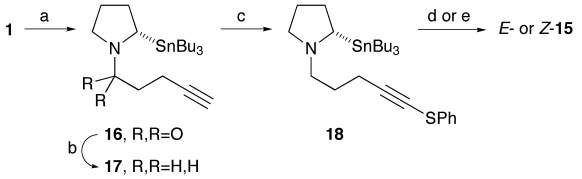
Reduction of the alkyne **12** with $LiAlH_4$ gave exclusively the vinyl sulfide *E*-**13**, whereas reduction with diisobutylaluminium hydride (DIBAL) gave exclusively the vinyl sulfide *Z*-**13**. Acid-catalyzed deprotection and Swern oxidation of the resulting alcohol gave the desired aldehydes *E*- and *Z*-**14**.

The synthesis of the stannanes *E*- and *Z*-**15** was achieved by reductive amination.[22] The best yields were obtained using the reducing agent $NaBH_3CN$ in the solvent nitromethane, which was not buffered with an acid (Scheme 10). Under these conditions the products **15** were obtained in good yield without any isomerization.



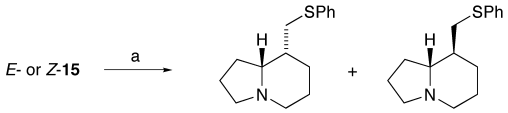
Scheme 10. Reductive amination to phenylthio-substituted substrates *E*- and *Z*-**15**. a) *B*-bromocatecholborane, CH_2Cl_2, RT, 10 min, then wash with aq NaOH, then $MeNO_2$, $NaBH_3CN$, *E*- or *Z*-**14**, RT, 15 min, *E*-**15** 72%, *Z*-**15** 69%.

An alternative route to the desired stannanes **15** was achieved from the carboxylic amide **16**, which was formed from the stannane **1** by deprotection and acylation with 4-pentynoyl chloride (Scheme 11). Reduction with $LiAlH_4$ gave the amine **17**. Subsequent sulfenylation of the alkynyl anion provides the alkynyl sulfide **18**. In this reaction the initial deprotonation of the alkyne must be accomplished in Et_2O, in order to avoid transmetallation of the stannane, a rapid process in THF. However, addition of diphenyl disulfide (activated with CH_3I) is best accomplished in THF. Reduction of the alkynyl sulfide **18** with $LiAlH_4$ gave the stannane *E*-**15**, whereas reduction with DIBAL gave the stannane *Z*-**15**.



Scheme 11. Acylation-reduction route to substrates *E*- and *Z*-**15**. a) *B*-bromocatecholborane, CH_2Cl_2, RT, 10 min, then $CH{\equiv}CCH_2CH_2COCl$, 59%; b) $LiAlH_4$, Et_2O, 0 °C, 20 min, 84%; c) *n*BuLi, Et_2O, 0 °C, then PhSSPh, MeI, THF, RT, 16 h, 66%; d) $LiAlH_4$, THF, 40 °C, 3 h, *E*-**15** 80%; e) DIBAL, hexane, −18 °C to RT, 7 h, *Z*-**15** 59%.

Treatment of the stannanes **15** with *n*BuLi in hexane/Et_2O (4:1) gave the diastereomeric cyclized products **19** and **20** (Scheme 12). From the stannane *E*-**15**, the major product was the indolizidine **19** (77%, 70:30, **19**:**20**), formed in good enantiomeric excess (**19**, 75% *ee*; **20**, 72% *ee*). The enantiomeric excess values were determined by reduction to the

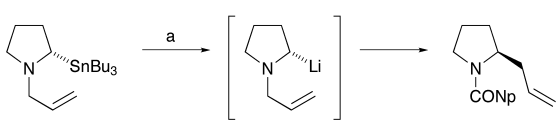


Scheme 12. Anionic cyclization to 1-(phenylthiomethyl)indolizidines. a) *n*BuLi, hexane/Et_2O 4:1, RT, 2 h, then MeOH, from *E*-**15** 77% (**19**:**20** 70:30), from *Z*-**15** 79% (**19**:**20** 50:50); or *n*BuLi, hexane/Et_2O/TMEDA 4:1:1, RT, 6 h, then MeOH, from *E*-**15** 71% (**19**:**20** 0:100), from *Z*-**15** 73% (**19**:**20** 0:100).

indolizidines **10** and **11** with Raney nickel. The organolithium species derived from the stannane *Z*-**15** cyclized to give a mixture of indolizidines **19** and **20** (79%, 50:50, **19**:**20**) in slightly lower enantiomeric excess (**19**, 55% *ee*; **20**, 53% *ee*). The transmetallation and cyclization of the stannanes **15** was complete within 1 h at room temperature and the much improved optical activity of the product indolizidines results from the faster rate of cyclization in comparison with the stannane **8**. It is possible that, in addition to the faster rate of cyclization, the organolithium species derived from *E*- or *Z*-**15** epimerize at a rate that is slower than the epimerization of the organolithium species **9**. Assuming, however, that the rate of epimerization of the organolithium species *E*-**15** is the same as that of the organolithium species **9** (in which $k_e \approx 3.4 \times 10^{-4}\,s^{-1}$ at 23 °C in hexane/Et_2O), then it is possible to calculate that the cyclization onto the vinylsulfide to produce the indolizidines with 75% *ee* would occur with a rate constant $k \approx 3 \times 10^{-3}\,s^{-1}$, corresponding to a half-life for cyclization, $t_{1/2} \approx 4$ min at 23 °C. Whilst this determination is based on the rate of epimerization of a different, although related substrate, it does indicate that the presence of a phenylthio substituent at the terminus of the alkene enhances the rate of cyclization to give a six-membered ring to a level that is similar to the cyclization onto an unactivated alkene to give a five-membered ring.

Using the solvent system hexane/Et_2O/TMEDA (4:1:1), the organolithium species derived from the stannanes *E*- or *Z*-**15** cyclized to give exclusively the indolizidine **20** in good yield (71–73%). The indolizidine **20** was formed as a racemic mixture in both cases. These results are similar to those obtained with the substrate **8** and we speculate that coordination of TMEDA to the lithium atom increases the rate of racemization of the organolithium species, in addition to altering the preferred conformation of the transition state for cyclization, such that only the product **20** is formed. Attempted cyclization of the alkynyl stannanes **17** or **18** was unsuccessful.

The successful intramolecular carbolithiation to give the indolizidine ring system and the more favourable cyclization with a pendent phenylthio substituent prompted us to investigate the possibility of forming a four-membered ring by this process. Gawley has described the addition of *n*BuLi to the stannane **21** (94% *ee*) to give the corresponding organolithium species **22** (Scheme 13).[27] This organolithium species does not undergo cyclization, but does rearrange by a combination of [2,3]- and [1,2]-sigmatropic rearrangement pathways. The [2,3]-sigmatropic rearrangement occurs with inversion of configuration at the carbanion centre, whereas the [1,2]-process occurs with racemization. The product was quenched with α-naphthoyl chloride to give the amide **23** (48% *ee*). It is interesting to note that the organolithium species **22** had significant configurational stability (on quenching after 2 h at 13 °C with tributyltin chloride, the stannane **21** was recovered in 65% *ee*). It is possible to calculate from this data that the half-life for epimerization of the organolithium species **22** must be approximately 7.5 h. This slow rate of epimerization supports our results with the lack of racemization of the organolithium species **4**, but contrasts with the much faster rate of epimerization of the organolithium species **9**.

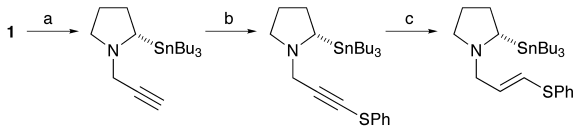


21 22 23

Scheme 13. Sigmatropic rearrangement of *N*-allyl-2-(tributylstannyl)pyrrolidine.[27] a) *n*BuLi, THF-TMEDA, 13 °C, 4 h, then α-naphthoyl chloride, 64%.

We postulated that the presence of a phenylthio substituent at the terminus of the allyl unit would promote cyclization in preference to rearrangement. We were intrigued by the possibility of influencing the reaction pathway and the enantioselectivity by a pendent phenylthio group and describe the results of this study below.

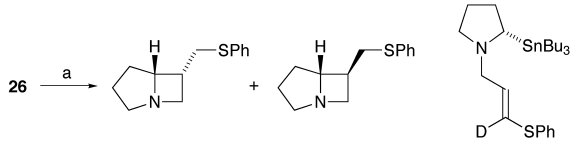
The desired substrate **26** bearing an *N*-(3-phenylthio)allyl substituent was prepared from the stannane **1** by N-deprotection and immediate alkylation with propargyl bromide (Scheme 14). Deprotonation of the resulting *N*-propargyl compound **24** in Et_2O (to avoid tin–lithium exchange) and addition of diphenyl disulfide (activated with CH_3I) in THF gave the alkynyl sulfide **25**. Reduction of the alkyne with $LiAlH_4$ led to the vinyl sulfide *E*-**26**. In this case, use of DIBAL for the reduction also led to the same *E*-stereoisomer, rather than the isomer *Z*-**26**.



24 25 26

Scheme 14. Preparation of phenylthio-substituted substrate *E*-**26**. a) *B*-bromocatecholborane, CH_2Cl_2, RT, 10 min, then $CH{\equiv}CCH_2Br$, 65%; b) *n*BuLi, Et_2O, 0 °C, 1 h, then PhSSPh, MeI, THF, RT, 1 h, 65%; c) $LiAlH_4$, THF, 40 °C, 1.5 h, *E*-**26** 80%.

Treatment of the stannane **26** with excess *n*BuLi in the low polarity solvent system hexane/Et_2O (4:1) at room temperature resulted in partial transmetallation. The desired cyclization products **27** and **28** were isolated (52%) with a high diastereoselectivity (10:1) in favour of the isomer **27** as determined by NMR spectroscopy (NOE experiments) on the inseparable mixture (Scheme 15). No products from [2,3]- or [1,2]-sigmatropic rearrangement were isolated. The remaining material was recovered stannane **26** (35%). Attempts to achieve complete transmetallation with further *n*BuLi or longer reaction times were unsuccessful and it was deter-



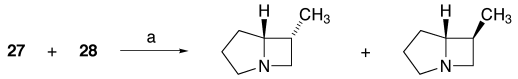
27 28 29

Scheme 15. Anionic cyclization to azabicyclo[3.2.0]heptanes. a) *n*BuLi, hexane/Et_2O 4:1, RT, 30 min, then MeOH, 52% (**27**:**28** 10:1), or a) *n*BuLi, THF, −78 °C, 2 min, then MeOH, 86% (**27**:**28** 1:1).

0947-6539/02/0801-0200 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 1

mined, by quenching the reaction with MeOD, that the recovered starting material was deuterated in the vinylic position to give **29**. Therefore tin–lithium exchange competes with deprotonation of this substrate in solvent of very low polarity at room temperature.

In order to determine the enantiomeric excess of the products **27** and **28**, the phenylthio group was removed by treatment with Raney nickel to give the amines **30** and **31** (Scheme 16). In a similar way to that used for the bicyclic amines **5**, **10** and **11**, addition of the chiral solvating agent (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol[17] to the amines **30** or



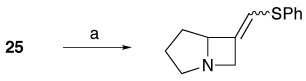
30 **31**

Scheme 16. Reduction of azabicyclo[3.2.0]heptanes **27** and **28**. a) Raney nickel, EtOH, 60 °C, 1 h, 54–71 %.

31 promoted splitting of the methyl doublet peaks in the ^{1}H NMR spectrum that allowed determination of the optical purity. We were pleased to find that the product **30**, and hence **27**, had been formed in 88–90 % *ee*. The enantiomeric excess of the minor diastereomer **28**/**31** could not be determined. The high enantiomeric excess of **27** must reflect a cyclization that is much more rapid than epimerization of the intermediate organolithium species in hexane/Et_2O. Cyclization to give an azetidine ring with a phenylthio-stabilized organolithium species therefore takes place with almost complete retention (or inversion) of configuration at the carbanion centre (we have not been able to determine the absolute configuration of the products **27** and **28** and these are drawn as if cyclization had occurred with retention of configuration).

The cyclization of the stannane **26** was sensitive to the solvent. The solvent system hexane/Et_2O/TMEDA (4:1:1) gave similar results (yield **27** + **28** 43 %, ratio 10:1, but with reduced enantioselectivity: **27** 54 % *ee*) in comparison with experiments in the absence of TMEDA (in contrast to the influence of TMEDA on the cyclization of the stannanes **8** and **15**). However, the use of THF caused a completely different outcome. In THF, transmetallation and cyclization were extremely rapid, being complete in less than 2 min at −78 °C. The yield (86 %) of the bicyclic amine products **27** and **28** was high using THF as the solvent, however, there was no diastereomeric excess and both **27** and **28** were formed in low enantiomeric excess (14–24 %). This result is surprising considering the known configurational stability of *N*-methyl-2-lithiopyrrolidine in THF at low temperature.[11a] Although the cyclization in THF gives only a low enantiomeric excess, the major enantiomer of **27** is the same as that formed in hexane/Et_2O.[28] It is not clear whether the low enantiomeric excess in THF is a result of rapid epimerization of this substrate in this solvent (at a rate that is competitive with cyclization) or whether there is a mixture of cyclization with retention and cyclization with inversion of configuration at the carbanion centre.

Attempted transmetallation and cyclization of the alkyne **24** led only to *N*-propargyl-pyrrolidine (80 %), although cyclization of the alkyne **25** was rapid in THF and a good yield (78 %) of the bicyclic ring system **32** was obtained (Scheme 17). The product was found to be a 1:1 mixture of alkene geometrical isomers. Attempts to determine the optical purity of these isomeric sulfides or to reduce the alkene or to cleave the phenylthio group (e.g. with Raney nickel or $NaBH_4/NiCl_2$) were unsuccessful.



32

Scheme 17. Anionic cyclization of phenylthio-substituted alkyne **25**. a) *n*BuLi, THF, −78 °C, 1.5 h, then MeOH, 78 %.

In conclusion, chiral organolithium species α- to a nitrogen atom of a tertiary amine can be used for the synthesis of bicyclic amines with high enantiomeric excess. 1-Azabicyclo-[3.2.0]heptane, 1-azabicyclo[3.3.0]octane and 1-azabicyclo-[4.3.0]nonane ring systems have been prepared and the stereoselectivity of the cyclization has been determined. Cyclization competes with epimerization of the organolithium species and a comparison of the rates of these processes has been achieved. High yields and high optical purities of the products can be obtained using, if necessary, a phenylthio-substituted alkene as the electrophilic tether.

Experimental Section

General: Optical rotations were measured on an Optical Activity Ltd. AA-1000 polarimeter, using a cell with a path length of 0.5 dm. IR spectra were recorded as liquid films on NaCl plates unless otherwise stated, using a Perkin–Elmer 881 or Nicolet FT-IR Magna 550 spectrometer. ^{1}H NMR spectra were recorded on a Bruker AC 300 MHz or Bruker DRX 400 MHz spectrometer using the residual solvent peak as an internal reference. Chemical shifts are given in parts per million. Coupling constants *J* are given in Hz. ^{13}C NMR spectra are recorded on the above spectrometers operating at 75 or 100 MHz, respectively, and are proton decoupled. Additional analysis by DEPT, HMQC and NOE experiments was performed when necessary. Mass spectra were measured on a Kratos Profile HV3 spectrometer or by the EPSRC mass spectrometry service, University of Wales Swansea. Elemental analyses were recorded on a Carlo Erba EA1110 elemental analyser.

THF was freshly distilled from sodium/benzophenone. Petrol refers to light petroleum ether (b.p. 40–60 °C). For the transmetallation reactions, hexane was distilled from calcium hydride and Et_2O from sodium/benzophenone. Flash column chromatography was performed on silica gel 60H (230–400 mesh) (Merck 9385) or on basic alumina (150 mesh) (Brockmann 1). Thin-layer chromatography was performed on silica-coated Merck Kieselgel $60F_{254}$ 0.25 mm plates, and visualised by UV irradiation at 254 nm or potassium permanganate dip.

(2*S*)-1-[2-(Tributylstannyl)pyrrolidin-1-yl]-but-3-en-1-one (2): *B*-Bromocatecholborane[15] (3.3 g, 16.5 mmol) in CH_2Cl_2 (80 mL) was added to carbamate (*S*)-**1**[14] (3.8 g, 8.2 mmol, 97:3 *er*) in CH_2Cl_2 (30 mL) at room temperature. After 30 min, 3-butenoyl chloride (1.0 g, 9.6 mmol) in CH_2Cl_2 (40 mL) was added. After 2 h, sat. aqueous $NaHCO_3$ (100 mL) was added and the mixture was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic extracts were dried ($MgSO_4$), evaporated and purified by column chromatography on silica gel, eluting with petrol/EtOAc 9:1 to give the stannane **2** (2.2 g, 65 %) as an oil; $R_f = 0.29$ (petrol/EtOAc 9:1); $[\alpha]_D^{23} = +189$ ($c = 2.8$ in EtOH); IR: $\tilde{\nu} = 1640$ (C=C), 1610 cm^{-1} (C=O); ^{1}H NMR (300 MHz, C_6D_6, 25 °C): $\delta = 0.94–1.07$ [m, 15H; Sn($CH_2CH_2CH_2CH_3$)$_3$], 1.34–1.48 [m, 6H; Sn($CH_2CH_2CH_2$)$_3$], 1.50–1.73 [m, 6H; Sn(CH_2CH_2)$_3$],

1.73–1.92 (m, 4H; $NCH_2CH_2CH_2$), 2.77 (d, ^3J(H,H) = 7 Hz, 2H; $OCCH_2$), 2.80–2.94 (m, 2H; 2 × NCH), 3.12 (dd, $^{3,3}J$(H,H) = 9, 7 Hz, 1H; NCH), 4.98 (dd, $^{3,3}J$(H,H) = 12.5, 2 Hz, 1H; CH^AH^B=), 5.03 (dd, $^{3,3}J$(H,H) = 6, 2 Hz, 1H; CHH^BH^B=), 5.97–6.12 (m, 1H; CH=); ^{13}C NMR (75 MHz, C_6D_6, 25 °C): δ = 11.2 (CH_2), 14.1 (CH_3), 27.9 (CH_2), 28.1 (CH_2), 29.8 (CH_2), 30.0 (CH_2), 40.0 (CH_2), 46.8 (CH, CH_2), 117.0 (=CH_2), 132.8 (=CH), 167.3 (C=O); MS (EI): calcd for $C_{20}H_{39}NO^{120}Sn$: 429.2054; found: 429.2060 $[M]^+$; *m*/*z* (%): 429 (0.5) $[M]^+$, 372 (62) $[M - Bu]^+$, 70 (100) $[C_4H_6O]^+$.

(2*S*)-*N*-(But-3-enyl)-2-(tributylstannyl)pyrrolidine (3): Aluminium chloride (133 mg, 0.97 mmol) and lithium aluminium hydride (96 mg, 2.9 mmol) in Et_2O (5 mL) were stirred at 0 °C for 15 min. The amide (*S*)-**2** (831 mg, 1.9 mmol) in Et_2O (5 mL) was added dropwise through cannula. After 2 h, aqueous NaOH (25 mL, 0.1M) and sodium potassium tartrate were added. The mixture was filtered and extracted with Et_2O (2 × 25 mL). The combined organic extracts were dried (Na_2SO_4), evaporated and purified by column chromatography on alumina, eluting with petrol/EtOAc 9:1 to give the amine **3** (718 mg, 89%) as an oil. R_f = 0.15 (petrol/EtOAc 4:1); $[\alpha]_D^{23}$ = +107 (*c* = 2.6 in EtOH); IR: $\tilde{\nu}$ = 1640 cm^{-1} (C=C); ^{1}H NMR (400 MHz, C_6D_6, 25 °C): δ = 1.04–1.12 [m, 15H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.43–1.53 [m, 6H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.62–1.84 [m, 6H; $Sn(CH_2CH_2CH_3)_3$], 1.84–2.10 (m, 5H; NCH_2CH_2CH=, NCH_2CH_2CH), 2.23–2.33 (m, 1H; CH), 2.33–2.45 (m, 2H; 2 × NCH), 2.52 (dd, $^{3,3}J$(H,H) = 9.5, 7.5 Hz, 1H; NCH), 2.97–3.10 (m, 2H; 2 × NCH), 5.11 (dd, $^{3,4}J$(H,H) = 10, 2 Hz, 1H; CH^AH^B=), 5.17 (dd, ^3J(H,H) = 17, 2 Hz, 1H; CHH^AH^B=), 6.00 (ddt, ^3J(H,H) = 17, 10, 7 Hz, 1H; CH=); ^{13}C NMR (100 MHz, C_6D_6, 25 °C): δ = 9.2 (CH_2), 13.7 (CH_3), 25.0 (CH_2), 27.7 (CH_2), 29.5 (CH_2), 29.7 (CH_2), 33.9 (CH_2), 53.7 (CH_2), 56.5 (CH_2), 57.5 (CH), 115.0 (CH_2), 137.2 (CH); MS (EI): calcd for $C_{20}H_{41}N^{120}Sn$: 415.2261; found: 415.2257 $[M]^+$; *m*/*z* (%): 415 (0.1) $[M]^+$, 124 (100) $[M - SnBu_3]^+$, 55 (72) $[C_4H_7]^+$; elemental analysis calcd (%) for $C_{20}H_{41}NSn$ (414.3): C 57.99, H 9.98, N 3.38; found: C 58.06, H 10.07, N 3.23.

(1*S*,8*R*)-1-Methylhexahydro-1*H*-pyrrolizine (pseudoheliotridane) (5): *n*-Butyllithium (1.5M in hexanes, 1.2 mL, 1.3 mmol) was added to the amine (*S*)-**3** (261 mg, 0.63 mmol) in dry hexane/Et_2O 9:1 (10 mL) under argon at −78 °C. The mixture was warmed to 25 °C for 4 h and was quenched with MeOH (0.5 mL) at −78 °C. The mixture was warmed to 25 °C and sat. aqueous NaCl (30 mL) was added. The mixture was extracted with Et_2O (2 × 25 mL). The combined organic extracts were dried ($NaSO_4$), evaporated and purified by column chromatography on alumina, eluting with petrol (b.p. 30–40 °C), then Et_2O to give pyrrolizidine **5**[16] (69 mg, 87%) as an oil. An excess of picric acid in EtOH was added and the mixture was purified by column chromatography on silica gel, eluting with MeOH/CH_2Cl_2 0:1 to 1:49 to give the picrate salt of the pyrrolizidine **5**. M.p. (picrate salt) 230–234 °C, lit.[16a] 234–236 °C; R_f (picrate salt) = 0.10 (CH_2Cl_2/MeOH/NH_3 9:1:0.1); $[\alpha]_D^{23}$ = +6.8 (*c* = 0.5 in EtOH, free base); IR (picrate salt, KBr disk): $\tilde{\nu}$ = 1560, 1365 cm^{-1} (NO_2); ^{1}H NMR (400 MHz, $CDCl_3$, picrate salt, 25 °C): δ = 1.21 (d, ^3J(H,H) = 6.5 Hz, 3H; CH_3), 1.80–2.33 (m, 7H; 3 × CH_2, CH), 2.82–2.92 (m, 1H; $NCH^AH^BCH_2CH$), 3.02–3.12 (m, 1H; $NCH^AH^BCH_2CH_2$), 3.65–3.75 (m, 1H; $NCH^AH^BCH_2CH_2$), 3.86–3.95 (m, 1H; NCH), 3.98–4.07 (m, 1H; $NCH^AH^BCH_2CH$), 8.85 (s, 2H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, picrate salt, 25 °C): δ = 16.7 (CH_3), 24.8 (CH_2), 29.3 (CH_2), 33.9 (CH_2), 40.0 (CH), 55.4 (CH_2), 55.6 (CH_2), 74.1 (CH), 126.6 (CH), 128.6 (C), 141.6 (C), 162.1 (C); MS (EI): calcd for $C_8H_{15}N$: 125.1204; found: 125.1201 $[M]^+$; *m*/*z* (%): 229 (4) [picric acid]$^+$, 125 (51) $[M]^+$, 83 (100) $[C_5H_9N]^+$; elemental analysis calcd (%) for $C_{14}H_{18}N_4O_7$ (354.3): C 47.46, H 5.12, N 15.81; found: C 47.47, H 5.04, N 15.51. The chiral solvating agent (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol[17] (0.03 mmol) split and shifted the CH_3 doublet of the free base, pseudoheliotridane (5 mg, 0.04 mmol) in $CDCl_3$ (0.7 mL) from δ = 1.02 (d, *J* = 6.5 Hz, 3H) to δ = 0.69 (d, *J* = 6.5 Hz, 3H) and δ = 0.67 (d, *J* = 6.5 Hz, 3H), thereby allowing the measurement of the *ee* of 94%.

(1*R*,8*R*)-1-(Monodeutereomethyl)hexahydro-1*H*-pyrrolizine (6a, E = D): In the same way as the amine **5**, *n*BuLi (2.5M in hexanes, 0.30 mL, 0.75 mmol), the amine **3** (150 mg, 0.36 mmol) in hexane/Et_2O 9:1 (7.5 mL) and MeOD (0.04 mL, 1.0 mmol), gave, after adding an excess picric acid in EtOH and purifying by column chromatography on silica gel, eluting with CH_2Cl_2/MeOH 1:0 to 98:2, the picrate salt of the amine **6a**, E = D (74 mg, 58%) as needles. M.p. 235–236 °C (picrate salt); R_f = 0.10 (CH_2Cl_2/MeOH/NH_3 9:1:0.1); $[\alpha]_D^{24}$ = +0.95 (*c* = 0.6 in $CHCl_3$, picrate salt); IR (picrate salt, $CDCl_3$): $\tilde{\nu}$ = 1570, 1365 cm^{-1} (NO_2); ^{1}H NMR (400 MHz, $CDCl_3$, picrate salt, 25 °C): δ = 1.18 (dt, ^3J(H,H) = 6.5 Hz, ^2J(H,D) = 2 Hz, 2H; CH_2D), 1.82–1.98 (m, 2H; 2 × CH), 1.98–2.16 (m, 2H; 2 × CH), 2.17–2.33 (m, 3H; 3 × CH), 2.84–2.93 (m, 1H; NCH), 3.03–3.13 (m, 1H; NCH), 3.64–3.74 (m, 1H; NCH), 3.85–3.95 (m, 1H; NCH), 3.99–4.05 (m, 1H; NCH), 8.82 (s, 2H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, picrate salt, 25 °C): δ = 16.2, 16.4/16.6 (CH_2D), 24.8 (CH_2), 29.3 (CH_2), 33.9 (CH_2), 39.9 (CH), 55.4 (CH_2), 55.6 (CH_2), 74.1 (CH), 126.6 (CH), 128.1 (C), 141.7 (C), 162.4 (C); MS (EI): calcd for $C_8H_{14}DN$: 126.1267; found: 126.1270 $[M]^+$; *m*/*z* (%): 229 (23) [picric acid]$^+$, 126 (25) $[M]^+$, 83 (100) $[C_5H_9N]^+$; elemental analysis calcd (%) for $C_{14}H_{17}DN_4O_7$ (355.3): C 47.33, H 4.82, N 15.77; found: C 47.80, H 5.18, N 15.62.

(1*R*,8*R*)-1-[2,2-Diphenyl-2-hydroxyethyl)hexahydro-1*H*-pyrrolizine (6b, E = C(OH)Ph$_2$): In the same way as the amine **5**, *n*BuLi (1.1M in hexanes, 0.92 mL, 0.97 mmol), the amine **3** (200 mg, 0.48 mmol) in hexane/Et_2O 9:1 (10 mL) and benzophenone (175 mg, 0.96 mmol) in Et_2O (1 mL), gave, after purification by column chromatography on alumina, eluting with petrol/EtOAc 1:0 to 0:1, the amine **6b**, E = C(OH)Ph_2 (92 mg, 62%) as needles. M.p. 164–166 °C; R_f = 0.11 (CH_2Cl_2/MeOH 9:1); $[\alpha]_D^{23}$ = +19.6 (*c* = 0.5 in EtOH); IR (KBr disc): $\tilde{\nu}$ = 3425 (OH), 1595, 1490 cm^{-1} (Ph); ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 1.34–1.45 (m, 2H; CH_2CO), 1.58–1.82 (m, 5H; 5 × CH), 2.30 (ddd, ^{2,3,3} = 11, 10, 6 Hz, 1H; CH), 2.38 (dd, $^{2,3}J$(H,H) = 13.5, 7.5 Hz, 1H; CH), 2.47–2.53 (m, 2H; 2 × NCH), 2.81 (dt, $^{2,3}J$(H,H) = 11, 6.5 Hz, 1H; NCH), 2.95–3.01 (m, 1H; NCH), 3.08 (td, $^{3,3}J$(H,H) = 8, 5 Hz, 1H; NCH), 7.10–7.18 (m, 2H; Ph), 7.22–7.30 (m, 4H; Ph), 7.41–7.48 (m, 4H; Ph); ^{13}C NMR (100 MHz, CD_3OD, 25 °C): δ = 24.7 (CH_2), 30.4 (CH_2), 34.9 (CH_2), 41.5 (CH), 45.3 (CH_2), 54.4 (CH_2), 54.5 (CH_2), 71.1 (CH), 77.1 (C), 125.9 (CH), 126.0 (CH), 126.1 (CH), 127.5 (2 × CH), 148.0 (C), 148.1 (C); MS (EI): calcd for $C_{21}H_{25}NO$: 307.1936; found: 307.1941 $[M]^+$; *m*/*z* (%): 307 (1.0) $[M]^+$, 183 (4.5) $[Ph_2COH]^+$, 124 (100) $[C_8H_{14}N]^+$.

(1*R*,8*R*)-1-(Trimethylsilylmethyl)hexahydro-1*H*-pyrrolizine (6c, E = SiMe$_3$): In the same way as the amine **5**, *n*BuLi (1.8M in hexane, 0.48 mL, 0.86 mmol), the amine **3** (180 mg, 0.43 mmol) in hexane/Et_2O 9:1 (10 mL) and Me_3SiCl (0.11 mL, 0.86 mmol), gave, after adding an excess picric acid in EtOH and purifying by column chromatography on silica gel, eluting with CH_2Cl_2/MeOH 1:0 to 98:2, the picrate salt of the amine **6c**, E = $SiMe_3$ (113 mg, 62%) as needles. M.p. 145–146 °C (picrate salt); R_f = 0.64 (CH_2Cl_2/MeOH 9:1); $[\alpha]_D^{23}$ = +5.3 (*c* = 0.7 in $CHCl_3$, picrate salt); IR (picrate salt, $CDCl_3$): $\tilde{\nu}$ = 1565, 1360 cm^{-1} (NO_2); ^{1}H NMR (400 MHz, $CDCl_3$, picrate salt, 25 °C): δ = 0.06 [s, 9H; $(CH_3)_3Si$], 0.70 (dd, $^{2,3}J$(H,H) = 14, 9.5 Hz, 1H; CHSi), 0.88 (dd, $^{2,3}J$(H,H) = 14, 4 Hz, 1H; CHSi), 1.59 (br s, 1H; NH), 1.80–2.34 (m, 7H; $NCH_2CH_2CH_2CHCHCH_2$), 2.79–2.92 (m, 1H; NCH), 3.03–3.11 (m, 1H; NCH), 3.63–3.74 (m, 1H; NCH), 3.84–3.95 (m, 1H; NCH), 3.97–4.08 (m, 1H; NCH), 8.87 (s, 2H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, picrate salt, 25 °C): δ = −1.1 (CH_3), 19.8 (CH_2), 24.7 (CH_2), 29.3 (CH_2), 34.2 (CH_2), 41.9 (CH), 55.4 (CH_2), 55.6 (CH_2), 75.5 (CH), 126.5 (CH), 128.0 (C), 141.7 (C), 162.4 (C); MS (EI): calcd for $C_{11}H_{23}NSi$: 197.1601; found: 197.1600 $[M]^+$; *m*/*z* (%): 229 (12) [picric acid]$^+$, 197 (9) $[M]^+$, 124 (28) $[C_8H_{14}N]^+$, 83 (100) $[C_5H_9N]^+$.

(1*R*,8*R*)-1-(Trimethylstannylmethyl)hexahydro-1*H*-pyrrolizine (6d, E = SnMe$_3$): In the same way as the amine **5**, *n*BuLi (2.5M in hexane, 0.3 mL, 0.75 mmol), the amine **3** (150 mg, 0.36 mmol) in hexane/Et_2O 9:1 (7.5 mL) and Me_3SnCl (0.8 mL, 1M in THF), gave, after adding an excess picric acid in EtOH and purifying by column chromatography on silica gel, eluting with CH_2Cl_2/MeOH 1:0 to 98:2, the picrate salt of the amine **6d**, E = $SnMe_3$ (126 mg, 68%) as needles. M.p. 146–148 °C (picrate salt); R_f = 0.53 (CH_2Cl_2/MeOH 9:1); $[\alpha]_D^{23}$ = +29.5 (*c* = 0.9 in $CHCl_3$, picrate salt); IR (picrate salt, $CDCl_3$): $\tilde{\nu}$ = 1565, 1360 cm^{-1} (NO_2); ^{1}H NMR (400 MHz, $CDCl_3$, picrate salt, 25 °C): δ = 0.12 [s, 9H; $(CH_3)_3Sn$], 0.87 (dd, $^{2,3}J$(H,H) = 13, 9.5 Hz, 1H; CHSn), 1.11 (dd, $^{2,3}J$(H,H) = 13, 5 Hz, 1H; CHSn), 1.82–1.95 (m, 3H; 3 × CH), 2.04–2.31 (m, 5H; 4 × CH, NH), 2.83–2.92 (m, 1H; NCH), 3.04–3.11 (m, 1H; NCH), 3.62–3.70 (m, 1H; NCH), 3.82–3.89 (m, 1H; NCH), 3.97–4.03 (m, 1H; NCH), 8.85 (s, 2H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, picrate salt, 25 °C): δ = −9.6 (CH_3), 13.5 (CH_2), 24.8 (CH_2), 29.3 (CH_2), 35.0 (CH_2), 44.0 (CH), 55.4 (CH_2), 55.5 (CH_2), 75.7 (CH), 126.6 (CH), 128.0 (C), 141.7 (C), 162.4 (C); MS (EI): calcd for $C_{11}H_{23}N^{120}Sn$: 289.0863; found: 289.0863 $[M]^+$; *m*/*z* (%): 289 (0.4) $[M]^+$, 126 (20) $[C_8H_{16}N]^+$, 124 (100) $[C_8H_{14}N]^+$.

(1*R*,8*R*,2′*RS*)-1-(2′-Hydroxy-2′-phenyl)ethylhexahydro-1*H*-pyrrolizine (6e, E = CH(OH)Ph): In the same way as the amine **5**, *n*BuLi (1.9M in hexanes, 0.56 mL, 1.06 mmol), the amine **3** (220 mg, 0.53 mmol) in hexane/Et_2O 9:1 (10 mL) and PhCHO (0.11 mL, 1.06 mmol), gave, after adding an

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excess of picric acid in EtOH and purifying by column chromatography on silica gel, eluting with CH_2Cl_2/MeOH 1:0 to 98:2, the picrate salt of the amine **6e**, E = CH(OH)Ph (102 mg, 41%) as a 1:1 mixture of diastereomers as needles. M.p. 140–143 °C (picrate salt); $R_f = 0.55$ (CH_2Cl_2/MeOH 9:1); IR (picrate salt, $CHCl_3$): $\tilde{\nu} = 3610$ (OH), 1610, 1495 (Ar), 1565, 1365 cm^{-1} (NO_2); ^1H NMR (400 MHz, $CDCl_3$, picrate salt, 25 °C): $\delta =$ 1.20–1.26 (m, 0.5H; 0.5 × CH), 1.75–1.84 (m, 0.5H; 0.5 × CH), 1.87–2.34 (m, 10H; 8 × CH, NH, OH), 2.79–2.83 (m, 1H; NCH), 3.00–3.13 (m, 1H; NCH), 3.63–3.74 (m, 1H; NCH), 3.98–4.18 (m, 2H; 2 × NCH), 4.71–4.79 (m, 1H; C*H*OH), 7.26–7.39 (m, 5H; Ph), 8.84 (s, 2H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, picrate salt, 25 °C): $\delta = 24.8$ (CH_2), 25.0 (CH_2), 29.9 (CH_2), 30.1 (CH_2), 32.1 (CH_2), 32.7 (CH_2), 41.2 (CH_2), 41.4 (CH_2), 41.9 (CH), 42.4 (CH), 55.2 (CH_2), 55.3 (CH_2), 55.4 (CH_2), 72.6 (CH), 72.7 (CH), 72.8 (CH), 73.0 (CH), 125.6 (CH), 126.6 (CH), 128.1 (C, CH), 128.2 (CH), 128.8 (CH), 141.6 (C), 143.8 (C) 144.0 (C), 162.3 (C); MS (EI): calcd for $C_{15}H_{21}NO$: 231.1623; found: 231.1622 $[M]^+$; *m*/*z* (%): 231 (20) $[M]^+$, 229 (16) [picric acid]$^+$, 124 (100) $[C_8H_{14}N]^+$, 109 (86).

(2*S*)-1-[2-(Tributylstannyl)pyrrolidin-1-yl]-pent-4-en-1-one (7): *B*-Bromocatechol borane[15] (4.4 mL, 1.3 mmol, 0.3 M in CH_2Cl_2) was added at room temperature to a solution of the carbamate **1** (0.5 g, 1.1 mmol) in CH_2Cl_2 (10 mL). After 5 min, aq NaOH (5 mL, 2 M) and 4-pentenoyl chloride (0.59 g, 5.0 mmol) were added. The mixture was stirred for 16 h, extracted into CH_2Cl_2 (3 × 5 mL), dried ($MgSO_4$) and evaporated. Purification by chromatography on silica gel eluting with petrol/EtOAc 9:1 gave the stannane (*S*)-**7** (318 mg, 65%) as an oil. $R_f = 0.35$ (petrol/EtOAc 9:1); $[\alpha]_D^{22} = +188$ ($c = 1.48$ in $CHCl_3$); IR: $\tilde{\nu} = 1615\ cm^{-1}$ (C=O); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 0.82$–0.95 [m, 15H; Sn(CH_2CH$_2$CH$_2$CH_3)$_3$], 1.22–1.38 [m, 6H; Sn(CH$_2$CH$_2$CH_2)$_3$], 1.43–1.58 [m, 6H; Sn(CH$_2$CH_2)$_3$], 1.86–2.02 (m, 3H; CH_2CH^AH^B), 2.11–2.20 (m, 1H; CH$_2$CH^AH^B), 2.31–2.46 (m, 4H; CH_2CO, CH_2C=), 3.32–3.41 (m, 2H; 2 × NCH), 3.47–3.55 (m, 1H; NCH), 5.00 (d, ^3J(H,H) = 9.5 Hz, 1H; CH^AH^B=), 5.08 (d, ^3J(H,H) = 16.5 Hz, 1H; CH^AH^B=), 5.82–5.95 (m, 1H; CH=); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 10.3$ (CH_2), 13.7 (CH_3), 27.5 (CH_2), 27.6 (CH_2), 29.1 (CH_2), 29.2 (CH_2), 29.6 (CH_2), 34.0 (CH_2), 46.9 (CH), 47.2 (CH_2), 114.9 (CH_2), 137.8 (CH), 169.1 (C=O); MS (CI): calcd for $C_{21}H_{41}NO^{120}Sn$: 443.2210; found: 443.2217 $[M]^+$; *m*/*z* (%): 443 (0.5) $[M]^+$, 386 (56) $[M - C_4H_9]^+$, 70 (100).

(2*S*)-*N*-(Pent-4-enyl)-2-(tributylstannyl)pyrrolidine (8): $LiAlH_4$ (0.70 mL, 0.70 mmol, 1 M in Et_2O) was added to a solution of the amide **7** (222 mg, 0.50 mmol) at 0 °C in Et_2O (5 mL). After 20 min at 0 °C, MeOH (0.5 mL) was added and the mixture was absorbed on alumina. Column chromatography on alumina, eluting with petrol/EtOAc 9:1 gave the stannane (*S*)-**8** (191 mg, 90%) as an oil. $R_f = 0.17$ (petrol/EtOAc 4:1); $[\alpha]_D^{20} = +67.5$ ($c =$ 1.20 in $CHCl_3$); IR: $\tilde{\nu} = 1630\ cm^{-1}$ (C=C); ^1H NMR (400 MHz, C_6D_6, 25 °C): $\delta = 0.92$–1.20 [m, 15H; Sn(CH_2CH$_2$CH$_2$CH_3)$_3$], 1.43–1.60 [m, 6H; Sn(CH$_2$CH$_2$CH_2)], 1.67–1.80 [m, 6H; Sn(CH$_2$CH_2)$_2$], 1.80–2.33 (m, 10H; 5 × CH_2), 2.53 (dd, $^{2,3}J$(H,H) = 11, 7.5 Hz, 1H; CH^AH^{B}N), 2.95 (ddd, $^{2,3,3}J$(H,H) = 11, 8, 7.5 Hz, 1H; CH^AH^BN), 3.03 (dd, $^{3,3}J$(H,H) = 8, 7.5 Hz, 1H; NCHSn), 5.10 (dd, $^{3,2}J$(H,H) = 10, 2 Hz, 1H; CH^AH^B=), 5.17 (dd, $^{3,2}J$(H,H) = 17, 2 Hz, 1H; CH^AH^B=), 5.94 (ddt, $^{3,3,3}J$(H,H) = 17, 10, 6.5 Hz, 1H; CH=); ^{13}C NMR (100 MHz, C_6D_6, 25 °C): $\delta = 9.2$ (CH_2), 13.7 (CH_3), 24.9 (CH_2), 27.7 (CH_2), 28.7 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 32.0 (CH_2), 53.8 (CH_2), 56.5 (CH_2), 57.7 (CH), 114.4 (CH_2), 138.8 (CH); MS (EI): calcd for $C_{21}H_{43}N^{120}Sn$: 429.2417; found: 429.2418 $[M]^+$; *m*/*z* (%): 429 (0.5) $[M]^+$, 176 (35), 138 (100).

Alternatively, the amine **8** could be prepared from **1** by deprotection and reductive amination: *B*-Bromocatecholborane[15] (2.2 mL, 0.66 mmol, 0.3 M in CH_2Cl_2) was added to carbamate (*S*)-**1**[14] (250 mg, 0.54 mmol) in CH_2Cl_2 (5 mL) at room temperature. After 10 min the mixture was washed rapidly with aq 2 M NaOH (3 × 5 mL), dried ($MgSO_4$) and evaporated. The residue was dissolved in $MeNO_2$ (2.5 mL) and $NaBH_3CN$ (126 mg, 2.0 mmol), 4-pentenal (92 mg, 1.1 mmol) and 4 Å molecular sieves were added at room temperature. After 15 min the mixture was absorbed on alumina and purified by column chromatography on alumina, eluting with petrol/EtOAc 9:1 to give the stannane (*S*)-**8** (143 mg, 62%) as an oil, data identical to above.

(1*R*,9*R*)-1-Methyloctahydroindolizine (10): The stannane **8** (84 mg, 0.20 mmol) in hexane/Et_2O (3 mL, 4:1) was treated with *n*-butyllithium (0.24 mL, 0.63 mmol, 2.5 M in hexanes) at room temperature. After 6 h, MeOH (0.5 mL) and picric acid (1.0 mL, 0.2 mmol, 0.2 M in EtOH) were added. The mixture was absorbed on silica gel and purified by column chromatography on silica gel, eluting with MeOH/CH_2Cl_2 0:1 to 1:49 to give an inseparable mixture of the picrate salts of **10**, **11** and *N*-pent-4-enylpyrrolidine (68 mg, 93%), consisting of amine **10**[29] (76%, 13% *ee*), amine **11** (4%) and *N*-pent-4-enylpyrrolidine (13%) as a powder. $R_f = 0.34$ (CH_2Cl_2/MeOH 9:1); IR (picrate salt, $CHCl_3$): $\tilde{\nu} = 1630$, 1610 (Ar), 1565, 1310 cm^{-1} (NO_2); ^1H NMR (400 MHz, $CDCl_3$, picrate salt, major product, 25 °C): $\delta = 1.02$ (d, ^3J(H,H) = 7 Hz, 3H; CH_3), 1.21–1.33 (m, 1H; CH^AH^{B}CHMe), 1.66–74 (m, 1H; CH^AH^BCHMe), 1.84–2.23 (m, 6H; CH_2CH_2CH, CH_2CH$_2$CHMe), 2.37–2.47 (m, 1H; C*H*Me), 2.64–2.74 (m, 1H; NCH^CH^D), 3.22 (ddd, $^{2,3,3}J$(H,H) = 13, 8, 3.5 Hz, 1H; NCH^EH^F), 3.42 (br d, ^2J(H,H) = 12 Hz, 1H; NCH^CH^D), 3.55–3.65 (m, 1H; NCH^EH^F), 3.79–3.87 (m, 1H; NCH), 8.88 (s, 2H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, picrate salt, 25 °C): $\delta = 18.3$ (CH_3), 19.0 (CH_2), 19.9 (CH_2), 22.8 (CH_2), 24.4 (CH_2), 29.5 (CH), 47.7 (CH_2), 54.2 (CH_2), 65.9 (CH), 126.6 (CH), 128.2 (C), 141.7 (C), 162.2 (C); MS (CI): calcd for $C_9H_{18}N$: 140.1439; found: 140.1438 $[M+H]^+$; *m*/*z* (%): 140 (52) $[M+H]^+$, 138 (42) $[M - H]^+$ 96 (55), 84 (100); elemental analysis calcd (%) for $C_{15}H_{20}N_4O_7$ (368.3): C 48.91, H 5.47, N 15.21; found: C 49.09, H 5.48, N 14.98.

The enantioselectivity of the cyclization reaction was determined by measuring (^1H NMR) the relative peak areas of the methyl doublets of the picrate salt of the amine **10** in the presence of the chiral solvating agent (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.[17]

(1*S*,9*R*)-1-Methyloctahydroindolizine (11): The stannane **8** (40 mg, 0.09 mmol) in hexane/Et_2O/TMEDA (2 mL, 4:1:1) was treated with *n*-butyllithium (0.17 mL, 0.37 mmol, 2.2 M in hexanes) at room temperature. After 6 h, MeOH (0.5 mL) and picric acid (0.45 mL, 0.09 mmol, 0.2 M in EtOH) were added. The mixture was absorbed on silica gel and purified by column chromatography on silica gel, eluting with MeOH/CH_2Cl_2 0:1 to 1:49 to give an inseparable mixture of the picrate salts of **10**, **11** and *N*-pent-4-enylpyrrolidine (33 mg, 97%), consisting of amine **10** (7.5%, 0% *ee*), amine **11**[29] (68.5%, 0% *ee*) and *N*-pent-4-enylpyrrolidine (21%) as a powder. $R_f = 0.34$ (CH_2Cl_2/MeOH 9:1); IR (picrate salt, $CHCl_3$): $\tilde{\nu} = 1630$, 1610 (Ar), 1565, 1320 cm^{-1} (NO_2); ^1H NMR (400 MHz, $CDCl_3$, picrate salt, major product, 25 °C): $\delta = 1.05$ (d, ^3J(H,H) = 7 Hz, 3H; CH_3), 1.88–2.30 (m, 9H; CH_2CH_2CHMeCHCH_2CH_2), 2.43–2.54 (m, 1H; NCH), 2.60–2.72 (m, 1H; NCH^AH^B), 2.76–2.88 (m, 1H; NCH^CH^D), 3.82–3.95 (m, 2H; NCH^AH^B, NCH^CH^D), 8.87 (s, 2H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, picrate salt, 25 °C): $\delta = 18.4$ (CH_3), 19.4 (CH_2), 22.9 (CH_2), 26.6 (CH_2), 31.6 (CH_2), 33.5 (CH), 52.9 (CH_2), 53.9 (CH_2), 73.5 (CH), 126.7 (CH), 128.2 (C), 141.7 (C), 161.9 (C); MS (EI): calcd for $C_9H_{18}N$: 139.1361; found: 139.1362 $[M]^+$; *m*/*z* (%): 139 (5) $[M]^+$, 138 (7) $[M - H]^+$ 96 (7), 84 (100); elemental analysis calcd (%) for $C_{15}H_{20}N_4O_7$ (368.3): C 48.91, H 5.47, N 15.21; found: C 48.87, H 5.46, N 14.80.

The enantioselectivity of the cyclization reaction was determined by measuring (^1H NMR) the relative peak areas of the methyl doublets of the free base of the amine **11** in the presence of the chiral solvating agent (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.[17]

***O*-(2′-Tetrahydropyranyl)-5-phenylthiopent-4-ynol (12)**: *n*BuLi (7.5 mL, 18.80 mmol, 2.5 M in hexanes) was added at 0 °C to a solution of alkyne *O*-(2′-tetrahydropyranyl)-pent-4-ynol[26] (3.0 g, 17.9 mmol) in THF (90 mL). After 1 h, a pre-mixed solution of PhSSPh (4.65 g, 21.5 mmol) and MeI (3.0 g, 21.3 mmol) in THF (75 mL) was added over 45 min. After 30 min, the mixture was warmed to room temp and stirred for 18 h. Water (75 mL) was added and the mixture was extracted into CH_2Cl_2 (3 × 40 mL), dried ($MgSO_4$), evaporated and purified by column chromatography on silica gel, eluting with petrol/EtOAc 19:1 to give the alkyne **12** (4.55 g, 92%) as an oil. $R_f = 0.38$ (petrol/EtOAc 10:1); IR: $\tilde{\nu} = 1580$, 1475 cm^{-1} (Ar); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 1.48$–1.86 (m, 6H; 3 × CH_2), 1.90 (quintet, ^3J(H,H) = 6.5 Hz, 2H; CH_2CH$_2$C≡), 2.59 (t, ^3J(H,H) = 6.5 Hz, 2H; CH_2), 3.47–3.55 (m, 2H; CH^AH^{B}O, CH^CH^{D}O), 3.84–3.91 (m, 2H; CH^AH^BO, CH^CH^DO), 4.62 (t, ^3J(H,H) = 3.5 Hz, 1H; CHO), 7.19 (t, ^3J(H,H) = 7.5 Hz, 1H; Ar), 7.32 (t, ^3J(H,H) = 7.5 Hz, 2H; Ar), 7.41 (d, ^3J(H,H) = 7.5 Hz, 2H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 17.3$ (CH_2), 19.5 (CH_2), 25.5 (CH_2), 28.9 (CH_2), 30.7 (CH_2), 62.2 (CH_2), 65.0 (CS), 65.8 (CH_2), 98.8 (CH), 99.3 (C), 125.8 (CH), 126.1 (CH), 129.1 (CH), 133.6 (C); MS (CI): calcd for $C_{16}H_{21}O_2S$: 277.1262; found: 277.1264 $[M+H]^+$; *m*/*z* (%): 277 (18%) $[M+H]^+$, 193 (13), 102 (100); elemental analysis calcd (%) for $C_{16}H_{20}O_2S$ (276.4): C 69.53, H 7.29; found: C 69.97, H 7.57.

***E*-*O*-(2′-Tetrahydropyranyl)-5-phenylthiopent-4-enol (13)**: Alkyne **12** (3.00 g, 10.9 mmol) in THF (30 mL) was added to a suspension of $LiAlH_4$

(800 mg, 21.0 mmol) in THF (20 mL). After heating at 40–45 °C for 3 h, the mixture was cooled to room temperature and stirred for 16 h. MeOH (5 mL) and water (50 mL) were added and the mixture was extracted into CH_2Cl_2 (3 × 50 mL), dried ($MgSO_4$) and evaporated. Purification by column chromatography on silica gel, eluting with petrol/EtOAc 9:1 gave the alkene *E*-**13** (2.81 g, 93%) as an oil. $R_f = 0.38$ (petrol/EtOAc 10:1); IR: $\tilde{\nu} = 1730$ (C=C), 1575, 1480 cm^{-1} (Ar); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 1.49-1.87$ (m, 8H; 4 × CH_2), 2.28 (dtd, $^{3,3,4}J(H,H) = 7$, 6.5, 1 Hz, 2H; CH_2C=), 3.43 (dt, $^{3,3}J(H,H) = 9.5$, 6.5 Hz, 1H; CH^AH^BO), 3.48–3.54 (m, 1H; CH^CH^DO), 3.78 (dt, $^{3,3}J(H,H) = 9.5$, 6.5 Hz, 1H; CH^AH^BO), 3.87 (ddd, $^{2,3}J(H,H) = 11$, 7.5, 3.5 Hz, 1H; CH^CH^DO), 4.59 (t, $^3J(H,H) = 3.5$ Hz, 1H; CHO), 6.00 (dt, $^{3,3}J(H,H) = 14.5$, 7 Hz, 1H; CH=), 6.18 (dt, $^{3,4}J(H,H) = 14.5$, 1 Hz, 1H; CHS), 7.17–7.21 (m, 1H; Ar), 7.27–7.33 (m, 4H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 19.7$ (CH_2), 25.5 (CH_2), 29.1 (CH_2), 29.8 (CH_2), 30.7 (CH_2), 62.4 (CH_2), 66.7 (CH_2), 98.9 (CHO), 121.4 (CHS), 126.1 (CH), 128.5 (CH), 128.9 (CH), 136.4 (C), 136.5 (CH); MS (CI): calcd for $C_{16}H_{26}NO_2S$: 296.1684; found: 296.1684 $[M+NH_4]^+$; *m*/*z* (%): 296 (10) $[M+NH_4]^+$, 278 (3) $[M]^+$,102 (100); elemental analysis calcd (%) for $C_{16}H_{22}O_2S$ (278.4): C 69.02, H 7.96; found: C 68.62, H 8.20.

***Z*-*O*-(2′-Tetrahydropyranyl)-5-phenylthiopent-4-enol (13)**: DIBAL (30 mL, 1M in hexane) over 45 min was added at −18 °C to a solution of the alkyne **12** (4.85 g, 17.6 mmol) in hexane (150 mL). The mixture was warmed to 0 °C for 1 h, and then to room temperature for 16 h. MeOH (2 mL) then aq NaOH (60 mL, 1M) were added and the mixture was extracted into hexane (3 × 50 mL), dried ($MgSO_4$) and evaporated. Purification by column chromatography on silica gel, eluting with petrol/EtOAc 9:1 gave the alkene *Z*-**13** (4.83 g, 99%) as an oil. $R_f = 0.38$ (petrol/EtOAc 10:1); IR: $\tilde{\nu} = 1730$ (C=C), 1580, 1480 cm^{-1} (Ar); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 1.48-1.94$ (m, 8H; 4 × CH_2), 2.36 (dt, $^{3,3}J(H,H) = 7.5$, 6.5 Hz, 2H; CH_2C=), 3.45 (dt, $^{3,3}J(H,H) = 10$, 6.5 Hz, 1H; CH^AH^BO), 3.47–3.54 (m, 1H; CH^CH^DO), 3.79 (dt, $^{3,3}J(H,H) = 10$, 6.5 Hz, 1H; CH^AH^BO), 3.84–3.91 (m, 1H; CH^CH^DO), 4.60 (t, $^3J(H,H) = 3.5$ Hz, 1H; CHO), 5.84 (dt, $^{3,3}J(H,H) = 9$, 7.5 Hz, 1H; CH=), 6.22 (d, $^3J(H,H) = 9$ Hz, 1H; CHS), 7.19 (t, $^3J(H,H) = 7$ Hz, 1H; Ar), 7.26–7.35 (m, 4H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 19.6$ (CH_2), 25.5 (CH_2), 25.9 (CH_2), 29.1 (CH_2), 30.7 (CH_2), 62.2 (CH_2), 66.8 (CH_2), 98.9 (CHO), 123.2 (CHS), 126.1 (CH), 128.7 (CH), 129.0 (CH), 132.7 (CH), 136.4 (C); MS (CI): calcd for $C_{16}H_{26}NO_2S$: 296.1684; found: 296.1685 $[M+NH_4]^+$; *m*/*z* (%): 296 (7) $[M+NH_4]^+$, 278 (2) $[M]^+$, 102 (100); elemental analysis calcd (%) for $C_{16}H_{22}O_2S$ (278.4): C 69.02, H 7.96; found: C 69.10, H 8.27.

***E*-5-(Phenylthio)pent-4-enal (14)**: Water (2.6 mL) and $TsOH \cdot H_2O$ (100 mg, 0.53 mmol) were added at room temperature to a solution of the sulfide *E*-**13** (2.60 g, 9.60 mmol) in MeOH (100 mL). After 16 h, K_2CO_3 (150 mg) and water (100 mL) were added. The mixture was extracted into CH_2Cl_2 (3 × 50 mL), dried ($MgSO_4$) and evaporated. Purification by column chromatography on silica gel, eluting with petrol/EtOAc 4:1 gave the alcohol (1.86 g, 100%) as an oil. $R_f = 0.48$ (petrol/EtOAc 1:1); IR: $\tilde{\nu} =$ 3350 (O-H), 1740 (C=C), 1540, 1480 cm^{-1} (Ar); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 1.44$ (s, 1H; OH), 1.72 (quintet, $^3J(H,H) = 6.5$ Hz, 2H; CH_2CH_2C=), 2.28 (qd, $^{3,4}J(H,H) = 6.5$, 1.5 Hz, 2H; CH_2C=), 3.69 (t, $^3J(H,H) = 6.5$ Hz, 2H; CH_2O), 5.98 (dt, $^{3,3}J(H,H) = 14.5$, 6.5 Hz, 1H; CH=), 6.20 (dt, $^{3,4}J(H,H) = 14.5$, 1.5 Hz, 1H; CHS), 7.17–7.22 (m, 1H; Ar), 7.27–7.36 (m, 4H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 29.4$ (CH_2), 31.9 (CH_2), 62.2 (CH_2), 121.8 (CHS), 126.2 (CH), 128.6 (CH), 129.0 (CH), 135.9 (CH), 136.2 (C); MS (CI): calcd for $C_{11}H_{18}NOS$: 212.1109; found: 212.1106 $[M+NH_4]^+$; *m*/*z* (%): 212 (52) $[M+NH_4]^+$, 195 (100) $[M+H]^+$, 102 (41); elemental analysis calcd (%) for $C_{11}H_{14}OS$ (194.3): C 68.00, H 7.26; found: C 68.00, H 7.46.

DMSO (1.6 mL, 20.0 mmol), followed by the above alcohol (1.92 g, 9.90 mmol) in CH_2Cl_2 (2 mL), was added to a solution of oxalyl chloride (0.90 mL, 10.0 mmol) in CH_2Cl_2 (25 mL) at −60 °C. After 15 min at −60 °C, Et_3N (6.2 mL, 45.0 mmol) was added and the mixture was stirred for a further 5 min then warmed to room temperature. Water (50 mL) was added and the mixture was extracted into CH_2Cl_2 (3 × 40 mL), dried ($MgSO_4$) and evaporated. Purification by column chromatography on silica gel, eluting with petrol/EtOAc 9:1 gave the aldehyde *E*-**14** (1.31 g, 69%) as an oil. $R_f = 0.35$ (petrol/EtOAc 10:1); IR: $\tilde{\nu} = 1740$ (C=O, C=C), 1540, 1480 cm^{-1} (Ar); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.48$ (q, $^3J(H,H) =$ 6.5 Hz, 2H; CH_2C=), 2.59 (t, $^3J(H,H) = 6.5$ Hz, 2H; CH_2CH_2C=), 5.92 (dt, $^{3,3}J(H,H) = 14$, 6.5 Hz, 1H; CH=), 6.22 (d, $^3J(H,H) = 14$ Hz, 1H; CHS), 7.18–7.24 (m, 1H; Ar), 7.27–7.36 (m, 4H; Ar) and 9.82 (s, 1H; CHO); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 25.5$ (CH_2), 42.9 (CH_2), 123.3 (CHS), 126.5 (CH), 128.9 (CH), 129.0 (CH), 133.2 (CH), 135.7 (C), 201.3 (CO); MS (EI): calcd for $C_{11}H_{12}OS$: 192.0609; found: 192.0608 $[M]^+$; *m*/*z* (%): 192 (25) $[M]^+$, 110 (80), 86 (100).

***Z*-5-(Phenylthio)pent-4-enal (14)**: In the same way as the aldehyde *E*-**14**, the sulfide *Z*-**13** (4.17 g, 15.0 mmol) in MeOH (200 mL) and water (4 mL) and $TsOH \cdot H_2O$ (100 mg, 0.53 mmol) gave, after purification by column chromatography on silica gel, eluting with petrol/EtOAc 4:1, the alcohol (2.91 g, 100%) as an oil. $R_f = 0.48$ (petrol/EtOAc 1:1); IR: $\tilde{\nu} = 3350$ (O-H), 1745 (C=C), 1575, 1475 cm^{-1} (Ar); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta =$ 1.63 (s, 1H; OH), 1.73 (tt, $^{3,3}J(H,H) = 7$, 6.5 Hz, 2H; CH_2CH_2C=), 2.35 (q, $^3J(H,H) = 7$ Hz, 2H; CH_2C=), 3.70 (t, $^3J(H,H) = 6.5$ Hz, 2H; CH_2O), 5.84 (dt, $^{3,3}J(H,H) = 9.5$, 7 Hz, 1H; CH=), 6.24 (d, $^3J(H,H) = 9.5$ Hz, 1H; CHS), 7.18–7.24 (m, 1H; Ar), 7.26–7.37 (m, 4H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 25.4$ (CH_2), 31.8 (CH_2), 62.2 (CH_2), 123.7 (CHS), 126.3 (CH), 128.9 (CH), 129.0 (CH), 132.2 (CH), 136.1 (C); MS (CI): calcd for $C_{11}H_{18}NOS$: 212.1109; found: 212.1104 $[M+NH_4]^+$; *m*/*z* (%): 212 (55) $[M+NH_4]^+$, 195 (100) $[M+H]^+$, 102 (41); elemental analysis calcd (%) for $C_{11}H_{14}OS$ (194.3): C 68.00, H 7.26; found: C 68.48, H 7.54.

In the same way as the aldehyde *E*-**14**, oxalyl chloride (0.60 mL, 6.7 mmol) in CH_2Cl_2 (15 mL), DMSO (1.1 mL, 13.4 mmol) and the alcohol (1.3 g, 6.70 mmol) in CH_2Cl_2 (2 mL) then Et_3N (4.1 mL, 30.0 mmol) gave, after purification by column chromatography on silica gel, eluting with petrol/EtOAc 9:1, the aldehyde *Z*-**14** (821 mg, 64%) as an oil. $R_f = 0.37$ (petrol/EtOAc 10:1); IR: $\tilde{\nu} = 1730$ (C=O, C=C), 1590, 1480 cm^{-1} (Ar); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.56-2.62$ (m, 4H; CH_2CH_2), 5.76–5.84 (m, 1H; CH=), 6.28 (d, $^3J(H,H) = 10.5$ Hz, 1H; CHS), 7.21–7.26 (m, 1H; Ar), 7.29–7.38 (m, 4H; Ar), 9.81 (s, 1H; CHO); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 21.9$ (CH_2), 43.0 (CH_2), 125.0 (CHS), 126.5 (CH), 129.0 (CH), 129.1 (CH), 130.1 (CH), 135.7 (C), 201.6 (CO); MS (ES): calcd for $C_{11}H_{13}OS$: 193.0687; found: 193.0684 $[M+H]^+$; *m*/*z* (%): 193 (100) $[M+H]^+$, 118 (87).

***E*-(2*S*)-*N*-(5-Phenylthiopent-4-enyl)-2-(tributylstannyl)pyrrolidine (*E*-15)**: In the same way as the alkene *E*-**13**, $LiAlH_4$ (90 mg, 2.4 mmol) and the alkyne **18** (388 mg, 0.73 mmol) gave, after purification by column chromatography on alumina, eluting with petrol/EtOAc 10:1, the stannane *E*-**15** (314 mg, 80%) as an oil. $R_f = 0.11$ (petrol/EtOAc 4:1); $[\alpha]_D^{20} = +55.3$ ($c = 1.14$ in $CHCl_3$); IR: $\tilde{\nu} = 1740$ (C=C), 1585, 1480 cm^{-1} (Ar); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 0.86-0.93$ [m, 15H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.26–1.37 [m, 6H; $Sn(CH_2CH_2CH_2)_3$], 1.45–1.52 [m, 6H; $Sn(CH_2CH_2)_3$], 1.59–2.90 (m, 13H; 6 × CH_2, CH), 5.95 (dt, $^{3,3}J(H,H) = 15$, 6.5 Hz, 1H; CH=), 6.16 (d, $^3J(H,H) = 15$ Hz, 1H; CHS), 7.16–7.24 (m, 1H; Ar), 7.27–7.34 (m, 4H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 9.3$ (CH_2), 13.7 (CH_3), 24.5 (CH_2), 26.8 (CH_2), 27.5 (CH_2), 27.8 (CH_2), 29.3 (CH_2), 31.1 (CH_2), 54.0 (CH_2), 56.3 (CH_2), 57.7 (CH), 121.6 (CH), 126.1 (CH), 128.6 (CH), 128.9 (CH), 134.7 (CH), 136.4 (C); MS (CI): calcd for $C_{27}H_{47}NS^{120}Sn$: 538.2529; found: 538.2530 $[M+H]^+$; *m*/*z* (%): 538 (18) $[M+H]^+$, 308 (33), 246 (100).

***Z*-(2*S*)-*N*-(5-Phenylthiopent-4-enyl)-2-(tributylstannyl)pyrrolidine (15)**: In the same way as the alkene *Z*-**13**, DIBAL (0.65 mL, 1M in hexane) and the alkyne **18** (169 mg, 0.32 mmol) gave, after purification by column chromatography on alumina, eluting with petrol/EtOAc 10:1, the alkene *Z*-**15** (101 mg, 59%) as an oil. $R_f = 0.13$ (petrol/EtOAc 4:1); $[\alpha]_D^{20} = +46$ ($c = 0.98$, $CHCl_3$); IR: $\tilde{\nu} = 1760$ (C=C), 1605, 1480 cm^{-1} (Ar); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 0.87-0.94$ [m, 15H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.26–1.38 [m, 6H; $Sn(CH_2CH_2CH_2)_3$], 1.46–1.54 [m, 6H; $Sn(CH_2CH_2)_3$], 1.59–3.00 (m, 13H; 6 × CH_2, CH), 5.80 (dt, $^{3,3}J(H,H) = 8.5$, 7 Hz, 1H; CH=), 6.24 (d, $^3J(H,H) = 8.5$ Hz, 1H; CHS), 7.20 (t, $^3J(H,H) = 7$ Hz, 1H; Ar), 7.27–7.34 (m, 4H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 9.7$ (CH_2), 13.7 (CH_3), 24.4 (CH_2), 27.0 (CH_2), 27.5 (CH_2), 27.6 (CH_2), 29.2 (CH_2), 31.1 (CH_2), 47.2 (CH_2), 53.8 (CH_2), 57.7 (CH), 123.9 (CH), 126.1 (CH), 128.7 (CH), 128.8 (CH), 131.7 (CH), 136.1 (C); MS (CI): calcd for $C_{27}H_{47}NS^{120}Sn$: 538.2529; found: 538.2533 $[M+H]^+$; *m*/*z* (%): 538 (4) $[M+H]^+$, 248 (100), 140 (95); elemental analysis calcd (%) for $C_{27}H_{47}NSSn$ (536.4): C 60.45, H 8.83, N 2.61; found: C 60.63, H 9.21, N 2.51.

Alternatively, the amines *E*- and *Z*-**15** could be prepared from **1** by deprotection and reductive amination with **14**: In the same way as the amine **8**, the stannane **1** (250 mg, 0.54 mmol), *B*-bromocatecholborane (2.2 mL, 0.66 mmol, 0.3M in CH_2Cl_2) then $NaBH_3CN$ (126 mg, 2.0 mmol) in $MeNO_2$ (2.5 mL) and the aldehyde *E*- or *Z*-**14** (211 mg, 1.1 mmol) gave,

0947-6539/02/0801-0204 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 1

after purification by column chromatography on alumina, eluting with petrol/EtOAc 10:1, the stannane *E*-**15** (209 mg, 72%) or *Z*-**15** (198 mg, 0.37 mmol, 69%), data identical to above.

(2*S*)-1-[2-(Tributylstannyl)pyrrolidin-1-yl]-pent-4-yn-1-one (16): In the same way as the amide **7**, *B*-bromocatechol borane[15] (4.4 mL, 1.2 mmol, 0.3 M in CH_2Cl_2), the carbamate (*S*)-**1**[14] (0.5 g, 1.1 mmol) in CH_2Cl_2 (10 mL) and 4-pentynoyl chloride (392 mg, 4.0 mmol) gave, after purification by column chromatography on silica gel eluting with petrol/EtOAc 9:1, the stannane **16** (279 mg, 59%) as an oil. $R_f = 0.36$ (petrol/EtOAc 4:1); $[\alpha]_D^{22} = +248$ ($c = 1.2$ in $CHCl_3$); IR: $\tilde{\nu} = 3305$ (≡C-H), 1615 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 0.80 - 0.90$ [m, 15H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.23 – 1.33 [m, 6H; $Sn(CH_2CH_2CH_2)_3$], 1.41 – 1.52 [m, 6H; $Sn(CH_2CH_2)_3$], 1.84 – 2.00 (m, 4H; ≡CH, $CH_2CH^AH^B$), 2.12 – 2.19 (m, 1H; CH^AH^B), 2.46 – 2.57 (m, 4H; $CH_2CH_2C\equiv$), 3.31 – 3.39 (m, 2H; 2 × NCH), 3.47 – 3.54 (m, 1H; NCH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta =$ 10.2 (CH_2), 13.8 (CH_3), 14.6 (CH_2), 27.5 (CH_2), 27.6 (CH_2), 29.2 (CH_2), 29.6 (CH_2), 33.6 (CH_2), 47.0 (CH), 47.2 (CH_2), 68.6 (CH), 83.8 (C), 167.5 (CO); MS (EI): calcd for $C_{21}H_{39}NO^{120}Sn$: 441.2054; found: 441.2054 $[M]^+$; *m*/*z* (%): 441 (5) $[M]^+$, 384 (100), 382 (78); elemental analysis calcd (%) for $C_{21}H_{39}NOSn$ (440.3): C 57.29, H 8.93, N 3.18; found: C 57.40, H 9.27, N 3.14.

(2*S*)-*N*-(Pent-4-ynyl)-2-(tributylstannyl)pyrrolidine (17): In the same way as the amine **8**, the amide **16** (183 mg, 0.42 mmol) and $LiAlH_4$ (0.60 mL, 0.60 mmol, 1 M in Et_2O) gave, after purification by column chromatography on alumina, eluting with petrol/EtOAc 19:1, the stannane **17** (151 mg, 84%) as an oil. $R_f = 0.18$ (petrol/EtOAc 4:1); $[\alpha]_D^{22} = +73.1$ ($c = 0.73$ in $CHCl_3$); IR: $\tilde{\nu} = 3310$ cm^{-1} (≡C-H); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 0.81 - 0.98$ [m, 15H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.24 – 1.35 [m, 6H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.41 – 1.56 [m, 6H; $Sn(CH_2CH_2CH_2)_3$], 1.68 – 1.90 (m, 5H; 5 × CH), 1.93 (t, $^4J(H,H) = 2$ Hz, 1H; ≡CH), 1.94 – 2.07 (m, 2H; 2 × CH), 2.09 – 2.33 (m, 3H; 3 × CH), 2.35 – 2.46 (m, 1H; CH), 2.79 – 3.03 (m, 2H; 2 × CH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 9.2$ (CH_2), 13.7 (CH_3), 16.5 (CH_2), 24.5 (CH_2), 27.5 (CH_2), 27.7 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 53.9 (CH_2), 55.7 (CH_2), 57.6 (CH), 68.5 (CH), 83.5 (C); MS (EI): calcd for $C_{21}H_{41}N^{120}Sn$: 427.2261; found 427.2250 $[M]^+$; *m*/*z* (%): 427 (6) $[M]^+$, 368 (42), 134 (100); elemental analysis calcd (%) for $C_{21}H_{41}NSn$ (426.3): C 59.17, H 9.69, N 3.29; found: C 59.43, H 10.13, N 3.21.

(2*S*)-*N*-(5-Phenylthiopent-4-ynyl)-2-(tributylstannyl)pyrrolidine (18): *n*BuLi (0.39 mL, 0.98 mmol, 2.5 M in hexanes) was added at 0 °C to a solution of the alkyne **17** (378 mg, 0.89 mmol) in Et_2O (5 mL). After 90 min, a pre-mixed solution of PhSSPh (243 mg, 1.07 mmol) and MeI (0.06 mL, 0.98 mmol) in THF (10 mL) was added. The mixture was allowed to warm to room temperature. After 16 h, the mixture was absorbed on alumina and purified by column chromatography on alumina, eluting with petrol/EtOAc 10:1 to give the alkyne **18** (312 mg, 66%) as an oil. $R_f = 0.14$ (petrol/EtOAc 4:1); $[\alpha]_D^{22} = +36.5$ ($c = 1.04$ in $CHCl_3$); IR: $\tilde{\nu} = 1595$, 1480 cm^{-1} (Ar); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 0.81 - 0.96$ [m, 15H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.21 – 1.39 [m, 6H; $Sn(CH_2CH_2CH_2)_3$], 1.41 – 1.55 [m, 6H; $Sn(CH_2CH_2)_3$], 1.61 – 2.23 (m, 8H; 3 × CH_2, 2 × CH), 2.38 – 2.57 (m, 3H; $CH_2C\equiv$, NCH), 2.80 – 2.99 (m, 2H; 2 × NCH), 7.19 (t, $^3J(H,H) = 7$ Hz, 1H; Ar), 7.31 (t, $^3J(H,H) = 7$ Hz, 2H; Ar), 7.41 (t, $^3J(H,H) = 7$ Hz, 2H; Ar); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 9.1$ (CH_2), 13.6 (CH_3), 14.2 (CH_2), 18.4 (CH_2), 24.5 (CH_2), 27.5 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 54.0 (CH_2), 55.9 (CH_2), 57.7 (CH), 60.4 (C), 99.2 (C), 125.7 (CH), 126.0 (CH), 129.0 (CH), 134.6 (C); MS (CI): calcd for $C_{27}H_{45}NS^{120}Sn$: 536.2373; found: 536.2373 $[M+H]^+$; *m*/*z* (%): 536 (7) $[M+H]^+$, 308 (50), 84 (100); elemental analysis calcd (%) for $C_{27}H_{45}NSSn$ (534.4): C 60.68, H 8.49, N 2.62; found: C 60.73, H 8.88, N 2.33.

Cyclization of the stannane *E*-15: The stannane *E*-**15** (1.16 g, 2.16 mmol) in hexane/Et_2O (25 mL, 4:1) was treated with *n*-butyllithium (2.6 mL, 6.50 mmol, 2.5 M in hexanes) at room temperature. After 2 h, MeOH (2 mL) was added, the solvent was removed under reduced pressure and the residue was purified by column chromatography on alumina, eluting with petrol-EtOAc (1:0 to 4:1) to give the amines **19** and **20** (409 mg, 77%) as a 7:3 ratio of diastereomers as an oil. IR: $\tilde{\nu} = 3020$, 2935 cm^{-1} (C-H); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 1.25 - 2.21$ (m, 12H; 4 × CH_2, 4 × CH), 2.46 – 2.50 (m, 0.3H; CH^AH^BN), 2.62 (dd, $^{2,3}J(H,H) = 12$, 8.5 Hz, 0.3H; CH^AH^BS), 2.93 – 3.03 (m, 1.7H; CH^AH^BN, CH^CH^DN), 3.05 (dd, $^{2,3}J(H,H) = 12$, 3.5 Hz, 0.3H; CH^AH^BS), 3.19 (dd, $^2J(H,H) = 12.5$, 9 Hz, 0.7H; CH^AH^BS), 3.32 (dd, $^{2,3}J(H,H) = 12.5$, 4.5 Hz, 0.7H; CH^AH^BS), 6.98 – 7.04 (m, 1H; Ar), 7.09 – 7.14 (m, 2H; Ar), 7.38 – 7.43 (m, 2H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 20.8$ (CH_2), 21.1 (CH_2), 25.7 (CH_2), 26.3 (CH_2), 28.5 (CH_2), 29.3 (CH_2), 31.4 (CH_2), 35.4 (CH), 37.7 (CH_2), 41.9 (CH), 52.5 (CH_2), 53.8 (CH_2), 54.4 (CH_2), 54.7 (CH_2), 66.6 (CH), 68.3 (CH), 125.3 (CH), 125.5 (CH), 127.7 (CH), 127.8 (CH), 128.8 (CH), 138.2 (C), 138.3 (C); MS (CI): calcd for $C_{15}H_{22}NS$: 248.1473; found: 248.1468 $[M+H]^+$; *m*/*z* (%): 248 (100) $[M+H]^+$, 140 (62) $[C_9H_{18}N]^+$, 138 (60) $[M - C_6H_5S]^+$. The enantioselectivity of the cyclization was determined by treating the mixture of amines **19** and **20** with Raney nickel in EtOH (60 °C, 30 min, 90%) to give the amines **10** and **11**.

Cyclization of the stannanes *E*- or *Z*-15 in the presence of TMEDA: The stannane *E*- or *Z*-**15** (1 mol equiv, 0.1 M) in hexane/Et_2O/TMEDA 4:1:1 was treated with *n*-butyllithium (3 mol equiv) at room temperature. After 2 h, MeOH (excess) was added, the solvent was removed under reduced pressure and the residue was passed through a plug of alumina, eluting with petrol/EtOAc 4:1 to give the amine **20** as an oil. Treatment with Raney nickel in EtOH (60 °C, 30 min), filtration and treatment with picric acid (1 mol equiv) gave, after chromatography on silica gel, eluting with MeOH/CH_2Cl_2 0:1 to 1:49, the amine **11** (71 – 73%), data identical to above.

(2*S*)-*N*-(Prop-2-ynyl)-2-(tributylstannyl)pyrrolidine (24): *B*-Bromocatechol borane[15] (4.4 mL, 0.3 M in CH_2Cl_2, 1.32 mmol) was added to the carbamate (*S*)-**1**[14] (0.5 g, 1.1 mmol) in CH_2Cl_2 (10 mL) at room temperature. After 10 min, aqueous NaOH (10 mL, 2 M) was added, followed by propargyl bromide (0.12 mL, 1.1 mmol, 80% *w*/*w* in PhMe). After 75 min, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), absorbed on alumina and purified by column chromatography on alumina, eluting with petrol/EtOAc 1:0 to 9:1 to give the alkyne **24** (280 mg, 65%) as an oil. $R_f = 0.65$ (petrol/EtOAc 4:1); $[\alpha]_D^{22} = +93.4$ ($c = 3.5$ in $CHCl_3$); IR: $\tilde{\nu} = 3320$ cm^{-1} (≡C-H); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 0.82 - 0.95$ [m, 15H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.30 [sextet, $^3J(H,H) = 7$Hz, 6H; $Sn(CH_2CH_2CH_2)_3$], 1.43 – 1.58 [m, 6H; $Sn(CH_2CH_2)_3$], 1.70 – 1.90 (m, 3H; 3 × CH), 1.96 – 2.10 (m, 1H; CH), 2.18 (t, $^4J(H,H) = 2.5$ Hz, 1H; ≡CH), 2.26 (q, $^3J(H,H) = 8.5$ Hz, 1H; CH), 2.47 – 2.53 (m, 1H; CH), 2.93 – 3.00 (m, 1H; CH), 3.36 (dd, $^{2,4}J(H,H) = 17$, 2.5 Hz, 1H; $NCH^AH^BC\equiv C$), 3.64 (dd, $^{2,4}J(H,H) = 17$, 2.5 Hz, 1H; $NCH^AH^BC\equiv C$); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 8.7$ (CH_2), 13.7 (CH_3), 24.8 (CH_2), 27.5 (CH_2), 29.3 (CH_2), 29.9 (CH_2), 43.0 (CH_2), 53.0 (CH_2), 53.7 (CH), 72.6 (CH), 79.2 (C); MS (CI): calcd for $C_{19}H_{38}N^{120}Sn$: 400.2026; found: 400.2028 $[M+H]^+$; *m*/*z* (%): 400 (2.8) $[M+H]^+$, 308 (3.0), 108 (13) $[M - SnBu_3]^+$, 70 (100) $[C_4H_8N]^+$.

(2*S*)-*N*-[3-(Phenylthio)prop-2-ynyl]-2-(tributylstannyl)pyrrolidine (25): In the same way as the sulfide **18**, the alkyne **24** (329 mg, 0.83 mmol) in Et_2O (6.5 mL), PhSSPh (230 mg, 1.0 mmol) and MeI (0.057 mL, 0.91 mmol) in THF (3.5 mL) gave, after allowing to warm to room temperature for 1 h and purification by column chromatography on alumina, eluting with petrol/EtOAc 100:1 to 9:1, the alkyne **25** (275 mg, 65%) as an oil. $R_f = 0.65$ (petrol/EtOAc 4:1); $[\alpha]_D^{22} = +88.8$ ($c = 1.1$ in $CHCl_3$); IR: $\tilde{\nu} = 1585$, 1485 cm^{-1} (Ar); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 0.89 - 0.98$ [m, 15H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.35 [sextet, $^3J(H,H) = 7$Hz, 6H; $Sn(CH_2CH_2CH_2)_3$], 1.49 – 1.59 [m, 6H; $Sn(CH_2CH_2)_3$], 1.78 – 2.13 (m, 4H; 4 × CH), 2.38 (q, $^3J(H,H) = 8.5$ Hz, 1H; CH), 2.59 (t, $^3J(H,H) = 8.5$ Hz, 1H; CH), 2.97 – 3.04 (m, 1H; CH), 3.65 (d, $^2J(H,H) = 18$ Hz, 1H; $NCH^AH^BC\equiv C$), 3.88 (d, $^2J(H,H) = 18$ Hz, 1H; $NCH^AH^BC\equiv C$), 7.24 – 7.45 (m, 5H; Ar); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 8.8$ (CH_2), 13.7 (CH_3), 24.9 (CH_2), 27.6 (CH_2), 29.3 (CH_2), 30.0 (CH_2), 44.5 (CH_2), 53.2 (CH_2), 53.8 (CH), 70.3 (C), 95.4 (C), 126.0 (CH), 126.3 (CH), 129.1 (CH), 133.2 (C); MS (CI): calcd for $C_{25}H_{42}NS^{120}Sn$: 508.2060; found: 508.2065 $[M+H]^+$; *m*/*z* (%): 508 (1.3) $[M+H]^+$, 308 (3.0), 216 (2.7) $[M - SnBu_3]^+$, 108 (13) $[M - SPh - SnBu_3]^+$, 70 (100) $[C_4H_8N]^+$.

***E*-(2*S*)-*N*-[3-(Phenylthio)prop-2-enyl]-2-(tributylstannyl)pyrrolidine (26)**: In the same way as the alkene *E*-**13**, $LiAlH_4$ (55 mg, 1.45 mmol) and the alkyne **25** (210 mg, 0.42 mmol) in THF (2 mL) gave, after 1.5 h at 45 °C and purification by column chromatography on alumina, eluting with petrol/EtOAc 1:0 to 4:1, the stannane *E*-**26** (172 mg, 80%) as an oil. $R_f = 0.22$ (petrol/EtOAc 4:1); $[\alpha]_D^{22} = +34.0$ ($c = 2.0$ in $CHCl_3$); IR: $\tilde{\nu} = 1585$, 1480 cm^{-1} (Ar); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 0.82 - 0.95$ [m, 15H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.35 [sextet, $^3J(H,H) = 7$ Hz, 6H; $Sn(CH_2CH_2CH_2)_3$], 1.42 – 1.58 [m, 6H; $Sn(CH_2CH_2)_3$], 1.62 – 2.08 (m, 5H; 5 × CH), 2.40 (t, $^3J(H,H) = 8.5$ Hz, 1H; CH), 2.74 – 2.88 (m, 1H; CH), 2.90 – 3.05 (m, 1H; CH), 3.49 (dd, $^{3,3}J(H,H) = 13.5$, 6.5 Hz, 1H; CH), 5.99 (dt, $^{3,3}J(H,H) = 14$, 7 Hz, 1H; $CH=CHS$), 6.35 (d, $^3J(H,H) = 14$ Hz, 1H; =CHS), 7.17 – 7.36 (m, 5H; Ar); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 9.1$ (CH_2), 13.7 (CH_3), 24.6 (CH_2), 27.6 (CH_2), 29.3 (CH_2), 29.6 (CH_2), 54.4

(CH_2), 56.9 (CH), 58.4 (CH_2), 124.3 (CH), 126.5 (CH), 129.0 (CH), 129.4 (CH), 132.2 (CH), 135.6 (C); MS (CI): calcd for $C_{25}H_{44}NS^{120}Sn$: 510.2216; found: 510.2217 $[M+H]^+$; *m/z* (%): 510 (24) $[M+H]^+$, 308 (26), 218 (86) $[M-SnBu_3]^+$, 70 (100) $[C_4H_8N]^+$; elemental analysis calcd (%) for $C_{25}H_{43}NSSn$ (508.4): C 59.06, H 8.53, N 2.76; found: C 58.88, H 8.76, N 2.52.

6-Phenylthiomethyl-1-azabicyclo[3.2.0]heptane (27 + 28): The stannane *E*-**26** (116 mg, 0.23 mmol) in hexane/Et_2O (3.2 mL, 4:1) was treated with *n*-butyllithium (0.23 mL, 0.58 mmol, 2.5 M in hexanes) at room temperature. After 30 min, MeOH (0.2 mL) and picric acid (1.1 mL, 0.23 mmol, 0.2 M in EtOH) were added and the mixture was absorbed on silica gel. Purification by column chromatography on silica gel, eluting with CH_2Cl_2/MeOH 1:0 to 50:1 gave the picrate salts of the amines **27** and **28** (52 mg, 52%) as a 10:1 ratio of diastereomers as a solid. M.p. (decomp.) 134 °C; $R_f = 0.45$ (CH_2Cl_2/MeOH 9:1); $[\alpha]_D^{18} = -1.1$ (*c* = 1.3 in $CHCl_3$); IR (picrate salt, $CHCl_3$): $\tilde{\nu}$ = 1630, 1615 (Ar), 1560, 1320 cm^{-1} (NO_2); ^1H NMR (400 MHz, $CDCl_3$, 25 °C, picrate salt, major product): δ = 1.99–2.04 (m, 1H; NCHCH^{E}H^F), 2.13–2.23 (m, 1H; NCHC*H*^{E}H^F), 2.34–2.42 (m, 2H; NCH_2CH_2), 2.52 (sextet, ^3J(H,H) = 7.5 Hz, 1H; NCH_2CH), 3.24–3.29 (m, 1H; NCH^{C}H^DCH_2), 3.33 (d, ^3J(H,H) = 8 Hz, 2H; CH_2S), 3.32–3.41 (m, 1H; NC*H*^{C}H^DCH_2), 3.56 (dd, $^{2,3}J$(H,H) = 11.5, 10 Hz, 1H; NCH^A*H*^{B}CH), 4.30 (dd, $^{2,3}J$(H,H) = 11.5, 7.5 Hz, 1H; NC*H*^{A}H^{B}CH), 4.76 (t, ^3J(H,H) = 7 Hz, 1H; NCH), 7.24–7.36 (m, 5H; Ph), 8.85 (s, 2H; Ar); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, picrate salt, major product) δ = 24.5 (CH_2), 30.7 (CH_2), 35.1 (CH), 36.7 (CH_2), 53.2 (CH_2), 55.6 (CH_2), 72.2 (CH), 126.6 (CH), 127.4 (CH), 128.2 (C), 129.3 (CH), 130.8 (CH), 133.7 (C), 141.7 (C), 162.4 (C); MS (CI): calcd for $C_{13}H_{18}NS$: 220.1160; found: 220.1159 $[M+H]^+$; *m/z* (%): 220 (100) $[M+H]^+$, 110 (23); elemental analysis calcd (%) for $C_{19}H_{20}N_4O_7S$ (448.5): C 50.89, H 4.50, N 12.49; found: C 50.55, H 4.30, N 12.30. In addition, the picrate salt of the stannane **26** (61 mg, 36%) was isolated.

Alternatively, the amines **27** and **28** could be prepared from **26** in THF: The stannane *E*-**26** (76 mg, 0.15 mmol) in THF (2 mL) was treated over 1 min with *n*-butyllithium (0.15 mL, 0.38 mmol, 2.5 M in hexanes) at −78 °C. After a further 1 min, MeOH (0.2 mL) and picric acid (0.73 mL, 0.15 mmol, 0.2 M in EtOH) were added and the mixture was warmed to room temperature and absorbed on silica gel. Purification by column chromatography on silica gel, eluting with CH_2Cl_2/MeOH 1:0 to 50:1 gave the picrate salts of the amines **27** and **28** (59 mg, 86%) as a 1:1 ratio of diastereomers as a solid. Data as above but ^1H NMR (300 MHz, $CDCl_3$, 25 °C, picrate salt): δ = 1.98–2.57 (m, 10H; 10 × CH), 2.93–3.06 (m, 2H; 2 × CH), 3.20–3.40 (m, 7H; 7 × CH), 3.56 (dd, $^{2,3}J$(H,H) = 11.5, 10 Hz, 1H; CH), 4.30 (dd, $^{2,3}J$(H,H) = 11.5, 7.5 Hz, 1H; CH), 4.48–4.63 (m, 1H; CH), 4.76 (t, ^3J(H,H) = 7 Hz, 1H; CH), 5.00 (t, ^3J(H,H) = 8 Hz, 1H; CH), 7.20–7.38 (m, 10H; 2 × SPh), 8.80 (s, 4H; 2 × Ar); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, picrate salt): δ = 24.5 (CH_2), 25.5 (CH_2), 25.8 (CH_2), 30.4 (CH), 30.7 (CH_2), 32.8 (CH_2), 35.1 (CH), 36.7 (CH_2), 53.1 (CH_2), 53.2 (CH_2), 55.6 (CH_2), 56.8 (CH_2), 69.7 (CH), 72.2 (CH), 126.6 (CH), 127.4 (CH), 127.7 (CH), 128.2 (C), 129.3 (CH), 129.5 (CH), 130.8 (CH), 131.3 (CH), 133.3 (C), 133.7 (C), 141.7 (C), 162.4 (C).

***E*-(2*S*)-*N*-[3-Deuterio-3-(phenylthio)prop-2-enyl]-2-(tributylstannyl)pyrrolidine (29)**: In the same way as the amines **27** + **28**, prepared in hexane/Et_2O 4:1, the stannane **26** (120 mg, 0.24 mmol) and *n*BuLi (0.24 mL, 0.60 mmol, 2.5 M in hexanes), gave, after quenching with MeOD (0.2 mL), addition of picric acid (1.2 mL, 0.24 mmol, 0.2 M in EtOH) and purification by column chromatography on silica gel, eluting with CH_2Cl_2/MeOH 1:0 to 50:1, the picrate salt of the stannane **29** (59 mg, 33%) as an oil. $R_f = 0.85$ (CH_2Cl_2/MeOH 9:1); IR (picrate salt, $CHCl_3$): $\tilde{\nu}$ = 1630, 1615 (Ar), 1570, 1330 cm^{-1} (NO_2); ^1H NMR (300 MHz, $CDCl_3$, 25 °C, picrate salt): δ = 0.79–1.08 [m, 15H; $Sn(CH_2CH_2CH_2CH_3)_3$], 1.18–1.54 [m, 12H; $Sn(CH_2CH_2CH_2)_3$], 1.96–2.08 (m, 1H; CH), 2.19–2.36 (m, 3H; 3 × CH), 2.56–2.68 (m, 1H; CH), 2.78–2.92 (m, 1H; CH), 3.50 (dt, $^{2,3}J$(H,H) = 13, 6.5 Hz, 1H; CH), 3.60–3.74 (m, 1H; CH), 4.08 (dd, $^{2,3}J$(H,H) = 13, 6.5 Hz, 1H; CH), 5.55 (t, ^3J(H,H) = 7.5 Hz, 1H; CH=CS), 7.22–7.40 (m, 5H; Ar), 8.87 (s, 2H; Ar); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, picrate salt): δ = 9.9 (CH_2), 13.6 (CH_3), 23.9 (CH_2), 27.3 (CH_2), 28.9 (CH_2), 29.4 (CH_2), 54.2 (CH_2), 55.3 (CH), 56.8 (CH_2), 115.7 (CH), 126.7 (CH), 128.0 (C), 128.4 (CH), 129.5 (CH), 131.7 (C), 132.0 (CH), 141.5 (C), 162.0 (C); MS (FAB): calcd for $C_{25}H_{43}DNS^{120}Sn$: 511.2273; found: 511.2279 $[M+H]^+$; *m/z* (%): 511 (57) $[M+H]^+$, 219 (40) $[M-SnBu_3]^+$, 150 (100).

6-Methyl-1-azabicyclo[3.2.0]heptane (30 + 31): Sulfides **27** + **28** (69 mg, 0.32 mmol, 1:1 mixture of the free bases) in EtOH (2 mL) at 60 °C were added to a suspension of Raney nickel (1.0 g) in EtOH (2 mL). After 1 h the mixture was filtered and picric acid (1.5 mL, 0.32 mmol, 0.2 M in EtOH) was added. The solution was absorbed on silica gel and purified by column chromatography on silica gel, eluting with CH_2Cl_2/MeOH 1:0 to 50:1, to give the picrate salts of the amines **30** + **31** (77 mg, 71%) as a 1:1 mixture of diastereomers as a solid. $R_f = 0.40$ (CH_2Cl_2/MeOH 9:1); IR (picrate salt, $CHCl_3$): $\tilde{\nu}$ = 1620 (Ar), 1575, 1320 cm^{-1} (NO_2); ^1H NMR (300 MHz, $CDCl_3$, 25 °C, picrate salt): δ = 1.15 (d, ^3J(H,H) = 7.5 Hz, 3H; CH_3), 1.39 (d, ^3J(H,H) = 7.5 Hz, 3H; CH_3), 2.07–2.56 (m, 10H; 10 × CH), 3.17–3.42 (m, 5H; 5 × CH), 3.61–3.71 (m, 1H; CH), 4.21 (dt, $^{2,3}J$(H,H) = 12, 7.5 Hz, 1H; CH), 4.58–4.71 (m, 2H; 2 × CH), 5.05 (q, ^3J(H,H) = 7.5 Hz, 1H; CH), 9.04 (s, 4H; 2 × Ar); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, picrate salt): δ = 13.0 (CH_3), 18.4 (CH_3), 24.5 (CH_2), 25.2 (CH_2), 25.7 (CH_2), 25.7 (CH), 30.4 (CH), 30.6 (CH_2), 52.9 (CH_2), 53.2 (CH_2), 57.6 (CH_2), 58.6 (CH_2), 70.5 (CH), 74.2 (CH), 126.6 (CH), 128.2 (C), 141.6 (C), 162.2 (C); MS (ES): calcd for $C_7H_{14}N$: 112.1126; found: 112.1124 $[M+H]^+$; *m/z* (%): 112 (100) $[M+H]^+$.

Alternatively, the free base of the amines **30** + **31** (10:1) could be prepared: To a suspension of Raney nickel (1.0 g) in EtOH (2 mL) was added sulfide **27** + **28** (82 mg, 0.37 mmol, 10:1) in EtOH (2 mL) at 60 °C. After 1 h, the mixture was filtered and evaporated to give the amines **30** + **31** (23 mg, 54%) as a 10:1 mixture of diastereomers as an oil. ^1H NMR (300 MHz, $CDCl_3$, 25 °C, major diastereomer): δ = 1.26 (d, ^3J(H,H) = 7.5 Hz, 3H; CH_3), 1.92–2.00 (m, 2H; 2 × CH), 2.15–2.40 (m, 3H; 3 × CH), 2.98–3.15 (m, 2H; 2 × CH), 3.40 (dd, $^{2,3}J$(H,H) = 10 Hz, 1H; CH), 3.95 (dd, $^{2,3}J$(H,H) = 10, 7.5 Hz, 1H; CH), 4.44 (t, ^3J(H,H) = 6 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 18.4 (CH_3), 24.5 (CH_2), 30.4 (CH), 30.7 (CH_2), 52.3 (CH_2), 56.4 (CH_2), 72.4 (CH); MS (CI): calcd for $C_7H_{14}N$: 112.1126; found: 112.1126 $[M+H]^+$; *m/z* (%): 112 (100) $[M+H]^+$.

The enantioselectivity of the cyclization reaction was determined by measuring (^1H NMR) the relative peak areas of the methyl doublets of the amines **30** + **31** (as their free bases) in the presence of the chiral solvating agent (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.[17]

***E*- and *Z*-6-Phenylthiomethylene-1-azabicyclo[3.2.0]heptane (32)**: *n*-Butyllithium (0.3 mL, 0.68 mmol, 2.5 M in hexanes) was added to the stannane **24** (139 mg, 0.27 mmol) in THF (2.5 mL) at −78 °C. After 1.5 h, MeOH (0.5 mL) was added and the mixture was absorbed on alumina. Purification by column chromatography on alumina, eluting with petrol/EtOAc 1:0 to 0:1 then EtOAc/MeOH 50:1 to 5:1, gave the amines *E*- and *Z*-**32** (45 mg, 78%) as a 1:1 mixture of geometrical isomers as an oil. $R_f = 0.07$ (MeOH); IR: $\tilde{\nu}$ = 1585, 1485 cm^{-1} (Ar); ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.76–2.15 (m, 8H; 2 × $NCH_2CH_2CH_2CH_2$), 2.66–2.87 (m, 4H; 2 × NCH_2CH_2), 3.44 (dt, $^{2,4}J$(H,H) = 15, 3.0 Hz, 1H; NCH^A*H*^{B}C=), 3.55 (ddd, $^{2,4,4}J$(H,H) = 15, 3.5, 2.5 Hz, 1H; NCH^A*H*^{B}C=), 4.23 (dd, $^{2,4}J$(H,H) = 15, 2.5 Hz, 1H; NC*H*^{A}H^{B}C=), 4.29 (dd, $^{2,4}J$(H,H) = 15, 1.5 Hz, 1H; NC*H*^{A}H^{B}C=), 4.57–4.66 (m, 2H; 2 × NCH), 5.87 (q, ^4J(H,H) = 1.0 Hz, 1H; CHS), 5.92 (q, ^4J(H,H) = 1.0 Hz, 1H; CHS), 7.14–7.32 (m, 10H; 2 × Ar); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 23.9 (CH_2), 23.9 (CH_2), 30.8 (CH_2), 32.7 (CH_2), 55.9 (CH_2), 56.0 (CH_2), 60.2 (CH_2), 60.8 (CH_2), 72.6 (CH), 73.0 (CH), 111.5 (2 × CH), 126.0 (CH), 126.1 (CH), 128.1 (CH), 128.3 (CH), 129.0 (CH), 136.0 (C), 136.4 (C), 145.6 (C), 146.3 (C); MS (CI): calcd for $C_{13}H_{16}NS$: 218.1003; found: 218.1002 $[M+H]^+$; *m/z* (%): 218 (43) $[M+H]^+$, 110 (100).

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[28] The absolute configuration of both diastereomers **27** and **28** is unknown; in all cases studied with a variety of different solvents and reaction conditions, the same major enantiomer of the diastereomer **27** is formed. However, in the few cases [using the solvent system hexane/Et_2O 2:1, which occurred with reasonable yield (58%) and diastereoselectivity (**27**:**28** 10:1) but lower enantioselectivity (31–34% *ee*) or using the solvent THF] where it has been possible to observe [^{1}H NMR in the presence of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol] the splitting of the methyl doublets of both **30** and **31** in the mixture of **30** + **31** derived from **27** + **28**, it appears that a different major enantiomer of the diastereomer **28** may have been formed in hexane/Et_2O 2:1 from that formed in THF as the solvent.
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