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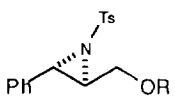
Studies of Regio- and Stereoselectivity in Some Nucleophilic Ring Opening Reactions of *N*-Tosyl-3-phenyl-2-aziridinemethanols and Derivatives

David Tanner* and Odd R. Gautun

Department of Organic Chemistry, University of Uppsala
Box 531, S-751 21 Uppsala, Sweden

Abstract: A study has been made of the regio- and stereoselectivity of the ring opening reactions of the 3-aryl substituted aziridines **1** and **2**. The regiochemical outcome is apparently decided by a balance of electronic activation at C-3 by the phenyl group and the chelating effects of C-1 oxygen functionality which can direct nucleophiles intramolecularly to C-2 or C-3. Good levels of regiocontrol for either C-3 or C-2 attack are obtained particularly for the reactions of aziridino alcohols **1a** and **2a** with hydride reagents, while methyl-transfer reagents such as $LiMe_2Cu$ and $AlMe_3$ tend to give exclusive C-3 attack with inversion (cuprate) or inversion plus retention (trialkylaluminum). Possible reaction mechanisms (inter- vs. intramolecular) are discussed.

We have previously shown how to achieve good to excellent regiocontrol in the ring opening of 2,3-aziridino alcohols by hydride and methyl-transfer reagents,[1, 2] and many of the results could be explained by assuming a mechanism involving complexation of the organometallic reagent to the hydroxyl group in the substrate, followed by intramolecular delivery of the nucleophile to the proximal carbon of the aziridine ring; for all the substrates studied, ring opening occurred with clean inversion. Recently, in connection with a project aimed at the total synthesis of some natural products via chiral aziridines,[3] we had occasion to investigate the reactions of isomeric 3-aryl substituted aziridino alcohols (and derivatives) such as **1** and **2**.



1a R = H
1b R = Bn
1c R = TBS

2a R = H
2b R = Bn

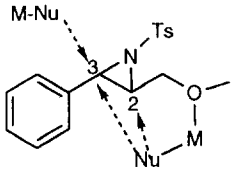
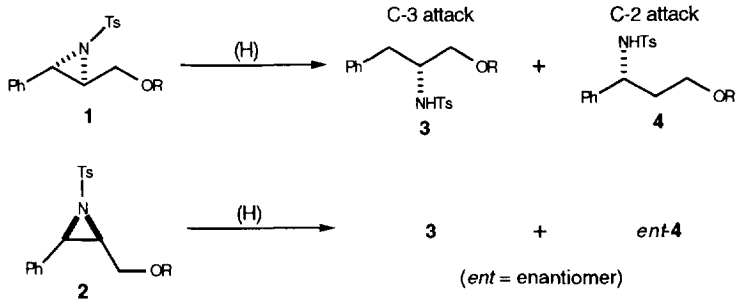


Fig. 1. Inter- vs. intramolecular attack

On the basis of our earlier results,[1, 2] and as shown schematically in Fig. 1, we expected that three major pathways should be open to these substrates for their reactions with organometallic nucleophiles: *(i)* an intermolecular reaction involving attack at the C-3 position, which is activated by the phenyl group, ring opening occuring with inversion or retention. For substrates **a** and **b**: *(ii)* an intramolecular reaction with attack at C-3, after complexation of the reagent to (or reaction with) the C-1 oxygen functionality (inversion or retention); *(iii)* intramolecular attack at C-2 (presumably with inversion). Prediction of the actual mode of attack is thus not simple, and it was of interest to try to find reaction conditions which would allow for synthetically useful levels of regio- and stereocontrol. Racemic substrates were used for these exploratory studies but, when our work was in progress, preparation of **1a**, **1c**, and **2a** in enantiomerically pure form was reported.[4] The results from ring opening of aziridino alcohols **1a** and **2a** by hydride reagents (Scheme 1) are shown in Table 1.



Scheme 1. Regio- and stereoisomers from ring opening of ***1*** *and* ***2*** *by hydride reagents. (Ent-****1*** *gives ent-****3*** *and ent-****4****; ent-****2*** *gives ent-****3*** *and* ***4****).*

Table 1. Ring opening of ***1a*** *and* ***2a*** *by hydride reagents and catalytic hydrogenolysis.*

Entry	Substrate	Reagent/Conditions	Ratio[a] **3** : **4**	%Yield[b]
1.	**1a**	Red-Al (2 eq.), -78°C, THF	8 : 92	70[c]
2.		Red-Al (4 eq.), 0 to 20 °C, THF	25 : 75	84
3.	**2a**	Red-Al (2 eq.), -30°C, THF	<1 : >99	80
4.		Red-Al (2 eq.), 20°C, THF	<1 : >99	78
5.	**1a**	$LiAlH_4$ (2 eq.), -78°C, THF	20 : 80	<10[c]
6.		$LiAlH_4$ (2 eq.), -30 to -20°C, THF	67 : 33	75[c]
7.	**2a**	$LiAlH_4$ (2 eq.), -30°C, THF	<1 : >99	65[c]
8.		$LiAlH_4$ (2 eq.), 20°C, THF	2 : 98	65
9.	**1a**	DIBAL (4 eq.), 0 to 20 °C, THF	96 : 4	90
10.	**2a**	DIBAL (4 eq.), 0 to 20 °C, THF	7 : 93	68[c]
11.	**1a**	10% Pd/C, H_2, EtOH	>99 : <1	100
12.	**2a**	10% Pd/C, H_2, EtOH	>99 : <1	98

[a] By ^1H NMR spectroscopy on crude product. [b] Total isolated yield. [c] Reaction incomplete.

Our previous studies[1] had shown that Red-Al and $LiAlH_4$ are "C-2 selective" reagents for 2,3-aziridino alcohols, and this is largely reflected also in the present cases (Table 1, entries 1 - 5, 7 and 8). We interpret this as being due to the chelate effect shown in Fig. 1 ("5-exo" mode) but we were surprised that the C-2 selectivity was much superior for the *cis* aziridine **2a**. Further, for the reactions with $LiAlH_4$, the C-2 selectivity for **2a** was not eroded to the same extent as for **1a** upon increasing the reaction temperature, and comparison of entries 5 and 6 in Table 1 may very well indicate that two different mechanisms (intra- *vs.* intermolecular) are operative for the *trans* substrate. (It may also be mentioned that the epoxy alcohol corresponding to **1a** gives a 4.5:1 ratio[5] in favour of the C-2 product in the reaction with Red-Al at 25°C, and this can be compared with entry 2 in Table 1). DIBAL, which cannot deliver hydride intramolecularly after reaction with the C-1 hydroxyl, was earlier found[1] to be a generally less reactive and less selective species than the other two complex hydrides, and it was therefore another surprise to find that this reagent gave useful chemical yields and high (but opposite!) selectivities for both **1a** and **2a** (Table 1, entries 9 and 10). We presume that this is due to two competing intermolecular processes, *i.e.* complexation of DIBAL blocks C-2 in the *trans* substrate and C-3 in the *cis* isomer. Finally, the results shown in entries 11 and 12 of Table 1 (hydrogenolysis at the benzylic position) are what would be expected.

Presumably, all three hydride reagents react with the hydroxyl groups in **1a** and **2a** before nucleophilic attack occurs. The effect of blocking the initial reaction was examined for the *trans* aziridine in the form of derivatives **1b** and **1c**, and the results are collected in Table 2.

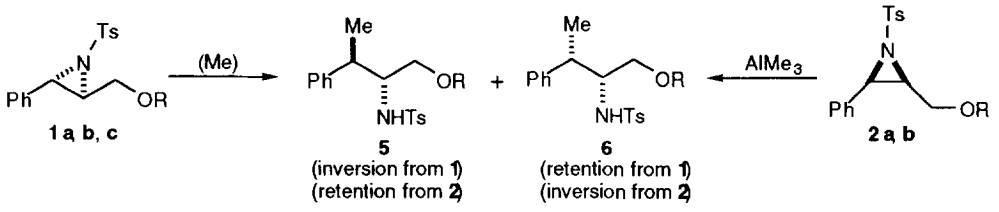
*Table 2. Ring opening of **1b** and **1c** by hydride reagents and catalytic hydrogenolysis.*

Entry	Substrate	Reagent/Conditions	Ratio[a] **3** : **4**	%Yield[b]
1.	**1c**	Red-Al (4 eq.), 20°C, THF	>99 : <1[c]	70
2.	**1b**	$LiAlH_4$ (4 eq.), 0 to 25°C, THF	>99 : <1	68
3.	**1c**	$LiAlH_4$ (4 eq.), 20°C, THF	>99 : <1[c]	77
4.	**1b**	DIBAL (4 eq.), 25 to 65 °C, THF	no reaction	
5.	**1c**	DIBAL (4 eq.), 25 to 65 °C, THF	no reaction	
6.	**1b**	10% Pd/C, H_2, EtOH	>99 : <1	81
7.	**1b**	10% Pd/C, EtOH, HCl	>99 : <1[d]	84

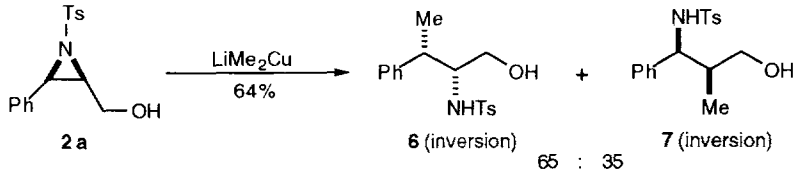
[a] *By ^1H NMR on crude product.* [b] *Total isolated yield.* [c] *Silylether also cleaved.* [d] *Benzyl ether also cleaved.*

In our earlier work with silyl-protected derivatives of aziridino alcohols[2] we found that such protecting groups are often labile towards hydride reagents, and this was also observed in the present case (Table 2, entries 1 and 3.). However, comparison of entry 1 in Table 2 with entry 2 in Table 1 implies that the ring opening reaction is occurring faster, and the exclusion of the chelate effect leads to reaction at the benzylic position only. The benzyl derivative **1b** also gives excellent C-3 regioselectivity with $LiAlH_4$, without loss of the protecting group (Table 2, entry 2). However, both **1b** and **1c** showed an unexpected lack of reactivity towards DIBAL, even under relatively harsh conditions (compare entry 4 in Table 2 with entry 9 in Table 1). Catalytic hydrogenation was once again C-3 selective and, for **1b**, the conditions could be varied to allow retention or removal of the protecting group (Table 2, entries 6 and 7). The results summarized in Tables 1 and 2 thus show that the desired chiral 1,2- or 1,3-amino alcohol derivatives can be prepared with useful regioselectivity by suitable combinations of substrate and reagent.

For the ring-opening reactions of 2,3-aziridino alcohols with methyl-transfer reagents such as $LiMe_2Cu$, we have shown[1] that the hydroxyl group plays an important role in determining regiochemistry. Further, the presence of Lewis-basic ether functions (such as OBn) can be exploited[1, 2] to exercise regiocontrol in reactions with trialkylaluminum reagents. The present substrates thus offered an opportunity to determine the directing power of such functional groups vis-à-vis the activating effect of the phenyl moiety, and the question of inversion *vs* retention at C-3 was also of interest. In the event, the effect of the phenyl group proved overwhelming for **1a - c** as well as for the reaction of **2a, b** with $AlMe_3$ (Scheme 2), while the directive effect of the hydroxyl began to compete in the ring opening of **2a** by $LiMe_2Cu$ (Scheme 3). The results from the reactions of the *trans* series are shown in Table 3.



*Scheme 2. Stereoisomers formed by C-3 attack of methyl-transfer reagents. For **1**, (Me) = $LiMe_2Cu$ or $AlMe_3$. $LiMe_2Cu$ gives only inversion; $AlMe_3$ gives inversion plus retention for both types of substrate.*



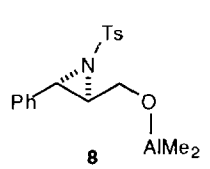
Scheme 3. Regio- and stereoisomers formed by attack, with inversion, of LiMe $_2$Cu on ***2a.***

Table 3. Ring opening of ***1a, b, c*** *by methyl-transfer reagents.*

Entry	Substrate	Reagent/Conditions	Ratio[a] **5** (inv.) : **6** (ret.)	%Yield[b]
1.	**1a**	$LiMe_2Cu$ (3 eq.), -20°C to RT, Et_2O	>99 : <1	70
2.	**1b**	$LiMe_2Cu$ (3 eq.), -20°C, Et_2O	>99 : <1	36[c]
3.	**1c**	$LiMe_2Cu$ (3 eq.), -20°C to RT, Et_2O	>99 : <1	35[d]
4.	**1a**	$AlMe_3$ (6 eq.), -78°C, toluene	70 : 30	48[e]
5.		$AlMe_3$ (6 eq.), -20°C, toluene	70 : 30	81
6.	**1b**	$AlMe_3$ (6 eq.), 0°C to RT, toluene	42 : 58	88
7.		$AlMe_3$ (6 eq.), 110°C, toluene	25 : 75	85
8.		$AlMe_3$ (6 eq.), 207°C, tetralin	10 : 90	47
9.	**1c**	$AlMe_3$ (6 eq.), 110°C, toluene	22 : 78	78[f]

[a] *By* ^{1}*H NMR on crude product.* [b] *Total isolated yield.* [c] *Bn ether of cinnamyl alcohol also isolated (49%).* [d] *TBS ether of cinnamyl alcohol also isolated (33%).* [e] *Reaction incomplete.* [f] *Silyl ether also cleaved.*

Reaction of **1a** with $LiMe_2Cu$ was completely C-3 selective, and the ring-opening process occurred with inversion (Table 3, entry 1). This behaviour is very similar to that observed for corresponding 2,3-epoxy alcohols.[6a, b] Substrates **1b** and **1c** also gave excellent C-3 selectivity, but unexpectedly large amounts of olefinic (elimination) products were also formed, presumably via initial generation of benzylic radicals (Table 3, entries 2 and 3). In the reactions of **1a** with $AlMe_3$ (Table 3, entries 4 and 5) we presume that the first equivalent of the reagent reacts to form the alkoxide **8**, followed by intermolecular attack (with inversion) by a second nucleophile molecule. The product of retention may derive from intramolecular delivery[7] of methyl via the zwitterion **9** (X = $AlMe_2$) and this result may be compared and contrasted with that from the reaction of the corresponding epoxy alcohol[6a] which gives near-exclusive retention (32:1 ratio). The epoxide oxygen is no doubt a stronger Lewis base than the tosylated nitrogen of the aziridine, and should better promote reaction via species akin to **9**. Blocking the free hydroxyl of the substrate with the TBS group led to a much slower reaction (no conversion at or below room temp., see Table 3, entry 9) and at the elevated temperature required for ring opening the protecting group was cleaved off. However, ring opening is likely to have occurred before loss of the TBS group (compare entries 5 and 9 in Table 3) and the intermediacy of **9** (X = TBS) can once again explain the results.



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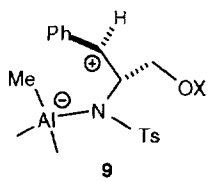

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The reaction of **1b** with $AlMe_3$ showed an interesting temperature dependence (Table 3, entries 6, 7, and 8). The inversion product could arise from initial complexation of the reagent to the benzyl ether, followed

by intramolecular delivery of the nucleophile to the activated benzylic position ("6-endo" mode,[8] Fig. 1), while the retention product presumably forms via an S_N1-type reaction involving **9** (X = Bn). The good regioselectivity (9:1 in favour of the retention product, Table 3, entry 8) obtained at the highest temperature was offset by the poorer yield, no doubt due to thermal decomposition of the substrate.[9]

Turning to the *cis* series, the regioselectivity in the reaction of aziridino alcohol **2a** with $LiMe_2Cu$ (Scheme 3) differed markedly from that found for the *trans* isomer (Table 3, entry 1). For **2a**, the previously observed directing effect of a free hydroxyl group[1] now became apparent, although the electronic activating effect of the C-3 phenyl group was still predominant. Table 4 shows the results from the reaction of **2a**, **b** with $AlMe_3$.

Table 4. Ring opening of ***2 a b*** *by* $AlMe_3$ *(6 eq.) in toluene.*

Entry	Substrate	Reaction temp.	Ratio[a] **5** (ret.) : **6** (inv.)	%Yield[b]
1.	**2 a**	-33°C	52 : 48	42[c]
2.		110°C	48 : 52	92
3.	**2 b**	0 to 23°C	16 : 84	92
4.		110°C	28 : 72	90

[a] *By* ^1H *NMR spectroscopy on crude product.* [b] *Total isolated yield.* [c] *Reaction incomplete.*

Aziridino alcohol **2a** (Table 4, entries 1 and 2) gave little or no regioselectivity, nor was there any significant temperature dependence; in the latter respect, the substrate resembles its *trans* isomer (Table 3, entries 4 and 5). However, benzyl ether **2b** gave predominantly inversion at room temperature (Table 4, entry 3) while **1b** gave mostly retention under the same conditions (Table 3, entry 6). For both substrates the proportion of retention product increased with temperature, and possible mechanisms have been outlined above in the discussion of the results with the *trans* isomer.

The regiochemistry of the ring opening reactions described here thus seems to be dependent on a delicate balance between steric and electronic effects, and several competing mechanisms can be envisioned. However, good regiocontrol can be exerted, particularly in the reactions involving hydride transfer, and applications of this methodology to the enantioselective total synthesis of natural products will be described elsewhere.

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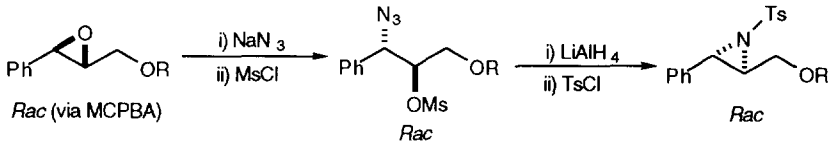
EXPERIMENTAL

General remarks. ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were obtained on a Varian XL 300 spectrometer ($CDCl_3$ as solvent and TMS as internal standard). Abbreviations: s, singlet; d, doublet; t, triplet; qt, quartet; qn, quintet; b, broad; app., apparent; J, coupling constant in Hz. IR spectra were run on a Perkin-Elmer 1600 FT-IR instrument, and only the strongest/structurally most important peaks are listed. Elemental analyses were performed by Analytische Laboratorien, Gummersbach, Germany. Red-Al (3.5M in toluene), $LiAlH_4$ (1M in THF), DIBAL (1M in hexanes) and $AlMe_3$ (2M in hexanes) were purchased from Aldrich and used as received. MeLi (1.6M in diethyl ether) was purchased from Merck and was titrated immediately before use. Copper(I) iodide was purified via the dimethyl sulfide adduct as described.[11] Tetrahydrofuran (THF)

and diethyl ether were distilled under nitrogen from Na/benzophenone. Toluene, methylene chloride, and triethylamine were distilled under nitrogen from calcium hydride. Tetralin was distilled at reduced pressure. Silica gel for flash chromatography was purchased from Grace-Amicon.

Synthesis of aziridines. The general scheme which was previously developed to transform epoxides to aziridines (see, e.g., refs. 2, 4, and 10) was followed. This is outlined in Scheme 4 for the *trans* series, and is described in detail below for **1b**. Compounds **1a**, **1c**, and **2a** have previously been synthesized in optically active form.[4]



Scheme 4. General route for stereospecific conversion of epoxides to aziridines.

Aziridine (±)-**1a** was synthesized according to the literature, and the ^{1}H NMR data were in accord with those published[4] for optically pure material. ^{13}C NMR: 144.4, 137.0, 134.5, 129.7, 128.6, 128.4, 127.1, 126.4, 60.6, 54.7, 46.3, 21.6. IR: 3250 (b), 1321, 1158 cm^{-1}. Anal. Calc. for $C_{16}H_{17}NO_3S$: C, 63.35%; H, 5.65. Found: C, 63.26; H, 5.77.

(±)-**1b** was synthesized from the benzyl ether of *trans* cinnamyl alcohol[12] according to Scheme 4 (R = Bn). Standard MCPBA epoxidation gave the oxirane, which was ring opened by sodium azide and converted to the azido mesylate as follows. The epoxide (0.461 g, 1.92 mmol) was dissolved in an 8:1 mixture of 2-methoxyethanol and water (13 mL) and sodium azide (0.754 g, 11.5 mmol) and ammonium chloride (0.207 g, 3.9 mmol) were added. The mixture was heated at 80°C for 4 h, cooled to RT and partitioned between ether (55 mL) and water (25 mL). The layers were separated and the aqueous phase was extracted with ether (3 x 25 mL). The combined organics were washed with water, dried ($MgSO_4$) and evaporated *in vacuo* to yield a residue which was purified by flash chromatography (ether/pentane, 1:1). A single regioisomer of the azido alcohol (*cf.* Scheme 4) was obtained as an oil (0.520 g, 96%).

Data for the *azido alcohol*. ^{1}H NMR: 7.54 - 7.30 (10H; m); 4.67 (1H; d, J = 6.8; C<u>H</u>N$_3$); 4.55 (2H; s); 4.06 - 3.97 (1H; m; C<u>H</u>OH); 3.60 (1H; dd, J = 9.8, 6.0; C<u>H</u>OBn); 3.55 (1H; dd, J = 9.8, 3.8; C<u>H</u>OBn); 2.48 (1H; d, J = 4.5; O<u>H</u>). ^{13}C NMR: 137.6, 136.0, 128.7, 128.5, 128.4, 127.9, 127.8, 73.5, 72.8, 70.2, 66.8. IR: 3444 (b), 2103.

The azido alcohol from above (0.495 g, 1.75 mmol) was dissolved with stirring in dry CH_2Cl_2 (6 mL) and cooled with stirring under nitrogen to 0°C. Triethylamine (0.4 mL) and mesyl chloride (0.17 mL, 2.1 mmol) were added and the mixture was allowed to warm up to room temperature. When reaction was complete according to TLC, the solvent was removed and the residue diluted with ether. The precipitate was filtered off and the filtrate was evaporated *in vacuo* to yield a residue which was purified by flash chromatography (ether/pentane, 1:1). The azido mesylate (Scheme 4, R = Bn) was obtained as an oil (0.620 g, 98%).

Data for the *azido mesylate*. ^{1}H NMR: 7.45 - 7.30 (10; m); 4.98 (1H; d, J = 6.0); 4.86 (1H; ddd, J = 6.0, 6.0, 3.4); 4.53 (2H; AB, J = 11.9); 3.79 (1H; dd, J = 11.0, 6.0); 3.62 (1H; dd, J = 11.0, 3.4); 2.72 (3H; s). ^{13}C NMR: 137.2, 134.9, 129.1, 128.9, 128.5, 128.0, 127.8, 82.5, 73.5, 68.1, 65.1, 38.1. IR: 2108, 1359, 1179. This material was ring-closed to the *N*-H aziridine (*cf.* Scheme 4) as follows.

The azido mesylate from above (0.577 g, 1.6 mmol) was dissolved with stirring under nitrogen in dry THF (16 mL) and the solution was cooled to 0°C before portionwise addition of lithium aluminum hydride (0.187 g, 4.91 mmol). The reaction mixture was allowed to reach room temperature over 2 h, and was then heated at 50°C until TLC analysis showed complete disappearance of starting material (a few hours). The reaction mixture was cooled to 0°C and water (0.2 mL) was added, followed by 15% NaOH (aq., 0.2 mL) and finally more water (0.4 mL). The granular precipitate was filtered off onto Celite and the filter cake was washed thoroughly with ethyl acetate. The combined filtrate and washings were dried over $MgSO_4$ and the solvent was removed to yield a residue which was purified by flash chromatography (ether/pentane, 80:20). The *N*-H aziridine was obtained as an oil (0.339 g, 89%).

Data for the *N*-H *aziridine*. ^{1}H NMR: 7.38 - 7.18 (10H; m); 4.56 (2H; s); 3.75 (1H; bdd, J = 10, 3); 3.59 (1H; bdd, J = 10, 5); 2.90 (1H; b"s"; aziridine); 2.35 (1H; b "s"; aziridine); 1.05 (1H; b"s"; NH). The signals are broadened, and the spectrum is temperature dependent, due to slow nitrogen inversion at ambient temperature. ^{13}C NMR: 139.6, 137.8, 128.4, 127.7, 127.6, 127.0, 125.7, 73.0, 70.4 (b), 40.3 (b), 36.3 (b). IR: 3290 (b).

The *N*-H aziridine from above (0.299 g, 1.25 mmol) was dissolved with stirring under nitrogen in dry CH_2Cl_2 (6 mL) and the solution was cooled to 0°C. Triethylamine (1 mL) was added, followed by tosyl chloride (0.238 g, 1.25 mmol) and the mixture was stored overnight at 0°C before being diluted with ether and washed with water. The organics were dried over $MgSO_4$ and evaporated *in vacuo* to give a residue which was purified by flash chromatography (ether/pentane, 40:60), to give the *N*-tosyl aziridine (±)-**1b** as an oil (0.392 g, 80%).

Data for (±)-**1b**. ^{1}H NMR: 7.82 (2H; AA' of AA'BB', J_{AB} = 8.4); 7.47 - 7.15 (12H; m); 4.60 (2H; s); 4.23 (1H; dd, J = 10.6, 5.8); 4.05 (1H; dd, J = 10.6, 6.3); 3.90 (1H; d, J = 4.2); 3.20 - 3.14 (1H; m); 2.38 (3H; s). ^{13}C NMR: 144.1, 137.7, 137.0, 134.5, 129.5, 128.5, 128.4, 128.3, 127.8, 127.4, 126.8, 73.4, 67.1, 50.5, 47.0, 21.6. IR: 1324, 1160. Anal. Calc. for $C_{23}H_{23}NO_3S$: C, 70.20%; H, 5.89. Found: C, 70.14; H, 6.03.

Data for (±)-**1c**. The ^{1}H NMR data were in accord with those published[4] for optically pure material. ^{13}C NMR: 144.0, 137.2, 134.7, 129.5, 128.4, 128.2, 127.4, 126.8, 60.7, 52.3, 47.5, 25.8, 21.6, 18.3, -5.3. IR: 1325, 1161, 1089. Anal. Calc. for $C_{22}H_{31}NO_3SSi$: C, 63.27%; H, 7.48. Found: C, 63.42; H, 7.49.

(±)-**2a**. was synthesized from *cis* cinnamyl alcohol[13] and the ^{1}H NMR data were in accord with those published[4] for optically pure material. ^{13}C NMR: 144.9, 134.4, 132.1, 129.8, 128.5, 128.14, 128.07, 127.2, 59.4, 45.9, 45.3, 21.7. IR: 3520 (b), 1325, 1157. Anal. Calc. for $C_{16}H_{17}NO_3S$: C, 63.35%; H, 5.65. Found: C, 63.16; H, 5.75.

(±)-**2b** was synthesized from the benzyl ether of *cis* cinnamyl alcohol (prepared as described[12] for the *trans* isomer) according to Scheme 4. The ring opening by azide is non-regioselective, but both azido alcohols give the same aziridine. The overall yield was 50%. Data for the *aziridine*. Mp 52 - 55°C. ^{1}H NMR: 7.90 and 7.31 (each 2H; AA'BB', J_{AB} = 8.3); 7.29 - 7.21 (8H; m); 7.09 - 7.06 (2H; m); 4.27 (2H; AB, J_{AB}= 11.5); 4.04 (1H; d, J = 6.5); 3.37 - 3.26 (3H, m); 2.41 (3H, s). ^{13}C NMR: 144.6, 137.6, 134.7, 132.3, 129.7, 128.3, 128.2, 128.09, 128.03, 127.6, 127.4, 72.8, 66.3, 44.3, 21.7. IR: 1326, 1160. Anal. Calc. for $C_{23}H_{23}NO_3S$: C, 70.20%; H, 5.89. Found: C, 70.08; H, 5.96.

Ring opening reactions with hydride reagents. The reactions were carried out according to the procedures described[1] previously, with the exception that ethyl acetate was used instead of ether during work-up and extraction of the products. In all cases, the crude products were analysed by ^{1}H NMR spectroscopy prior to

chromatographic purification (ether used as eluent for **3/4** (R = H); 40% ether/pentane when R = Bn). Examination of the purified materials indicated that the chromatography did not affect the product ratio. Reaction conditions, product ratios and total yields are shown in Tables 1 and 2. (Note that reaction of **1c** with Red-Al and $LiAlH_4$ yielded **3** (R = H) as the product).

Data for (±)-**3** (R = H). Mp 95 - 96°C (from ether/hexane, lit.[14] for (*S*)-enantiomer: 73 - 74°C). ^1H NMR: 7.59 (2H; AA' of AA'BB', J_{AB} = 8.4); 7.22 - 7.14 (5H; m); 7.01 - 6.94 (2H; m); 5.09 (1H; bd, J = 7); 3.63 (1H; dd, J = 11.0, 3.7); 3.55 - 3.39 (2H; m); 2.78 (1H; dd, J = 13.4, 7); 2.67 (1H; dd, J = 13.4, 7.3); 2.47 (1H; bs); 2.40 (3H; s). The ^{13}C NMR spectrum was in accordance with that reported[13] for the (*S*)-enantiomer. IR (KBr): 3534 (b), 3241 (b), 1320, 1152.

Data for (±)-**4** (R = H). Mp 129 - 130°C (from ethyl acetate/hexane, lit.[15] for (*S*)-enantiomer: 140 - 141°C). The ^1H NMR spectrum was in accordance with that reported[15] for the (*S*)-enantiomer. ^{13}C NMR: 143.1, 140.6, 137.3, 129.3, 128.5, 127.4, 127.1, 126.3, 59.4, 55.9, 39.2, 21.5. IR (KBr): 3470 (b), 3145 (b), 1320, 1158.

Data for (±)-**3** (R = Bn). ^1H NMR: 7.62 (2H; AA' of AA'BB', J_{AB} = 8.3); 7.39 - 7.14 (10H; m); 7.04 - 6.96 (2H; m); 4.88 (1H; bd, J = 7.6); 4.37 (2H; s); 3.60 - 3.48 (1H; m); 3.27 (2H; AB of ABX, J_{AB} = 9.5, J_{AX} = 4.7, J_{BX} = 3.6); 2.81 (2H; AB of ABX, J_{AB} = 14, J_{AX} = 7.5, J_{BX} = 6.5); 2.39 (3H; s). ^{13}C NMR: 143.1, 137.63, 137.56, 137.1, 129.6, 129.3, 128.47, 128.42. 127.83, 127.76, 126.9, 126.5, 73.2, 69.9, 54.6, 38.3, 21.5. IR: 3281 (b), 1330, 1159.

Ring opening by catalytic hydrogenolysis. (a) Aziridine **1a** (40.9 mg, 0.135 mmol) was dissolved with stirring in 95% ethanol (2 mL). 10% Pd/C catalyst (2.8 mg) was added, the flask was evacuated and then an atmosphere of hydrogen was secured. The mixture was stirred under balloon pressure of hydrogen for 1 h (reaction complete according to TLC). The mixture was filtered through Celite, the filter cake was washed with ethyl acetate, and the combined filtrate and washings were evaporated to dryness to give **3** (R = H) in quantitative yield. The same procedure was used for **2a**. *(b)* Catalytic hydrogenolysis of **1b** was performed under the same conditions, and gave **3** (R = Bn) in 81% yield after flash chromatography (40% ether/pentane). When the reaction was carried out in the presence of a catalytic amount of conc. HCl, hydrogenation for 36 h gave **3** (R = H) in 84% yield after flash chromatography (ether).

Ring opening with $LiMe_2Cu$. CuI (59 mg, 0.310 mmol) was slurried in dry ether (1 mL) and cooled with stirring under nitrogen to -20°C. A solution of MeLi (1.18M in ether, 0.530 mL, 0.625 mmol) was added dropwise to give a clear solution of the cuprate reagent. To the cuprate solution was added a solution of **1a** (31.2 mg, 0.103 mmol) in ether (1 mL) and the mixture was stirred at -20°C for 4 h (starting material consumed according to TLC analysis). The reaction mixture was allowed to warm up to room temperature and NH_4Cl (aq.) was added. The mixture was diluted with ether, and air was bubbled through the mixture until the solids had been digested. The organic layer was separated, washed with brine, dried ($MgSO_4$) and the solvent removed to give the crude product which was analysed by ^1H NMR spectroscopy. Only **5** (R = H) could be detected, and the material was obtained pure in 70% yield after flash chromatography (80% ether/pentane).

Data for (±)-**5** (R = H). ^1H NMR: 7.56 (2H; AA' of AA'BB', J_{AB} = 8.4; tosyl); 7.23 - 7.13 (5H; m; tosyl, phenyl); 7.00 - 6.95 (2H; m; phenyl); 4.55 (1H; bd, J = 7; NH); 3.77 - 3.68 (1H; m; CHOH); 3.65 - 3.56 (1H; m; CHOH); 3.32 - 3.25 (1H; m; CHNHTs); 2.96 (1H; app. qn, J = 7; PhCHMe); 2.41 (3H; s; tosyl Me); 2.09 (1H; bt, J = 7; OH); 1.19 (3H; d, J = 7.0; Me). Assignments were made on the basis of decoupling experiments. ^{13}C NMR: 143.3, 141.8, 136.6, 129.6, 128.7, 127.6, 127.0, 126.9, 62.7, 60.2, 40.4, 21.5,

17.9. IR: 3505 (b), 3286 (b), 1324, 1157. Anal. Calc. for $C_{17}H_{21}NO_3S$: C, 63.92%; H, 6.63. Found: C, 64.10; H, 6.58.

Substrates **1b** and **1c** were reacted with the cuprate in the same way, to yield **5** (R = Bn) and **5** (R = TBS), respectively. (In addition to ring opening, elimination to the corresponding ethers of cinnamyl alcohol also occurred in these cases; the products were identified by their ^{1}H NMR spectra).

Data for (±)-**5** (R = Bn). ^{1}H NMR: 7.55 (2H; AA' of AA'BB', J_{AB} = 8.4; tosyl); 7.38 - 7.13 (10H; m; tosyl, phenyl); 7.06 - 7.03 (2H; m; phenyl); 4.46 (1H; bd, J = 8.5; NH); 4.37 (2H; AB, J = 11.9; benzyl); 3.53 - 3.45 (1H; m; CHNHTs); 3.38 (1H; dd, J = 9.5, 4.0; CHOBn); 3.25 (1H; dd, J = 9.5, 6.0; CHOBn); 3.15 (1H; app. qn, J = 7.0; PhCHMe); 2.39 (3H; s; tosyl Me); 1.18 (3H; d, J = 7.0; Me). Assignments made on the basis of decoupling experiments. ^{13}C NMR: 142.9, 141.8, 137.9, 137.5, 129.4, 128.46, 128.39, 128.0, 127.8, 127.0, 126.7, 73.2, 69.5, 57.9, 40.2, 21.5, 17.2. IR: 3285 (b), 1329, 1159.

Data for (±)-**5** (R = TBS). ^{1}H NMR: 7.58 (2H; AA' of AA'BB', J_{AB} = 8; tosyl); 7.26 - 7.18 (5H; m; tosyl, phenyl); 7.11 - 7.05 (2H; m; phenyl); 4.42 (1H; bd, J = 8.5; NH); 3.50 - 3.45 (1H; m; CHOTBS); 3.38 - 3.28 (2H; m; CHOTBS and CHNHTs); 3.13 (1H; app. qn, J = 7.0; PhCHMe); 2.40 (3H; s; tosyl Me); 1.22 (3H; d, J = 7.0; Me); 0.88 (9H; s; *t*-Bu); -0.02 (6H; 2 x s; $SiMe_2$). IR: 3287 (b), 1333, 1161, 1092.

Reaction of **2a** with $LiMe_2Cu$ gave a chromatographically inseparable mixture of **6** and **7** (R = H). However, the signals from the individual isomers were well separated in the ^{1}H NMR spectrum of the mixture, and **7** was identified by comparison with literature data.[16]

Data for (±)-**6** (R = H). ^{1}H NMR: 7.72 and 7.09 (each 2H; AA'BB', J_{AB} = 8; tosyl); 7.30 - 7.16 (5H; m; phenyl); 5.05 (1H; bd, J = 8.8; NH); 3.40 - 3.23 (3H; m; CHNHTs and CH_2OH); 2.89 (1H; app. qn, J *ca.* 7; PhCHMe); 2.41 (3H; s; tosyl Me); 1.86 (1H; bs; OH); 1.20 (3H; d, J = 7.0; Me). Assignments made on the basis of decoupling experiments. ^{13}C NMR: 143.4, 142.8, 137.6, 129.7, 128.7, 127.4, 127.0, 126.8, 62.5, 60.7, 41.1, 30.3, 18.2.

Ring opening with $AlMe_3$. A 0.1M solution of the aziridine in dry toluene or tetralin under nitrogen (0.1M) was stirred at the appropriate temperature (see Tables 3 and 4) and a solution of $AlMe_3$ (2M in hexane, 6 equiv.) was added dropwise. (Use of less reagent leads to much slower or no reaction). Stirring and heating (or cooling) were continued while the reaction was monitored by TLC. The reaction mixture was brought to 0°C and diluted with ether before addition of NH_4Cl (aq.). The resultant mixture was filtered through Celite and the filter cake washed thoroughly with ethyl acetate. The combined organics were dried ($MgSO_4$) and the solvents removed to give the crude product which was analysed by ^{1}H NMR spectroscopy prior to flash chromatographic purification. Compounds **5** and **6** (R = H or Bn) could not be separated by chromatography. (Note that the reaction of **1c** with $AlMe_3$ gave **5/6** (R = H) as the product).

Data for (±)-**6** (R = Bn). 7.67 (2H; AA' of AA'BB', J_{AB} = 8.4; tosyl); 7.38 - 7.02 (12H; m; tosyl, phenyl); 5.01 (1H; bd, J = 9.5; NH); 4.17 (2H; AB, J = 12; benzyl); 3.41 - 3.33 (1H; m; CHNHTs); 3.09 (1H; dq, J = 9.8, 7; PhCHMe); 2.90 (2H; AB of ABX, J_{AB} = 9.5, J_{AX} = 3.5, J_{BX} = 2.5; CH_2OBn); 2.38 (3H; s; tosyl Me); 1.28 (3H; d, J = 7.0; Me). Assignments made on the basis of decoupling experiments. ^{13}C NMR: 143.5, 143.0, 138.2, 137.6, 129.5, 128.5, 128.4, 127.8, 127.7, 127.6, 126.9, 126.6, 73.1, 68.7, 59.3, 41.3, 21.5, 18.6. Further structural proof was provided by catalytic hydrogenation of **5/6** (R = Bn) with H_2, 10% Pd/C, EtOH (see procedure given above for hydrogenolysis) to give **5/6** (R = H).

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