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A Regio- and Stereodivergent Route to All Isomers of *vic*-Amino Alcohols

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Received July 17, 2002

Vicinal amino alcohols are substructures in several important natural products. They are also frequently employed ligands in asymmetric synthesis. Many enantioselective syntheses of *vic*-amino alcohols have been reported, but each structure has required its own synthetic route. This study presents a synthetic strategy leading to all eight possible isomers of a given β-amino alcohol, starting from vinyl epoxides. The developed strategy focuses on the propensity of vinyl epoxides and vinylaziridines to be selectively ring-opened at the allylic position by suitable hard nucleophiles. Within this strategy, a novel large-scale aminolysis reaction and the synthesis of a trisubstituted *N*-H vinylaziridine are detailed.

Introduction

The β-amino alcohol moiety is found in a wide variety of biologically active alkaloids and peptides;[1] it is consequently a common building block in the synthesis of natural products.[2] The importance of vicinal amino alcohols is also well-recognized in asymmetric synthesis, as many chiral auxiliaries and ligands contain this substructure.[3] Existing synthetic routes to enantiopure amino alcohols often rely on the derivatization of the available pool of amino acids, which limits the number of accessible derivatives.[4] Large efforts to develop asymmetric routes to 1,2-amino alcohols have been made and can be divided into two strategically different categories.

In the first class, the amino alcohol moiety is formed by concomitant creation of a new C−C bond. Reported enantio- or diastereoselectivities can be high, but the reactions are often limited to substrates containing certain functional groups. When one of the two stereocenters is set, the other can be created with good diastereoselectivity, as in the case of addition of organometallic nucleophiles to α-aminocarbonyls.[4] By concurrent creation of two stereocenters, amino alcohols can be obtained with high enantioselectivity, i.e., by addition of nucleophiles to nitroalkenes[5] or imines.[1,6] Similar selectivities can be obtained by reaction of chiral aminoallylboranes and aldehydes.[7] In this category, the addition of α-alkoxyenolates to aldimines is the most flexible reaction, as the choice of enolate decides which isomer (syn/anti) will be the major product.

Alternatively, the amino alcohol moiety may be constructed without alteration of the carbon skeleton. The substrates are primarily alkenes or alkene derivatives, and the reactions proceed stereospecifically. Regioselectivity is often a problem that can be circumvented only when the substrate is substituted with groups having different electronic or steric influence. This dilemma can be exemplified by Sharpless aminohydroxylation of alkenes, which proceeds with high enantioselectivity but often with moderate yields due to poor regioselectivity.[8] With the advancement of diastereo- and enantioselective syntheses of epoxides, cleavage of oxiranes by nitrogen nucleophiles has become one of the most investigated routes to vicinal amino alcohols.[9] Both *syn*- and *anti*-amino alcohols are available by employing *cis*- or *trans*-epoxides, respectively. Also aziridines,[10,11] cyclic sulfates,[12] and carbonates[13] can be ring-opened to give amino alcohols.

Despite the great interest in the field of 1,2-amino alcohols, no divergent route from a common starting

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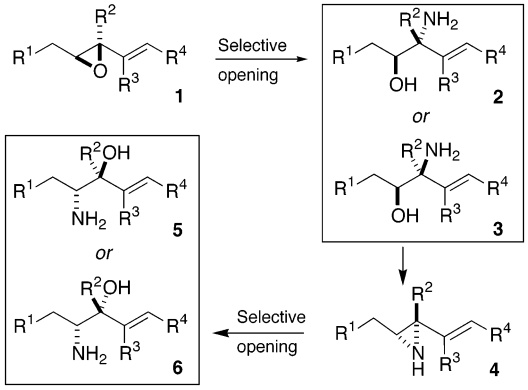
10.1021/jo0262053 CCC: $22.00
Published on Web 11/08/2002

SCHEME 1. Synthetic Strategy



material toward all possible regio- and stereoisomers of a vicinal amino alcohol has been documented, thus complicating the synthetic planning substantially by the requirement of a separate synthetic route for each isomer. A divergent route leading to all possible isomers would be a great simplification for studies on structure−activity relationships of pharmacologically active derivatives incorporating this structural motif. Such a route would also allow optimization of the performance of chiral ligands and auxiliaries containing this substructure.

We recently reported our preliminary findings on the development of a route leading to all eight possible isomers of a given 1,2-amino alcohol starting from a readily synthesized substrate.[14] The present paper describes investigations on the scope and limitations of the reaction scheme, including a simplified synthesis of vinyl epoxides by application of the enantioselective epoxidation of dienes developed by Shi and co-workers.[15] Furthermore, a novel, large-scale aminolysis reaction and the synthesis of a trisubstituted *N*-H vinylaziridine are detailed.

The requirements for a generally applicable synthetic route were readily available starting materials, flexibility, predictability, and high regio- and diastereoselectivity. These demands could be met by choosing vinyl epoxides as substrates, both enantiomers being readily available in high enantiomeric excess, as they are known to be ring-opened selectively at the allylic position by hard nucleophiles.[16] As depicted in Scheme 1, the synthesis strategy designed to fulfill the above specifications starts by ring-opening of epoxides **1** with a nitrogen nucleophile. The opening can be performed either with inversion or retention of stereochemistry, giving *anti*- and *syn*-amino alcohols **2** and **3**, respectively. Ring closure of **2** to the corresponding vinylaziridines **4** and subsequent ring-opening with an oxygen nucleophile, either with inversion or retention, would then give *anti*- and *syn*-amino alcohols **5** and **6**, all reactions taking place regioselectively at the allylic position. The remaining set

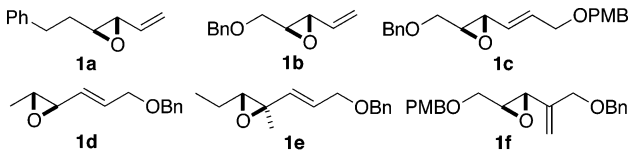
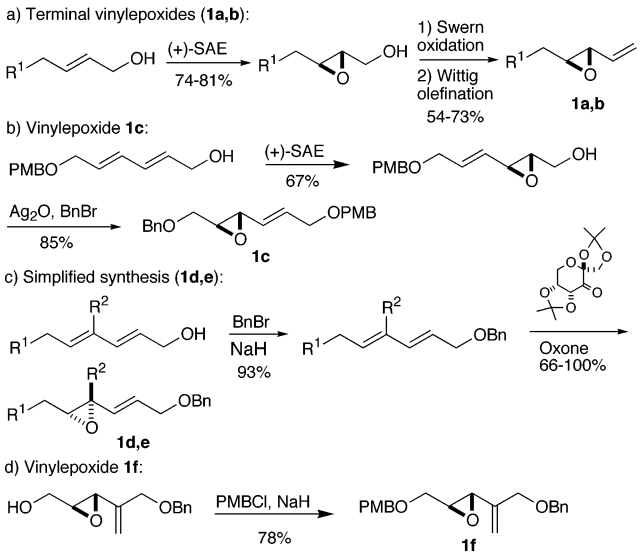


FIGURE 1. Vinyl epoxides used in the present study.

SCHEME 2. Synthesis of Vinyl Epoxides 1



of enantiomeric amino alcohol isomers can simply be obtained by starting from *ent*-**1**.

Results and Discussion

Figure 1 depicts a set of vinyl epoxides used in the present study. The substrates were chosen to represent variations of electronic character (**1a** vs **1b**), terminal vs internal olefin (**1b** vs **1c**), steric hindrance (**1d** vs **1e**), and position of vinyl group substituent (**1c**−**e** vs **1f**).

Vinyl epoxides **1a**,**b** were obtained from the corresponding allylic alcohols using Sharpless asymmetric epoxidation (SAE) followed by the Swern/Wittig procedure (Scheme 2a),[17] whereas **1c** was obtained with SAE of the corresponding dienol followed by benzylation (Scheme 2b).[18] The synthesis of vinyl epoxides **1d**,**e** was simplified by application of the recently published asymmetric epoxidation of dienes.[15] This reaction was reported with TMS-protected dienols, but could be applied to Bn-protected dienols giving slightly lower enantioselectivities (Scheme 2c). Epoxidation of benzylated hexadienol yielded **1d** in 66% together with 10% of the corresponding regioisomer, whereas **1e** was epoxidized with complete regioselectivity in 100% yield. Vinyl epoxide **1f** was synthesized by *p*-methoxybenzyl (PMB) protection of corresponding epoxy alcohol (Scheme 2d).[19,20] Enantiomeric excesses were analyzed on the corresponding epoxy alcohols for **1a**,**b**,**f** to ≥95% and on vinyl epoxides **1c**−**e** to ≥90%.[21]

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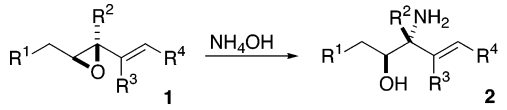
TABLE 1. Aminolysis of Vinyl Epoxides 1 to *anti*-Amino Alcohols 2



						yield of **2** (%)[a]	
entry	substrate	R^1	R^2	R^3	R^4	microwave[b]	oil bath[c]
1	**1a**	$PhCH_2$	H	H	H	93	91[d]
2	**1b**	BnO	H	H	H	87	93
3	**1c**	BnO	H	H	CH_2OPMB	88	
4	**1d**	H	H	H	CH_2OBn	100[d]	82[e]
5	**1e**	Me	Me	H	CH_2OBn	89[f]	78[f]
6	**1f**	PMBO	H	CH_2OBn	H	84	

[a] Isolated yields. [b] 20−30 W, 8−15 min. [c] 125−170 °C, 1−4.5 h. [d] Regioisomeric mixture 11:1. [e] Regioisomeric mixture 9:1. [f] Regioisomeric mixture 2:1.

Synthesis of *anti*-Amino Alcohols 2. Epoxides are commonly ring-opened by sodium azide to afford azido alcohols, which can be reduced to the corresponding amino alcohols.[22] Unfortunately, when vinyl epoxides are treated with sodium azide, a mixture of products is obtained due to a thermal [3,3]-rearrangement of the initially formed allylic azide.[23] Instead, vinyl epoxides **1** could be regioselectively and stereospecifically ring-opened with ammonia to afford *anti*-amino alcohols **2**. The aminolysis of vinyl epoxides was originally performed by prolonged heating in neat ammonia with tosic acid as catalyst.[24] Although this method gives good yields with sterically unhindered substrates, it suffers from impractical handling, long reaction times and modest yields of sterically hindered amino alcohols. To circumvent these drawbacks a microwave-assisted aminolysis procedure was designed, using ammonium hydroxide as nucleophile.[25,26] With this protocol the synthesis of *anti*-amino alcohols **2** could be greatly improved due to simplified handling, short reaction times, and high yielding reactions also with sterically hindered substrates (Table 1). When vinyl epoxides **1a**,**b**,**f** were irradiated at 30 W for 8 min in NH_4OH, amino alcohols **2a**,**b**,**f** were formed with complete regioselectivity (>20:1) in high yields (entries 1−3 and 6).[27] Microwave irradiation of **1c** afforded **2c**, together with a byproduct, which could be minimized by decreasing the power to 15 W for 20 min (entry 3). Vinyl epoxide **1d** afforded amino alcohol **2d** as a regioisomeric mixture (11:1), the reason for which is unclear (entry 4). When **1d** was irradiated for 5 min at 50 W, the selectivity was 6:1, whereas 10 min at 30 W gave an 11:1 selectivity. This selectivity optimization confirmed the earlier observed trend that decreased power gives improved regioselectivity.[25] Amino alcohol **2e** was, as expected, obtained with poor regioselectivity due to steric hindrance at the allylic position (entry 5). The selectivity could be improved from 2:1 to 3.5:1, at the expense of decreased yield, when decreasing the power from 40 W for 11 min to 30 W for 15 min.

As large-scale microwave chemistry is difficult to perform, the aminolysis reaction was further investigated using vinyl epoxides **1a**,**b**. Our first strategy involved the use of protic solvents and excess ammonium hydroxide, as amines have participated in epoxide openings performed in various organic solvents.[28] Pleasingly, when **1a** was subjected to 10 equiv of NH_4OH in EtOH at 70 °C in a sealed flask, slow formation of **2a** occurred. The reaction rate could be improved by employing a large excess of NH_4OH, which yielded **2a** in 73% after 48 h of heating. Addition of a catalytic amount of $TsOH\cdot H_2O$ caused formation of the corresponding diol without increasing the rate of formation of **2a**. The change of solvent to 2-methoxyethanol, which allowed heating to 120 °C, did not improve the results. Compared to the original procedure with neat ammonia, the use of excess NH_4OH in protic solvents simplifies the handling without shortening the reaction time.

Not satisfied with these results, we investigated if there was a microwave effect[29] in the aminolysis reaction or if it would proceed with conventional heating. Gratifyingly, by heating vinyl epoxide **1b** in NH_4OH in a sealed metal cylinder to 170 °C,[30] complete conversion was achieved within 4.5 h and **2b** could be isolated in 93% yield (Table 1, entry 2). This procedure was applied to vinyl epoxide **1d**, giving **2d** in 72% yield and 6:1 regioselectivity after only 1 h heating (entry 4). The result could easily be improved to 82% and 9:1 regioselectivity by decreasing the temperature to 140 °C, which was sufficient also for the ring-opening of **1e** (entry 5). The reaction temperature could be decreased even further, and amino alcohol **2a** was isolated in excellent yield after 1 h at only 125 °C, albeit in 11:1 regioselectivity (entry 1). These results clearly indicate the absence of a microwave effect. The regioisomeric mixtures obtained with some substrates can most likely be optimized by fine-tuning of reaction temperature and time. This novel aminolysis method is the first practical large-scale protocol described for ring-opening of vinyl epoxides with ammonia. The reaction is fast, stereospecific, and highly regioselective. Furthermore, no special equipment is needed, as the pressure reached at 125 °C in NH_4OH is moderate.

Synthesis of *syn*-Amino Alcohols 3. Pd(0)-catalyzed ring-opening of vinyl epoxides **1** in the presence of tosyl isocyanate gave oxazolidinones **7** in high yields with retention of configuration (Scheme 3, Table 2).[31] Conversion of **1** to **7** took place with complete diastereoselectivity (>95%) when **1** contained additional vinylic substituents (**1c**−**f**, entries 3−6). Unfortunately, the terminal vinyl epoxides **1a**,**b** afforded **7a**,**b** as unseparable diastereomeric mixtures, the ratio of which could only be slightly improved by optimizing the reaction conditions. Gratify-

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(30) 170 °C was the maximum temperature reached in microwave reactions in NH_4OH at 50 W for 8 min.
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SCHEME 3. Synthesis of *syn*-Amino Alcohols 3

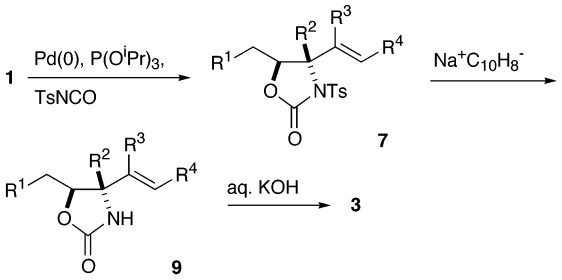

TABLE 2. Synthesis of *syn*-Amino Alcohols 3

						yield (%)[a]		
entry	substrate	R^1	R^2	R^3	R^4	**7**	**9**	**3**
1	**1a**	$PhCH_2$	H	H	H	82[b]	93[c]	100
2	**1b**	BnO	H	H	H	88[d]	75[c]	97
3	**1c**	BnO	H	H	CH_2OPMB	87	72	91
4	**1d**	H	H	H	CH_2OBn	*e*	61[f]	95
5	**1e**	Me	Me	H	CH_2OBn	94	80	98
6	**1f**	PMBO	H	CH_2OBn	H	93	84	86

[a] Isolated yields. [b] Before separation of diastereomers. [c] dr 6:1. [d] dr 14:1. [e] Not isolated; see the text. [f] Yield from **1d**.

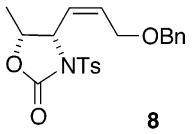

FIGURE 2. (*Z*)-4,5-*cis*-Oxazolidinone **8**.

ingly, by equilibration of the initial product mixtures, the kinetically obtained, poor ratios could be significantly enhanced (**1a** dr = 2:1 → 6:1, **1b** dr = 2:1 → 14:1, entries 1 and 2).[27] A similar palladium-assisted equilibration of vinyloxazolines was recently reported.[32]

Oxazolidinone **7d** was formed along with a byproduct in a 3:1 ratio, the structure of which has been identified as (*Z*)-4,5-*cis*-oxazolidinone **8** (Figure 2). To the best of our knowledge, an *E* → *Z* isomerization has not previously been reported in this reaction. As opposed to the equilibration results above, the byproduct ratio could be improved to 9:1 by decreasing the temperature (entry 4).[33]

Amino alcohols **3** could in principle be obtained from **7** either by sequential detosylation and hydrolysis or by hydrolysis prior to detosylation. The latter method proved inferior, as the corresponding *N*-tosyl amino alcohols could not be selectively deprotected. Oxazolidinones **7** were detosylated using sodium naphthalide in THF to the corresponding *N*-H derivatives **9** (Scheme 3, Table 2).[34] At this stage the diastereomers of **9a**,**b** could be separated by flash chromatography. Due to troublesome purification of *N*-tosyl oxazolidinone **7d**, the best yield from **1d** to **9d** was obtained when **7d** was used in unpure form (entry 4). Subsequent basic hydrolysis of **9** afforded *syn*-amino alcohols **3** in excellent yields (Scheme 3, Table 2). The hydrolysis of **9e** was retarded due to sterical

SCHEME 4. Synthesis of Aziridines 4 and *anti*-Amino Alcohols 5

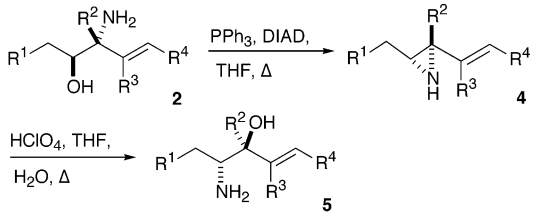

TABLE 3. Synthesis of Aziridines 4 and *anti*-Amino Alcohols 5

						yield (%)[a]	
entry	substrate	R^1	R^2	R^3	R^4	**4**	**5**
1	**2a**	$PhCH_2$	H	H	H	80	80
2	**2b**	BnO	H	H	H	72	84
3	**2c**	BnO	H	H	CH_2OPMB	60[b]	82
4	**2d**	H	H	H	CH_2OBn	62[c]	74[d]
5	**2e**	Me	Me	H	CH_2OBn	80[e]	67[f]
6	**2f**	PMBO	H	CH_2OBn	H	63	71

[a] Isolated yields. [b] 23% **2c** was recovered. [c] Isolation problems; see the text. [d] dr 10:1. [b] 13% **2e** was recovered. [f] dr 2.5:1.

hindrance; 8 h reflux was needed for completion compared to 1 h for **9a**−**d**,**f**.

Synthesis of N-H Vinylaziridines 4. The two remaining amino alcohols **5** and **6** are regioisomers of **2** and **3**. We envisaged the synthesis of **5** and **6** by ring-opening of *N*-H vinylaziridines **4**, which could be obtained from *anti*-amino alcohols **2** (Scheme 1). Cyclization of amino alcohols into *N*-H aziridines is known to be difficult, having neither a nitrogen activating group nor a good leaving group.[35] We recently investigated this transformation, and the best results were obtained with an optimized Mitsunobu protocol employing PPh_3 and diisopropylazodicarboxylate (DIAD).[36] Using this procedure, aziridines **4** could be obtained in good yields without involving activating groups (Scheme 4, Table 3). *N*-H Vinylaziridines **4** were found to be unstable on silica gel, which made purification on deactivated silica important. With this technique, the yield of aziridine **4b** could be raised from 30% to 72% (entry 2). However, aziridine **4c** was too unstable to allow for the difficult separation from the formed $Ph_3P{=}O$. This problem could be circumvented by employing polymer-bound triphenylphosphine, although this decreased the reaction rate, and **4c** was isolated in 78% (entry 3). Surprisingly, aziridine **4d** coevaporated with EtOAc, which made purification troublesome, but it could finally be isolated in 62% yield (entry 4).[37]

Syntheses of trisubstituted *N*-H aziridines are rare and described yields are moderate.[38] This might be due to

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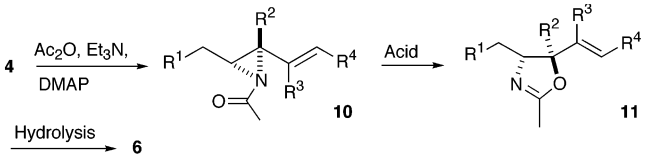
(38) (a) Viallon, L.; Reinaud, O.; Capdevielle, P.; Maumy, M. *Tetrahedron* **1996**, *52*, 13505−13614. (b) Wipf, P.; Henninger, T. C.; Geib, S. J. *J. Org. Chem.* **1998**, *63*, 6088−6089.

difficulties both in forming precursors as **2e** and ring-closing to aziridines, the reactions being retarded because of sterical hindrance. To our delight, ring closure of **2e** to trisubstituted aziridine **4e** was successful, and the relatively unpolar **4e** was easily isolated from $Ph_3P{=}O$. Although the reaction stopped before full conversion,[39] **4e** could be isolated in 80% and the remaining **2e** was readily recovered (entry 5). The yield based on recovered **2e** was an excellent 92%. Regioisomeric mixtures of **2** and **5**, obtained in the aminolysis, can be used without separation as both ring closures give aziridines **4**. Surprisingly, also the mixture of **2e** and **5e** obtained by aminolysis of **1e** could be ring-closed to **4e** in good yield, despite the sterical hindrance in **5e**.

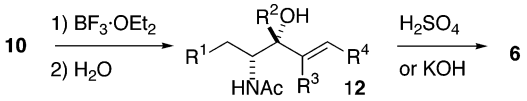
Synthesis of *anti*-Amino Alcohols 5. Acidic hydrolysis of activated aziridines[40] has been reported to proceed with rather poor regioselectivity.[10,41] There are no reports on hydrolysis of *N*-H aziridines, which might be due to the low reactivity of unactivated aziridines.[35] To our delight, *N*-H vinylaziridines **4** could be hydrolyzed into *anti*-amino alcohols **5** (Scheme 4) under acidic conditions. Initial hydrolysis attempts with **4a** were performed with tosic acid in THF/H_2O, affording **5a** in moderate yield. This result could be improved with $HClO_4$, and **5a** was formed with complete regioselectivity (>20:1) in 80% yield (Table 3, entry 1). The method was applied to aziridines **4b**−**f**, affording *anti*-amino alcohols **5b**−**f** in good yields. The reaction proceeded with clean S_N2 inversion for substrates **4a**−**c**,**f**, whereas amino alcohol **5d** surprisingly was formed in 10:1 diastereomeric ratio (entry 4). As expected, trisubstituted vinylaziridine **4e** behaved differently than **4a**−**d**,**f** under acidic conditions. Amino alcohol **5e** was formed as a 1:1 diastereomeric mixture, and optimization attempts with perchloric acid failed. Also, $LiClO_4$ was ineffective for this transformation.[42] Turning to Lewis acids, $InCl_3$ at pH 4 gave a 2:1 mixture of **6e** and **5e**, i.e., the unwanted diastereomer was the major compound. This might be explained by internal delivery of water from $In(H_2O)_6^{3+}$ coordinated to nitrogen.[43] Fortunately, employment of 2 equiv of $BF_3{\cdot}OEt_2$ in THF/H_2O 10:1 yielded **5e** in a 2.5:1 ratio (entry 5).[41,44] Treatment with BBr_3 instead resulted in partial epimerization of aziridine **4e**. The poorer diastereoselectivity obtained in the Brønsted acid mediated solvolysis of **4e** can be reationalized by invoking a carbocation-type of intermediate, the formation of which is somewhat retarded when using Lewis acids.

Synthesis of *syn*-Amino Alcohols 6. Ring-opening of aziridines **4** with retention of configuration would yield *syn*-amino alcohols **6**. Our synthetic strategy focused on an S_Ni rearrangement of *N*-acetylaziridines **10** into oxazolines **11**, followed by hydrolysis to **6** (Scheme 5). Acetylation of aziridines **4** proceeded in nearly quantitative yields, and *N*-acetylaziridines **10** were used as crude products in the subsequent reaction, as they were unstable to standard purification.[45] Acetylation of trisubstituted aziridine **4e** was troublesome; standard conditions (Ac_2O, Et_3N, catalytic amount DMAP) afforded a mixture of **10e** and an unidentified byproduct. When **4e** was subjected to Ac_2O and Et_3N without DMAP, solely byproduct was formed, as was the case with AcCl and Et_3N. A large excess of Et_3N (20 eqviv) and a catalytic amount of DMAP improved the ratio. Surprisingly, clean acetylation could be obtained with Ac_2O and a stoichiometric amount of DMAP. To circumvent the problematic workup of acid labile **10e**, polymer-bound DMAP was employed.

SCHEME 5. Synthesis of *syn*-Amino Alcohols 6



SCHEME 6. Rearrangement and in Situ Hydrolysis to Hydroxy Amides 12 Followed by Hydrolysis to 6



Several methods reported to cause the S_Ni rearrangement were scanned with *N*-acetylaziridines **10a**; reflux in chloroform was unsuccessful[46] and $TsOH{\cdot}H_2O$ instead afforded hydroxy amide **12a** in moderate yield (Scheme 6).[47] Early attempts with sodium iodide gave oxazoline **11a** as a diastereomeric mixture,[48] but fine-tuning of the reaction conditions caused a slow, but clean, rearrangement to **11a**. Turning to Lewis acids, treatment with $BF_3{\cdot}OEt_2$ resulted in a smooth rearrangement into oxazoline **11a**,[49] whereas reaction with copper triflate was slow.[50] Despite the clean rearrangement, **11a** could only be isolated in 55% yield. Unexpectedly, **11a** was partly hydrolyzed during purification,[51] furnishing a mixture of **11a** and hydroxy amide **12a** after flash chromatography.

The lability of oxazoline **11a** caused us to focus on formation of **12a** instead. Returning to the $TsOH{\cdot}H_2O$-catalyzed reaction, the results indicated in situ hydrolysis of **11a** to **12a**. This could be proved by treating oxazoline **11a** with $TsOH{\cdot}H_2O$, which afforded **12a** in high yield. Apparently, when present during the rearrangement, water causes byproduct formation. Unfortunately, rearrangement was retarded both with anhydrous TsOH and camphorsulfonic acid. As Brønstedt acids seemed ineffective, we speculated if in situ hydrolysis of **11a** to **12a** would be possible also in the $BF_3{\cdot}OEt_2$ rearrangement. Indeed, by addition of 10% water to the reaction mixture after complete formation of **11a**, hydroxy amide **12a** was slowly formed along with byproducts (Scheme 6). Changing the solvent from toluene to THF considerably in-

(39) Optimization attempts failed; neither prolonged reaction time nor a large excess of reagents improved the conversion; instead, a byproduct was formed.

(40) Ibuka, T.; Nakai, K.; Habashita, H.; Hotta, Y.; Otaka, A.; Tamamura, H.; Fujii, N. *J. Org. Chem.* **1995**, *60*, 2044−2058.

(41) Prasad, B. A. B.; Sekar, G.; Singh, V. K. *Tetrahedron Lett.* **2000**, *41*, 4677−4679.

(42) (a) Parrodi, C. A.; Vazquez, V.; Quintero, L.; Juraristi, E. *Synth. Commun.* **2001**, *31*, 3295−3302. (b) Yadav, J. S.; Reddy, B. V. S.; Jyothirmai, B.; Murty, M. S. R. *Synlett* **2002**, 53−56.

(43) (a) Yadav, J. S.; Reddy, B. V. S.; Abraham, S.; Sabitha, G. *Tetrahedron Lett.* **2002**, *43*, 1565−1567. (b) Fringuelli, F.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **2001**, *66*, 3554−3558.

(44) Reduced temperature considerably decreased the reactivity, and with a catalytic amount of acid, the reaction proceeded only at reflux with poor selectivity (dr 1.3:1).

(45) Lindström, U. M.; Somfai, P. *J. Am. Chem. Soc.* **1997**, *119*, 8385−8386.

(46) Cardillo, G.; Gentilucci, L.; Tolomelli, A.; Tomasini, C. *Tetrahedron Lett.* **1997**, *38*, 6953−6956.

TABLE 4. Synthesis of *syn*-Amino Alcohols 6

						yield (%)[a]	
entry	substrate	R^1	R^2	R^3	R^4	**12**	**6**
1	**4a**	$PhCH_2$	H	H	H	71	95[b]
2	**4b**	BnO	H	H	H	73	92[b]
3	**4c**	BnO	H	H	CH_2OPMB	73	91[c]
4	**4d**	H	H	H	CH_2OBn	74[d]	93[b]
5	**4e**	Me	Me	H	CH_2OBn	70	*e*
6	**4f**	PMBO	H	CH_2OBn	H	73	84[c]

[a] Isolated yields. [b] Acidic hydrolysis. [c] Basic hydrolysis. [d] dr 10:1. [e] See the text.

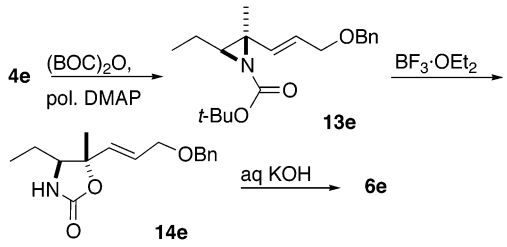
creased the hydrolysis rate, and **12a** could be isolated in 71% yield from **4a**. (Table 4, entry 1).

The rearrangement proceeded, as expected, with complete diastereoselectivity (dr > 20:1) and gratifyingly also with complete regioselectivity (>20:1). The latter can be rationalized by the stabilizing effect of the vinyl group on the transition state, thus favoring attack of the carbonyl oxygen at the allylic position. The timing of the water addition is crucial: when added too early, the diastereoselectivity is diminished, as water opens the *N*-acetylaziridine; when added too late, the formation of byproducts increases.

Also hydroxy amides **12b**−**f** were formed with complete regioselectivity in >70% yield over two steps (Table 4, entries 2−6). The diastereoselectivity was likewise high (dr > 20:1) in all cases apart from **12d** (dr 10:1), the reason for which is unclear. When **10e** was rearranged with byproduct present, **12e** was formed as a diastereomeric mixture, the ratio of which depended on the amount of byproduct.

Hydroxy amides **12a**,**b**,**e** were hydrolyzed in 5% aqueous H_2SO_4, giving *syn*-amino alcohols **6a**,**b**,**e** in excellent yields (Scheme 6, Table 4). Due to the acid lability of the PMB group, hydroxy amides **12c**,**f** were hydrolyzed in 1 M KOH, which gave a slower reaction (Table 4, entries 3 and 6). In all cases the reaction proceeded without alterations of the stereochemistry. The hydrolysis of **12e** was severely retarded by sterical hindrance. Several reaction conditions were screened without success; acidic media caused decomposition, whereas basic media was ineffective.[52] Conversion of **12e** to the corresponding acyloxazolidinone followed by LiOOH treatment only resulted in recovered amide **12e**.[53] Alternative strategies toward *syn*-amino alcohol **6e** avoiding hydroxy amide **12e** were investigated. Oxazoline **11e** could be isolated in 89%, but reduction of this species with $NaBCNH_3$ in acidic medium followed by hydrolysis gave a mixture of compounds.[54] Instead, **6e** could be obtained via BOC-protection of aziridine **4e** to BOC-aziridine **13e** and subsequent rearrangement to oxazolidinone **14e** (Scheme 7).[55] The $BF_3{\cdot}OEt_2$-induced rearrangement was conducted with crude **13e**, and **14e** was obtained as a separable mixture of diastereomers (2.3:1) in 66% combined yield. Oxazolidinone **14e** was easily hydrolyzed with 1 M KOH to *syn*-amino alcohol **6e** in 98% yield (Scheme 7).

SCHEME 7. Rearrangement to Oxazolidinone 14e Followed by Hydrolysis to 6e



Determination of Relative Stereochemistry. Amino alcohols **2**, **5**, and **6** were converted into the corresponding oxazolidinones.[18] The ring protons (H_4, H_5) of these compounds have coupling constants ($J_{H4,H5}$) that are larger for the cis- than the trans-configuration.[7] When *anti*-amino alcohols **2a**−**d**,**f** and **5a**−**d**,**f** were converted into oxazolidinones **15a**−**d**,**f** and **16a**−**d**,**f**, the coupling constants of the ring protons were 7.8−8.3 and 7.2−8.3 Hz, respectively, which is consistent with the cis-configuration. Oxazolidinones **9a**−**f** (Scheme 3) show the relative configuration of *syn*-amino alcohols **3a**−**f**. Compounds **9a**−**d**,**f** have coupling constants ranging from 5.0 to 7.2 Hz, confirming the trans-configuration. Finally, *syn*-amino alcohols **6a**−**d**,**f** yielded oxazolidinones **14a**−**d**,**f** with coupling constants between 5.5 and 6.6 Hz, agreeing with the trans-configuration. The relative configurations of **9e**, **14e**, **15e**, and **16e** were confirmed by NOESY experiments. Interactions between the ring proton (H_4) and the methyl group at C_5 were present for oxazolidinones **15e** and **16e**, indicating the cis-configuration.

Conclusions

We have presented a synthetic strategy that provides a straightforward route from vinyl epoxides **1** to the four isomeric *vic*-amino alcohols **2**, **3**, **5**, and **6**. Since *ent*-**1** is available from the same starting material as **1**, this protocol has the potential of delivering all eight possible isomers of a given amino alcohol. The presented strategy focuses on the propensity of vinyl epoxides and vinylaziridines to be ring-opened at the allylic position by suitable nucleophiles, using reactions that perform such transformations selectively with either inversion or retention of configuration. The synthesis of vinyl epoxides has been simplified by application of an enantioselective

(47) Nishiguchi, T.; Tochio, H.; Nabeya, A.; Iwakura, Y. *J. Am. Chem. Soc.* **1968**, *91*, 5835−5845.
(48) Foglia, T. A.; Gregory, L. M.; Maerker, G. *J. Org. Chem.* **1970**, *35*, 3779−3785.
(49) Hori, K.; Nishiguchi, T.; Nabeya, A. *J. Org. Chem.* **1997**, *62*, 3081−3088.
(50) Ferraris, D.; Drury, W. J., III; Cox, C.; Lectka, T. *J. Org. Chem.* **1998**, *63*, 4568−4569.
(51) (a) Lee, K.-Y.; Kim, Y.-H.; Park, M.-S.; Oh, C.-Y.; Ham, W.-H. *J. Org. Chem.* **1999**, *64*, 9450−9458. (b) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, 1999.
(52) Acidic conditions gave no reaction/decomposition: 5% H_2SO_4, rt to reflux; 5% H_2SO_4 in THF/H_2O 1:1, rt to reflux; 5 equiv $BF_3{\cdot}OEt_2$ in THF/H_2O 10:1, rt to reflux; 10 equiv $TsOH{\cdot}H_2O$ in THF, rt to reflux. Basic conditions gave no reaction: 1 M KOH in EtOH/H_2O 1:1, 150 °C; NH_4OH in EtOH/H_2O 1:1, 140 °C; NH_4OH in H_2O, 50 W 15 min; LiOH, H_2O_2 in THF/H_2O 3:1, reflux. NaOEt in EtOH, reflux. NH_2-$NH_2{\cdot}H_2O$ afforded reduced alkene with intact amide group; Ca/NH_3 cleaved both the amide and benzyl group.
(53) Evans, D. A.; Ratz, A. M.; Huff, B. E.; Sheppard, G. S. *J. Am. Chem. Soc.* **1995**, *117*, 3448−3467.
(54) Gosmann, G.; Guillaume, D.; Husson, H.-P. *Tetrahedron Lett.* **1996**, *37*, 4369−4372.
(55) Sepulveda-Arques, J.; Armero-Alarte, T.; Acero-Alarcon, A.; Zaballos-Garcia, E.; Solesio, B. Y.; Carrera, J. E. *Tetrahedron* **1996**, *52*, 2097−2102.

diene epoxidation. Furthermore, a novel, practical, large-scale aminolysis reaction and the successful synthesis of a trisubstituted *N*-H vinylaziridine have been detailed.

Experimental Section

This Experimental Section contains typical procedures for formation of compounds **2**−**7**, **9**, **10**, **12**, and **13** and analytical data of all amino alcohols. For general experimental details and analytical data of the remaining compounds, see the Supporting Information.

Typical Procedure for the Aminolysis of Epoxides 1 to *anti*-Amino Alcohols 2. (3*S*,4*R*)-4-Amino-1-phenylhex-5-en-3-ol (2a):[23] Microwave Irradiation. Vinyl epoxide **1a** (15.0 mg, 86 μmol) in NH_4OH (25%, 2.5 mL) was subjected to focused microwave irradiation at 30 W for 8 min. The solvent was evaporated at reduced pressure and the crude product chromatographed (EtOAc/MeOH 6:1 + 1% NH_3) to give *anti*-amino alcohol **2a** as a yellow oil in 93% yield (15.3 mg, 80 μmol).

Conventional Heating. Vinyl epoxide **1a** (0.55 g, 3.1 mmol) in NH_4OH (25%, 7 mL) in a sealed tube was heated to 125 °C, in a preheated oil bath, for 1 h. The mixture was extracted with 4 × 10 mL of Et_2O, then the organic phase was dried (Na_2SO_4) and concentrated. Flash chromatography as above afforded **2a** in 91% combined yield (regioisomeric mixture 11:1).

(2*R*,3*R*)-3-Amino-1-benzyloxypent-4-en-2-ol (2b)[23] was prepared from vinyl epoxide **1b** as described for **2a**. Microwave irradiation at 30 W for 8 min gave 87% yield. Conventional heating at 170 °C for 4.5 h gave 93% yield.

(2*R*,3*R*)-3-Amino-1-benzyloxy-6-(4-methoxybenzyloxy)-4(*E*)-hexen-2-ol (2c) was prepared from vinyl epoxide **1c** as described for **2a**. Microwave irradiation at 15 W for 20 min gave **2c** as a low-melting solid in 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.27 (m, 5H), 7.25 (d, 2H, J = 8.7 Hz), 6.87 (d, 2H, J = 8.7 Hz), 5.75 (m, 2H), 4.52 (s, 2H), 4.42 (s, 2H), 3.97 (d, 2H, J = 4.2 Hz), 3.80 (s, 3H), 3.77 (m, 1H), 3.51 (m, 3H), 2.16 (br s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 159.2, 138.0, 133.4, 130.3, 129.4, 128.4, 128.3, 127.8, 113.8, 73.5, 72.7, 71.9, 71.7, 70.0, 55.6, 55.3. IR (neat): 3583, 3377 (br), 3922, 2852 cm^{-1}. $[\alpha]_D$: +2.5 (*c* 0.25, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{21}H_{28}NO_4$ (M + H): 358.2018. Found: 358.2014.

(2*R*,3*S*)-3-Amino-6-benzyloxy-4(*E*)-hexen-2-ol (2d)[23] was prepared from vinyl epoxide **1d** as described for **2a**. Microwave irradiation at 30 W for 10 min gave **2d** in 100% combined yield (regioisomeric ratio 11:1). Conventional heating at 140 °C for 1 h gave 82% combined yield (regioisomeric ratio 9:1). $[\alpha]_D$: −6.8 (*c* 1.00, CH_2Cl_2).

(3*R*,4*S*)-4-Amino-7-benzyloxy-4-methyl-5(*E*)-hepten-3-ol (2e) was prepared from vinyl epoxide **1e** as described for **2a**. Microwave irradiation at 40 W for 11 min gave **2e** as a colorless oil in 89% combined yield (regioisomeric ratio 2:1). Conventional heating at 140 °C for 1 h gave 78% combined yield (regioisomeric ratio 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.26 (m, 5H), 5.81 (d, 1H, J = 15.8 Hz), 5.72 (dt, 1H, J = 15.8, 5.6 Hz), 4.52 (s, 2H), 4.04 (d, 2H, J = 5.6 Hz), 3.17 (dd, 1H, J = 10.5, 2.2 Hz), 1.88 (br s, 3H), 1.51 (ddq, 1H, J = 13.9, 7.3, 2.2 Hz), 1.21 (s, 3H), 1.18 (m, 1H), 1.00 (t, 3H, J = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 138.2, 128.3, 127.7, 127.6, 125.1, 79.4, 72.2, 70.6, 56.8, 26.1, 24.8, 11.3. IR (neat): 3356, 2964, 2873 cm^{-1}. $[\alpha]_D$: +21.6 (*c* 0.76, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{15}H_{24}NO_2$ (M + H): 250.1807. Found: 250.1811.

(2*R*,3*R*)-3-Amino-4-benzyloxymethyl-1-(4-methoxybenzyloxy)pent-4-en-2-ol (2f)[20] was prepared from vinyl epoxide **1f** as described for **2a**. Microwave irradiation at 30 W for 8 min gave **2e** in 84% yield.

Typical Procedures for the Ring Opening of Vinyl Epoxides 1 To Give Oxazolidinones 7. With Equilibration: (4*S*,5*S*)-5-Phenethyl-3-(toluene-4-sulfonyl)-4-vinyloxazolidin-2-one (7a). To a solution of $(dba)_3Pd_2{\cdot}CHCl_3$[56] (15.0 mg, 15 μmol) in THF (1 mL) was added distilled $(^iPrO)_3P$ (36 μL, 0.146 mmol). The mixture was stirred for 20 min before addition of distilled TsNCO (44 μL, 0.292 mmol) and vinyl epoxide **1a** (25.0 mg, 0.146 mmol) in THF (1 mL), and the resultant mixture was refluxed for 36 h. Water was added, and the mixture was extracted with Et_2O. The organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. Flash chromatography (pentane/EtOAc 5:1 → 2:1) afforded oxazolidinone **7a** as a yellow oil in 82% yield (43.7 mg, 0.117 mmol). NMR analysis indicated a diastereomeric ratio of 4.5:1. ^{1}H NMR (300 MHz, $CDCl_3$, major isomer): δ 7.92 (d, 2H, J = 8.5 Hz), 7.38−7.12 (m, 7H), 5.77 (ddd, 1H, J = 16.8, 9.9, 8.2 Hz), 5.42 (d, 1H, J = 16.8 Hz), 5.36 (d, 1H, J = 9.9 Hz), 4.46 (dd, 1H, J = 8.2, 4.6 Hz), 4.12 (dt, 1H, J = 8.0, 4.6 Hz), 2.85−2.63 (m, 2H), 2.45 (s, 3H), 2.08−1.87 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.3, 145.4, 139.6, 134.9, 133.5, 129.6, 128.5, 128.4, 128.3, 126.3, 120.5, 79.1, 64.7, 35.4, 30.7, 21.8. IR (neat): 2926, 2864, 1782, 1369 cm^{-1}. HRMS (EI+) exact mass calcd for $C_{20}H_{21}NO_4S$ (M): 371.1191. Found: 371.1182.

Without Equilibration: (4*S*,5*R*)-5-Benzyloxymethyl-4-[3-(4-methoxybenzyloxy)-1(*E*)-propenyl]-3-(toluene-4-sulfonyl)oxazolidin-2-one (7c) was prepared from vinyl epoxide **1c** as described for **7a**, except that the reaction was run at room temperature for 1 h. The product was isolated as a yellow oil in 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, 2H, J = 8.4 Hz), 7.37−7.22 (m, 7H), 7.19 (d, 2H, J = 8.7 Hz), 6.89 (d, 2H, J = 8.7 Hz), 5.98 (dt, 1H, J = 15.4, 5.0 Hz), 5.77 (ddt, 1H, J = 15.4, 8.3, 1.5 Hz), 4.83 (dd, 1H, J = 8.3, 3.8 Hz), 4.47 (s, 2H), 4.46 (s, 2H), 4.24 (q, 1H, J = 3.8 Hz), 4.03 (dd, 2H, J = 5.0, 1.5 Hz), 3.81 (s, 3H), 3.56 (dd, 1H, J = 11.1, 3.8 Hz), 3.52 (dd, 1H, J = 11.1, 3.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 151.9, 145.7, 137.4, 135.5, 133.4, 130.4, 139.9, 129.8, 129.0, 128.5, 128.2, 128.1, 114.3, 79.1, 74.0, 72.7, 69.2, 69.0, 60.9, 55.7, 22.1. IR (neat): 3062, 2983, 1784, 1371 cm^{-1}. $[\alpha]_D$: −11.2 (*c* 1.80, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{29}H_{31}NO_7S$ (M): 537.1821. Found: 537.1819.

Typical Procedure for the Detosylation of 7 to Oxazolidinones 9. (4*S*,5*S*)-5-Phenethyl-4-vinyloxazolidin-2-one (9a). Sodium naphthalide was prepared by stirring naphthalene (200 mg, 1.6 mmol) and small pieces of sodium (50 mg, 2.2 mmol) in freshly distilled DME (3 mL) overnight. To a solution of oxazolidinone **7a** (30.0 mg, 81 μmol) in THF (0.5 mL) at −78 °C was dropwise added sodium naphthalide until the blackish color persisted. The mixture was stirred for 15 min, quenched with EtOH, and allowed to reach 0 °C before addition of phosphate buffer (pH 7). The mixture was extracted with Et_2O, then the organic phase was washed with water and brine, dried (Na_2SO_4), and concentrated. The diastereomers could be separated by careful flash chromatography (pentane/EtOAc 4:1 → 1:1), affording the *N*-H oxazolidinone **9a** as a colorless oil in 93% yield (16.3 mg, 75 μmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.17 (m, 5H), 5.76 (ddd, 1H, J = 17.4, 10.2, 7.4 Hz), 5.40 (br s, 1H), 5.30−5.22 (m, 2H), 4.21 (ddd, 1H, J = 11.3, 7.0, 4.3 Hz), 3.96 (br t, 1H, J = 7.0 Hz), 2.87 (ddd, 1H, J = 14.3, 9.8, 5.3 Hz), 2.73 (ddd, 1H, J = 14.3, 9.4, 7.2 Hz), 2.12−1.93 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 140.3, 135.3, 128.4, 129.3, 126.1, 119.1, 81.4, 61.3, 35.7, 31.3. IR (neat): 3361 (br), 2933,2808, 1749 cm^{-1}. $[\alpha]_D$: −45.7 (*c* 0.14, CH_2Cl_2). HRMS (EI+) exact mass calcd for $C_{13}H_{15}NO_2$ (M): 217.1103. Found: 217.1103.

Typical Procedure for the Hydrolysis of 9 to *syn*-Amino Alcohols 3. (3*S*,4*S*)-4-Amino-1-phenyl-5-hexen-3-ol (3a). A solution of oxazolidinone **9a** (12.6 mg, 58 μmol) in 1 M KOH (EtOH/H_2O 2:1) was refluxed for 1.5 h. Aqueous NaOH (2 M) was added, and the mixture was extracted several times with Et_2O. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The crude product was pushed through a short silica plug to afford *syn*-amino alcohol **3a** as a yellow oil in 100% yield (11.1 mg, 58 μmol). ^{1}H NMR (400

(56) dba = dibenzylideneacetone.

MHz, $CDCl_3$): δ 7.30−7.16 (m, 5H), 5.78 (ddd, 1H, J = 17.2, 10.5, 7.4 Hz), 5.19 (dt, 1H, J = 17.2, 1.2 Hz), 5.13 (dt, 1H, J = 10.5, 1.2 Hz), 3.32 (ddd, 1H, J = 10.2, 7.4, 3.1 Hz), 3.14 (t, 1H, J = 7.4 Hz), 2.88 (ddd, 1H, J = 13.9, 10.2, 5.1 Hz), 2.69 (ddd, 1H, J = 13.9, 10.2, 7.0 Hz), 2.17 (br s, 3H), 1.85 (m, 1H), 1.69 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 139.9, 128.3, 128.2, 125.6, 115.8, 73.2, 59.5, 35.7, 32.2. IR (neat): 3357 (br), 2920, 2860 cm^{-1}. $[\alpha]_D$: −27.5 (*c* 0.63, CH_2Cl_2). HRMS (EI+) exact mass calcd for $C_{12}H_{18}NO$ (M + H): 192.1388. Found: 192.1377.

(2*R*,3*S*)-3-Amino-1-benzyloxy4-penten-2-ol (3b) was prepared from oxazolidinone **9b** as described for **3a** and isolated as a low-melting solid in 97% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38−7.24 (m, 5H), 5.82 (ddd, 1H, J = 17.3, 10.4, 6.9 Hz), 5.20 (d, 1H, J = 17.3 Hz), 5.11 (d, 1H, J = 10.4 Hz), 4.56 (AB-q, 2H, J = 11.9 Hz), 3.58 (m, 2H), 3.50 (m, 1H), 3.40 (br t, 1H, J = 6.9 Hz), 2.00 (br s, 3H). ^{13}C NMR (100 MHz, $CDCl_2$): δ 139.2, 137.8, 128.3, 127.6, 115.9, 73.5, 73.0, 71.7, 56.2. IR (neat): 3356 (br), 2904, 2864 cm^{-1}. $[\alpha]_D$: −9.1 (*c* 0.65, CH_2Cl_2). HRMS (EI+) exact mass calcd for $C_{12}H_{18}NO_2$ (M + H): 208.1338. Found: 208.1340.

(2*R*,3*S*)-3-Amino-1-benzyloxy-6-(4-methoxybenzyloxy)-4(*E*)-hexen-2-ol (3c) was prepared from oxazolidinone **9c** as described for **3a** and isolated as yellow crystals in 91% yield. mp 70−71 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.27 (m, 5H), 7.25 (d, 2H, J = 8.7 Hz), 6.88 (d, 2H, J = 8.7 Hz), 5.75 (dt, 1H, J = 15.6, 4.8 Hz), 5.69 (dd, 1H, J = 15.6, 6.0 Hz), 4.56 (AB-q, 2H, J = 12.1 Hz), 4.42 (s, 2H), 3.95 (d, 2H, J = 4.8 Hz), 3.80 (s, 3H), 3.59−3.40 (m, 4H), 1.96 (br s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 138.0, 130.2, 129.4, 128.4, 128.3, 127.8, 113.8, 73.5, 73.3, 72.0, 71.8, 69.9, 55.3, 55.3. IR (neat): 3583, 3357 (br), 2920, 2856 cm^{-1}. $[\alpha]_D$: −20.3 (*c* 1.10, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{21}H_{28}NO_4$ (M + H): 358.2018. Found: 358.2021.

(2*R*,3*R*)-3-Amino-6-benzyloxy-4(*E*)-hexen-2-ol (3d) was prepared from oxazolidinone **9d** as described for **3a** and isolated as a colorless oil in 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.27 (m, 5H), 5.78 (dt, 1H, J = 15.6, 5.2 Hz), 5.70 (dd, 1H, J = 15.6, 6.8 Hz), 4.52 (s, 2H), 4.02 (d, 2H, J = 5.2 Hz), 3.45 (dq, 1H, J = 7.0, 6.2 Hz), 3.06 (br t, 1H, J = 6.9 Hz), 2.06 (br s, 3H), 1.18 (d, 3H, J = 6.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.6, 135.3, 128.8, 128.4, 128.2, 128.1, 72.8, 70.7, 70.7, 60.4, 20.1. IR (neat): 3356, 2970, 2858 cm^{-1}. $[\alpha]_D$: +14.8 (*c* 0.60, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{13}H_{20}NO_2$ (M + H): 222.1494. Found: 222.1492.

(3*R*,4*R*)-4-Amino-7-benzyloxy-4-methyl-5(*E*)-hepten-3-ol (3e) was prepared from oxazolidinone **9e** as described for **3a** and isolated as a yellow oil in 98% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.27 (m, 5H), 5.79 (d, 1H, J = 15.8 Hz), 5.73 (dt, 1H, J = 15.8, 4.8 Hz), 4.52 (s, 2H), 4.03 (d, 2H, J = 4.8 Hz), 3.15 (dd, 1H, J = 10.3, 2.0 Hz), 1.97 (br s, 3H), 1.50 (m, 1H), 1.28 (m, 1H), 1.11 (s, 3H), 1.02 (t, 3H, J = 7.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.1, 138.2, 128.4, 127.8, 127.7, 125.0, 78.6, 72.4, 70.6, 56.8, 24.0, 21.3, 11.6. IR (neat): 3356, 2970, 2873 cm^{-1}. $[\alpha]_D$: +15.9 (*c* 2.02, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{15}H_{24}NO_2$ (M + H): 250.1807. Found: 250.1814.

(2*R*,3*S*)-3-Amino-4-benzyloxymethyl-1-(4-methoxybenzyloxy)-4-penten-2-ol (3f) was prepared from oxazolidinone **9f** as described for **3a** and isolated as a low-melting solid in 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.14 (m, 7H), 6.80 (d, 2H, J = 8.8 Hz), 5.12 (m, 2H) 4.44 (m, 2H), 4.39 (br s, 2H), 3.98 (AB-q, 2H, J = 12.1 Hz), 3.74−3.68 (m, 1H), 3.73 (s, 3H), 3.52−3.36 (m, 3H), 2.00 (br s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.2, 147.0, 137.8, 130.2, 129.3, 128.4, 127.7, 115.0, 113.8, 73.0, 72.5, 71.7, 71.7, 71.4, 56.2, 55.2. IR (neat) 3373 (br), 2910, 2860 cm^{-1}. $[\alpha]_D$ −6.9 (*c* 1.00, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{21}H_{28}NO_4$ (M + H): 358.2018. Found: 358.2019.

Typical Procedure for the Ring Closure of Amino Alcohols 2 to Aziridines 4. With Regular Triphenylphosphine: (2*R*,3*R*)-2-Phenethyl-3-vinylaziridine (4a).[23] To a solution of PPh_3 (0.19 mg, 0.73 mmol) in THF (2 mL) at 0 °C was added DIAD (0.14 mL, 0.73 mmol). After 20 min amino alcohol **2a** (0.10 g, 0.52 mmol) in THF (1.5 mL) was added, and the resultant mixture was refluxed for 17 h. The solvent was evaporated at reduced pressure, Et_2O was added to the crude product, and the mixture was stored overnight in the freezer. Precipitated Ph_3PO was removed by filtration and careful flash chromatography on deactivated silica (10% Et_3N during packing), (pentane → pentane/EtOH 10:1) afforded vinylaziridine **4a** in 80% yield.

With Polymer-Bound Triphenylphosphine: (2*S*,3*R*)-2-Benzyloxymethyl-3-[3-(4-methoxybenzyloxy)-1(*E*)-propenyl]aziridine (4c). To amino alcohol **2c** (8.1 mg, 23 μmol) and polymer-bound PPh_3 (15.2 mg, 45 μmol (3 mmol/g)) in THF (1 mL) at 0 °C was added DIAD (8.7 μL, 45 μmol). The resultant mixture was refluxed for 26 h, after which some **2c** still remained. The solvent was evaporated at reduced pressure, then careful flash chromatography on deactivated silica (10% Et_3N during packing, pentane/EtOAc 8:1 → EtOAc/MeOH 10:1 + 1% NH_4OH) afforded vinylaziridine **4c** as a colorless oil in 78% yield (4.6 mg, 13.6 μmol) based on recovered **2c** (1.9 mg, 5.3 μmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.27 (m, 5H), 7.26 (d, 2H, J = 8.7 Hz), 6.88 (d, 2H, J = 8.7 Hz), 5.88 (dt, 1H, J = 15.4, 5.8 Hz), 5.32 (dd, 1H, J = 15.4, 8,3 Hz), 4.55 (d, 2H, J = 2.5 Hz), 4.44 (s, 2H), 3.97 (d, 2H, J = 5.8 Hz), 3.80 (s, 3H), 3.60 (dd, 1H, J = 10.3, 4.0 Hz), 3.47 (dd, 1H, J = 10.3, 5.5 Hz), 2.37 (br d, 1H, J = 8.0 Hz), 2.19 (br s, 1H), 1.60 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 132.6, 132.5, 130.7, 129.8, 128.8, 128.1, 114.2, 73.5, 72.4, 70.13, 55.7. IR (neat): 3377 (br), 2956, 2858 cm^{-1}. $[\alpha]_D$: +11.9 (*c* 1.08, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{21}H_{26}NO_3$ (M + H): 340.1913. Found: 340.1912.

Typical Procedure for the Solvolysis of Aziridines 4 into anti-Amino Alcohols 5. $HClO_4$ Procedure: (3*S*,4*R*)-4-Amino-6-phenyl-1-hexen-3-ol (5a). To a solution of vinylaziridine **4a** (30.0 mg, 0.173 mmol) in THF (3 mL) and H_2O (2.4 mL) was added $HClO_4$ (15 μL, 0.173 mmol), and the solution was heated to 50 °C for 7 h. After addition of K_2CO_3, the mixture was stirred for 20 min, filtered, and concentrated. Flash chromatography (EtOAc/MeOH 10:1+ 1% NH_4OH) afforded amino alcohol **5a** as a low-melting solid in 80% yield (26.6 mg, 0.139 mmol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33−7.16 (m, 5H), 5.86 (ddd, 1H, J = 17.3, 10.7, 6.1 Hz), 5.34 (dt, 1H, J = 17.3, 1.5 Hz), 5.25 (dt, 1H, J = 10.7, 1.5 Hz), 4.07 (br s, 1H), 2.94−2.76 (m, 3H), 2.62 (ddd, 1H, J = 14.0, 9.9, 6.9 Hz), 1.94 (br s, 3H), 1.91−1.76 (m, 1H). 1.63−1.49 (m, 1H). ^{13}CNMR (67.5 MHz, $CDCl_3$): δ 141.8, 136.6, 128.5, 128.3, 125.9, 117.0, 75.0, 54.5, 35.4, 32.8. IR (neat): 3373 (br), 2922, 2864 cm^{-1}. $[\alpha]_D$: −15.8 (*c* 5.23, CH_2Cl_2). HRMS (EI+) exact mass calcd for $C_{12}H_{18}NO$ (M + H): 192.1388. Found: 192.1390.

(2*S*,3*S*)-2-Amino-1-benzyloxypent-4-en-3-ol (5b) was prepared from aziridine **4b** as described for **5a** and isolated as a colorless oil in 84% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39−7.24 (m, 5H), 5.84 (ddd, 1H, J = 17.3, 10.4, 6.0 Hz), 5.31 (dt, 1H, J = 17.3, 1.7 Hz), 5.20 (dt, 1H, J = 10.4, 1.7 Hz), 4.50 (s, 2H), 4.11 (br t, 1H, J = 5.8 Hz), 3.51 (m, 2H), 3.06 (br q, 1H, J = 6.0 Hz), 2.01 (br s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.7, 137.3, 128.3, 127.7, 127.6, 116.5, 74.6, 73.5, 72.3, 54.6. IR (neat): 3343 (br), 2908, 2860 cm^{-1}. $[\alpha]_D$: −11.4 (*c* 0.69, CH_2Cl_2). HRMS (EI+) exact mass calcd for $C_{12}H_{18}NO_2$ (M + H): 208.1338. Found: 208.1344.

(2*S*,3*S*)-2-Amino-1-benzyloxy-6-(4-methoxybenzyloxy)-4(*E*)-hexen-3-ol (5c) was prepared from aziridine **4c** as described for **5a** and isolated as a low-melting solid in 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.24 (m, 7H), 6.88 (d, 2H, J = 8.6 Hz), 5.88 (dt, 1H, J = 15.6, 5.5 Hz), 5.73 (dd, 1H, J = 15.6, 6.0 Hz), 4.52 (s, 2H), 4.44 (s, 2H), 4.15 (br t, 1H, J = 5.7 Hz), 4.00 (d, 2H, J = 5.5 Hz), 3.81 (s, 3H), 3.54 (dd, 1H, J = 9.5, 5.0 Hz), 3.50 (dd, 1H, J = 9.5, 6.0 Hz), 3.06 (br q, 1H, J = 5.5 Hz), 2.75 (br s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 138.3, 132.1, 130.7, 129.8, 129.6, 128.9, 128.3, 128.2. 114.2, 74.4, 73.9, 72.8, 72.4, 70.2, 55.7, 55.1. IR (neat): 3585,

3357 (br), 2913, 2858 cm^{-1}. $[\alpha]_D$: +11.4 (*c* 0.07, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{21}H_{28}NO_4$ (M + H): 358.2018. Found: 358.2020.

(2*S*,3*R*)-2-Amino-6-benzyloxy-4(*E*)-hexen-3-ol (5d) was prepared from aziridine **4d** as described for **5a** and isolated as a colorless oil in 74% combined yield (ds 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.27 (m, 5H), 5.88 (dtd, 1H, *J* = 15.6, 5.6, 0.9 Hz), 5.75 (ddt, 1H, *J* = 15.6, 6.1, 1.2 Hz), 4.52 (s, 2H), 4.04 (d, 2H, *J* = 5.6 Hz), 4.00 (dt, 1H, *J* = 5.1, 0.9 Hz), 3.00 (dq, 1H, *J* = 6.6, 4.2 Hz), 2.06 (br s, 3H), 1.04 (d, 3H, *J* = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2, 131.7, 129.1, 128.4, 127.7, 127.6, 75.3, 72.2, 70.1, 50.7, 18.4. IR (neat): 3354, 2925, 2856 cm^{-1}. $[\alpha]_D$: +16.7 (*c* 1.75, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{13}H_{20}NO_2$ (M + H): 222.1494. Found: 222.1501.

(2*S*,3*S*)-4-Amino-2-benzyloxymethyl-5-(4-methoxybenzyloxy)-1-penten-3-ol (5f) was prepared from aziridine **4f** as described for **5a** and isolated as a yellow oil in 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.21 (m, 7H), 6.88 (d, 2H, *J* = 8.6 Hz), 5.28 (s, 1H), 5.26 (s, 1H), 4.54 (m, 2H), 4.42 (m, 2H), 4.10 (d, 1H, *J* = 6.3 Hz), 4.08 (m, 2H), 3.79 (s, 3H), 3.58 (dd, 1H, *J* = 9.2, 4.3 Hz), 3.52 (dd, 1H, *J* = 9.2, 6.3 Hz), 3.12 (td, 1H, *J* = 6.3, 4.3 Hz), 1.80 (br s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.3, 144.7, 137.9, 130.0, 129.4, 128.5, 127.8, 127.7, 116.0, 113.9, 77.6, 73.2, 72.6, 71.1, 55.3, 53.0. IR (neat): 3369 (br), 2914, 2860, 2360 cm^{-1}. $[\alpha]_D$: +7.0 (*c* 0.50, CH_2Cl_2). HRMS (CI+): exact mass calcd for $C_{21}H_{28}NO_4$ (M + H): 358.2018. Found: 358.2019.

BF_3·OEt_2 Procedure: (4*R*,5*S*)-5-Amino-1-benzyloxy-4-methyl-2(*E*)-hepten-4-ol (5e). To a solution of vinylaziridine **4e** (50 mg, 0.216 mmol) in THF (2 mL) and H_2O (0.2 mL) at 0 °C was added BF_3·OEt_2 (56 μL, 0.43 mmol), and the solution was stirred at room temperature for 5 h. The reaction was quenched with 2 M NaOH, and THF was removed in vacuo. To the residue was added CH_2Cl_2 (2 mL), and the mixture was filtered through an Extrelut NT3 tube, which was eluted with CH_2Cl_2 (15 mL). The solution was concentrated, and flash chromatography (EtOAc/MeOH 10:1+ 1% NH_4OH) afforded amino alcohol **5e** as a diastereomeric mixture (2.5:1) in 67% yield (36 mg, 0.145 mmol). The diastereomers could be separated with careful flash chromatography, which gave **5e** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.27 (m, 5H), 5.90 (dt, 1H, *J* = 15.6, 5.6 Hz), 5.73 (dd, 1H, *J* = 15.6, 1.2 Hz), 4.52 (s, 2H), 4.06 (dd, 2H, *J* = 5.6, 1.2 Hz), 2.44 (dd, 1H, *J* = 9.2, 2.1 Hz), 2.34 (br s, 3H), 1.71 (m, 1H), 1.29 (s, 3H), 1.06 (m, 1H), 0.98 (t, 3H, *J* = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 135.7, 128.3, 127.7, 127.6, 126.2, 73.4, 72.1, 70.4, 62.1, 26.0, 25.3, 11.8. IR (neat): 3396, 2968, 2873 cm^{-1}. $[\alpha]_D$: −5.2 (*c* 0.66, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{15}H_{24}NO_2$ (M + H): 250.1807. Found: 250.1809.

Typical Procedure for the Acylation of Vinylaziridines 4 to *N*-Acetylaziridines 10, Followed by Rearrangement to 11 and *in Situ* Hydrolysis into Hydroxy Amides 12: (2*R*,3*R*)-1-(2-Phenethyl-3-vinylaziridin-1-yl)-ethanone (10a). A solution of vinylaziridine 4a (100 mg, 0.58 mmol), Et_3N (0.160 mL, 1.2 mmol), and DMAP (catalytic amount) in CH_2Cl_2 (1.5 mL) was cooled to −78 °C before addition of Ac_2O (60 μL, 0.63 mmol). After 15 min the reaction was quenched with H_2O and the mixture was extracted with Et_2O. The organic phase was washed with water, saturated $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated to give the crude *N*-acetyl vinylaziridine **10a** (126.2 mg) that was taken directly on to the next step. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.18 (m, 5H), 5.40 (m, 1H), 5.25 (m, 2H), 2.87−2.71 (m, 3H), 2.52 (dt, 1H, *J* = 6.3, 2.7 Hz), 2.07 (s, 3H), 1.98 (m, 1H), 1.74 (m, 1H).

(1*R*,2*R*)-*N*-(2-Hydroxy-1-phenethyl-3-butenyl)acetamide (12a): To a solution of the crude **10a** (10.0 mg, 46 μmol) in THF (0.5 mL) at −25 °C was added BF_3·OEt_2 (12 μL, 92 μmol). After 1.5 h full conversion into the corresponding oxazoline was achieved, H_2O (0.05 mL) was added, and the resultant mixture was stirred at room temperature for 2 h. Aqueous NaOH (2 M) was added, and the mixture was extracted several times with Et_2O. The organic phase was washed with saturated $NaHCO_3$, dried (Na_2SO_4), and concentrated. Flash chromatography (EtOAc) afforded *syn*-hydroxy amide **12a** as white crystals in 71% yield (7.6 mg. 33 μmol). mp 73−74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30−7.16 (m, 5H), 5.85 (ddd, 1H, *J* = 17.2, 10.5, 5.9 Hz), 5.61 (br d, 1H, *J* = 8.9 Hz), 5.28 (dt, 1H, *J* = 17.2, 1.6 Hz), 5.18 (dt, 1H, *J* = 10.5, 1.6 Hz), 4.16 (br t, 1H, *J* = 4.7 Hz), 3.97 (ddd, 1H, *J* = 14.1, 9.0, 4.7 Hz), 2.68 (t, 2H, *J* = 8.0 Hz), 2.40 (br s, 1H), 2.03−1.80 (m, 2H), 1.95 (s, 3H). ^{13}CNMR (100 MHz, $CDCl_3$): δ 170.5, 141.5, 138.0, 128.4, 128.2, 125.9, 116.2, 74.4, 53.5, 33.5, 32.7, 23.4. IR (neat): 3296 (br), 2929, 2862, 1647 cm^{-1}. $[\alpha]_D$: +22.2 (*c* 0.46, CH_2Cl_2). HRMS (EI+) exact mass calcd for $C_{14}H_{20}NO_2$ (M + H): 234.1494. Found: 234.1490.

Typical Procedures for the Hydrolysis of Amides 12 to *syn*-Amino Alcohols 6. Acidic Hydrolysis: (3*R*,4*R*)-4-Amino-6-phenyl-1-hexen-3-ol (6a). Hydroxy amide **12a** (21.0 mg, 90 μmol) in aqueous H_2SO_4 (5%) was refluxed for 1 h, then aqueous NaOH (2 M) was added, and the mixture was extracted several times with Et_2O. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The crude product was pushed through a short silica plug to afford *syn*-amino alcohol **6a** as a low-melting solid in 95% yield (16.4 mg, 86 μmol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30−7.21 (m, 5H), 5.83 (ddd, 1H, *J* = 17.3, 10.4, 6.0 Hz), 5.33 (dt, 1H, *J* = 17.3, 1.4 Hz), 5.21 (dt, 1H, *J* = 10.4, 1.4 Hz), 3.85 (br t, 1H, *J* = 6.0 Hz), 2.79 (ddd, 1H, *J* = 15.4, 10.2, 5.8 Hz), 2.67 (m, 2H), 1.94 (m, 1H), 1.58 (m, 1H). ^{13}CNMR (100 MHz, $CDCl_3$): δ 141.6, 138.7, 128.3, 128.2, 125.8, 116.6, 75.4, 54.9, 35.8, 32.7. IR ($CDCl_3$): 3602, 3300 (br), 3155, 2924 cm^{-1}. $[\alpha]_D$: +13.8 (*c* 0.86, CH_2Cl_2). HRMS (EI+) exact mass calcd for $C_{12}H_{18}NO$ (M + H): 192.1388. Found: 192.1387.

(2*S*,3*R*)-2-Amino-1-benzyloxy-4-penten-3-ol (6b) was prepared from hydroxy amide **12b** as described for **6a** and isolated as a yellow oil in 92% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39−7.27 (m, 5H), 5.82 (ddd, 1H, *J* = 17.3, 10.4, 5.3 Hz), 5.33 (dt, 1H, *J* = 17.3, 1.4 Hz), 5.20 (dt, 1H, *J* = 10.4, 1.4 Hz), 4.54 (AB-q, 2H, *J* = 11.8 Hz), 4.08 (br t, 1H, *J* = 5.3 Hz), 3.60 (dd, 1H, *J* = 9.3, 4.4 Hz), 3.51 (m, 1H), 2.97 (br m, 1H), 2.34 (br s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 137.6, 128.3, 127.7, 127.6, 116.5, 73.4, 72.7, 72.3, 54.7. IR (neat): 3332 (br), 2912, 2864 cm^{-1}. $[\alpha]_D$: +14.4 (*c* 0.55, CH_2Cl_2). HRMS (EI+) exact mass calcd $C_{12}H_{18}NO_2$ (M + H): 208.1338. Found: 208.1334.

(2*S*,3*S*)-2-Amino-6-benzyloxy-4(*E*)-hexen-3-ol (6d) was prepared from hydroxy amide **12d** as described for **6a** and isolated as a colorless oil in 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.26 (m, 5H), 5.89 (dtd, 1H, *J* = 15.5, 5.6, 0.9 Hz), 5.73 (ddt, 1H, *J* = 15.5, 6.3, 1.3 Hz), 4.52 (s, 2H), 4.05 (d, 2H, *J* = 5.6 Hz), 3.73 (dt, 1H, *J* = 6.3, 0.9 Hz), 2.81 (qvi, 1H, *J* = 6.5 Hz), 2.05 (br s, 3H), 1.10 (d, 3H, *J* = 6.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2, 133.4, 128.8, 128.4, 127.7, 127.6, 76.3, 72.2, 70.1, 51.1, 20.4. IR (neat): 3313, 2970, 2860 cm^{-1}. $[\alpha]_D$: +3.4 (*c* 1.59, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{13}H_{20}NO_2$ (M + H): 222.1494. Found: 222.1505.

Basic Hydrolysis: (2*S*,3*R*)-2-Amino-1-benzyloxy-6-(4-methoxybenzyloxy)-4(*E*)-hexen-3-ol (6c). Hydroxy amide **12c** (12.0 mg, 30 μmol) in 1 M KOH (EtOH/H_2O 2:1) was refluxed for 24 h. NaOH (2 M) was added, and the mixture was extracted several times with Et_2O. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The crude product was pushed through a short silica plug to afford *syn*-amino alcohol **6c** as low-melting solid in 91% yield (9.8 mg, 27 μmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.25 (m, 7H), 6.88 (d, 2H, *J* = 8.4 Hz), 5.88 (dt, 1H, *J* = 15.6, 5.5 Hz), 5.73 (dd, 1H, *J* = 15.6, 4.8 Hz), 4.53 (AB-q, 2H, *J* = 11.8 Hz), 4.44 (s, 2H), 4.08 (br t, 1H, *J* = 4.8 Hz), 4.01 (d, 2H, *J* = 5.5 Hz), 3.81 (s, 3H), 3.57 (dd, 1H, *J* = 9.0, 4.3 Hz), 3.48 (dd, 1H, *J* = 9.0, 6.3 Hz), 2.94 (br q, 1H, *J* = 4.8 Hz), 1.86 (br s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 137.6, 132.6, 130.0, 129.5, 128.8, 128.5, 127.9, 127.8, 113.6, 73.5, 72.6, 72.1, 71.9, 69.7, 55.3, 54.5. IR (neat): 3394 (br), 2933, 2858 cm^{-1}. $[\alpha]_D$:

+3.8 (*c* 0.29, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{21}H_{28}NO_4$ (M + H): 358.2018. Found: 358.2022.

(2*S*,3*R*)-4-Amino-2-benzyloxymethyl-5-(4-methoxybenzyloxy)-1-penten-3-ol (6f) was prepared from hydroxy amide **12f** as described for **6c** and isolated as a yellow oil in 84% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28−7.14 (m, 7H), 6.81 (m, 2H), 5.21 (br s, 1H), 5.19 (br s, 1H), 4.43 (m, 2H), 4.36 (m, 2H), 4.02 (m, 2H), 3.92 (m, 1H), 3.74 (s, 3H), 3.49 (m, 1H), 3.40 (m, 1H), 3.04 (m, 1H), 1.72 (br s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.3, 145.5, 138.0, 130.0, 129.4, 128.4, 127.7, 114.9, 113.9, 113.8, 73.2, 73.1, 72.8, 72.3, 70.9, 55.3, 52.9. IR (neat): 3361 (br), 2918, 2856 cm^{-1}. $[\alpha]_D$: +7.8 (*c* 0.75, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{21}H_{28}NO_4$ (M + H): 358.2018. Found: 358.2022.

Typical Procedure for the BOC-Protection of Vinylaziridines 4 to *N*-BOC-Aziridines 13, Followed by Rearrangement to *trans*-Oxazolidinones 14: (2*S*,3*R*)-2-(3-Benzyloxypropenyl)-3-ethyl-2-methylaziridine-1-carboxylic Acid *tert*-Butyl Ester 13e. A slurry of vinylaziridine **4e** (17.0 mg, 73 μmol) and polymer-bound DMAP (5.5 mmol/g, 27 mg, 0.15 mmol) in CH_2Cl_2 (1.0 mL) was cooled to 0 °C before addition of BOC_2O (32.0 mg, 0.15 mmol), stirred at room temperature for 2 h, quenched with saturated $NaHCO_3$, and filtered through an Extrelut NT3 tube, which was eluted with CH_2Cl_2 (15 mL). The solution was concentrated to give the crude *N*-BOC-vinylaziridine **13e** (24.4 mg), which was taken directly on to the next step. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.26 (m, 5H), 5.89 (dt, 1H, J = 15.6, 5.7 Hz), 5.30 (d, 1H, J = 15.6 Hz), 4.51 (s, 2H), 4.03 (d, 2H, J = 5.7 Hz), 2.39 (t, 1H, J = 6.7 Hz), 1.50 (m, 2H), 1.41 (s, 9H 1.38 (s, 3H), 1.04 (t, 3H, J = 7.5 Hz).

(4*S*,5*S*)-5-(3-Benzyloxy-1(*E*)-propenyl)-4-ethyl-5-methyloxazolidin-2-one (14e). To a solution of the crude **13e** (12.5 mg, 38 μmol) in THF (0.7 mL) at −78 °C was added $BF_3{\cdot}OEt_2$ (7.2 μL, 57 μmol), and the resulting mixture was stirred at −78 °C for 2 h. The reaction was quenched with saturated $NaHCO_3$, and THF was removed in vacuo. To the residue was added CH_2Cl_2 (2 mL), and the mixture was filtered through an Extrelut NT3 tube, which was eluted with CH_2Cl_2 (15 mL). The solution was concentrated, and flash chromatography (pentane:EtOAc 1:1 → 1:2) afforded *trans*-oxazolidinone **14e** as a diastereomeric mixture (2:1) in 66% yield (6.8 mg. 25 μmol). The diastereomers could be separated with careful flash chromatography or by HPLC (Zorbax Rx-Sil semipreparative column, 95% hexane, 5% *i*-PrOH, 5 mL/min) to give **14e** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38−7.27 (m, 5H), 5.93 (dt, 1H, J = 15.7, 4.9 Hz), 5.85 (dt, 1H, J = 15.7, 1.2 Hz), 5.41 (br s, 1H), 4.53 (s, 2H), 4.06 (dd, 2H, J = 4.9, 1.2 Hz), 3.49 (dd, 1H, J = 9.3, 4.4 Hz), 1.61−1.45 (m, 2H), 1.42 (s, 3H), 0.97 (t, 3H, J = 7.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.3, 138.0, 133.4, 128.4, 127.7, 127.7, 127.1, 84.2, 72.6, 69.6, 62.6, 23.3, 19.8, 11.1. IR (neat): 3265, 2937, 2856, 1747 cm^{-1}. $[\alpha]_D$: −11.4 (*c* 0.26, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{16}H_{22}NO_3$ (M + H): 276.1600. Found: 276.1601.

(4*S*,5*S*)-5-Amino-1-benzyloxy-4-methyl-2(*E*)-hepten-4-ol (6e) was prepared by hydrolysis of *trans*-oxazolidinone **14e** as described for **3a** and isolated as a colorless oil in 98% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.25 (m, 5H), 5.89 (dt, 1H, J = 15.6, 5.5 Hz), 5.77 (d, 1H, J = 15.6 Hz), 4.52 (s, 2H), 4.06 (d, 2H, J = 5.5 Hz), 2.60 (br s, 3H), 2.55 (app. d, 1H, J = 10.2 Hz), 1.67 (m, 1H), 1.19 (s, 3H), 1.17 (m, 1H), 0.98 (t, 3H, J = 7.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.4, 138.3, 128.4, 127.8, 127.6, 126.0, 73.4, 72.2, 70.4, 60.6, 24.1, 21.9, 11.7. IR (neat): 3357, 2931, 2858 cm^{-1}. $[\alpha]_D$: +22.0 (*c* 0.14, CH_2Cl_2). HRMS (CI+) exact mass calcd for $C_{15}H_{23}NO_2$ (M + H): 250.1807. Found: 250.1811.

Acknowledgment. This work was supported financially by the Swedish Research Council.

Supporting Information Available: Synthesis of vinyl epoxides **1c**−**e** and oxazolidinones **14a**−**d**,**f**, **15**, and **16** and analytical data of **4b**,**d**−**f**, **7b**,**d**−**f**, **8**, **9b**−**f**, **10b**−**f**, **11a**, and **12b**−**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0262053