

Introduction

1

One of the main objectives in organic chemistry is the synthesis of natural products, as they often can be isolated only in minor amounts from Nature. As early as in the 1950s very complicated molecules could be synthesized, albeit in poor total yields. In the last decades chemists have, besides synthesizing even more complicated compounds, focused on optimizing and finding new reactions which could simplify and shorten these syntheses. Large efforts in developing libraries of efficient reactions for each type of transformation have been made, in order to simplify the design of complex molecules. With these libraries at hand, each subunit in a complex molecule can be synthesized with well-known techniques, presupposed that the subunits can be combined in a later stage.

Many natural products contain one or more stereogenic centers, which complicates their synthesis substantially. Asymmetric synthesis has become one of the most expanding fields in organic chemistry since it was recognized in the 1960s that one enantiomer of a chiral compound can be a potent drug, whereas the other can be strongly poisonous (Figure 1).

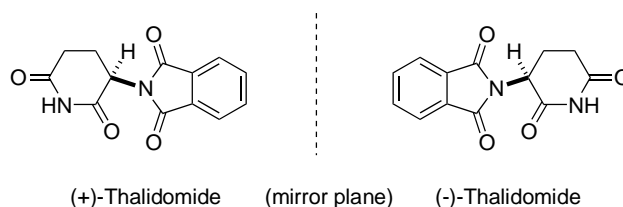


Figure 1: The structure of thalidomide, a drug prescribed for pregnant women in the 1960s. Both enantiomers have the desired sedative effect, but the (-)-enantiomer also caused foetal deformities.

Asymmetric reactions are often developed from well-known procedures; chiral auxiliaries or catalysts bearing chiral ligands can be utilized to afford induction towards one of the two isomers that can be formed. As the research on new asymmetric processes is continuously increasing, the need for novel chiral auxiliaries and ligands is extensive.¹

1.1 Vicinal amino alcohols

The β -amino alcohol moiety is found in a wide variety of biologically active alkaloids and peptides,² it is consequently a common building block in the synthesis of natural products.³ Figure 2 displays some alkaloids incorporating the 1,2-amino alcohol substructure; deoxynojirimycin is an α -glycosidase inhibitor with therapeutic potential due to its low cytotoxicity. Sphingosine is the major backbone in glycosphinglipids, which are vital in cell recognition events such as growth, differentiation and immune response. Quinine, present in the bark of China trees, is used as drug when treating malaria, high fever and other diseases.

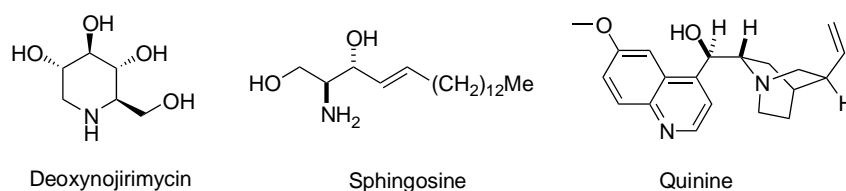


Figure 2: Examples of natural products incorporating a *vic*-amino alcohol functionality.

The importance of vicinal amino alcohols is also well recognized in asymmetric synthesis, as many chiral auxiliaries and ligands contain this substructure. Some representative examples of amino alcohol-derived compounds are shown in Figure 3. Evans' oxazolidinones are utilized as chiral auxiliaries in various reactions, e.g. asymmetric alkylations.¹ Bisoxazolines are

¹ Ager, D. J.; Prakash, I.; Schaad, D. R. *Chemical Reviews* **1996**, *96*, 835-875. Seyden-Penne, J. *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*; Wiley: New York, 1995.

² Kobayashi, S.; Ishitani, H.; Ueno, M. *J. Am. Chem. Soc.* **1998**, *120*, 431-432 and references therein.

³ Castejon, P.; Moyano, A.; Pericas, M. A.; Riera, A. *Tetrahedron* **1996**, *52*, 7063-7086.

used as ligands in enantioselective cyclopropanations and aziridinations,¹ whereas cinchomidinium salts are employed in asymmetric phase transfer catalysis.⁴

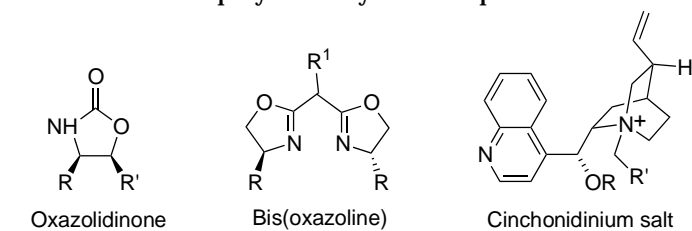


Figure 3: Vic-amino alcohol derivatives used in asymmetric synthesis.

1.2 Background to amino alcohols

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.⁵ Large efforts to develop asymmetric routes to 1,2-amino alcohols have been made, and can be divided into two strategically different categories.

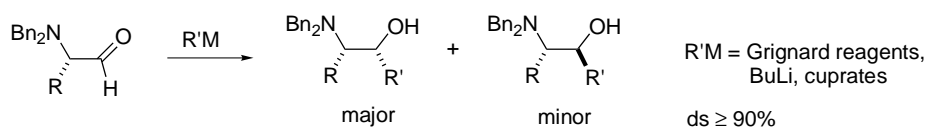
1.2.1 C-C bond forming reactions

The first category contains reactions where the amino alcohol moiety is formed by concomitant creation of a new C-C bond. The reactions are regiospecific and give rise to two diastereomers. Reported diastereoselectivities are high, but the reactions are often limited by structural demands on the substrates.

In the stereoselective addition of nucleophiles to α -aminocarbonyls, derived from chiral amino acids, the asymmetric induction can be interpreted with the Felkin-Ahn non-chelation control model (Scheme 1).⁵

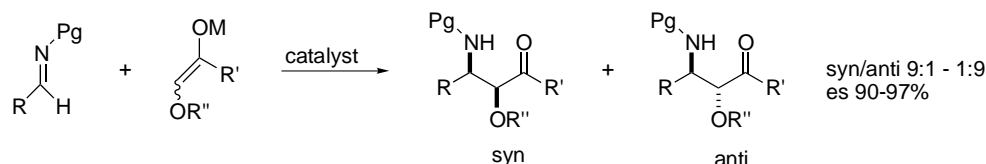
⁴ Nelson, A. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 1583-1585.

⁵ Reetz, M. T. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1531-1546.



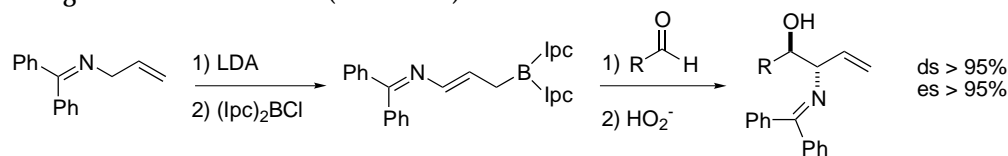
Scheme 1: Nucleophilic addition to α -aminocarbonyls .

Stereoselective nucleophilic additions to nitroalkenes⁶ or imines^{2,7} afford amino alcohols in high enantioselectivity. In the addition of α -alkoxyenolates to aldimines, the choice of enolate decides which isomer (syn/anti) will be the major product (Scheme 2).



Scheme 2: Nucleophilic addition to imines.

Addition of allylic imines to aldehydes primarily gives γ -amino alcohols. To obtain α -addition, the imine can be transformed into a 3-aminoallylborane. When chiral boron reagents are used, vinylic 1,2-amino alcohols can be obtained in high enantioselectivities (Scheme 3).⁸



Scheme 3: Aminoallylborane addition to aldehydes.

1.2.2 Reactions not altering the carbon skeleton

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,

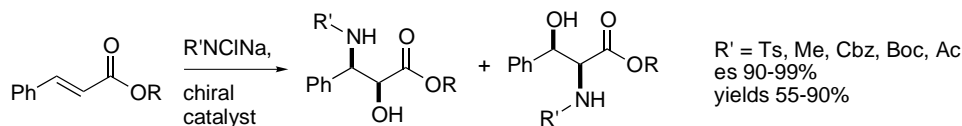
⁶ Enders, D.; Haertwig, A.; Raabe, G.; Runsink, J. *Eur. J. Org. Chem* **1998**, 1771-1792. Enders, D.; Haertwig, A.; Runsink, J. *Eur. J. Org. Chem* **1998**, 1793-1802.

⁷ Hattori, K.; Yamamoto, H. *Tetrahedron* **1994**, *50*, 2785-2792.

⁸ Barrett, A. G. M.; Seefeld, M. A.; White, A. J. P. *J. Org. Chem.* **1996**, *61*, 2677-2685.

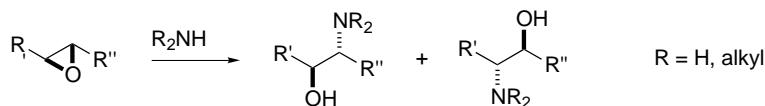
which can be circumvented only when the substituents on the alkene (derivative) have different electrostatic or steric influence.

Alkenes can be converted to 1,2-amino alcohols by the Sharpless aminohydroxylation procedure (Scheme 4).⁹ The reaction proceeds with high enantioselectivity but often with moderate yields due to poor regioselectivity.



Scheme 4: Asymmetric aminohydroxylation.

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 *anti*-amino alcohols.¹⁰ This strategy, however, is often limited by poor regioselectivity, except for terminal oxiranes (Scheme 5). Substituents on the oxirane ring have both sterical and electronical influence on the regioselectivity; conjugating substituents, e.g. phenyl and vinyl, usually promote ring opening at the adjacent carbon.¹¹



Scheme 5: Nucleophilic opening of epoxides.

Cyclic sulfates¹² and carbonates,¹³ derived by asymmetric dihydroxylation of the corresponding alkenes, can be ring-opened with nitrogen nucleophiles to give

⁹ O'Brien, P. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 326-329. Li, G.; Chang, H.-T.; Sharpless, B. K. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 451.

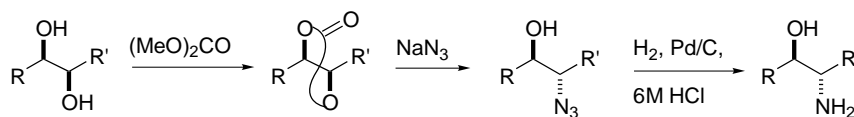
¹⁰ Larrow, J. F.; Schaus, S. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1996**, *118*, 7420-7421. Mitsunobu, O. *Synthesis of amines and ammonium salts*; Trost, B. M. and Fleming, I., Ed.; Pergamon: Oxford, 1991; Vol. 6, pp Chapter 1.3. Zwanenburg, B. *Pure Appl Chem* **1999**, *71*, 423-430. Hayakawa, H.; Okada, N. M., M.; Miyashita, M. *Tetrahedron Lett.* **1999**, *40*, 4589-4592. Sekar, G.; Singh, V. K. *J. Org. Chem.* **1999**, *64*, 287-289.

¹¹ Jaime, C.; Ortuno, R. M.; Font, J. *J. Org. Chem.* **1988**, *53*, 139-141.

¹² Lohray, B. B.; Gao, Y.; Sharpless, K. B. *Tetrahedron Lett.* **1989**, *30*, 2623-2626. Lohray, B. B.; Ahuja, J. R. *J. Chem. Soc., Chem. Commun.* **1991**, 95-97.

¹³ Chang, H.-T.; Sharpless, B. *Tetrahedron Lett.* **1996**, *37*, 3219-3222. Cho, G. Y.; Ko, S. Y. *J. Org. Chem.* **1999**, *64*, 8745-8747.

anti-amino alcohols. The opening occurs in the most activated position with overall yields of 70-80% (Scheme 6).¹³



Scheme 6: Nucleophilic opening of cyclic carbonates.

Enantioselective aziridination has proven more difficult than asymmetric epoxidation, and there are no general methods reported. Ring-opening of aziridines with oxygen nucleophiles to afford 1,2-amino alcohols are consequently not as common, yet interesting.¹⁴

1.3 Aim of the study

Despite the great interest in the field of 1,2-amino alcohols, no divergent route from a common starting material towards all possible regio- and stereoisomers of a vicinal amino alcohol has been documented. The requirement of a separate synthesis route for each isomer complicates the synthetic planning substantially. A divergent route leading to all possible isomers would be a great simplification for studies on structure-activity relationships for pharmacologically active derivatives incorporating the amino alcohol moiety. A divergent route would also allow optimization of the performance of chiral ligands containing this structural motif. We therefore set out to develop a route leading to all eight possible isomers of a given 1,2-amino alcohol starting from a common substrate that can be readily synthesized.

¹⁴ Takeuchi, H.; Koyama, K. *Journal of the Chemical Society, Perkin Transactions 2* **1981**, 121-126. Ibuka, T.; Nakai, K.; Akaji, M.; Tamamura, H.; Fujii, N.; Yamamoto, Y. *Tetrahedron* **1996**, *52*, 11739-11752. Hwang, G.-I.; Chung, J.-H.; Lee, W. K. *J.Org. Chem.* **1996**, *61*, 6183-6188. Cantrill, A. A.; Osborn, H. M. I.; Sweeney, J. *Tetrahedron* **1998**, *54*, 2181-2208.

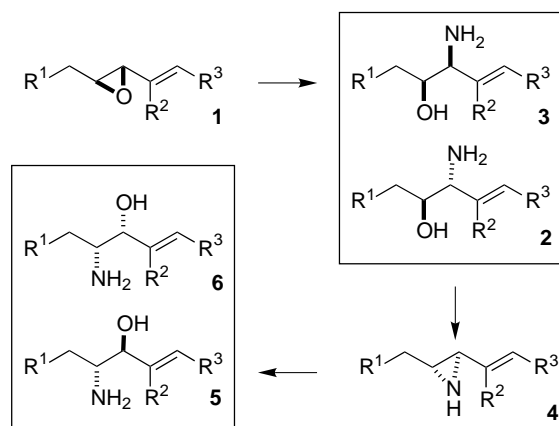
Synthetic strategy

2

The requirements for a generally applicable synthetic route towards all possible isomers of vicinal amino alcohols are readily available starting materials and highly regio- and stereoselective reactions affording predictable products. These demands can be met by choosing vinyloxyepoxides as substrates, since they are known to be ring opened regioselectively at the allylic position by hard nucleophiles¹⁵ and both enantiomers are readily available in high enantiomeric excess.¹⁵

As depicted in Scheme 7, the synthetic strategy 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. To obtain the two regioisomers **5** and **6**, *anti*-amino alcohols **2** are ring-closed to the corresponding vinylaziridines **4**. Subsequently, this species can be ring opened with a suitable oxygen nucleophile, either with inversion or retention of stereochemistry, to give *anti*- and *syn*-amino alcohols **5** and **6**. The reactions used should be stereospecific or highly stereoselective, and the nucleophiles are expected to attack at the allylic position only. The remaining set of enantiomeric amino alcohol isomers can be obtained simply by starting from the enantiomeric vinyloxyepoxides (*ent*-**1**).

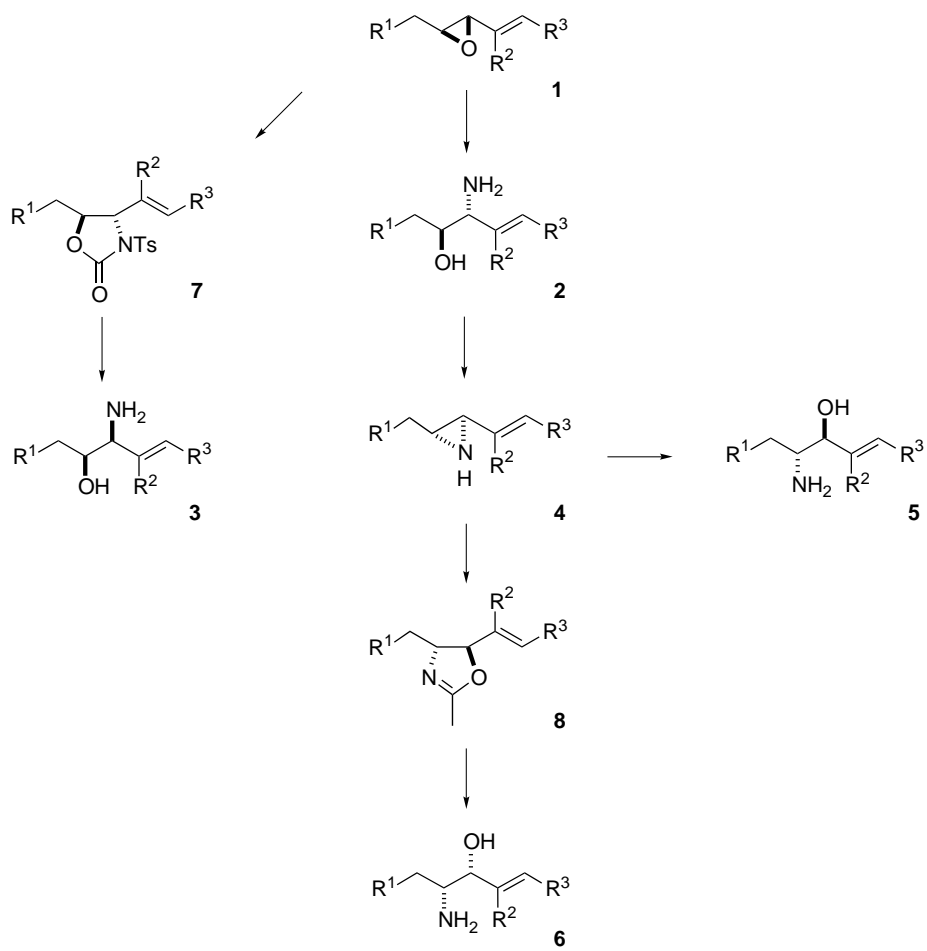
¹⁵ See Chapter 3 and Appendix B.



Scheme 7: Synthetic strategy.

2.1 Project plan

The synthetic plan is outlined in Scheme 8 and consists of four parts, leading to one amino alcohol each. In the first part vinyl epoxides **1** are exposed to microwave-assisted aminolysis affording *anti*-amino alcohols **2**. To achieve the diastereomers of **2**, epoxides **1** are transformed into the corresponding oxazolidinones **7** by palladium(0)-catalyzed ring opening with tosyl isocyanate, resulting in retention of stereochemistry. The formed oxazolidinones are then detosylated and hydrolyzed into *syn*-amino alcohols **3**. The third part starts with ring closure of *anti*-amino alcohols **2** under Mitsunobu conditions to yield aziridines **4**, which subsequently can be hydrolyzed under acidic conditions to give *anti*-amino alcohols **5**. Alternatively, aziridines **4** can be acetylated and rearranged with retention of configuration into oxazolines **8**, delivering *syn*-amino alcohols **6** upon acidic or basic hydrolysis.



Scheme 8: Synthesis of all isomers of a given vic-amino alcohol.

Vinylepoxides^{I,II}

3

Vinylepoxides **1a-d** have been used as substrates in the study (Figure 4). Compound **1a** has a benzylic side chain, **1b** has a benzyloxy side chain whereas **1c** and **1d** have additional substitution on the vinyl group.

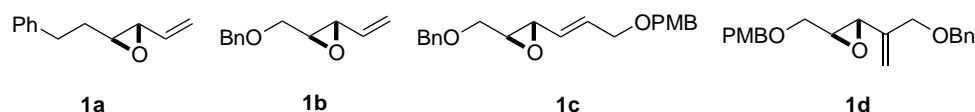


Figure 4: Vinylepoxides used in the present study.

Vinylepoxides **1a,b** were prepared from the corresponding allylic alcohols using Sharpless asymmetric epoxidation (SAE) followed by the Swern/Wittig procedure.¹⁶ Vinylepoxide **1c** was obtained by SAE on the corresponding dienol and subsequent benzylation, whereas compound **1d** was synthesized by PMB-protection of the corresponding epoxyalcohol.¹⁷ All epoxyalcohols had es $\geq 95\%$ as analyzed by chiral HPLC and the syntheses are outlined in Appendix B.

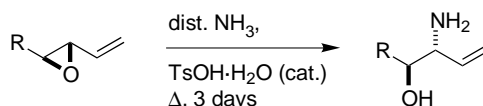
In the aminolysis study (Chapter 3.1), several additional vinylepoxides were used to illustrate the scope and limitations of the reaction. These substrates (**1e-i**) were prepared from the corresponding allylic alcohols as described for **1a,b**.

¹⁶ Díez-Martin, D. *et al Tetrahedron* **1992**, *48*, 7899-7938

¹⁷ Weigand, S.; Brückner, R. *Synlett* **1997**, 225-228.

3.1 Aminolysis with inversion of stereochemistry I

The ring-opening of 1,2-disubstituted vinyloxydes in neat ammonia, with tosic acid as catalyst, has been developed in our group.¹⁸ The reaction proceeds stereospecifically and regioselectively with an S_N2 attack at the allylic carbon, affording the corresponding vicinal amino alcohols in good yields (Scheme 9). The scope of the reaction is rather limited as it requires prolonged heating in neat ammonia in a sealed metal cylinder, and when sterically hindered substrates are used the reaction is retarded. Stogryn and Brois showed that monosubstituted vinyloxydes can be opened using ammonium hydroxide,¹⁹ but with more substituted substrates the reaction becomes too slow for synthetic purposes. In order to make the aminolysis more synthetically useful, the development of a reaction less sensitive to steric hindrance and with shorter reaction time was needed.



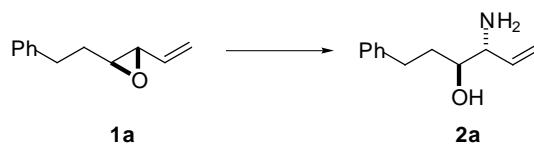
Scheme 9: Aminolysis.

In recent years, the application of microwave-assisted reactions in organic synthesis has received considerable attention, and compared to conventional heating microwave irradiation often gives greatly enhanced reaction rates and less by-products.²⁰ A microwave-assisted aminolysis protocol, that hopefully would circumvent the drawbacks of previous methods, was designed using ammonium hydroxide as nitrogen source. The three procedures were carried out with vinyloxyde **1a**, and the results are summarized in Table 1. The procedure of Storgyn and Brois afforded amino alcohol **2a** in only 13% yield after 10 days (entry 1), whereas heating the same substrate in neat ammonia and tosic acid monohydrate (cat.) afforded **2a** in 77% yield after 3 days (entry 2). Gratifyingly, with the microwave assisted procedure compound **2a** could be obtained in 93% yield in only 8 minutes (entry 3).

¹⁸ Lindström, U. M.; Franckowiak, R.; Pinault, N.; Somfai, P. *Tetrahedron Lett.* **1997**, *38*, 2027-2030.

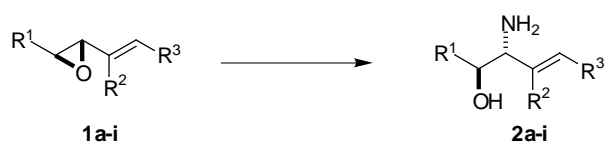
¹⁹ Stogryn, E. L.; Brois, S. J. *J. Am. Chem. Soc.* **1967**, *89*, 605-609.

²⁰ Caddick, S. *Tetrahedron* **1995**, *51*, 10403-10432. Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacquault, P.; Mathé, D. *Synthesis* **1998**, 1213-1233. Stambouli, A.; Chastrette, M.; Soufiaoui, M. *Tetrahedron Lett.* **1991**, *32*, 1723-1724.

Table 1: Investigation of the aminolysis of **1a**.

Entry	Conditions	Reaction time	Yield (%)
1	NH ₄ OH, rt →Δ	10 days	13
2	NH ₃ , TsOH·H ₂ O (0.05 eq), 80 °C	3 days	77
3	NH ₄ OH, microwave irradiation, 30W	8 min	93

When di- and trisubstituted vinyloxydes **1a-i** were subjected to microwave irradiation at 30W in NH₄OH, complete conversion into amino alcohols **2a-i** was generally obtained within 8 min (Table 2). The yields for the unhindered disubstituted substrates are better or as good as the previously reported results (entries 1,2). The aminolysis of **1c**, with additional substitution on the double bond, was initially problematic due to byproduct formation, but could be optimized to 88% by decreasing the power (entry 3). Also more sterically hindered substrates are efficiently converted into amino alcohols, as derivative **1e** gave a yield of 90% compared to only 23% after 4 days in neat ammonia at 130 °C (entry 5). The procedure is effective even for trisubstituted substrates (entries 6,7); the 2,2,3-trisubstituted vinyloxyde **1f** afforded **2f** in 76% yield whereas the cyclic substrate **1g**, with a quaternary allylic carbon, gave **2g** and its regioisomer (1:1) in a combined yield of 77%. The latter results are remarkable, as trisubstituted substrates were inert or reacted sluggishly using the original protocol. Aminolysis of **1h** gave a 2:1 mixture of amino alcohol **2h** and its regioisomer, reflecting a competition between the allylic and benzylic position (entry 8). More surprisingly, **1i** also gave a regioisomeric mixture, the explanation for which is less obvious. Interestingly, by decreasing the irradiation power from 30W to 5W and increasing the reaction time, it was possible to suppress ring opening at the homoallylic position, and the regioisomeric ratio increased from 6:1 to 9:1.

Table 2: Comparison of yields using different aminolysis procedures.

Entry	Vinylepoxyde	NH ₄ OH, 30 W, 8 min. ^{a,b} Yield (%)	NH ₃ , 130 °C, 3 days. ^{b,c} Yield (%)
1	1a	93	77 ^d
2	1b	87	93
3	1c	88 ^e	-
4	1d	84	86
5	1e	90	23 ^f
6	1f	76 ^g	25
7	1g	77 Ratio 1:1	- ^h
8	1h	98 Ratio 2:1	70 Ratio 4:1
9	1i	95 30W, 8 min →6:1 5W, 30 min →9:1	75 Ratio 5:1

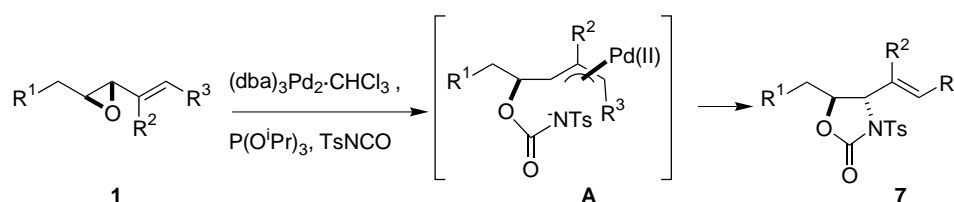
^aReaction conditions used except where noted, not optimized for each substrate. ^bIsolated yields. ^cCatalytic amount TsOH·H₂O (0.05 eq) used. ^d80 °C. ^e20 min, 15W. ^f4 days. ^g2*8 min, 30W. ^hSee text.

General drawbacks of microwave chemistry are the difficulties in scaling up reactions and differences between microwave ovens, which sometimes cause reproducibility problems.

3.2 Ring-opening with retention of stereochemistry^{II}

3.2.1 Formation of oxazolidinones **7**

Vinylepoxides **1** could be ring opened with double inversion, i.e. retention, using palladium(0)-catalysis as previously reported by Trost.²¹ The reaction starts by formation of a π -allyl palladium complex, after which the oxygen anion attacks tosyl isocyanate to form intermediate **A**. This species subsequently ring-closes with retention of configuration to *N*-tosyl oxazolidinones **7** (Scheme 10). The reaction is reported to take place with complete stereoselectivity (*ds*>95%), but this was true only for vinylepoxides containing additional vinylic substituents (**1c,d**), whereas the unsubstituted compounds **1a,b** gave a diastereomeric mixture of oxazolidinones.²²



Scheme 10: Palladium(0)-catalyzed epoxide opening with tosyl isocyanate.

An investigation on the influence of various reaction parameters on the diastereoselectivity was made on vinylepoxide **1a**. The reported conditions²¹ (0.01 eq $(dba)_3Pd_2 \cdot CHCl_3$, 0.06 eq $(PrO)_3P$, TsNCO, THF, rt) gave poor selectivity (*ds* 67%) and low conversion. Refluxing overnight was sufficient to reach full conversion, but the selectivity was still low. Increased amounts of $(dba)_3Pd_2 \cdot CHCl_3$ (0.1 eq) and triisopropylphosphite (0.6 eq) gave slightly better results, further increase of $(PrO)_3P$ to 1.0 eq gave a diastereoselectivity of 78%. Variation of the amount of TsNCO from 1.1 - 20 eq caused no difference in selectivity. Only when the mixing order was changed so that the addition of $(PrO)_3P$ occurred last, did the reaction take place at rt. This might be due to catalysis by $(dba)_3Pd_2 \cdot CHCl_3$ instead of $Pd[P(PrO)_3]_4$ and gave only 67% diastereoselectivity.

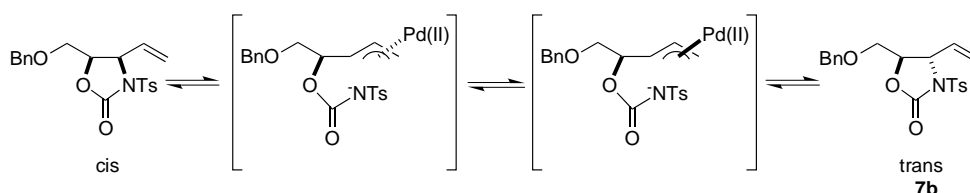
²¹ Trost, B. M.; Sudhakar, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 3792-3794.

²² Determination of *ds* was made by integration on ¹H NMR.

Vinylepoide **1b** reacted remarkably fast compared to **1a**; only 30 min at rt gave complete conversion to **7b** under optimized conditions,²³ albeit in low diastereoselectivity (Table 3, entry 1). The selectivity was slightly increased when the reaction was performed in refluxing THF (entry 2), which indicated an equilibration of the two diastereomers at elevated temperatures (Scheme 11). The poor selectivity could indeed be drastically improved by equilibration of the initial, kinetically obtained, product mixture, thus favoring the more stable *trans*-oxazolidinone (entries 3,4, see also Table 4).

Table 3: Reaction conditions versus selectivity for **7b**.

Entry	Temp.	Time	ds (%)
1	rt	30 min	67
2	reflux	1.5 h	75
3	reflux	2 days	91
4	reflux	5 days	93



Scheme 11: Equilibration of *trans*-oxazolidinone **7b** and its diastereomer.

Equilibration was performed with the catalyst at reflux for 2-5 days, where longer reflux time gave better ds but also caused more degradation of the product. The reaction of **1a** could be equilibrated to 86% ds, but the best total yield of **2a** was achieved when the equilibration was stopped at 82% ds (Table 4). Microwave-assisted equilibration of **2a** gave similar results as conventional heating; with prolonged heating (50W, 30+60+90 min) a diastereoselectivity of 81% could be obtained.

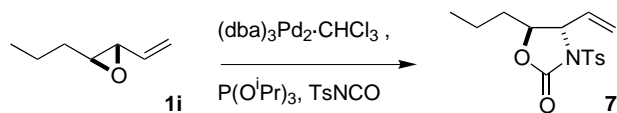
²³ 0.1 eq (dba)₃Pd₂CHCl₃, 1.0 eq (PrO)₃P, 2 eq TsNCO, THF.

Table 4. Formation of *N*-tosyl oxazolidinones **7**.^a

Substrate	R ¹	R ²	R ³	Yield of 7 (%)
1a	PhCH ₂	H	H	82 ^b
1b	BnO	H	H	88 ^b
1c	BnO	H	CH ₂ OPMB	87 ^c
1d	PMBO	CH ₂ OBn	H	93

^aIsolated yields. ^bDiastereomeric mixture, see text. ^cOnly the (*E*)-isomer observed.

A recently published palladium(0)-catalyzed transformation of vinyl-oxazolidinones into vinyloxazolines shows the same equilibration trend; when R¹ changes from alkyl to alkoxy the selectivity increases.²⁴ To further prove this trend, vinyloxy **1i** was exposed to the reaction conditions. Oxazolidinone **7i** was formed with poor diastereoselectivity, only 63%, which could not be improved by equilibration attempts (Scheme 12).

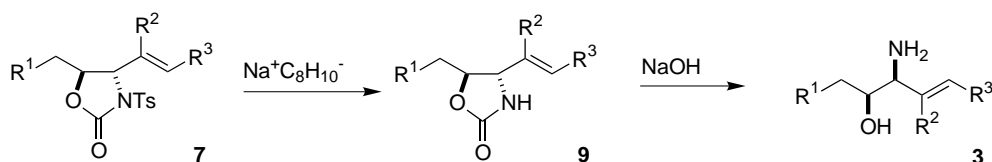
**Scheme 12:** Formation of oxazolidinone **7i**.

3.2.2 Detosylation and hydrolysis

Detosylation of oxazolidinones **7** could be affected by titration with carefully prepared sodium naphthalide solution at -78 °C (Scheme 13, Table 5).²⁵ Compound **9a** was formed in high yield whereas **9b-d** were formed in about 70%, which might be due to partial deprotection of the Bn and PMB groups. After detosylation the diastereomers of both **9a** and **9b** could be separated by careful flash chromatography.

²⁴ Cook, G. R.; Shanker, S. *Tetrahedron Lett.* **1998**, 39, 3405-3408.

²⁵ Heathcock, C. H.; Blumenkopf, T. A.; Smith, K. M. *J. Org. Chem.* **1989**, 54, 1548-1562.



Scheme 13: Detosylation of **7** into **9** and hydrolysis to yield *syn*-amino alcohols **3**.

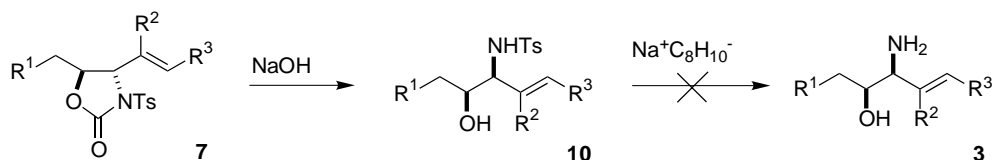
Hydrolysis of the *N*-H oxazolidinones **9** into *syn*-amino alcohols **3** was performed both under basic and acidic conditions. The basic hydrolysis was much faster, giving **3** in excellent yields (Scheme 13, Table 5).

Table 5. Yields of oxazolidinones **9** and *syn*-amino alcohols **3**.^a

Substrate	R ¹	R ²	R ³	Yield (%)	
				9	3
1a	PhCH ₂	H	H	93	100
1b	BnO	H	H	75	97
1c	BnO	H	CH ₂ OPMB	72	91
1d	PMBO	CH ₂ OBn	H	84	86

^aIsolated yields.

An earlier strategy with hydrolysis of **7** into *N*-tosyl amino alcohol **10** prior to detosylation showed that the hydrolysis works very well, but the detosylation is difficult (Scheme 14). No reaction took place also when allowing the temperature to reach -20 °C, further increase of the temperature would cause selectivity problems between the tosyl group and other protecting groups (Bn, PMB).



Scheme 14: Hydrolysis of **7** prior to detosylation to yield amino alcohols **3**.

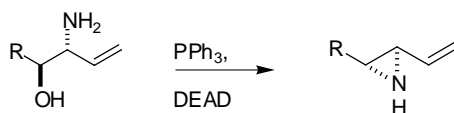
Vinylaziridines II

4

To obtain the two remaining amino alcohols **5** and **6**, which are the regioisomers of **2** and **3**, the amino group and the hydroxy group must be interchanged. This can be done via ring-closure of *anti*-amino alcohols **2** to the corresponding *N*-H vinylaziridines **4**, as described in Chapter 4.1. Subsequent solvolysis of **4** yields *anti*-amino alcohols **5** (Chapter 4.2) whereas a rearrangement reaction is needed to obtain *syn*-amino alcohols **6** (Chapter 4.3).

4.1 Aziridine formation

N-H Aziridines can be synthesized by ring-closure of *anti*-amino alcohols under Mitsunobu conditions (Scheme 15).²⁶ Cyclization of primary amines is known to be difficult,²⁷ and previous reports show moderate yields of the corresponding *N*-H aziridines. Furthermore, carbamates **11** were sometimes formed as major product instead of the aziridines (Figure 5).²⁶



Scheme 15: The Mitsunobu reaction.

The influence of various reaction parameters was investigated using racemic amino alcohol **12** (Figure 5), and Table 6 lists the scanned alternatives. The

²⁶ Lindström, U. M.; Somfai, P. *Synthesis* **1998**, 109.

²⁷ Hughes, D. L. *Org. Prep. Proc. Int.* **1996**, *28*, 127-164. Tanner, D. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 599-619. Osborn, H. M. I.; Sweeney, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1693-1715. Pearson, W. H.; Lian, B. W.; Bergmeier, S. C. *Aziridines and azirines: monocyclic*; Padwa, A., Ed.; Pergamon, 1996; Vol. 1A, pp 1-96.

temperature during addition of substrate to the preformed PPh₃-diazo complex seems unimportant (entry 1), and the reaction temperature is limited to reflux due to low reactivity at rt (entry 2). As solvent, THF was superior to toluene, presumably due to increased solubility of **12**, which increased the reaction rate (entry 3). The preferred diazo reagent is DIAD, as the bulky isopropyl groups give less probability of carbamate formation compared to ethyl groups (entry 4). Under these optimized conditions, the N-H aziridine of **12** could be isolated in 74% yield, which should be compared to previously reported yields around 50%.

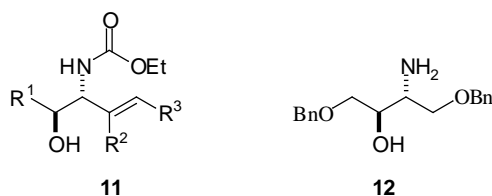


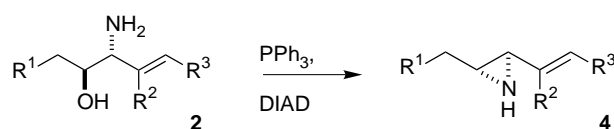
Figure 5: Carbamate **11** and amino alcohol **12**.

Table 6: Investigated parameters of the Mitsunobu reaction.^a

Entry	Parameters	Alternatives	Optimized
1	addition temperature ^b	-78, -20, 0, rt, 50 °C	0 °C
2	reaction temperature	rt, reflux	reflux
3	solvent	toluene, THF	THF
4	diazo reagent	DEAD, DIAD	DIAD

^aReported procedure:²³ PPh₃ and DEAD are dissolved in toluene, the amino alcohol is added and the mixture is refluxed overnight. ^bOf **12** to PPh₃-diazo complex.

Anti-amino alcohols **2** could be ring-closed into vinylaziridines **4** in yields ranging from 80% for **4a** down to 30% for **4b** (Scheme 16, Table 7). The moderate yield of **4b** could be increased to 72% by careful purification on deactivated silica, indicating that the purification might be more important than the reaction conditions. Aziridine **4c** was formed in 93% yield according to integration on crude NMR, but due to its instability even on deactivated silica the isolated yield was poor. This could partially be circumvented by using polymer bound PPh₃, which gave an easily purified crude product but decreased reaction rate. With this protocol, aziridine **4c** could be isolated in 78% yield based on recovered starting material.



Scheme 16: Formation of vinylaziridines **4**.

Table 7. Yield of vinylaziridines **4**.^a

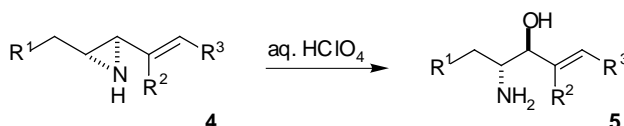
Substrate	R ¹	R ²	R ³	Yield of 4 (%)
2a	PhCH ₂	H	H	80
2b	BnO	H	H	72
2c	BnO	H	CH ₂ OPMB	78 ^b
2d	PMBO	CH ₂ OBn	H	63

^aIsolated yields. ^bBased on recovered starting material, polymer bound PPh₃ used.

4.2 Solvolysis with inversion of stereochemistry

Acidic hydrolysis of activated aziridines has been reported to proceed with rather poor regioselectivity.²⁸ There are no reports on hydrolysis of *N*-H aziridines, which might be due to the low reactivity of unactivated aziridines.²⁹

Vinylaziridines **4** could be stereospecifically and highly regioselectively hydrolyzed into *anti*-amino alcohols **5** under acidic conditions (Scheme 17, Table 8). Initial attempts to hydrolyze **4** in aq TsOH gave **5** in modest yields and regioselectivity (9:1), whereas complete regioselectivity (>20:1) was obtained with HClO₄ (1 eq) in THF/H₂O 1:1.



Scheme 17: Solvolysis of vinylaziridines **4**.

²⁸ Takeuchi, H.; Koyama, K. *J. Chem. Soc., Perkin Trans. 2* **1981**, 121-126. Prasad, B. A. B.; Sekar, G.; Singh, V. K. *Tetrahedron Lett.* **2000**, *41*, 4677-4679.

²⁹ Tanner, D. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 599-619.

Table 8. Solvolysis of vinylaziridines **4**.^a

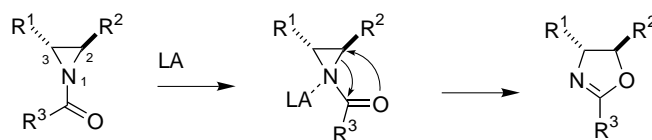
Substrate	R ¹	R ²	R ³	Yield of 5 (%)
4a	PhCH ₂	H	H	80
4b	BnO	H	H	84
4c	BnO	H	CH ₂ OPMB	82
4d	PMBO	CH ₂ OBn	H	71

^aIsolated yields.

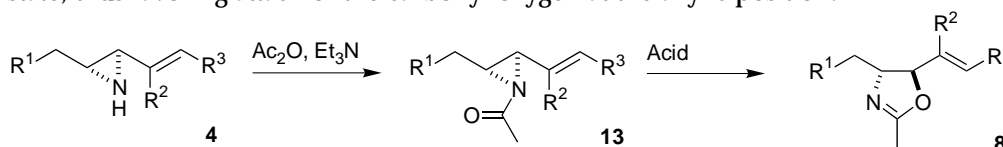
4.3 Rearrangement with retention of stereochemistry

4.3.1 Rearrangement to oxazolines **8**

To obtain the last isomer, *syn*-amino alcohol **6**, vinylaziridine **4** must be ring-opened with retention of stereochemistry by an oxygen nucleophile. This can be achieved either by a reaction proceeding with double inversion or by an intramolecular rearrangement. The Lewis acid-catalyzed rearrangement of acylaziridines into the corresponding oxazolines is reported to proceed with an S_Ni mechanism to give retention of stereochemistry, as outlined in Scheme 18.³⁰ The Lewis acid coordinates to the aziridine nitrogen, which is more basic than the carbonyl oxygen, and weakens the C2-N bond. C2 is then attacked by the carbonyl oxygen in a front-side manner, giving the corresponding oxazoline with retention of configuration. The two cases reported have R¹ = H and R² = Me or Ph, which explains the regioselectivity observed as a partial positive charge on C2 is better stabilized than on C3. When both R¹ and R² = alkyl, the regioselectivity might become problematic. Also Brønsted acids can be used to achieve the oxazoline, although the mechanism in these cases might be different.

**Scheme 18:** The S_Ni mechanism.³⁰ Hori, K.; Nishiguchi, T.; Nabeya, A. *J. Org. Chem.* **1997**, *62*, 3081-3088.

Acetylation of vinylaziridines **4** into acylaziridines **13** was clean, and **13** were used as crude products in the rearrangement due to instability on silica gel (Scheme 19).³¹ Several methods reported to cause the reaction were scanned with **13a** as substrate; reflux in chloroform³² was unsuccessful, treatment with sodium iodine³³ gave oxazolines **8a** and its diastereomer (proceeds via double inversion), tosic acid³⁴ gave hydroxyamide **14a** (Scheme 20) as major product and only minor amounts of **8a**. When the acylaziridine was treated with $\text{BF}_3\cdot\text{OEt}_2$ rearrangement into oxazoline **8a** ensued,²⁸ and reaction with copper triflate³⁵ gave comparable results (Scheme 19). The reaction proceeded as expected with complete diastereoselectivity, and gratifyingly also with complete regioselectivity. 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.



Scheme 19: Acetylation and rearrangement into **8**.

$\text{BF}_3\cdot\text{OEt}_2$ was the Lewis acid of choice for further investigations. The rearrangement was initially performed in refluxing benzene,³ but due to the increased reactivity stemming from the vinyl group, toluene at low temperature was sufficient for full conversion. Although the reaction was clean on TLC and crude NMR, **8** could never be isolated in more than 55% yield. Instead, oxazolines **8** surprisingly proved to be unstable towards purification,³⁶ giving a mixture of **8** and hydroxyamides **14** (Scheme 20) after flash chromatography. In the $\text{TsOH}\cdot\text{H}_2\text{O}$ reaction the partial hydrolysis of **8** into **14** occurred spontaneously, which indicated that **8** might be the completely hydrolyzed *in situ* upon addition of a small amount of water. This strategy was evaluated using $\text{TsOH}\cdot\text{H}_2\text{O}$ in toluene; at complete conversion of acylaziridine **13** into **8**, excess

³¹ Lindström, U. M.; Somfai, P. *J. Am. Chem. Soc.* **1997**, *119*, 8385-8386.

³² Cardillo, G.; Gentilucci, L.; Tolomelli, A.; Tomasini, C. *Tetrahedron Lett.*, **1997**, *39*, 6953-6956.

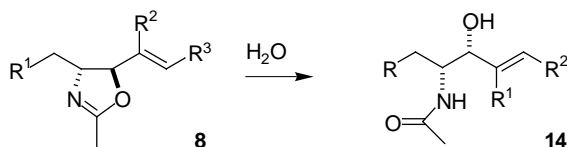
³³ Foglia, T.A.; Gregory, L.M.; Maerker, G. *J. Org. Chem.*, **1970**, *11*, 3779-3785.

³⁴ Nishiguchi, T.; Tochio, H.; Nabeya, A.; Iwakura, Y. *J. Am. Chem. Soc.*, **1969**, *21*, 5835-5846.

³⁵ Ferraris, D.; Drury III, W. J.; Cox, C.; Lectka, T. *J. Org. Chem.* **1998**, *63*, 4568-4569.

³⁶ Lee, K.-Y.; Kim, Y.-H.; Park, M.-S.; Oh, C.-Y.; Ham, W.-H. *J. Org. Chem.* **1999**, *64*, 9450-9458.
Greene, T. W.; Wuts, P. G. M. *Protective groups in organic synthesis*, 3rd ed.; Wiley: New York, 1999.

water was added and the reaction was kept at rt, which caused slow hydrolysis into **14** accompanied by by-product formation. Change of solvent into THF gave a faster rearrangement followed by complete conversion into **14**, albeit as a diastereomeric mixture caused by partial ring-opening of acylaziridine **13** by the water present in the acid.³⁷ The reaction was repeated using dried TsOH, but this gave a sluggish reaction with byproducts, as was also the case when using camphorsulfonic acid.



Scheme 20: Hydrolysis into hydroxyamide **14**.

$\text{BF}_3 \cdot \text{OEt}_2$ proved better, giving a fast and clean rearrangement in THF at $-25\text{ }^\circ\text{C}$ followed by hydrolysis at rt, to yield **14** in ca 70% from vinylaziridines **4** (Table 9). The timing of the water addition is crucial for the successful outcome of the reaction; when added too early the diastereoselectivity is diminished as water opens the acylaziridine, when added too late the formation of byproducts increases.

Table 9: Acetylation and rearrangement of vinylaziridines **4**.^a

Substrate	R ¹	R ²	R ³	Yield of 14 (%)
4a	PhCH ₂	H	H	71
4b	BnO	H	H	73
4c	BnO	H	CH ₂ OPMB	73
4d	PMBO	CH ₂ OBn	H	73

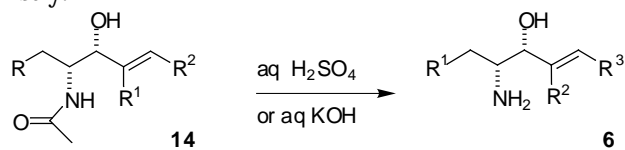
^aIsolated yields over two steps.

4.3.2 Hydrolysis of hydroxyamides **14**

Hydroxyamides **14a,b** were hydrolyzed in 0.5% H_2SO_4 , giving *syn*-amino alcohols **6a,b** in excellent yields. Due to the lability of the PMB group, hydroxyamides **14c,d** were hydrolyzed in 1M KOH with slightly lower yields

³⁷ Also in the initial experiments **14** was isolated as a diastereomeric mixture.

(Scheme 21, Table 10). In all cases the reaction proceeded without alterations of the stereochemistry.³⁸



Scheme 21: Hydrolysis of hydroxyamides **14**.

Table 10. Hydrolysis of hydroxyamides **14**.^a

Substrate	R ¹	R ²	R ³	Yield of 6 (%)
14a	PhCH ₂	H	H	95 ^b
14b	BnO	H	H	92 ^b
14c	BnO	H	CH ₂ OPMB	91 ^c
14d	PMBO	CH ₂ OBn	H	84 ^c

^aIsolated yields. ^bAcidic hydrolysis. ^cBasic hydrolysis.

³⁸ Lai, C. K.; Buckanin, R. S.; Chen, S. J.; Zimmerman, D. F.; Sher, F. T.; Berchtold, G. *A.J. Org. Chem.* **1982**, *47*, 2364-2369. Koft, E. R.; Dorff, P.; Kulling, R. *J. Org. Chem.* **1989**, *54*, 2936-2940.

Determination of regiochemistry and relative stereochemistry

5

Trans-oxazolidinones are known to have smaller coupling constants between the ring protons in ^1H NMR than the corresponding *cis*-oxazolidinones. Reported values for *N*-H oxazolidinones are 3-7 Hz and 7-9 Hz respectively (Figure 6).^{8,39} Accordingly, by converting amino alcohols into the corresponding oxazolidinones (Scheme 22), their relative stereochemistry can be revealed, as *syn*-amino alcohols give *trans*-oxazolidinones and *anti*-amino alcohols give *cis*-oxazolidinones. Also the regiochemistry can be disclosed when the amino alcohols have a vinylic substituent, since the allylic ring-proton shifts downfield in ^1H NMR.

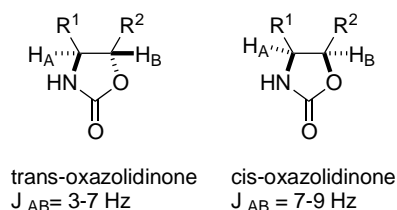
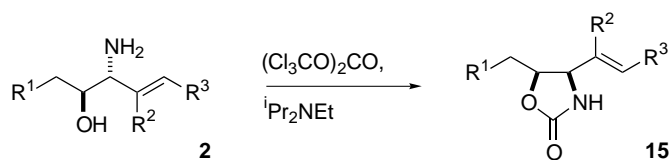


Figure 6: Coupling constants between H_a and H_b in *cis*- and *trans*-oxazolidinones.

When *anti*-amino alcohols **2** and **5** were converted into *cis*-oxazolidinones **15** and **16**, the coupling constants ranged from 7.8 to 8.3 Hz (Table 11). *Syn*-amino alcohols **3** and **6** yielded *trans*-oxazolidinones **9** and **17**, with coupling constants between 5.0 and 7.0 Hz.

³⁹ Bergmeier, S. C.; Stanchina, D. M. *Tetrahedron Lett.* **1995**, *36*, 4533-4536 and references therein.



Scheme 22: Conversion of *trans*-amino alcohol **2** to *cis*-oxazolidinones **15**.

Table 11: Oxazolidinone coupling constants (J_{AB}).^a

Amino alcohol	Oxazolidinone	J_{AB} (Hz)			
		a	b	c	d
2	15	8.2	8.2	8.3	8.3
3	9	7.0	6.6	6.8	5.0
5	16	8.0	8.3	8.3	7.8
6	17	6.6	6.6	6.0	5.5

^aFor definitions of R¹, R² and R³ see Table 10.

Anti-amino alcohols **2e,h,i** (Table 2) showed coupling constants of 7.8-8.1 Hz upon conversion into oxazolidinones. The relative configurations of **2f,g** were determined by NOE-experiments on the corresponding oxazolidinones.

Concluding remarks

A synthetic strategy that provides a straightforward route from vinyloxyepoxides **1** to the four isomeric *vic*-amino alcohols **2**, **3**, **5** and **6** has been presented. Since *ent*-**1** is available from the same starting material as **1**, all eight possible isomers of a given amino alcohol can be synthesized using this procedure. The strategy focuses on the propensity of vinyloxyepoxides 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.

Furthermore an efficient, microwave-assisted protocol for the regioselective and stereospecific synthesis of vicinal amino alcohols from vinyloxyepoxides has been presented. Compared to previous methods, this procedure uses milder reaction conditions, shorter reaction times, generally gives higher yields and is applicable to a larger set of substrates.

Further investigations to define the scope and limitations of the presented synthetic strategy towards amino alcohols are underway, mainly focusing on the rearrangement of vinylaziridines and improving the diastereoselectivities in the Pd(0)-catalyzed epoxide opening. The strategy will also be applied to natural product synthesis.

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I would like to thank...

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Appendix A

Experimental details for compounds 2-7, 8a, 9, 13 and 14.

General. ^1H and ^{13}C NMR spectra were recorded on Varian Mercury 300/400 MHz, JEOL 270 MHz or Bruker dpx 400/500 MHz spectrometers in CHCl_3 , using the residual peak of CHCl_3 (^1H NMR δ 7.26, ^{13}C NMR δ 77.0), or added TMS (δ 0.00), as internal standard. Chemical shifts are reported in the δ -scale with multiplicity (b=broad, s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), integration and coupling constants (Hz). Optical rotations, $[\alpha]_{\text{D}}$, were measured on a Perkin Elmer 343 polarimeter at the sodium D line at ambient temperature. Infrared spectra were recorded on an ATI Mattson FTIR spectrophotometer and only the strongest/structurally most important peaks (ν , cm^{-1}) are listed. High resolution mass spectra were recorded on a JEOL SX-102 spectrometer. Analytical thin layer chromatography was performed on Merck silica gel 60 F_{254} plates, the plates were visualized with UV light and phosphomolybdic acid/cerium sulfate staining reagent (purchased from Aldrich as a 20 wt% solution in ethanol but diluted to ca 5 wt% before use). Flash chromatography employed Grace Amicon silica gel 60 (35-70 μm). Air- and moisture sensitive reactions were carried out in flame-dried, septum-capped flasks under an atmospheric pressure of nitrogen. All liquid reagents were transferred via oven-dried syringes. THF and DME were distilled from sodium-benzophenone ketyl before use; dichloromethane was distilled from CaH_2 .

Typical procedure for the aminolysis of epoxides 1 to *anti*-amino alcohols 2:

Spectroscopic data for compounds 2a,b see ref 26.

(2R,3R)-3-Amino-1-benzyloxy-6-(4-methoxybenzyloxy)-hex-4-en-2-ol (2c):

Vinylepoxyde **1c** (7.0 mg, 21 μmol) in NH_4OH (25%, 2.5 mL) was subjected to focused microwave irradiation at 15W for 20 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 **2c** in 88% yield (6.5 mg, 18 μmol). ^1H 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} ; $[\alpha]_{\text{D}}$: +2.5 (c 0.25, CH_2Cl_2); HRMS (CI+) Exact mass calcd for $\text{C}_{21}\text{H}_{28}\text{NO}_4$ (M+H): 358.2018. Found: 358.2014.

(2R,3R)-3-Amino-4-benzyloxy-methyl-1-(4-methoxy-benzyloxy)-pent-4-en-2-ol (2d):

Prepared from vinyl epoxide **1d** in 93% yield as described for **2c**. ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.21 (m, 7H), 6.87 (d, 2H, $J = 8.8$ Hz), 5.24 (m, 1H), 5.21 (m, 1H), 4.52 (m, 2H), 4.45 (m, 2H), 4.12 (d, 1H, $J = 11.8$ Hz), 4.00 (d, 1H, $J = 11.8$ Hz), 3.83 (m, 1H), 3.78 (s, 3H), 3.63 (d, 1H, $J = 6.0$ Hz), 3.53 (m, 2H), 2.18 (br s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 159.2, 146.2, 137.7, 130.2, 129.3, 128.4, 127.7, 115.9, 113.8, 73.0, 72.6, 72.1, 71.4, 71.3, 57.4, 55.2; IR (neat): 3369 (br), 2910, 2860 cm^{-1} ; $[\alpha]_{\text{D}}$ +0.8 (c 1.00, CH_2Cl_2); HRMS (EI+) Exact mass calcd for $\text{C}_{21}\text{H}_{28}\text{NO}_4$ (M+H): 358.2018. Found: 358.2043.

Typical procedures for the ring opening of vinyl epoxides 1 to give oxazolidinones 7:

With equilibration:

(4S,5S)-5-Phenethyl-3-(toluene-4-sulfonyl)-4-vinyloxazolidin-2-one (7a):

To a solution of $(\text{dba})_3\text{Pd}_2\cdot\text{CHCl}_3$ (15.0 mg, 15 μmol) in THF (1 mL) was added dist. $(^i\text{PrO})_3\text{P}$ (36 μL , 0.146 mmol). The mixture was stirred for 20 min before addition of dist. 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 concd. Flash chromatography (pentane/EtOAc 5:1 \rightarrow 2:1) afforded oxazolidinone **7a** in 82% yield (43.7 mg, 0.117 mmol). NMR analysis indicated a diastereomeric ratio of 4.5:1. ^1H 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 $\text{C}_{20}\text{H}_{21}\text{NO}_4\text{S}$ (M): 371.1191. Found: 371.1182.

(4R,5R)-5-Benzyloxymethyl-3-(toluene-4-sulfonyl)-4-vinylloxazolidin-2-one (7b):

Prepared from vinyl epoxide **1b** in 88% yield as described for **7a**. ^1H NMR (400 MHz, CDCl_3 , major isomer): δ 7.87 (d, 2H, $J = 8.6$ Hz), 7.36-7.21 (m, 7H), 5.87 (ddd, 1H, $J = 17.2, 10.2, 7.8$ Hz), 5.44 (d, 1H, $J = 17.2$ Hz), 5.36 (d, 1H, $J = 10.2$ Hz), 4.81 (dd, 1H, $J = 7.8, 3.9$ Hz), 4.45 (s, 2H), 4.24 (q, 1H, $J = 3.9$ Hz), 3.56 (t, 2H, $J = 3.9$ Hz), 2.38 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 151.3, 145.1, 136.9, 134.8, 134.1, 129.4, 128.4, 128.4, 127.9, 127.8, 119.9, 78.5, 73.5, 68.5, 61.1, 21.7; IR (neat): 2931, 2868, 1780, 1371 cm^{-1} ; HRMS (EI+) Exact mass calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_5\text{S}$ (M): 387.1140. Found: 387.1150.

Without equilibration:

(4S,5R)-5-Benzyloxymethyl-4-[3-(4-methoxybenzyloxy)-propenyl]-3-(toluene-4-

sulfonyl)-oxazolidin-2-one (7c): Prepared from vinyl epoxide **1c** in 87% yield as described for **7a**, except that the reaction was run at rt for 1 h. ^1H 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} ; $[\alpha]_{\text{D}}$: -11.2 (c 1.80, CH_2Cl_2); HRMS (CI+) Exact mass calcd for $\text{C}_{29}\text{H}_{31}\text{NO}_7\text{S}$ (M): 537.1821. Found: 537.1819.

(4S,5R)-4-(1-Benzyloxymethylvinyl)-5-(4-methoxybenzyloxymethyl)-3-toluene-4-

sulfonyl)-oxazolidin-2-one (7d): Prepared from vinyl epoxide **1d** in 93% yield as described for **7c**. ^1H NMR (400 MHz, CDCl_3): δ 7.85 (d, 2H, $J = 8.3$ Hz), 7.34-7.22 (m, 5H), 7.17 (d, 2H, $J = 8.3$ Hz), 7.08 (d, 2H, $J = 8.4$ Hz), 6.82 (d, 2H, $J = 8.4$ Hz), 5.30 (s, 1H), 5.29 (s, 1H), 4.88 (d, 1H, $J = 3.3$ Hz), 4.44 (s, 2H), 4.38 (q, 1H, $J = 3.3$ Hz), 4.27 (s, 2H), 4.07 (AB-q, 2H, $J = 11.9$ Hz), 3.78 (s, 3H), 3.42 (br d, 2H, $J = 2.9$ Hz), 2.35 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 159.8, 152.5, 145.7, 143.5, 137.9, 135.1, 129.8, 129.6, 129.0, 129.0, 128.9, 128.3, 116.7, 114.3, 79.8, 73.5, 73.4, 73.4, 71.8, 69.0, 61.5, 55.7, 55.7, 22.1; IR (neat) 2953, 2864,

1719, 1365 cm^{-1} ; $[\alpha]_{\text{D}} + 22.9^{\circ}$ (*c* 0.90, CH_2Cl_2); HRMS (EI+) Exact mass calcd for $\text{C}_{29}\text{H}_{31}\text{NO}_7\text{S}$ (M): 537.1821. Found: 537.1826.

Typical procedure for the detosylation of 7 to oxazolidinones 9:

(4S,5S)-5-Phenethyl-4-vinylloxazolidin-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 dist. 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 *concd.* The diastereomers could be separated by careful flash chromatography (pentane/EtOAc 4:1 \rightarrow 1:1) affording the *N*-H oxazolidinone **9a** in 93% yield (16.3 mg, 75 μmol). ^1H 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} ; $[\alpha]_{\text{D}}: -45.7$ (*c* 0.14, CH_2Cl_2); HRMS (EI+) Exact mass calcd for $\text{C}_{13}\text{H}_{15}\text{NO}_2$ (M): 217.1103. Found: 217.1103.

(4R,5R)-5-Benzyloxymethyl-3-(toluene-4-sulfonyl)-4-vinylloxazolidin-2-one (9ba):

Prepared from oxazolidinone **7b** in 75% yield as described for **9a**. ^1H NMR (300 MHz, CDCl_3): δ 7.40-7.29 (m, 5H), 5.82 (ddd, 1H, $J = 17.3, 10.2, 7.2$ Hz), 5.68 (br s, 1H), 5.34-5.23 (m, 2H), 4.61 (AB-q, 1H, $J = 12.1$ Hz), 4.36 (dt, 1H, $J = 6.6, 4.1$ Hz), 4.25 (br t, 1H, $J = 6.6$ Hz), 3.70 (dd, 1H, $J = 11.0, 4.1$ Hz), 3.64 (dd, 1H, $J = 11.0, 4.1$ Hz); ^{13}C NMR (75 MHz, CDCl_3): δ 158.5, 137.3, 135.5, 128.3, 127.8, 127.6, 118.6, 80.8, 73.6, 69.0, 57.2; IR (neat): 3292 (br), 2924, 2866 cm^{-1} ; $[\alpha]_{\text{D}}: -25.9$ (*c* 0.51, CH_2Cl_2); HRMS (EI+) Exact mass calcd for $\text{C}_{13}\text{H}_{16}\text{NO}_3$ (M+H): 234.1130. Found: 234.1123.

(4S,5R)-5-Benzyloxymethyl-4-[3-(4-methoxybenzyloxy)-propenyl]-oxazolidin-2-one (9c): Prepared from oxazolidinone **7c** in 72% yield as for **9a**. ^1H NMR (400 MHz, CDCl_3): δ 7.38-7.24 (m, 5H), 7.25 (d, 2H, $J = 8.7$ Hz), 6.88 (d, 2H, $J = 8.7$

Hz), 5.80 (dt, 1H, $J = 15.4, 5.0$ Hz), 5.71 (ddt, 1H, $J = 15.4, 7.3, 1.0$ Hz), 5.60 (br s, 1H), 4.58 (AB-q, 2H, $J = 12.1$ Hz), 4.44 (s, 2H), 4.34 (dt, 1H, $J = 6.8, 4.2$ Hz), 4.24 (br t, 1H, $J = 7.1$ Hz), 3.97 (dd, 2H, $J = 5.0, 1.0$ Hz), 3.80 (s, 3H), 3.67 (dd, 1H, $J = 11.1, 4.2$ Hz), 3.60 (dd, 1H, $J = 11.1, 4.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 159.3, 158.4, 137.5, 131.4, 129.9, 129.7, 129.5, 128.5, 127.9, 127.7, 113.9, 80.9, 73.5, 72.4, 69.0, 68.9, 56.2, 55.3; IR (neat): 3288 (br), 2929, 2860, 1757 cm^{-1} ; $[\alpha]_{\text{D}}$: -62.0 (c 0.20, CH_2Cl_2); HRMS (CI+) Exact mass calcd for $\text{C}_{22}\text{H}_{26}\text{NO}_5$ (M+H): 384.1811. Found: 384.1808.

(4S,5R)-4-(1-Benzyloxymethylvinyl)-5-(4-methoxybenzyloxymethyl)-oxazolidin-2-one (9d): Prepared from oxazolidinone **7d** in 85% yield as described for **9a**. ^1H NMR (400 MHz, CDCl_3): δ 7.34–7.17 (m, 7H), 6.83 (d, 2H, $J = 9.1$ Hz), 5.22 (m, 2H), 5.17 (br s, 1H), 4.46 (AB-q, 2H, $J = 12.1$ Hz), 4.43 (m, 3H), 4.28 (d, 1H, $J = 5.0$ Hz), 3.97 (AB-q, 2H, $J = 11.8$ Hz), 3.76 (s, 3H), 3.57 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 159.3, 158.6, 143.7, 137.5, 129.6, 129.3, 128.6, 128.5, 127.9, 127.8, 115.3, 113.8, 80.2, 73.2, 72.8, 70.8, 69.4, 56.5, 55.2; IR (neat): 3288 (br), 2923, 2862, 1755 cm^{-1} ; $[\alpha]_{\text{D}}$: -19.9 (c 0.89, CH_2Cl_2); HRMS (EI+) Exact mass calcd for $\text{C}_{22}\text{H}_{25}\text{NO}_5$ (M): 383.1733. Found: 383.1740.

Typical procedure for the hydrolysis of **9** to *syn*-amino alcohols **3**:

(3S,4S)-4-Amino-1-phenylhex-5-en-3-ol (3a):

A solution of the oxazolidinone **9a** (12.6 mg, 58 μmol) in 1M KOH (EtOH/ H_2O 2:1) was refluxed for 1.5 h. Aq NaOH (2M) was added, and the mixture was extracted several times with Et_2O . The organic phase was washed with brine, dried (Na_2SO_4) and concd. The crude product was pushed through a short silica plug to afford *syn*-amino alcohol **3a** in 100% yield (11.1 mg, 58 μmol). ^1H NMR (400 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} ; $[\alpha]_{\text{D}}$: -27.5 (c 0.63, CH_2Cl_2); HRMS (EI+) Exact mass calcd for $\text{C}_{12}\text{H}_{18}\text{NO}$ (M+H): 192.1388. Found: 192.1377.

(2R,3S)-3-Amino-1-benzoyloxypent-4-en-2-ol (3b):

Prepared from oxazolidinone **9b** in 97% yield as described for **3a**. ¹H NMR (300 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₂): 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; [α]_D: -9.1 (*c* 0.65, CH₂Cl₂); HRMS (EI+) Exact mass calcd for C₁₂H₁₈NO₂ (M+H): 208.1338. Found: 208.1340.

(2R,3S)-3-Amino-1-benzoyloxy-6-(4-methoxybenzyloxy)-hex-4-en-2-ol (2c):

Prepared from oxazolidinone **9c** in 91% yield as described for **3a**. ¹H NMR (400 MHz, CDCl₃): 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 (dd, 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); ¹³C NMR (100 MHz, CDCl₃): δ 159.2, 138.0, 130.2, 129.4, 128.4, 128.3, 127.8, 113.8, 77.2, 73.5, 73.3, 72.0, 71.8, 69.9, 55.3; IR (neat): 3583, 3357 (br), 2920, 2856 cm⁻¹; [α]_D: -20.3 (*c* 1.10, CH₂Cl₂); HRMS (CI+) Exact mass calcd for C₂₁H₂₈NO₄ (M+H): 358.2018. Found: 358.2021.

(2R,3S)-3-Amino-4-benzoyloxymethyl-1-(4-methoxybenzyloxy)-pent-4-en-2-ol (2d):

Prepared from oxazolidinone **9d** in 86% yield as described for **3a**. ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (125 MHz, CDCl₃): 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; [α]_D: -6.9 (*c* 1.00, CH₂Cl₂); HRMS (CI+) Exact mass calcd for C₂₁H₂₈NO₄ (M+H): 358.2018. Found: 358.2019.

Typical procedure for the ring-closure of amino alcohols 2 to aziridines 4:

Spectroscopic data for compounds 4a,b see ref 26.

(2S,3R)-2-Benzoyloxymethyl-3-[3-(4-methoxybenzyloxy)-propenyl]-aziridine (4c):

To amino alcohol **2c** (8.1mg, 23 μmol) and polymer bound PPh₃ (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% Et₃N during packing), (pentane/EtOAc 8:1 → EtOAc/MeOH 10:1+1%NH₄OH) afforded vinylaziridine **4c** (4.6 mg, 13.6 μmol) in 78% yield based on recovered **2c** (1.9 mg, 5.3 μmol). ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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; [α]_D: +11.9 (*c* 1.08, CH₂Cl₂); HRMS (CI⁺) Exact mass calcd for C₂₁H₂₆NO₃ (M+H): 340.1913. Found: 340.1912.

(2R,3S)-2-(1-Benzyloxymethylvinyl)-3-(4-methoxybenzyloxymethyl)-aziridine (4d):

To a solution of PPh₃ (50.5 mg, 78 μmol) in THF (1 mL) at 0 °C was added DIAD (15 μL, 78 μmol). After 20 min amino alcohol **3d** (20.0 mg, 56 μmol) in THF (1 mL) was added, and the resultant mixture was refluxed for 24 h. The solvent was evaporated at reduced pressure, Et₂O was added to the crude product, and the mixture was stored overnight in the freezer. Precipitated Ph₃PO was removed by filtration and careful flash chromatography on deactivated silica (10% Et₃N during packing), (pentane → pentane/EtOH 10:1) afforded vinylaziridine **4d** in 63% yield (12.0 mg, 35 μmol). ¹H NMR (CDCl₃, 300 MHz): δ 7.37–7.23 (m, 7H), 6.87 (m, 2H), 5.18 (br s, 1H), 5.14 (t, 1H, *J* = 1.3 Hz), 4.48 (m, 4H), 4.01 (AB-q, 2H, *J* = 12.1 Hz), 3.79 (s, 3H), 3.58 (m, 1H), 3.46 (dd, 1H, *J* = 9.8, 4.8 Hz), 2.45 (br s, 1H), 2.27 (br s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 159.2, 143.2, 137.9, 130.2, 129.3, 128.4, 127.7, 127.6, 114.1, 114.0, 114.0, 113.9, 113.8, 72.6, 72.0, 71.4, 55.2, 37.2, 37.2, 37.1, 21.9; IR (neat): 3408 (br), 2933, 2858 cm⁻¹; [α]_D: +7.0 (*c* 0.50, CH₂Cl₂); HRMS (CI⁺) Exact mass calcd for C₂₁H₂₆NO₃ (M+H): 340.1913. Found: 340.1916.

Typical procedure for the solvolysis of aziridines 4 into anti-amino alcohols 5:

(3S,4R)-4-Amino-6-phenylhex-1-en-3-ol (5a):

To a solution of vinylaziridine **4a** (30.0 mg, 0.173 mmol) in THF (3 mL) and H₂O (2.4 mL) was added HClO₄ (15 μL, 0.173 mmol) and the solution was

heated to 50 °C for 7 h. After addition of K₂CO₃, the mixture was stirred for 20 min, filtered and concd. Flash chromatography (EtOAc/MeOH 10:1+ 1% NH₄OH) yielded amino alcohol **5a** in 80% (26.6 mg, 0.139 mmol). ¹H NMR (300 MHz, CDCl₃): 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); ¹³C NMR (67.5 MHz, CDCl₃): 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; [α]_D: -15.8 (c 5.23, CH₂Cl₂); HRMS (EI+) Exact mass calcd for C₁₂H₁₈NO (M+H): 192.1388. Found: 192.1390.

(2S,3S)-2-Amino-1-benzyloxypent-4-en-3-ol (5b):

Prepared from aziridine **4b** in 84% yield as described for **5a**. ¹H NMR (300 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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; [α]_D: -11.4 (c 0.69, CH₂Cl₂); HRMS (EI+) Exact mass calcd for C₁₂H₁₈NO₂ (M+H): 208.1338. Found: 208.1344.

(2S,3S)-2-Amino-1-benzyloxy-6-(4-methoxybenzyloxy)-hex-4-en-3-ol (5c):

Prepared from aziridine **4c** in 82% yield as described for **5a**. ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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; [α]_D: +11.4 (c 0.07, CH₂Cl₂); HRMS (CI+) Exact mass calcd for C₂₁H₂₈NO₄ (M+H): 358.2018. Found: 358.2020.

(2S,3S)-4-Amino-2-benzyloxymethyl-5-(4-methoxybenzyloxy)-pent-1-en-3-ol (5d):

Prepared from aziridine **4d** in 71% yield as described for **5a**. ¹H NMR (400 MHz, CDCl₃): 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), 3.15 (dt,

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} ; $[\alpha]_{\text{D}}$: +7.0 (c 0.50, CH_2Cl_2); HRMS (CI+): Exact mass calcd for $\text{C}_{21}\text{H}_{28}\text{NO}_4$ (M+H): 358.2018. Found: 358.2019.

Typical procedure for the acylation of vinylaziridines 4 to *N*-acetylaziridines 13, followed by rearrangement to 8 and hydrolysis into hydroxyamides 14 :

(2R,3R)-1-(2-Phenethyl-3-vinylaziridin-1-yl)-ethanone (13a):

A solution of vinylaziridine **4a** (100 mg, 0.58 mmol), Et_3N (0.160 mL, 1.2 mmol) and DMAP (cat.) 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, sat. NaHCO_3 and brine, dried (Na_2SO_4) and concd to give the crude *N*-acetyl vinylaziridine **13a** (126.2 mg) that was taken directly on to the next step. ^1H 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);

(4R,5R)-2-Methyl-4-phenethyl-5-vinyl-4,5-dihydrooxazole (8a):

^1H NMR (400 MHz, CDCl_3): δ 7.35-7.17 (m, 5H), 5.89 (ddd, 1H, $J = 17.3, 10.3, 7.3$ Hz), 5.33 (dt, 1H, $J = 17.2, 1.0$ Hz), 5.24 (dt, 1H, $J = 10.3, 1.0$ Hz), 4.50 (t, 1H, $J = 7.3$ Hz), 3.78 (br q, 1H, $J = 7.3$ Hz), 2.92-2.68 (m, 2H), 2.06 (s, 3H), 2.00-1.81 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 161.9, 136.1, 128.2, 125.8, 117.3, 85.9, 71.7, 37.2, 32.2, 17.1; HRMS (EI+) Exact mass calcd $\text{C}_{14}\text{H}_{17}\text{NO}$ (M): 215.1310. Found: 215.1314.

(1R,2R)-*N*-(2-Hydroxy-1-phenethylbut-3-enyl)-acetamide (14a):

To a solution of the crude **13a** (10.0 mg, 46 μmol) in THF (0.5 mL) at -25 °C was added $\text{BF}_3 \cdot \text{OEt}_2$ (12 μL , 92 μmol). After 1.5 h full conversion into the corresponding oxazoline was achieved, and H_2O (0.05 mL) was added, the resultant mixture was stirred at rt for 2 h. Aq NaOH (2M) was added, and the mixture was extracted several times with Et_2O . The organic phase was washed with sat. NaHCO_3 , dried (Na_2SO_4) and concd. Flash chromatography (EtOAc) afforded *syn*-hydroxyamide **14a** in 71% yield (7.6 mg, 33 μmol). ^1H 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}C NMR (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 cm^{-1} ; $[\alpha]_{\text{D}}$: +22.2 (c 0.46, CH_2Cl_2); HRMS (EI+) Exact mass calcd for $\text{C}_{14}\text{H}_{20}\text{NO}_2$ (M+H): 234.1494. Found: 234.1490.

(1S,2R)-*N*-(1-Benzyloxymethyl-2-hydroxybut-3-enyl)-acetamide (14b):

Prepared in two steps from aziridine **4b** in 73% yield as described for **14a**.

13b: ^1H NMR (400 MHz, CDCl_3): δ 7.37-7.25 (m, 5H), 5.52-5.28 (m, 3H), 4.53 (s, 2H), 3.69 (dd, 1H, $J = 10.9, 4.3$ Hz), 3.65 (dd, 1H, $J = 10.9, 4.7$ Hz), 3.08 (dd, 1H, $J = 8.0, 2.7$ Hz), 2.74 (td, 1H, $J = 4.3, 2.7$ Hz), 2.09 (s, 3H);

14b: ^1H NMR (300 MHz, CDCl_3): δ 7.39-7.27 (m, 5H), 6.12 (br d, 1H, $J = 7.9$ Hz), 5.80 (ddd, 1H, $J = 17.3, 10.4, 5.2$ Hz), 5.31 (dt, 1H, $J = 17.3, 1.6$ Hz), 5.17 (dt, 1H, $J = 10.4, 1.6$ Hz), 4.52 (s, 2H), 4.45 (m, 1H), 4.08 (td, 1H, $J = 12.6, 4.4$ Hz), 3.69 (m, 1H), 3.40 (br s, 1H), 1.98 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.4, 137.3, 137.1, 128.4, 127.9, 127.7, 116.1, 73.6, 73.0, 71.2, 52.5, 23.3; IR (neat) 3338 (br), 3929, 2868, 1653 cm^{-1} ; $[\alpha]_{\text{D}}$ +4.8 (c 0.52, CH_2Cl_2); HRMS (EI+) Exact mass calcd for $\text{C}_{14}\text{H}_{20}\text{NO}_3$ (M+H): 250.1443. Found: 250.1428.

(1S,2R)-*N*-[1-Benzyloxymethyl-2-hydroxy-5-(4-methoxybenzyloxy)-pent-3-enyl]-

acetamide (14c): Prepared in two steps from aziridine **4c** in 73% yield as described for **14a**.

13c: ^1H NMR (400 MHz, CDCl_3): δ 7.39-7.26 (m, 5H), 7.25 (d, 2H, $J = 8.7$ Hz), 6.88 (d, 2H, $J = 8.7$ Hz), 6.04 (dt, 1H, $J = 15.4, 5.5$ Hz), 5.31 (ddt, 1H, $J = 15.4, 8.6, 1.5$ Hz), 4.53 (s, 2H), 4.44 (s, 2H), 4.00 (dd, 2H, $J = 5.5, 1.5$ Hz), 3.81 (s, 3H), 3.70 (dd, 1H, $J = 10.8, 4.0$ Hz), 3.64 (dd, 1H, $J = 10.8, 4.5$ Hz), 3.10 (dd, 1H, $J = 8.6, 2.8$ Hz), 2.74 (td, 1H, $J = 4.3, 2.8$ Hz), 2.09 (s, 3H);

14c: ^1H NMR (400 MHz, CDCl_3): δ 7.38-7.24 (m, 7H), 6.87 (d, 2H, $J = 8.7$ Hz), 6.09 (br d, 1H, $J = 8.6$ Hz), 5.87 (dtd, 1H, $J = 15.6, 5.5, 1.3$ Hz), 5.69 (ddt, 1H, $J = 15.6, 5.5, 1.3$ Hz), 4.53 (d, 2H, $J = 2.2$ Hz), 4.50 (m, 1H), 4.42 (s, 2H), 4.06 (m, 1H), 3.98 (dd, 2H, $J = 5.5, 1.3$ Hz), 3.80 (s, 3H), 3.71 (dd, 1H, $J = 9.6, 3.5$ Hz), 3.67 (dd, 1H, $J = 9.6, 4.2$ Hz), 1.99 (s, 3H), 1.62 (br s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.0, 159.5, 137.7, 132.1, 131.3, 129.8, 129.3, 129.0, 128.5, 128.2, 114.2, 74.1, 73.1, 72.2, 71.8, 70.1, 55.7, 53.1, 23.4; IR (neat): 3315 (br), 2922, 2856, 1651 cm^{-1} ; $[\alpha]_{\text{D}}$: -1.3 (c 0.15, CH_2Cl_2); HRMS (CI+) Exact mass calcd for $\text{C}_{23}\text{H}_{30}\text{NO}_5$ (M+H): 400.2124. Found: 400.2124.

(1S,2R)-N-[3-Benzoyloxymethyl-2-hydroxy-1-(4-methoxybenzyloxymethyl)-but-3-enyl]-acetamide (14d): Prepared in two steps from aziridine **4d** in 73% yield as described for **14a**.

13d: ¹H NMR (400 MHz, CDCl₃): δ 7.31–7.19 (m, 5H), 7.15 (m, 2H), 6.82 (m, 2H), 5.23 (br s, 1H), 5.18 (br s, 1H), 4.45 (m, 2H), 4.34 (m, 2H), 3.94 (m, 2H), 3.77–3.71 (m, 1H), 3.74 (s, 3H), 3.63 (m, 1H), 3.09 (br s, 1H), 2.74 (br s, 1H), 2.02 (s, 3H);

14d: ¹H NMR (500 MHz, CDCl₃): δ 7.29–7.19 (m, 5H), 7.16 (d, 2H, *J* = 8.7 Hz), 6.81 (d, 2H, *J* = 8.7 Hz), 6.02 (d, 1H, *J* = 8.4 Hz), 5.19 (s, 1H), 5.13 (s, 1H), 4.50 (br s, 1H), 4.42 (AB-q, 2H, *J* = 11.7 Hz), 4.37 (s, 2H), 4.18 (m, 1H), 4.05 (d, 1H, *J* = 12.2 Hz), 3.95 (d, 1H, *J* = 12.2 Hz), 3.74 (s, 3H), 3.61 (d, 2H, *J* = 4.0 Hz), 3.54 (br s, 1H), 1.87 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 170.4, 159.4, 144.6, 138.0, 129.5, 128.4, 127.7, 114.5, 113.9, 73.3, 72.9, 72.2, 71.3, 55.3, 50.7, 23.2; IR (neat): 3325 (br), 2952, 2858, 1641 cm⁻¹; [α]_D: -5.5 (c 0.43, CH₂Cl₂); HRMS (CI+) Exact mass calcd for C₂₃H₃₀NO₅ (M+H): 400.2124. Found: 400.2129.

Typical procedures for the hydrolysis of amides **14** to *syn*-amino alcohols **6**:

Acidic hydrolysis:

(3R,4R)-4-Amino-6-phenylhex-1-en-3-ol (6a):

Hydroxyamide **14a** (21.0 mg, 90 μmol) in aq H₂SO₄ (5%) was refluxed for 1 h, then aq NaOH (2M) was added, and the mixture was extracted several times with Et₂O. The organic phase was washed with brine, dried (Na₂SO₄) and concd. The crude product was pushed through a short silica plug to afford *syn*-amino alcohol **6a** in 95% yield (16.4 mg, 86 μmol). ¹H NMR (300 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): δ 141.6, 138.7, 128.3, 128.2, 125.8, 116.6, 75.4, 54.9, 35.8, 32.7; IR (CDCl₃): 3602, 3300 (br), 3155, 2924 cm⁻¹; [α]_D: +13.8 (c 0.86, CH₂Cl₂); HRMS (EI+) Exact mass calcd for C₁₂H₁₈NO (M+H): 192.1388. Found: 192.1387.

(3R,4S)-4-Amino-5-benzyloxy-pent-1-en-3-ol (6b):

Prepared from hydroxyamide **14b** in 92% yield as described for **6a**. ¹H NMR (300 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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; [α]_D: +14.4 (c 0.55, CH₂Cl₂); HRMS (EI+) Exact mass calcd C₁₂H₁₈NO₂ (M+H): 208.1338. Found: 208.1334.

Basic hydrolysis:

(2S,3R)-2-Amino-1-benzyloxy-6-(4-methoxybenzyloxy)-hex-4-en-3-ol (6c):

Hydroxyamide **14c** (12.0 mg, 30 μmol) in 1M KOH (EtOH/H₂O 2:1) was refluxed for 24 h. Aq NaOH (2M) was added, and the mixture was extracted several times with Et₂O. The organic phase was washed with brine, dried (Na₂SO₄) and concd. The crude product was pushed through a short silica plug to afford *syn*-amino alcohol **6c** in 91% yield (9.8 mg, 27 μmol). ¹H NMR (400 MHz, CDCl₃): 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); ¹³C NMR (125 MHz, CDCl₃): 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; [α]_D: +3.8 (c 0.29, CH₂Cl₂); HRMS (CI+) Exact mass calcd for C₂₁H₂₈NO₄ (M+H): 358.2018. Found: 358.2022.

(2S,3R)-4-Amino-2-benzyloxymethyl-5-(4-methoxybenzyloxy)-pent-1-en-3-ol (6d):

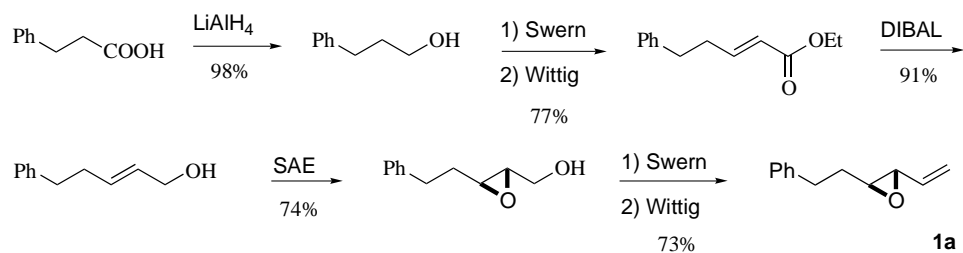
Prepared from hydroxyamide **14d** in 84% yield as described for **6c**. ¹H NMR (500 MHz, CDCl₃): δ 7.38-7.20 (m, 7H), 6.87 (m, 2H), 5.28 (br s, 1H), 5.26 (br s, 1H), 4.55-4.41 (m, 4H), 4.15-3.95 (m, 3H), 3.80 (s, 3H), 3.56 (m, 1H), 3.48 (m, 1H), 3.11 (m, 1H), 1.80 (br s, 3H); ¹³C NMR (125 MHz, CDCl₃): 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; [α]_D: +7.8 (c 0.75, CH₂Cl₂); HRMS (CI+) Exact mass calcd for C₂₁H₂₈NO₄ (M+H): 358.2018. Found: 358.2022.

Appendix B

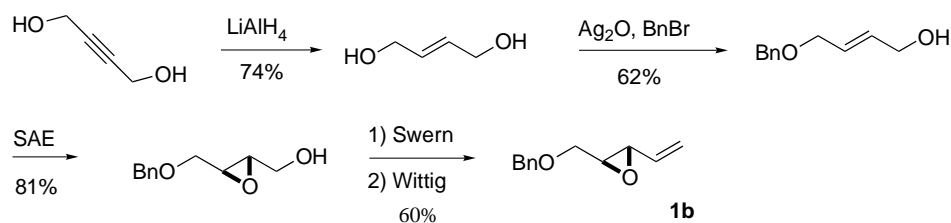
Synthesis of vinylepoxides **1** and oxazolidinones **15-17**.

General. As detailed in Appendix A.

Synthesis of vinylepoxide **1a**:²⁶

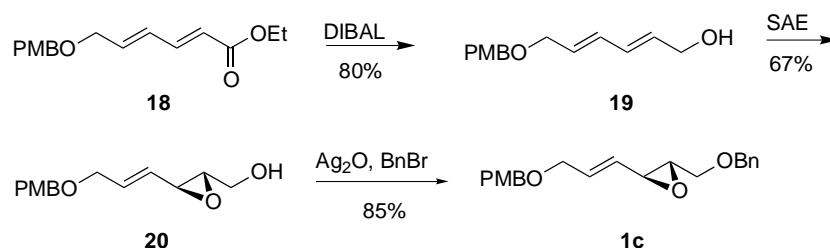


Synthesis of vinylepoxide **1b**:^{26,40}



⁴⁰ Löfstedt, J.; Pettersson-Fasth, H.; Bäckvall, J.-E. *Tetrahedron* **2000**, *56*, 2225-2230.

Synthesis of vinyl epoxide **1c** from the previously described ester **18**:⁴¹



6-(4-Methoxy-benzyloxy)-hexa-2,4-dien-1-ol (**19**):

Ester **2** (1.60 g, 5.8 mmol) in CH₂Cl₂ (35 mL) was cooled to -70 °C before slow addition of DIBAL (14.5 mL, 1M solution, 14.5 mmol). The mixture was stirred at -70 °C for 1.5 h, quenched with MeOH and purified on Rochelle salt. The mixture was extracted with CH₂Cl₂, the organic phase was washed with brine, dried (MgSO₄) and concentrated. Flash chromatography on deactivated silica (pentane/EtOAc 3:1→1:1) afforded dienol **3** in 80% yield (1.09 g, 4.7 mmol). ¹H NMR (400 MHz, CDCl₃): δ 7.26 (m, 2H), 6.87 (d, 2H, *J* = 8.7 Hz), 6.26 (m, 1H), 5.82 (m, 1H), 4.44 (s, 2H), 4.19 (d, 2H, *J* = 5.5 Hz), 4.03 (d, 1H, *J* = 5.5 Hz), 3.80 (s, 3H), 1.42 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 158.6, 132.5, 131.7, 129.7, 129.5, 129.0, 128.9, 113.3, 71.4, 69.7, 62.3, 54.9; IR (neat): 3386, 2935, 2837 cm⁻¹; [α]_D: +0.9 (*c* 0.95, CH₂Cl₂); HRMS (CI⁺) Exact mass calcd for C₁₄H₁₉O₃ (M+H): 235.1334. Found: 235.1342.

(2S,3S)-{3-[3-(4-Methoxy-benzyloxy)-propenyl]-oxiranyl}-methanol (**20**):

Molecular sieves (11 mg, 4 Å) in CH₂Cl₂ (3 mL) were cooled to -30 °C before sequential addition of (+)-DIPT (12.0 μL, 53 μmol), Ti(O^{*i*}Pr)₄ (10.5 μL, 35 μmol) and TBHP (0.30 mL, 2.49 M, 0.71 mmol). The mixture was stirred at -25 °C for 30 min, then dienol **3** (83 mg, 0.35 mmol) in CH₂Cl₂ (2 mL) was added, and the mixture was stored in the freezer overnight. The reaction was quenched with water, stirred with 30% NaOH in sat. NaCl and extracted with CH₂Cl₂. The organic phase was washed with brine, dried (MgSO₄) and concentrated. Flash chromatography on deactivated silica (pentane /EtOAc 4:1→ pure EtOAc) afforded epoxyalcohol **4** (40.1 mg, 0.16 mmol) in 67% yield based on recovered starting material (30.5 mg, 37%). Enantiomeric purity was measured using chiral HPLC to 95% es. ¹H NMR (400 MHz, CDCl₃): δ 7.25 (m, 2H), 6.88 (d, 2H, *J* =

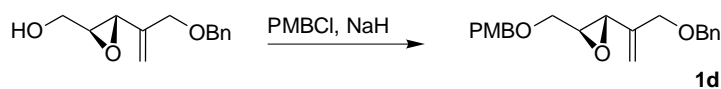
⁴¹ Lindström, U. M.; Somfai, P. *Tetrahedron Lett.* **1998**, *39*, 7173-7176.

8.6 Hz), 6.05 (dt, 1H, $J = 15.6, 5.5$ Hz), 5.51 (dd, 1H, $J = 15.6, 8.2$ Hz), 4.44 (s, 2H), 4.00 (dd, 2H, $J = 5.5, 1.4$ Hz), 3.92 (m, 1H), 3.80 (s, 3H), 3.67 (m, 1H), 3.42 (dd, 1H, $J = 8.2, 2.0$ Hz), 3.07 (ddd, 1H, $J = 4.3, 2.3$ Hz), 1.80 (t, 1H, $J = 5.8$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 159.1, 132.5, 130.0, 129.2, 128.9, 113.7, 72.1, 69.3, 61.1, 60.0, 55.3, 55.1; IR (neat): 3421, 2933, 2862, 1637 cm^{-1} ; $[\alpha]_{\text{D}}^{25}$: -14.3 (c 0.90, CH_2Cl_2); HRMS (CI+) Exact mass calcd for $\text{C}_{14}\text{H}_{18}\text{O}_4$ (M): 250.1205. Found: 250.1200.

(2S,3S)-2-Benzyloxymethyl-3-[3-(4-methoxybenzyloxy)-propenyl]-oxirane (1c):

Epoxyalcohol **4** (180 mg, 0.72 mmol) and freshly prepared Ag_2O (252 mg, 1.1 mmol) were dissolved in toluene (15 mL), BnBr (96 μL , 0.79 mmol) was added and the mixture was heated to 50 $^\circ\text{C}$ for 45 min.⁴² Then 0.5 eq Ag_2O (84 mg, 0.36 mmol) was added and the heating continued for 45 min. The mixture was filtered through celite, concd and purified by flash chromatography on deactivated silica (pentane/EtOAc 4:1 \rightarrow 1:2) to afford vinyl epoxide **1c** (114 mg, 0.33 mmol) in 85% yield based on recovered starting material (81.5 mg, 45%). ^1H NMR (400 MHz, CDCl_3): δ 7.39-7.27 (m, 5H), 7.25 (d, 2H, $J = 8.6$ Hz), 6.88 (d, 2H, $J = 8.6$ Hz), 6.04 (dt, 1H, $J = 15.6, 5.5$ Hz), 5.51 (ddt, 1H, $J = 15.6, 8.0, 1.5$ Hz), 4.57 (AB-q, 2H, $J = 11.7$ Hz), 4.45 (s, 2H), 4.01 (dd, 2H, $J = 5.5, 1.5$ Hz), 3.80 (s, 3H), 3.75 (dd, 1H, $J = 11.7, 3.1$ Hz), 3.52 (dd, 1H, $J = 11.7, 5.5$ Hz), 3.30 (dd, 1H, $J = 8.0, 2.0$ Hz) 3.11 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 159.0, 137.6, 132.3, 129.9, 129.2, 129.1, 128.2, 127.6, 113.7, 73.3, 72.0, 69.8, 69.3, 58.7, 55.3, 55.3; IR (neat): 2932, 2856, 1612 cm^{-1} ; $[\alpha]_{\text{D}}^{25}$: -1.0 (c 0.37, CH_2Cl_2); HRMS (CI+) Exact mass calcd for $\text{C}_{21}\text{H}_{23}\text{O}_4$ (M-H): 339.1596. Found: 339.1599.

Synthesis of vinyl epoxide 1d from (2S,3S)-[3-(1-benzyloxymethylvinyl)-oxiranyl]-methanol:¹⁷



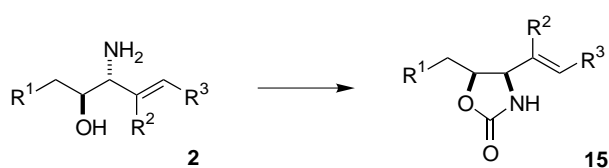
⁴² Bouzide, A.; Sauv , G. *Tetrahedron Lett.*, **1997**, 5945-5948.

(2S,3S)-[3-(1-Benzyloxymethylvinyl)-oxiranyl]-methanol (1d):

A solution of (2S,3R)-4-benzyloxymethyl-2,3-epoxy-4-penten-1-ol (0.40 g, 1.80 mmol) in DMF (3 mL) was transferred slowly to a suspension of NaH (48 mg, 1.98 mmol) in DMF (3 mL) at -20 °C. The mixture was stirred for 20 min at this temperature before addition of PMBCl (0.30 mL, 2.18 mmol). The solution was stirred at -20 °C for 1 h and then stored in a freezer at -20 °C for 24 h. The suspension was poured into Et₂O and water, the aqueous phase was extracted with Et₂O, the combined organic phases were washed with brine, dried (Na₂SO₄) and concd. Flash column chromatography (pentane/EtOAc 3:1) gave **1d** as a colourless oil (0.478 g, 78%). ¹H NMR (400 MHz, CDCl₃): δ 7.35–7.25 (m, 7H), 6.90 (br d, 2H, *J* = 6.8 Hz), 5.38 (s, 1H), 5.31 (s, 2H), 4.52 (m, 2H), 4.00 (s, 2H), 3.83 (s, 3H), 3.76 (dd, 1H, *J* = 11.6, 3.0 Hz), 3.48 (dd, 1H, *J* = 11.6, 3.0 Hz), 3.39 (d, 1H, *J* = 2.0 Hz), 3.30 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 158.9, 141.1, 137.7, 130.2, 129.6, 129.1, 128.1, 127.4, 115.8, 113.5, 72.7, 71.9, 69.5, 69.3, 58.3, 55.5, 55.1; [α]_D: +2.0 (*c* 1.00, CH₂Cl₂); HRMS (CI+) Calcd for C₂₁H₂₃O₄ (M-H): 339.1596. Found: 339.1602.

Typical procedure for the conversion of amino alcohols to the corresponding oxazolidinones:

To a solution of amino alcohol (0.140 mmol) and Pr₂NEt (37 μL, 0.210 mmol) in CH₂Cl₂ (2 mL) at 0 °C was added (Cl₃CO)₂CO (63 mg, 0.210 mmol) and the mixture was stirred overnight. H₂O was added and the mixture was extracted with Et₂O. The organic phase was washed with water and brine, dried (Na₂SO₄) and concd. Flash chromatography (pentane/EtOAc 1:1) gave the corresponding *N*-H oxazolidinone in 92% yield (0.129 mmol).

Oxazolidinones 15 from *anti*-amino alcohols 2:

(4R,5S)-5-Phenethyl-4-vinylloxazolidin-2-one (15a):

¹H NMR (400 MHz, CDCl₃): δ 7.31-7.17 (m, 5H), 5.80 (ddd, 1H, *J* = 17.6, 10.2, 7.8 Hz), 5.48 (br s, 1H), 5.34-5.26 (m, 2H), 4.63 (ddd, 1H, *J* = 11.7, 8.2, 3.9 Hz), 4.26 (br t, 1H, *J* = 7.8 Hz), 2.88 (ddd, 1H, *J* = 14.1, 9.4, 5.1 Hz), 2.69 (ddd, 1H, *J* = 14.1, 9.0, 7.4 Hz), 2.00 (m, 1H), 1.78 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 158.8, 140.4, 132.8, 128.4, 128.4, 126.1, 119.5, 79.0, 58.2, 32.5, 31.9; IR (neat): 3275 (br), 2953, 2864, 1747 cm⁻¹; [α]_D: -10.4 (c 1.05, CH₂Cl₂); HRMS (EI+) Exact mass calcd for C₁₃H₁₅NO₂ (M): 217.1103. Found: 217.1103.

(4R,5R)-5-Benzyloxymethyl-4-vinylloxazolidin-2-one (15b):

¹H NMR (400 MHz, CDCl₃): δ 7.38-7.27 (m, 5H), 5.87 (ddd, 1H, *J* = 17.2, 10.2, 7.0 Hz), 5.33 (d, 1H, *J* = 17.2 Hz), 5.32 (s, 1H), 5.29 (d, 1H, *J* = 10.2 Hz), 4.81 (dt, 1H, *J* = 8.2, 5.5 Hz), 4.54 (AB-q, 2H, *J* = 11.7 Hz), 4.42 (br t, 1H, *J* = 8.2 Hz), 3.62 (dd, 1H, *J* = 9.4, 5.5 Hz), 3.60 (dd, 1H, *J* = 9.4, 5.5 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 158.3, 137.3, 132.5, 128.3, 127.8, 127.6, 119.4, 78.0, 73.6, 68.1, 57.0; IR (neat): 3309 (br), 2927, 2870, 1757 cm⁻¹; [α]_D: -22.4 (c 0.45, CH₂Cl₂); HRMS (EI+) Exact mass calcd for C₁₃H₁₆NO₃ (M+H): 234.1130. Found: 234.1133.

(4R,5R)-5-Benzyloxymethyl-4-[3-(4-methoxybenzyloxy)-propenyl]-oxazolidin-2-one (15c):

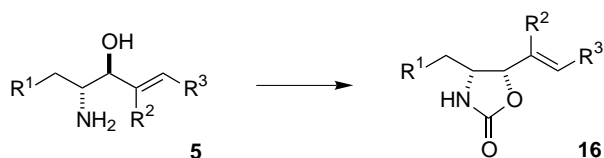
¹H NMR (400 MHz, CDCl₃): δ 7.35-7.25 (m, 5H), 7.24 (d, 2H, *J* = 8.7 Hz), 6.87 (d, 2H, *J* = 8.7 Hz), 5.86 (dt, 1H, *J* = 15.6, 4.8 Hz), 5.78 (dd, 1H, *J* = 15.6, 7.3 Hz), 5.03 (br s, 1H), 4.79 (dt, 1H, *J* = 8.3, 5.5 Hz), 4.53 (d, 2H, *J* = 5.1 Hz), 4.45 (br t, 1H, *J* = 7.7 Hz), 4.44 (s, 2H), 3.96 (d, 2H, *J* = 4.8 Hz), 3.81 (s, 3H), 3.62 (dd, 2H, *J* = 10.5, 5.5 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 159.3, 158.2, 137.4, 132.3, 129.9, 129.4, 128.5, 127.9, 127.8, 126.5, 113.9, 78.1, 73.7, 72.4, 69.1, 68.1, 56.2, 55.3; IR (neat): 3311 (br), 2935, 2862, 1757 cm⁻¹; [α]_D: -2.1 (c 0.33, CH₂Cl₂); HRMS (CI+) Exact mass calcd for C₂₂H₂₆N₂O₅ (M+H): 384.1811. Found: 384.1808.

(4R,5R)-4-(1-Benzyloxymethylvinyl)-5-(4-methoxybenzyloxymethyl)-oxazolidin-2-one (15d):

¹H NMR: (400 MHz, CDCl₃): δ 7.38-7.26 (m, 5H), 7.19 (d, 2H, *J* = 8.8 Hz), 6.85 (d, 2H, *J* = 8.8 Hz), 5.33 (s, 1H), 5.29 (s, 1H), 5.27 (br s, 1H), 4.82 (dt, 1H, *J* = 8.3, 5.8 Hz), 4.57 (d, 1H, *J* = 8.3 Hz), 4.46 (s, 2H), 4.38 (AB-q, 2H, *J* = 11.5 Hz), 3.95 (m, 2H), 3.78 (s, 3H), 3.53 (m, 2H); ¹³C NMR: (125 MHz, CDCl₃):

δ 159.7, 159.2, 141.7, 138.1, 130.1, 129.8, 128.9, 128.3, 128.2, 116.2, 114.2, 78.4, 73.6, 73.4, 72.2, 68.6, 56.6, 55.7; IR (neat): 3373 (br), 2925, 2864 cm^{-1} ; $[\alpha]_{\text{D}}$: -16.7 (*c* 0.75, CH_2Cl_2); HRMS (CI+): Exact mass calcd for $\text{C}_{22}\text{H}_{26}\text{NO}_5$ (M+H): 384.1811. Found: 384.1807.

Oxazolidinones 16 from *anti*-amino alcohols 5:



(4*R*,5*S*)-4-Phenethyl-5-vinyloxazolidin-2-one (16a):

^1H NMR (300 MHz, CDCl_3): δ 7.35-7.14 (m, 5H), 5.90 (ddd, 1H, $J = 17.2, 10.4, 7.1$ Hz), 5.48 (dt, 1H, $J = 17.2, 1.1$ Hz), 5.40 (dt, 1H, $J = 10.4, 1.1$ Hz), 5.05 (br t, 1H, $J = 8.0$ Hz), 3.88 (td, 1H, $J = 8.0, 5.5$ Hz), 2.86-2.57 (m, 3H), 1.86-1.76 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3): δ 158.0, 140.2, 130.7, 128.7, 128.2, 126.4, 120.3, 80.5, 55.4, 32.9, 32.5; IR (neat): 3327 (br), 2932, 2868, 1749 cm^{-1} ; $[\alpha]_{\text{D}}$: +9.7 (*c* 0.35, CH_2Cl_2); HRMS (EI+) Exact mass calcd for $\text{C}_{13}\text{H}_{15}\text{NO}_2$ (M): 217.1103. Found: 217.1111.

(4*S*,5*S*)-4-Benzylloxymethyl-5-vinyloxazolidin-2-one (16b):

^1H NMR (400 MHz, CDCl_3): δ 7.32-7.20 (m, 5H), 5.88 (ddd, 1H, $J = 17.2, 10.5, 6.7$ Hz), 5.40 (dt, 1H, $J = 17.2, 1.2$ Hz), 5.29 (d, 1H, $J = 10.5, 1.2$ Hz), 5.21 (br s, 1H), 5.07 (br t, 1H, $J = 8.0$ Hz), 4.41 (AB-q, 2H, $J = 11.9$ Hz), 4.04 (td, 1H, $J = 8.3, 3.9$ Hz), 3.40-3.29 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 158.8, 137.6, 130.5, 129.0, 128.5, 128.2, 120.7, 78.9, 74.1, 69.9, 55.5; IR (neat): 3267 (br), 2924, 2858, 1755 cm^{-1} ; $[\alpha]_{\text{D}}$: +33.0 (*c* 0.14, CH_2Cl_2); HRMS (EI+) Exact mass calcd for $\text{C}_{13}\text{H}_{16}\text{NO}_3$ (M+H): 234.1130. Found: 234.1121.

(4*S*,5*S*)-4-Benzylloxymethyl-5-[3-(4-methoxybenzyloxy)-propenyl]-oxazolidin-2-one (16c):

^1H NMR (400 MHz, CDCl_3): δ 7.35-7.23 (m, 7H), 6.88 (d, 2H, $J = 8.6$ Hz), 6.01 (dt, 1H, $J = 15.6, 4.4$ Hz), 5.76 (dd, 1H, $J = 15.6, 7.3$ Hz), 5.18 (br s, 1H), 5.13 (br t, 1H, $J = 7.8$ Hz), 4.51 (d, 2H, $J = 3.3$ Hz), 4.44 (s, 2H), 4.01 (m, 3H), 3.81 (s, 3H), 3.47 (dd, 1H, $J = 9.3, 4.3$ Hz), 3.41 (t, 1H, $J = 9.3$ Hz); ^{13}C NMR (125

MHz, CDCl₃): δ 158.8, 137.7, 133.7, 130.4, 129.7, 129.0, 128.5, 128.2, 124.0, 114.3, 78.4, 74.1, 72.6, 69.9, 69.3, 55.8, 55.7; IR (neat): 3323 (br), 2927, 2858, 1749 cm⁻¹; [α]_D: +23.3 (c 0.36, CH₂Cl₂); HRMS (CI+) Exact mass calcd for C₂₂H₂₆NO₅ (M+H): 384.1811. Found: 384.1808.

(4S,5S)-5-(1-Benzyloxymethylvinyl)-4-(4-methoxybenzyloxymethyl)-oxazolidin-2-one (16d):

¹H NMR (400 MHz, CDCl₃): δ 7.38-7.25 (m, 5H), 7.17 (d, 2H, *J* = 8.7 Hz), 6.86 (d, 2H, *J* = 8.7 Hz), 5.40 (s, 1H), 5.31 (s, 1H), 5.27 (br s, 1H), 5.17 (d, 1H, *J* = 7.8 Hz), 4.47 (AB-q, 2H, *J* = 11.7 Hz), 4.34 (AB-q, 2H, *J* = 11.2 Hz), 4.02 (AB-q, 2H, *J* = 11.9 Hz), 3.98 (ddd, 1H, *J* = 9.4, 7.8, 3.8 Hz), 3.79 (s, 3H), 3.43 (dd, 1H, *J* = 9.4, 3.8 Hz), 3.26 (t, 1H, *J* = 9.4 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 159.8, 158.8, 138.8, 129.9, 129.8, 128.9, 128.3, 128.1, 115.6, 114.3, 78.2, 73.7, 73.3, 71.9, 70.2, 55.7, 55.4; IR (neat): 3298 (br), 2924, 2858, 1759 cm⁻¹; [α]_D: +42.0 (c 0.50, CH₂Cl₂); HRMS (EI+): Exact mass calcd for C₂₂H₂₅NO₅ (M): 383.1733. Found: 383.1728.

Oxazolidinones 17 from *syn*-amino alcohols 6:



(4R,5R)-4-Phenethyl-5-vinyloxazolidin-2-one (17a):

¹H NMR (300 MHz, CDCl₃): δ 7.34-7.17 (m, 5H), 5.89 (ddd, 1H, *J* = 17.2, 10.4, 7.1 Hz), 5.58 (br s, 1H), 5.43 (dt, 1H, *J* = 17.2, 0.8 Hz), 5.33 (dt, 1H, *J* = 10.4, 0.8 Hz), 4.60 (br t, 1H, *J* = 6.6 Hz), 3.55 (br q, 1H, *J* = 6.6 Hz), 2.71 (br t, 1H, *J* = 7.7 Hz), 2.02-1.86 (m, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 158.5, 140.0, 133.8, 128.7, 128.2, 126.4, 119.3, 83.0, 57.8, 36.2, 32.1; IR (neat): 3282 (br), 2931, 2862, 1751 cm⁻¹; [α]_D: +40.0 (c 0.37, CH₂Cl₂); HRMS (EI+) Exact mass calcd for C₁₃H₁₅NO₂ (M): 217.1103. Found: 217.1103.

(4R,5S)-4-Benzyloxymethyl-5-vinyloxazolidin-2-one (17b):

¹H NMR (400 MHz, CDCl₃): δ 7.39-7.27 (m, 5H), 5.90 (ddd, 1H, *J* = 17.2, 10.6, 6.6 Hz), 5.40 (d, 1H, *J* = 17.2 Hz), 5.31 (d, 1H, *J* = 10.6 Hz), 5.26 (br s, 1H), 4.65 (t, 1H, *J* = 6.6 Hz), 4.55 (s, 2H), 3.74 (m, 1H), 3.51 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 158.0, 137.0, 133.9, 128.5, 128.0, 127.7, 118.8, 79.2, 73.7, 71.2, 57.6; IR (neat): 3296 (br), 2922, 2862, 1757 cm⁻¹; [α]_D: +48.9 (c 0.28, CH₂Cl₂);

HRMS (EI+) Exact mass calcd for C₁₃H₁₆NO₃ (M+H): 234.1130. Found: 234.1129.

(4S,5R)-4-Benzylloxymethyl-5-[3-(4-methoxy-benzyloxy)-propenyl]-oxazolidin-2-one (17c):

¹H NMR (400 MHz, CDCl₃): δ 7.39-7.27 (m, 5H), 7.26 (d, 2H, *J* = 8.7 Hz), 6.88 (d, 2H, *J* = 8.7 Hz), 5.93 (dt, 1H, *J* = 15.6, 4.8 Hz), 5.83 (ddt, 1H, *J* = 15.6, 6.5, 1.5 Hz), 5.19 (br s, 1H), 4.67 (br t, 1H, *J* = 6.3 Hz), 4.55 (s, 2H), 4.45 (s, 2H), 4.02 (dt, 2H, *J* = 4.0, 1.5 Hz), 3.81 (s, 3H), 3.74 (m, 1H), 3.52 (dd, 1H, *J* = 9.3, 4.5 Hz), 3.45 (dd, 1H, *J* = 9.3, 7.3 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 159.7, 158.5, 137.6, 132.3, 130.4, 129.8, 129.0, 128.5, 128.2, 127.9, 114.3, 79.1, 74.1, 72.7, 71.6, 69.3, 58.1, 55.7; IR (neat): 3298 (br), 2919, 2860, 1757 cm⁻¹; [α]_D: +31.6 (*c* 0.38, CH₂Cl₂); HRMS (CI+) Exact mass calcd for C₂₂H₂₆NO₅ (M+H): 384.1811. Found: 384.1815.

(4S,5R)-5-(1-Benzylloxymethylvinyl)-4-(4-methoxybenzyloxymethyl)-oxazolidin-2-one (17d):

¹H NMR (400 MHz, CDCl₃): δ 7.38-7.26 (m, 5H), 7.21 (d, 2H, *J* = 8.8 Hz), 6.83 (d, 2H, *J* = 8.8 Hz), 5.32 (s, 1H), 5.29 (s, 1H), 5.14 (br s, 1H), 4.74 (d, 1H, *J* = 5.5 Hz), 4.48 (br s, 2H), 4.42 (br s, 2H), 4.14 (d, 1H, *J* = 12.3 Hz), 4.05 (d, 1H, *J* = 12.3 Hz), 3.91 (m, 1H), 3.81 (s, 3H), 3.48 (dd, 1H, *J* = 9.3, 4.0 Hz), 3.42 (dd, 1H, *J* = 9.3, 7.6 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 159.5, 159.2, 141.9, 137.6, 129.4, 129.3, 128.5, 127.9, 127.8, 115.4, 114.0, 78.8, 73.2, 72.7, 71.5, 70.1, 56.9, 55.3; IR (neat): 3309 (br), 2924, 2856, 1755 cm⁻¹; [α]_D: +20.0 (*c* 0.26, CH₂Cl₂); HRMS (CI+) Exact mass calcd for C₂₂H₂₆NO₅ (M+H): 384.1811. Found: 384.1815.