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Synthesis and Lewis acid catalyzed Claisen rearrangement of 2-(1,3-oxazolin-2-yl)-substituted allyl vinyl ethers

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Abstract—Allyl vinyl ethers containing an acceptor function in the 2-position are useful substrates for the Lewis acid-catalyzed Claisen rearrangement. The first synthesis of acyclic 2-(1,3-oxazolin-2-yl)-substituted allyl vinyl ethers is reported. The Lewis acid catalyzed Claisen rearrangement of these allyl vinyl ethers afforded the rearrangement products with low to moderate diastereo- and enantioselectivity. The catalyzed rearrangement of chiral allyl vinyl ethers was investigated. The combination of substrate- and catalyst-induced diastereoselectivity led to unexpected and unprecedented results.

1. Introduction

The potential of the Claisen rearrangement as CC-bond forming reaction is well established.[1] Consequently, the development of a catalytic asymmetric Claisen rearrangement is of outstanding importance.[2] In general, chiral catalysts for other pericyclic reactions like cycloadditions and ene reactions are well known.[3] However, the catalysis of the Claisen rearrangement of allyl vinyl ethers even with achiral catalysts is undoubtedly underdeveloped.[4] One reason for this disparity may be that a variety of suitable substrates for catalyzed cycloadditions and ene reactions are easily accessible so that one can concentrate on the identification and optimization of the chiral catalyst. The problem in developing a catalyst for the Claisen rearrangement is more fundamental because allyl vinyl ethers containing a stereogenic vinyl ether double bond are not easily accessible as single double bond isomers. Consequently, the most important variants of Claisen rearrangements are based on allyl vinyl ethers generated in situ.[1c] Furthermore, substituents on the allyl vinyl ether exert a dramatic influence on the rate of thermal rearrangement.[5] Consequently, in order to develop a successful catalytic asymmetric Claisen rearrangement, a judicious choice of the structure of the allyl vinyl ether is required. We have recently shown that 2-alkoxycarbonyl-substituted allyl vinyl ethers are accessible as single vinyl ether double bond isomers, thermally stable and, most important, reactive in Lewis acid catalyzed Claisen rearrangements.[6] Our studies culminated in the publication of the first catalytic enantioselective Claisen rearrangement.[7] In terms of reactivity and stereoselectivity, the presence of an acceptor function in the 2-position of the allyl vinyl ether is crucial. The acceptor function together with the allylic ether oxygen atom offers the possibility of chelation of the Lewis acid, a prerequisite for high stereoselectivities in many Lewis acid catalyzed transformations (Fig. 1).

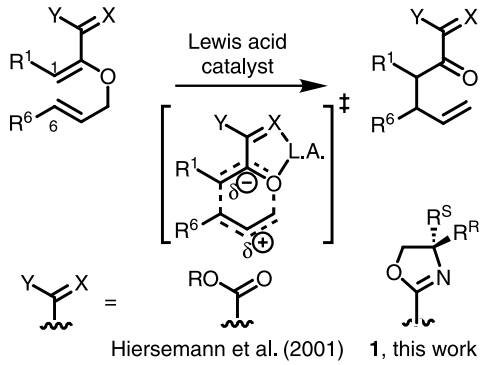

Figure 1. 2-Acceptor-substituted allyl vinyl ethers **1** as substrate of choice for Lewis acid (L.A.) catalyzed Claisen rearrangements.

In order to broaden the concept of 2-acceptor-substituted allyl vinyl ethers as an ideal substrate class for Lewis acid catalyzed Claisen rearrangements, we currently study the properties of different 2-acceptor substituted allyl vinyl ethers. The purpose of this article is to report synthesis and Lewis acid catalyzed Claisen rearrangement of 2-(1,3-oxazolin-2-yl)-substituted allyl vinyl ethers **1**, a novel type of a 2-acceptor substituted allyl vinyl ether.

2. Allyl vinyl ether synthesis

The synthesis of the 2-(1,3-oxazolin-2-yl)-substituted allyl

Keywords: Claisen rearrangement; catalysis; Lewis acid; copper(II) bis(oxazoline); allyl vinyl ether.

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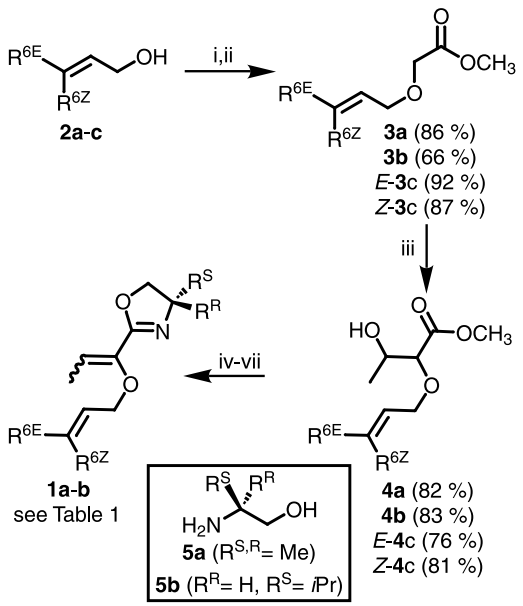


Scheme 1. Synthesis of allyl vinyl ethers **1**. *Reagents and conditions*. (i) *n*BuLi, THF, −78°C then ICH_2CO_2Na, −78°C to rt; (ii) DCC, DMAP, CH_2Cl_2, CH_3OH, 0°C, 30 min; (iii) LDA, THF, −78°C, 10 min; CH_3CHO, −78°C, 30 min; (iv) **5**, 80°C, sealed tube; (v) MsCl, Et_3N, CH_2Cl_2, 0°C, 20 min; (vi) Et_3N, CH_2Cl_2, 50°C, sealed tube; (vii) NaHMDS, THF, rt.

vinyl ethers **1** started from the commercially available allylic alcohols **2a–c** (Scheme 1). Etherification followed by esterification afforded the α-allyloxy-substituted acetates **3**. An aldol addition provided access to β-hydroxy esters **4** which were transformed into the allyl vinyl ethers **1** by a sequence consist of amide formation, bis(mesylation), base-induced cyclization and elimination.[8] The allyl vinyl ethers **1** were isolated as a mixture of vinyl ether double bond isomers which were separated by preparative HPLC (Table 1).

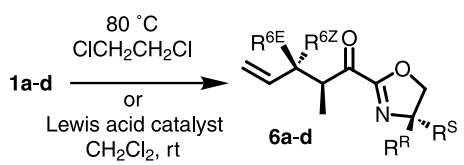
Table 1. Synthesis of allyl vinyl ethers **1**

Entry	Compound[a]	R^S	R^R	R^{6E}	R^{6Z}	Yield[b] (%)	*Z*/*E*[c]
1	**1a**	Me	Me	Me	Me	62	1/4
2	**1b**	Me	Me	H	H	35	1/4
3	*E*-**1c**	Me	Me	*n*Pr	H	45	1/4
4	*Z*-**1c**	Me	Me	H	*n*Pr	51	1/3
5	**1d**	*i*Pr	H	Me	Me	40	1/3

[a] *E*/*Z* descriptors indicate the allylic ether double bond configuration. Yield after chromatographic purification prior to preparative HPLC.
[b] Isolated yield from **4a–c**.
[c] *E*/*Z* ratio of the vinyl ether double bond generated under the reaction conditions outlined in Scheme 1. *E*/*Z* ratio may be variable depending on the purity of the NaHMDS.

3. Thermal Claisen rearrangement

Although not our primary objective, we briefly studied the thermal Claisen rearrangement of allyl vinyl ethers **1** (Scheme 2, Table 2).



Scheme 2. Thermal Claisen rearrangement. Results see Table 2.

The thermal rearrangement of the allyl vinyl ethers **1** proceeded at elevated temperature (80°C) and prolonged reaction times (39 to 95 h) with outstanding chemoselectivity to provide the rearrangement products **6** in almost quantitative yield (Table 2). With respect to catalysis, we conclude that a thermal background reaction should be insignificant at rt. The simple diastereoselectivity of the thermal Claisen rearrangement of allyl vinyl ether **1c** was exceptionally high (Table 2, entry 5–8). The relative configuration of the preferentially formed diastereomer **6c** can be explained by a chair-like transition state geometry for the Claisen rearrangement.

The thermal Claisen rearrangement of allyl vinyl ether **1d** proceeded without any auxiliary-induced diastereoselectivity (Table 2, entry 9,10). This somewhat surprising result may be explained assuming a lack of diastereoface differentiating capability of the chiral 1,3-oxazoline moiety due to the 1,5-relationsship between the chiral center and the prochiral C-1. Alternatively or additionally, a conformational flexibility between the auxiliary and the rearrangement system could undermine a potential diastereoface differentiating capability of the chiral auxiliary (Fig. 2).

4. Catalysis with achiral Lewis acids

Initially, we studied the general aptitude of different metal triflates as Lewis acid catalysts using *E*-**1a** as substrate (Scheme 2, Table 3). The experiments were performed with 5 mol% of the Lewis acid in CH_2Cl_2 at rt in the presence of activated molecular sieves to insure optimal chemoselectivity and reactivity. The Lewis acids were chosen based on experiences gained during our studies of the Lewis acid catalyzed Claisen rearrangement of 2-alkoxycarbonyl-substituted allyl vinyl ethers.[4]

Within an acceptable reaction time, $Cu(OTf)_2$ catalyzed the transformation of *E*-**1a** into the rearrangement product **2a**. $Lu(OTf)_3$ and $Sc(OTf)_3$ also catalyzed the rearrangement, but with incomplete conversion (Table 3, entry 2,4). A prolonged reaction time did not significantly improve the conversion (Table 3, entry 3,5). These results may be explained by an irreversible coordination of the catalyst to the rearrangement product. $Sn(OTf)_2$ was completely inefficient as Lewis acid catalyst (Table 3, entry 6).

Having identified $Cu(OTf)_2$ as the Lewis acid catalyst of choice, we next investigated the influence of different substituents on the result of the catalyzed rearrangement (Table 4).

The number of alkyl substituents on the C-6 of the allyl vinyl ether is of pivotal importance for the reactivity. Allyl vinyl ethers **1a**,**d** featuring a trisubstituted allylic ether double bond required a decreased catalyst loading and a shorter reaction time for complete conversion compared to the allyl vinyl ethers **1b**,**c** (Table 4, entries 9,10). This result supports the assumption of a highly polarized pericyclic transition state for the Lewis acid catalyzed Claisen rearrangement (Fig. 1). The increased number of alkyl substituents on the C-6 of the allyl vinyl ether **1a**,**d** helps to stabilize a partial positive charge in a highly polarized

Table 2. Thermal Claisen rearrangement of allyl vinyl ethers **1a**–**d**. High yields and high simple diastereoselectivity

	Substrate[a]	Product	R^S	R^R	R^{6E}	R^{6Z}	*t* (h)	Yield (%)	*syn*/*anti*
1	*E*-**1a**	**6a**	Me	Me	Me	Me	39	96	–
2	*Z*-**1a**	**6a**	Me	Me	Me	Me	39	98	–
3	*E*-**1b**	**6b**	Me	Me	H	H	89	99	–
4	*Z*-**1b**	**6b**	Me	Me	H	H	89	99	–
5	*E*,*E*-**1c**	*syn*-**6c**	Me	Me	*n*Pr	H	95	97	96/4[b]
6	*Z*,*E*-**1c**	*anti*-**6c**	Me	Me	H	*n*Pr	95	95	1/99[b]
7	*E*,*Z*-**1c**	*anti*-**6c**	Me	Me	H	*n*Pr	39	99	4/96[b]
8	*Z*,*Z*-**1c**	*syn*-**6c**	Me	Me	*n*Pr	H	39	99	99/1[b]
9	*E*-**1d**	**6d**	*i*Pr	H	Me	Me	48	99	1/1[c]
10	*Z*-**1d**	**6d**	*i*Pr	H	Me	Me	48	99	1/1[c]

[a] The first *E*/*Z* descriptor indicates the vinyl ether ether double bond configuration the second the allylic ether double bond configuration.
[b] Simple (*syn*/*anti*) diastereoselectivity.
[c] Auxiliary-induced diastereoselectivity.

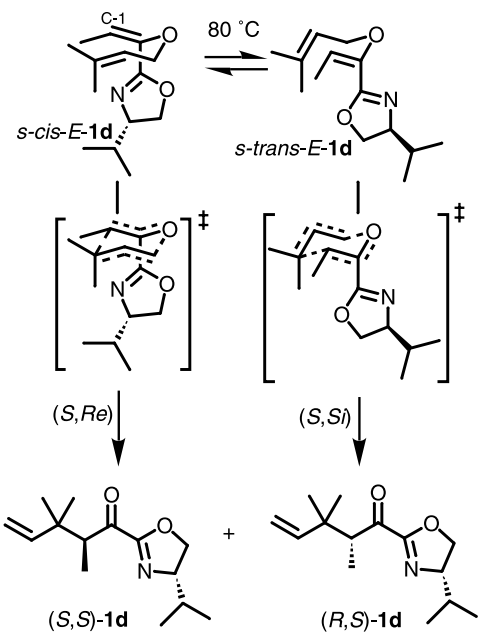


Figure 2. The *s-cis* and *s-trans* conformation may be available for allyl vinyl ether **1d**. This conformational mobility of the auxiliary relative to the prochiral C-1 makes two transition states accessible which lead to opposite diastereoface-differentiation {(*S*,*Re*) vs (*S*,*Si*)}.

transition state.[9] Consequently, the allyl vinyl ether **1b** without alkyl substituent on C-6 was the least reactive substrate (Table 4, entry 8) and an intermediate reactivity was found for the allyl vinyl ether **1c** (Table 4, entries 1–7).

The double bond configuration of **1c** also influenced the rate of conversion. The following order of reactivity was obtained: *Z*,*E*-**1c**>*E*,*E*-**1c**>*Z*,*Z*-**1c**>*E*,*Z*-**1c** (Table 4, entries 1–7). This order may be explained assuming a chair-like transition state geometry in which R^{6E} adopts an equatorial and R^{6Z} an axial position. No explanation is yet available for the observation that the allyl vinyl ethers **1c** containing *Z*-configured vinyl ether double bonds are more reactive than there *E*-configured relatives.

The simple (*syn*/*anti*) diastereoselectivity of the $Cu(OTf)_2$ catalyzed rearrangement was moderate for *E*,*E*- and *Z*,*E*-**1c** (Table 4, entries 2–5). With *E*,*Z*- and *Z*,*Z*-**1c** as substrates though, the rearrangement product **6c** was obtained as single diastereomer. This remarkable relationship between diastereoselectivity and allylic ether double bond configuration was previously reported for the Lewis acid catalyzed Claisen rearrangement of 2-alkoxycarbonyl-substituted allyl vinyl ethers.[4] We briefly studied the $Cu(OTf)_2$-catalyzed Claisen rearrangement of the allyl vinyl ether **1d** containing a chiral 1,3-oxazoline moiety (Table 4, entry 10,11). Unfortunately, the rearrangement afforded the product **6d** with very low auxiliary-induced diastereoselectivity.

Experiments were performed to shed light on the role of the molecular sieves. Generally, in the absence of molecular

Table 3. Lewis acid (5 mol%) catalyzed Claisen rearrangement of *E*-**1a** in the presence of 3 Å molecular sieves in CH_2Cl_2 at rt

Entry	Lewis acid	*t* (h)	Yield (%)[a]	**6a**/*E*-**1a**[b]
1	$Cu(OTf)_2$	3	92	1/0
2	$Lu(OTf)_3$	18	80	78/22
3	$Lu(OTf)_3$	89	80	78/22
4	$Sc(OTf)_3$	18	84	37/63
5	$Sc(OTf)_3$	89	84	43/57
6	$Sn(OTf)_2$	101	85	9/91

[a] Isolated yield after removal of the catalyst by filtration through a 4×0.5 cm silica gel column.
[b] Ratio determined by ^1H NMR.

Table 4. $Cu(OTf)_2$-Catalyzed Claisen rearrangement in the presence of 3 Å MS in CH_2Cl_2 at rt. The nature of the substituents and the double bond configuration profoundly influence the reactivity and stereoselectivity of the $Cu(OTf)_2$-catalyzed Claisen rearrangement

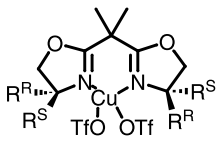
Entry	Substrate	$Cu(OTf)_2$ (mol%)	*t* (h)	Product	Yield (%)[a]	*syn*/*anti*[b]
1	*E*,*E*-**1c**	5	117	**6c**	78 (9)	72/28
2	*E*,*E*-**1c**	10	5	**6c**	72	72/28
3	*E*,*E*-**1c**	5[c]	68	**6c**	41 (54)	82/18
4	*Z*,*E*-**1c**	5[c]	67	**6c**	95	22/78
5	*Z*,*E*-**1c**	5	22	**6c**	87	35/65
6	*Z*,*Z*-**1c**	10	24	**6c**	87	>95/5
7	*E*,*Z*-**1c**	10	120	**6c**	67(23)	<5/95
8	*E*-**1b**	10	87	**6d**	23(54)	–
9	*Z*-**1a**	5	3	**6a**	96	–
10	*E*-**1d**	5	3.5	**6d**	92	58/42[d]
11	*Z*-**1d**	5	4.5	**6d**	96	42/58[d]

[a] Isolated yield after removal of the catalyst by filtration through a 4×0.5 cm silica gel column. In parentheses: % substrate reisolated.
[b] Ratio determined by ^1H NMR.
[c] In absence of molecular sieves.
[d] Ratio (2*R*)-**6d**/(2*S*)-**6d**.

sieves, the rate of the rearrangement decreased (Table 4, entry 3,4). Furthermore a slightly increased simple diastereoselectivity was observed in the absence of molecular sieves (Table 4, entry 3,4).

5. Catalysis with chiral Lewis acids

The copper(II) bis(oxazolines) **7** and **8** have been used successfully to catalyze the Claisen rearrangement of 2-alkoxycarbonyl-substituted allyl vinyl ethers affording an *ee* up to 90% (Fig. 3).[7,10]



R^R= Ph, R^s= H: [Cu{(*R*,*R*)-Ph-box}](OTf)$_2$, ***R*,*R*-7**
R^R= H, R^S= Ph: [Cu{(*S*,*S*)-Ph-box}](OTf)$_2$, ***S*,*S*-7**
R^R= H, R^S= *t*Bu: [Cu{(*S*,*S*)-Ph-box}](OTf)$_2$, ***R*,*R*-8**

Figure 3. The chiral copper bis(oxazolines) used to catalyze the Claisen rearrangement.

Initially, we had hoped that the presence of a 1,3-oxazoline moiety at the C-2 of the allyl vinyl ether would improve the enantioselectivity of the catalyzed rearrangement. In order to validate our original proposal, we studied the catalysis using the copper(II) bis(oxazolines) **7** and **8** (Scheme 2, Table 5).

Using **1a** as the substrate, reactivity and enantioselectivity was generally very low (Table 5, entries 1–4). The reactivity and enantioselectivity further decreased for allyl vinyl ether **1b** (Table 5, entries 5–7). Even after prolonged reaction times and in the presence of molecular sieves as well as 10 mol% of catalyst **7**, mainly substrate **1b** was reisolated. A combination of steric and electronic factors may be responsible for the very low reactivity. The bulky 1,3-oxazoline moiety in the substrate **1a**,**b** could decelerate the formation of the substrate-catalyst-complex. Additionally, in the case of **1b**, without alkyl substituents on C-6, the proposed partial positive charge in the transition state is less efficiently stabilized.

Table 5. Cu^{II} (bis)oxazoline-catalyzed Claisen rearrangement in CH_2Cl_2 at rt

Entry	Substrate	Catalyst	*t* (h)	Product	Yield (%)[a]	2*S*/2*R*[b]
1	*Z*-**1a**	5 mol% *R*,*R*-**7**	117	**6a**	97	66/34
2	*Z*-**1a**	5 mol% *S*,*S*-**7**	117	**6a**	98	34/66
3	*E*-**1a**	5 mol% *R*,*R*-**7**	111	**6a**	82	44/56
4	*Z*-**1a**	5 mol% *S*,*S*-**8**	95	**6a**	78	52/48
5	*Z*-**1b**	10 mol% *R*,*R*-**7**[c]	96	**6b**	23 (73)	47/53
6	*Z*-**1b**	10 mol% *S*,*S*-**7**[c]	70	**6b**	20 (59)	53/47
7	*E*-**1b**	10 mol% *R*,*R*-**7**[c]	96	**6b**	27 (70)	52/48
8	*Z*-**1d**	5 mol% *R*,*R*-**7**	2	**6d**	95	18/82
9	*Z*-**1d**	5 mol% *S*,*S*-**7**	2	**6d**	93	19/81
10	*Z*-**1d**	10 mol% *S*,*S*-**8**	21	**6d**	89	18/82
11	*E*-**1d**	5 mol% *R*,*R*-**7**	3	**6d**	88	68/32
12	*E*-**1d**	5 mol% *R*,*R*-**7**[c]	1	**6d**	97	69/31
13	*E*-**1d**	5 mol% *S*,*S*-**7**	2	**6d**	92	51/49
14	*E*-**1d**	5 mol% *S*,*S*-**8**	24	**6d**	92	63/37
15	*E*-**1d**	10 mol% *S*,*S*-**8**[c]	2	**6d**	93	83/17

[a] Isolated yield after removal of the catalyst by filtration through a 4×0.5 cm silica gel column. In parentheses: % substrate reisolated.
[b] Ratio determined by ^{1}H NMR.
[c] In the presence of molecular sieves.

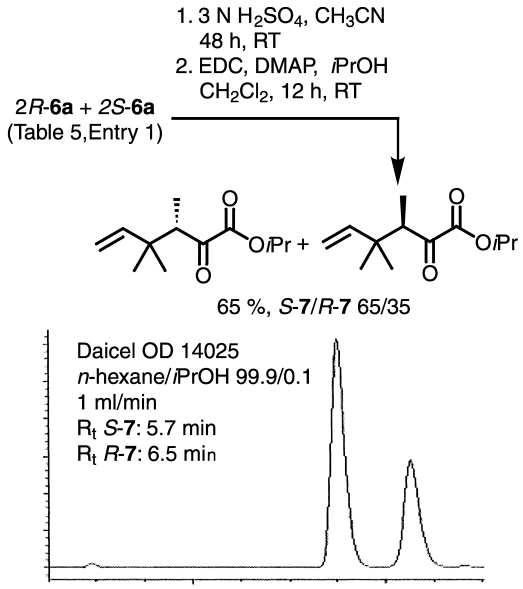
The allyl vinyl ether **1d** containing the *i*Pr-substituted chiral 1,3-oxazoline moiety was the most reactive substrate (Table 5, entries 8–15). In comparison with the less reactive **1a**, this result may be explained by the decreased steric hindrance between the monosubstituted 1,3-oxazoline moiety in **1d** and the bis(oxazoline) moiety of the catalyst **7**. The stereochemical results of the rearrangement are remarkable. Generally, the diastereoselectivities depended on the vinyl ether double bond configuration of **1d**. For *Z*-**1d**, we observed diastereoselectivities of 4/1 in the favor of the 2*R* configured rearrangement product **6d** (Table 5, entries 8–10). This ratio was not altered by the nature of the ligand on the Cu^{II} which may lead to the conclusion that the stereochemical result of the catalyzed rearrangement of *Z*-**1d** is solely the result of a substrate-induced diastereoselectivity which is more efficient with **7** or **8** than with $Cu(OTf)_2$ without chiral ligands. Using *E*-**1d** as the substrate, the 2*S* configured rearrangement product was preferentially formed utilizing **7** or **8** as the catalyst (Table 5, entries 11–15). However, in contrast to *Z*-**1d**, the diastereoselectivity of the rearrangement significantly depended on the catalyst and the reaction conditions. *R*,*R*-**7** catalyzed the rearrangement of *E*-**1d** to afford **6d** in a 2*S*/2*R*=68/32 ratio (Table 5, entry 11). The presence of molecular sieves increased reactivity and yield but did not alter the diastereoselectivity (Table 5, entry 12). A decreased diastereoselectivity was observed when *S*,*S*-**7** was used as the catalyst (Table 5, entry 13). Finally, the attempt to improve the diastereoselectivity by using *S*,*S*-**8** as catalyst failed, only a moderate diastereoselectivity was observed, even in the presence of molecular sieves (Table 5, entry 14,15).

6. Stereochemical assignment

Transformation of the 1,3-oxazoline **6** into the 2-oxo ester **9** enabled a comparison of analytical data and retention times (chiral HPLC) with previously reported data.[7] A typical example is depicted in Scheme 3.

7. Conclusion

We have successfully established an access to the novel 2-(1,3-oxazolin-2-yl)-substituted allyl vinyl ethers **1**. The unprecedented thermal Claisen rearrangement of **1** proceeded with high chemo- and simple diastereoselectivity. However, in the presence of a chiral 1,3-oxazoline moiety, we did not observe auxiliary-induced diastereoselectivities. For the first time, we showed that achiral metal triflates are Lewis acid catalysts for the Claisen rearrangement of 2-(1,3-oxazolin-2-yl)-substituted allyl vinyl ethers **1**. $Cu(OTf)_2$ was the most efficient catalyst in terms of reactivity. Substrate structure significantly influenced the reactivity and diastereoselectivity. As a general rule, alkyl substituents on C-6 accelerate the Lewis acid catalyzed



Scheme 3. Hydrolytic cleavage of the 1,3-oxazoline followed by EDC mediated esterification afforded the 2-oxo ester **7** as mixture of enantiomers. The enantiomeric ratio was determined by chiral HPLC. The absolute configuration was assigned by comparison of retention times with literature known data.[7]

Claisen rearrangement presumably by stabilizing a partial positive charge in highly polarized pericyclic transition state. Chiral Cu^{II} bis(oxazolines) catalyzed the Claisen rearrangement with low to moderate enantioselectivities. Future work aiming at the optimization of the substituent pattern on the 1,3-oxazoline ring system should pave the way for increased stereoselectivity and reactivity.

8. Experimental

Unless otherwise noted, all reactions were performed in flame-dried septum-sealed round bottom flasks under an atmosphere of argon. Solvents and reagents were transferred by means of syringes. Solvents were dried according to standard procedures. Reagents were used as purchased unless otherwise noted. (*S*)-Valinol[11] and the β-hydroxy-esters[8] **4a–c** were prepared according to known procedures. Flash chromatography was performed using silica gel 60 (Merck, 0.04–0.063 mm). ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 or 500 MHz using TMS or $CDCl_3$ as internal standard. The terms H^{major} and H^{minor} are used to assign distinguishable signals for the major and the minor diastereomer of diastereomeric mixtures. The ratio of enantiomers was determined by HPLC using a Daicel Chiracel OD14025 column. The diastereomeric ratio was determined either from ^{1}H NMR data or by HPLC (Machery-Nagel EC 250/4, Nucleosil 70-5, hexane/*i*-PrOH). The double bond isomers of the allyl vinyl ethers **1** were separated on gram scale by preparative HPLC (Nucleosil 50-7, 32×250 mm). IR spectra were recorded with a Nicolet 205 FT-IR spectrometer. Elemental Analyses were obtained with a EUROVECTOR EA3000.

8.1. General procedure A. Synthesis of 2-(1,3-oxazolin-2-yl)-substituted allyl vinyl ethers (1a–d)

An oven dried pressure tube with a threaded plug was equipped with a magnetic stirring bar and charged under an argon atmosphere with the β-hydroxy methyl ester **4a–d** (1 equiv.) and the amino alcohol **5** (2.5–5 equiv.). The pressure tube was sealed and heated for 24–48 h to 80°C (oil bath temperature). The excess of amino alcohol **5** was removed by Kugelrohr distillation and the residue was purified by flash chromatography (heptane/ethyl acetate 1/2).

An oven dried round bottom flask was equipped with a magnetic stirring bar, flushed with Argon and sealed with a rubber septum. The β-hydroxy amide (1 equiv.) was dissolved in CH_2Cl_2 (1 mL/mmol β-hydroxy amide) and the solution was cooled with an ice/water bath. Triethylamine (3.3 equiv.) and methanesulfonyl chloride (2.5 equiv.) were then added slowly. The reaction mixture was stirred for 20 min at rt and then quenched by the careful addition of sat. aqueous $NaHCO_3$ solution. The layers were separated and the aqueous phase extracted with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$ and then concentrated in vacuo. The crude bis(mesylate) was dissolved in CH_2Cl_2 (1 mL/mmol β-hydroxy amide) and triethylamine (3 equiv.) in a sealed tube under an argon atmosphere. The reaction mixture was heated for 50–110 h to 70°C until the starting material had disappeared (TLC-control) and then quenched with sat. aqueous $NaHCO_3$ solution. The layers were separated and the aqueous phase was extracted two times with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography heptane/ethyl acetate 1/1) to provide the mesylated 1,3-oxazolines.

To a cooled (ice bath) solution of the mesylated 1,3-oxazolines in THF (5 mL/mmol substrate) was added solid NaHMDS (2 equiv.). The mixture was warmed to rt and stirred until the starting material was consumed (TLC control). The reaction was quenched by the addition of saturated aqueous NH_4Cl solution. The phases were separated and the aqueous layer was extracted two times with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography (heptane/ethyl acetate 2/1) to provide the 2-(1,3-oxazolin-2-yl)-substituted allyl vinyl ethers **1** as a mixture of double bond isomers. The *E*/*Z* ratio may vary depending on the condition (partially hydrolyzed) of the solid NaHMDS.

8.1.1. (*E*)- and (*Z*)-4,4-Dimethyl-2-[1-(3-methyl-but-2-enyloxy)-propenyl]-4,5-dihydro-oxazoline (1a). According to the general procedure A, the β-hydroxy ester **4a** (3.28 g, 16.22 mmol) afforded **1a** (2.25 g, 10.12 mmol, 62%) as a *Z*:*E*=1:4 mixture of double bond isomers. The isomers were separated by HPLC (Nucleosil 70-5, 20×250 mm, 40 mL/min heptane/ethyl acetate 3/1). R_t(*Z*)=11 min, R_t(*E*)=12 min. *Z*-**1a**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.30 (s, 6H), 1.66 (s, 3H), 1.73 (s, 3H), 1.73 (d, 3H, *J*=7.0 Hz), 3.94 (s, 2H), 4.42 (d, 2H, *J*=7.25 Hz), 5.39–5.44 (m, 1H), 5.95 (q, 1H, *J*=7.0 Hz). ^{13}C NMR

($CDCl_3$, 75.5 MHz) δ 11.1, 18.0, 25.8, 28.3, 67.5, 68.2, 78.7, 120.3, 120.5, 137.9, 143.5, 158.9. IR (neat film) ν 2970, 2930, 2870, 1670 cm^{-1}. Anal. calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found C, 70.30; H, 9.88; N, 6.38. *E*-**1a**: ^1H NMR ($CDCl_3$, 500 MHz) δ 1.32 (s, 6H), 1.67 (s, 3H), 1.73 (s, 3H), 1.89 (d, 3H, J=7.6 Hz), 3.98 (s, 2H), 4.26 (d, 2H, J=6.6 Hz), 5.17 (q, 1H, J=7.4 Hz), 5.37–5.43 (m, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.6, 18.1, 25.8, 28.3, 65.3, 67.3, 78.5, 106.8, 119.9, 137.1, 143.8, 158.6. IR (neat film) ν 2930, 2890, 1650, 1620 cm^{-1}. Anal. calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found C, 69.89; H, 9.75; N, 6.61.

8.1.2. (*E*)- and (*Z*)-2-(1-Allyloxy-propenyl)-4,4-dimethyl-4,5-dihydro-oxazoline (1b). According to the general procedure A, the β-hydroxy ester **4b** (2.09 g, 11.97 mmol) afforded **1b** (0.81 g, 4.19 mmol, 35%) as a *Z*:*E*=1:4 mixture of double bond isomers. The isomers were separated by HPLC (Nucleosil 70-5, 20×250 mm, 40 mL/min heptane/ethyl acetate 3/1). $R_t(Z)$=14 min, $R_t(E)$=18 min. *Z*-**1b**: ^1H NMR (300 MHz, $CDCl_3$) δ 1.30 (s, 6H), 1.74 (d, 3H, J=7.1 Hz), 3.94 (s, 2H), 4.42 (dt, 2H, J_1=6.2, J_2=1.1 Hz), 5.14–5.33 (m, 2H), 5.92–6.07 (m, 2H). ^{13}C NMR (CDCl3, 75.5 MHz) δ 11.1, 15.9, 28.0, 28.3, 67.6, 72.9, 78.7, 118.0, 120.3, 134.1, 143.6, 158.7. IR (neat film) ν 2970, 2930, 1670, 1620, 1290 cm^{-1}. Anal. calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found C, 68.06; H, 9.09; N, 7.29. *E*-**1b**: ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (s, 6H), 1.79 (d, 3H, J=7.1 Hz), 3.89 (s, 2H), 4.20 (dt, 2H, J_1=4.6 Hz, J_2=1.4 Hz), 5.05–5.26 (m, 3H), 5.80–5.95 (m, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.5, 28.3, 67.3, 69.5, 78.5, 107.5, 117.8, 133.3, 143.5, 158.5. IR (neat film) ν 2970, 2930, 1650, 1370 cm^{-1}. Anal. calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found C, 67.73; H, 8.90; N, 7.00.

8.1.3. (1′*Z*2″*E*)- and (1′*E*,2″*E*)-2-(1′-Hex-2″-enyloxy-propenyl)-4,4-dimethyl-4,5-dihydro-oxazoline (*E*/*Z*,*E*-1c). According to the general procedure A, the β-hydroxy ester *E*-**4c** (2.56 g, 11.86 mmol) afforded **1c** (1.26 g, 5.28 mmol, 45%) as a *Z*:*E*=1:4 mixture of double bond isomers. The isomers were separated by HPLC (Nucleosil 70-5, 20×250 mm, 40 mL/min heptane/ethyl acetate 3/1). $R_t(Z)$=13 min, $R_t(E)$=14 min. *Z*,*E*-**1c**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.79 (t, 3H, J=7.5 Hz), 1.21 (s, 6H), 1.23–1.37 (m, 2H), 1.64 (d, 3H, J=7.1 Hz), 1.87–1.97 (m, 2H), 3.85 (s, 2H), 4.27 (d, 2H, J=5.5 Hz), 5.47–5.66 (m, 2H), 5.87 (q, 1H, J=7.0 Hz). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.2, 13.7, 22.1, 28.0, 28.2, 34.3, 67.5, 72.7, 78.6, 120.3, 125.7, 135.8, 143.4, 158.9. IR (neat film) ν 2894, 2930, 1624, 1668, 1364, 1350 cm^{-1}. Anal. calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found C, 70.96; H, 10.01; N, 6.09. *E*,*E*-**1c**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3H, J=7.3 Hz), 1.32 (s, 6H), 1.32–1.46 (m, 2H), 1.88 (d, 3H, J=7.1 Hz), 2.01 (q, 2H, J=6.9 Hz), 3.98 (s, 2H), 4.23 (d, 2H, J=5.8 Hz), 5.18 (q, 1H, J=7.2 Hz), 5.54–5.78 (m, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.6, 13.7, 22.1, 28.0, 28.3, 34.4, 67.3, 69.4, 78.4, 107.2, 124.9, 135.4, 143.6, 158.6. IR (neat film) ν 2930, 2890, 1650, 1620 cm^{-1}. Anal. calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found C, 71.20; H, 10.03; N, 6.19.

8.1.4. (1′*E*,2″*Z*)- and (1′*Z*,2″*Z*)-2-(1′-Hex-2″-enyloxy-propenyl)-4,4-dimethyl-4,5-dihydro-oxazoline (*E*/*Z*,*Z*-1c). According to the general procedure A, the β-hydroxy ester *Z*-**4c** (3.04 g, 14.07 mmol) afforded the allyl vinyl ether *Z*-**1c** (1.83 g, 7.74 mmol, 55%) as a *Z*:*E*=1:3 mixture of double bond isomers. The isomers were separated by HPLC (Nucleosil 70-5, 20×250 mm, 40 mL/min heptane/ethyl acetate 3/1). $R_t(Z)$=13 min, $R_t(E)$=14 min. *Z*,*Z*-**1c**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3H, J=7.3 Hz), 1.31 (s, 6H), 1.36 (td, 2H, J_1=14.8 Hz, J_2=7.4 Hz), 1.74 (d, 3H, J=7.1 Hz), 2.02 (q, 2H, J=6.8 Hz), 3.94 (s, 2H), 4.51 (d, 2H, J=5.5 Hz), 5.52–5.69 (m, 2H), 5.97 (q, 1H, J=7.1 Hz). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.2, 13.7, 22.7, 28.3, 29.6, 67.2, 67.6, 78.7, 120.4, 125.4, 134.2, 143.9, 159.5. IR (neat film) ν 2970, 2890, 1670, 1620 cm^{-1}. Anal. calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found C, 71.14; H, 9.74; N, 6.13. *E*,*Z*-**1c**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.75 (t, 3H, J=7.5 Hz), 1.19 (s, 6H), 1.25 (td, 2H, J_1=14.5 Hz, J_2=7.2 Hz,), 1.75 (d, 3H, J=7.5 Hz), 1.89 (q, 2H, J=7.2 Hz), 3.85 (s, 2H), 4.21 (d, 2H, J=4.6 Hz), 5.04 (q, 1H, J=7.4 Hz), 5.37–5.52 (m, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.5, 13.7, 22.6, 28.3, 29.7, 64.5, 67.3, 78.5, 107.2, 125.1, 133.5, 143.6, 161.1. IR (neat film) ν 2960, 2930, 2890, 2870, 1650 cm^{-1}. Anal. calcd for $C_{14}H_{23}NO_2$: C,70.85; H, 9.77; N, 5.90. Found C, 71.03; H, 9.75; N, 6.19.

8.1.5. (*E*,*S*)- and (*Z*,*S*)-4-Isopropyl-2-[1-(3-methyl-but-2-enyloxy)-propenyl]-4,5-dihydro-oxazoline (1d). According to the general procedure A, the β-hydroxy ester **4a** (1.8 g, 8.9 mmol) afforded the allyl vinyl ether **1d** (0.84 g, 3.54 mmol, 40%) as a *Z*:*E*=1:3 mixture of double bond isomers. The isomers were separated by HPLC (Nucleosil 50-7, 20×250 mm, 40 mL/min heptane/ethyl acetate 3/1). $R_t(Z)$=9 min, $R_t(E)$=10 min. *Z*-**1d**: ^1H NMR ($CDCl_3$, 500 MHz) δ 0.88 (d, 3H, J=6.6 Hz), 0.97 (d, 3H, J=6.6 Hz), 1.68 (s, 3H), 1.74 (s, 3H), 1.74 (d, 3H, J=7.2 Hz), 1.80 (dt, 1H, J_1=6.7 Hz, J_2=13.1 Hz), 3.95–4.04 (m, 2H), 4.2–4.27 (m, 1H), 4.34–4.49 (m, 2H), 5.42–5.47 (m, 1H), 5.95 (q, 1H, J=7.1 Hz). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 11.1, 18.0, 18.1, 18.9, 25.8, 32.7, 68.3, 69.6, 72.5, 120.3, 120.4, 138.0, 143.6, 160.2. IR (neat film) ν 2960, 2930, 2890, 2360, 1670 cm^{-1}. Anal. calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found C, 71.20; H, 9.9; N, 5.86. *E*-**1d**: ^1H NMR ($CDCl_3$, 500 MHz) δ 0.89 (d, 3H, J=6.6 Hz), 0.99 (d, 3H, J=6.6 Hz), 1.66 (s, 3H), 1.73 (s, 3H), 1.80 (dt, 1H, J_1=6.7 Hz, J_2=13.1 Hz), 1.91 (d, 3H, J=7.2 Hz), 3.97–4.05 (m, 2H), 4.2–4.32 (m, 3H), 5.18 (q, 1H, J=7.3 Hz), 5.38–5.43 (m, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.7, 18.2, 19.0, 25.8, 32.7, 65.4, 69.5, 72.5, 106.9, 119.8, 137.3, 143.8, 159.9. IR (neat film) ν 2960, 2920, 2870, 2360, 1650 cm^{-1}. Anal. calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found C, 71.01; H, 9.85; N, 6.02.

8.2. General procedure B for the Cu^{II} bis(oxazoline)-catalyzed Claisen rearrangement

The reaction was performed in an oven dried, Argon flushed and septum sealed 10 mL round bottom flask equipped with a magnetic stirring bar. BOX and $Cu(OTf)_2$ were weighted under a non-inert atmosphere. The bis(oxazoline) ligand (6–12 mol%) was dissolved in CH_2Cl_2 (5 mL/mmol allyl vinyl ether). Solid copper(II) triflate (5–12 mol%) was added and the mixture was stirred for 1 h. The homogenous mixture was colored between light green and dark green, sometimes blue, depending on the ligand utilized. If

appropriate, molecular sieves 3 Å (1 g/mmol allyl vinyl ether) may be added at this point. A solution of the allyl vinyl ether **1** (0.4 mmol) in CH_2Cl_2 (5 mL/mmol) was then added. The reaction mixture was stirred at ambient temperature until TLC indicated complete consumption of the starting material. The reaction mixture was diluted with heptane/ethyl acetate 10/1 (5 mL) and then filtered through a 0.5×3 cm silica gel column. The organic solvents were then removed in vacuo to provide the rearrangement product as a colorless to light yellow oil.

8.2.1. (2*R*)- and (2*S*)-1-(4′,4′-Dimethyl-4′,5′-dihydro-oxazol-2′-yl)-2,3,3-trimethyl-pent-4-en-1-one (6a). According to the general procedure B, $Cu(OTf)_2$ (5 mol%, 6.98 mg, 0.019 mmol), (*R*)-(+)-2,2′-isopropylidene-bis(4-phenyl-2-oxazoline) (*R*,*R*)-**7** (6 mol%, 7.75 mg, 0.023 mol) and the allyl vinyl ether *E*-**1a** (86.1 mg, 0.4 mmol) afforded **6a** (70.5 mg, 0.32 mmol, 82%). HPLC: (Daicel OD 14025, 0.46×25 cm, hexane/*i*PrOH 98/2) R_t(2*S*-**7a**)=4.6 min, R_t(2*R*-**7a**)=5.3 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88–0.93 (m, 9H), 1.21 (s, 6H), 3.49 (q, 1H, J=7.0 Hz), 3.92 (s, 2H), 4.74–4.84 (m, 2H), 5.75 (dd, 1H, J_1=10.7 Hz, J_2=17.2 Hz). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.0, 23.7, 24.3, 27.8, 27.9, 39.8, 49.0, 68.5, 79.6, 111.9, 145.8, 159.2, 197.1. IR (neat film) ν 2970, 2940, 1740, 1710 cm^{-1}. Anal. calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found C, 70.39; H, 9.62; N, 5.92.

8.2.2. (2*R*)- and (2*S*)-1-(4′,4′-Dimethyl-4′,5′-dihydro-oxazol-2′-yl)-2-methyl-pent-4-en-1-one (6b). According to the general procedure B, $Cu(OTf)_2$ (10 mol%, 7.23 mg, 0.02 mmol), (*R*)-(+)-2,2′-isopropylidene-bis(4-phenyl-2-oxazoline) (*R*,*R*)-**7** (12 mol%, 8.03 mg, 0.024 mol), 200 mg 3 Å mole sieves and the allyl vinyl ether *Z*-**1b** (39.2 mg, 0.2 mmol) afforded a mixture (37.9 mg, not separated) of **6b** (23%) and *Z*-**1b** (77%). HPLC (Nucleosil 70-5, 0.46×25 cm, hexane/*i*PrOH 99/1): R_t(2*S*-**6b**)=6.5 min, R_t(2*R*-**6b**)=7.0 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (d, 3H, J=6.8 Hz), 1.35 (s, 6H), 2.32 (tdd, 2H, J_1=7.2 Hz, J_2=14.2 Hz, J_3=89.5 Hz), 3.50 (tq, 1H, J_1=J_2=6.9 Hz), 4.07 (s, 2H), 4.97–5.08 (m, 2H), 5.65–5.81 (m, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 15.9, 28.0, 36.8, 42.1, 68.6, 79.4, 117.1, 135.1, 157.7, 196.3. IR (neat film) ν 2960–2870, 1670, 1630 cm^{-1}. Anal. calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found C, 68.73; H, 7.90; N, 7.00.

8.2.3. (2*R,3*S**)-1-(4′,4′-Dimethyl-4′,5′-dihydro-oxazol-2′-yl)-2-methyl-3-propyl-pent-4-en-1-one (*syn*-6c).** According to the general procedure B, $Cu(OTf)_2$ (10 mol%, 6.48 mg, 0.018 mmol) and the allyl vinyl ether *Z*,*Z*-**1c** (42.5 mg, 0.18 mmol) afforded *syn*-**6c** (37 mg, 0.16 mmol, 87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, 3H, J=7.1 Hz), 1.11 (d, 3H, J=7.1 Hz), 1.14–1.5 (m, 4H), 1.34 (s, 3H), 2.24–2.37 (m, 1H), 3.52 (dt, J_1=14.5 Hz, J_2=7.2 Hz), 4.05 (s, 2H), 4.91–5.01 (m, 2H), 5.54–5.64 (m, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.7, 13.9, 20.1, 20.4, 27.9, 28.0, 33.1, 46.1, 46.8, 68.5, 79.4, 116.2, 139.8, 158.4, 196.9. IR (neat film) ν 2960, 1710, 1630, 1460 cm^{-1}. Anal. calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found C, 70.70; H, 9.55; N, 5.71.

8.2.4. (2*R,3*R**)-1-(4,4-Dimethyl-4,5-dihydro-oxazol-2-yl)-2-methyl-3-propyl-pent-4-en-1-one (*anti*-6c).** According to the general procedure B, $Cu(OTf)_2$ (10 mol%, 14.47 mg, 0.04 mmol), 400 mg 3 Å mol sieves and the allyl vinyl ether *E*,*Z*-**1c** (94.1 mg, 0.4 mmol) afforded *anti*-**6c** (85 mg isolated, 68% *anti*-**6c**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76 (t, 3H, J=7.0 Hz), 0.96 (d, 3H, J=7.1 Hz), 1.14–1.25 (m, 4H), 1.27 (s, 3H), 1.27 (s, 3H), 2.32–2.46 (m, 1H), 3.33 (dt, 1H, J_1=14.5 Hz, J_2=7.2 Hz), 3.98 (s, 2H), 4.83–4.99 (m, 2H), 5.37 (dt, 1H, J_1=17.0 Hz, J_2=9.8 Hz). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.7, 13.8, 20.4, 28.0, 35.0, 46.2, 46.3, 68.6, 79.4, 116.9, 138.9, 158.2, 196.8. IR (neat film) ν 2970, 1710, 1630, 1470 cm^{-1}. Anal. calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found C, 70.75; H, 9.55; N, 6.04.

8.2.5. (2*R,4′*S*)-1-(4′-Isopropyl-4′,5′-dihydro-oxazol-2′-yl)-2,3,3-trimethyl-pent-4-en-1-one (6d).** According to the general procedure B, $Cu(OTf)_2$ (5 mol%, 7.23 mg, 0.02 mmol), (*R*)-(+)-2,2′-isopropylidene-bis(4-phenyl-2-oxazoline) (*R*)-**7** (6 mol%, 8.02 mg, 0.024 mol) and the allyl vinyl ether *Z*-**1d** (94 mg, 0.4 mmol) afforded **6d** (87.2 mg, 0.37 mmol, 93%). HPLC: (Nucleosil 70-5, 0.46×25 cm, hexane/*i*PrOH 99/1) R_t(2*R*,4′*S*-**7d**)=3.6 min, R_t(2*S*,4′*S*-**7d**)=3.9 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87–1.10 (m, 9H), 1.86 (td, 1H, J_1=13.2 Hz, J_2=6.7 Hz), 3.64 (q, 1H^{syn}, J=7.0 Hz), 3.69 (q, 1H^{anti}, J=7.0 Hz), 4.05–4.18 (m, 2H), 4.29–4.44 (m, 1H), 4.89–4.99 (m, 2H), 5.86 (dd, 1H^{syn}, J_1=10.9 Hz, J_3=3.4 Hz), 5.92 (dd, 1H^{anti}, J_1=11.0 Hz, J_2=3.5 Hz). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.2, 12.4, 18.8, 18.3, 18.8, 24.0, 24.1, 24.2, 24.3, 32.3, 32.5, 39.7, 39.8, 48.8, 49.1, 70.7, 70.9, 72.9, 73.0, 111.9, 112.0, 145.8, 160.3, 160.7, 196.8. IR (neat film) ν 2970, 2930, 2880, 1710, 1690 cm^{-1}. Anal. calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found C, 70.71; H, 10.07; N, 5.51.

8.3. General procedure C. Assignment of the absolute configuration

The diastereomeric mixture of (2*R**,4′*S*)-1-(4′-isopropyl-4′,5′-dihydro-oxazol-2′-yl)-2,3,3-trimethyl-pent-4-en-1-one (**6d**) was dissolved in 3N aqueous H_2SO_4 and acetonitrile. The reaction mixture was stirred for 48 h at ambient temperature. The mixture was then extracted three times with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The crude product was dissolved in 2 mL CH_2Cl_2, DMAP (0.5 equiv.), isopropanol (2 equiv.) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC, 1.1 equiv.) were added successively. The mixture was stirred over night at ambient temperature and then diluted with H_2O. The layers were separated and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were concentrated in vacuo. The crude product mixture was purified by flash chromatography (heptane/ethyl acetate 5/1) to afford the known 3,4,4-trimethyl-2-oxo-hex-5-enoic acid propyl ester **9**. The absolute configuration was assigned by comparison of the data from chiral HPLC.

8.3.1. 3,4,4-Trimethyl-2-oxo-hex-5-enoic acid propyl ester (7). According to procedure C, a 66:34 enantiomeric mixture of **6a** (60.2 mg, 0.25 mmol) generated by the [Cu{(*R*,*R*)-Ph-box}](OTf)$_2$ catalyzed Claisen rearrangement of (*Z*)-**1a** afforded 3,4,4-trimethyl-2-oxo-hex-5-enoic

acid propyl ester **7** (41.8 mg, 0.2 mmol, 52%, (3*S*):(3*R*)=65:35). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (s, 3H), 1.05 (s, 3H), 1.07 (d, 3H, J=7.1 Hz), 1.32 (d, 6H, J=6.2 Hz), 1.35 (d, 6H, J=6.2 Hz), 3.46 (q, 1H, J=7.0 Hz), 4.96 (dd, 1 H, J_1=17.4, J_2=1.1 Hz), 4.97 (dd, 1H, J_1=10.9, J_2=1.1 Hz), 5.10 (sept, 1H, J=6.3 Hz), 5.86 (dd, 1H, J_1=17.2 Hz, J_2=10.7 Hz). HPLC: (Daicel OD 14025, 0.46×25 cm, hexane/*i*PrOH 99.9/0.1) R_t(3*S*)=5.7 min, R_t(3*R*)=6.5 min.

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