Electrogenerated Chiral 4-Methoxy-2-oxazolidinones as Diastereoselective Amidoalkylation Reagents for the Synthesis of β-Amino Alcohol Precursors

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A flexible and efficient synthesis of enantiomerically pure 4,5-substituted 2-oxazolidinones – important target molecules as precursors of pharmacologically active 2-oxazolidinones, β-amino alcohols, β-blockers and azasugar derivatives – is described. As starting materials, the enantiopure storage forms of chiral *N*-acyliminium ions (4*RS*,5*S*)-5-chloromethyl-4-methoxy-1,3-oxazolidin-2-one (**2**) and (4*RS*,5*R*)-4-methoxy-5-methyl-1,3-oxazolidin-2-one (**3**) were used; these are readily available from the chiral pool with the aid of electrochemical transformations. Substitution of the 4-methoxy group in building blocks **2** and **3** with a large variety of organometallic nucleophiles resulted in the *trans*-diastereoselective formation of enantiopure 4,5-disubstituted 2-oxazolidinones, with a high degree of flexibility in the substituent at the 4-position.

Introduction

Enantiomerically pure 4,5-disubstituted 2-oxazolidinones are important target molecules in organic synthesis because of their pharmacological properties. This is not only true of the oxazolidinones themselves, which can act as antibiotics against highly resistant Gram-positive bacteria,[1] but even more of β-amino alcohols, which can be obtained from 2-oxazolidinones by basic hydrolysis. The β-amino alcohol subunit is an important structural element in a number of different enzyme inhibitors[2] and β-blockers.[3] In addition, ring-annulated 2-oxazolidinones are precursors of azasugar structures,[4] which can act as glycosidase inhibitors.[5]

For these reasons, many publications deal with the use of chiral oxazolidinones[6] in organic synthesis, especially for the formation of chiral β-amino alcohols.[7] Important strategies for their synthesis make use, for example, of amino acids,[8] amino aldehydes, amino ketones[9] or cyclic sulfates[10] as starting materials. However, most of these methods are not very flexible in the choice of substituents allowed.

It was therefore our goal to develop a strategy for a very flexible and efficient synthesis of a whole class of enantiomerically pure 2-oxazolidinones, with scope for a large structural variety of functionalities in the 4- and 5-positions, starting from readily available building blocks.

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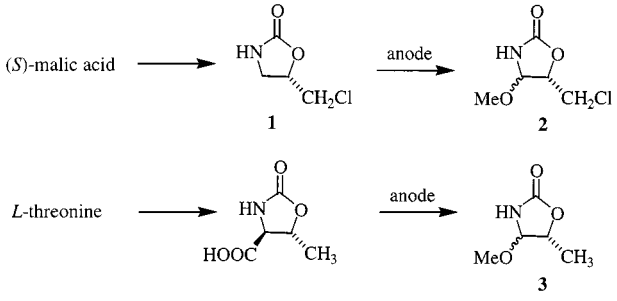
We accomplished this goal by the use of (4*RS*,5*S*)- or (4*RS*,5*R*)-5-chloromethyl-4-methoxy-2-oxazolidinone (**2**) and (4*RS*,5*R*)- or (4*RS*,5*S*)-4-methoxy-5-methyl-2-oxazolidinone (**3**) as chiral building blocks. Compounds **2** and **3** are readily available from the chiral pool,[11,12] through use of electrochemical transformations as the key steps, as we have described elsewhere. (Scheme 1)



Scheme 1. Electrochemical key step in the synthesis of 2 and 3

The oxazolidinones **2** and **3** are chiral *N*,*O*-acetals, which can be used as stable precursors of chiral *N*-acyliminium ions. They are established as valuable amidoalkylation reagents.[13] Starting from the *N*,*O*-acetals **2** and **3**, the *N*-acyliminium cations are generated in situ and can react with a variety of nucleophiles with good to excellent *trans* diastereoselectivities.[4,12,14] When oxazolidinone **2** is used, further functionalization though the chloromethyl group in the 5-position is possible.

In this publication we demonstrate the application of the chiral *N*,*O*-acetals **2** and **3** as flexible amidoalkylation reagents with different types of organometallic nucleophiles. A broad variety of substituents can be introduced into the 4-position of the oxazolidinones with good to excellent *trans* selectivities. This route produces a large variety of

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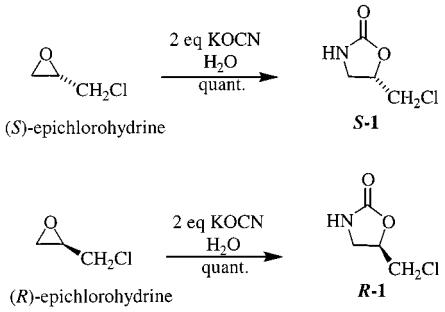
enantiomerically pure 4,5-substituted β-amino alcohol precursors.

Results and Discussion

One step in our previously described synthesis of enantiopure **1** occurred with an unsatisfactory yield of 50%.

We avoided this problem by starting with chiral epichlorohydrin, which is commercially available in both enantiomerically pure forms. This starting material can be transformed in one step into the respective enantiomer of 5-chloromethyl-2-oxazolidinone (**1**), in nearly quantitative yield, using potassium cyanate as nucleophile for the opening of the epoxide (Scheme 2). The products can be isolated and used in further reactions without purification.

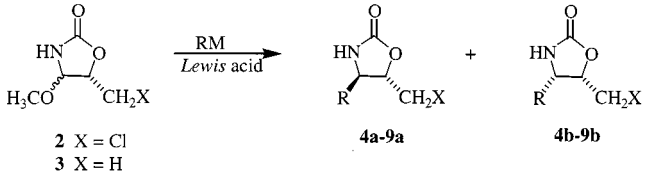


Scheme 2. Alternative sequence forming compound *S*-**1** or *R*-**1**

This synthesis has been described previously for racemic 5-chloromethyl-2-oxazolidinone *rac*-(**1**), starting from racemic epichlorohydrin.[15]

The stereospecific course of the epoxide transformation was demonstrated by determination of the enantiomeric purity of the products by means of chiral NMR shift experiments and by comparison of the optical rotations of the reaction products with literature data.[11a]

Oxazolidinones **2** and **3**, generated by anodic methoxylation as we described earlier,[16] have been intensively studied as chiral precursors of *N*-acyliminium ions, using different organometallic nucleophiles in the presence of Lewis acids. Under these conditions, it is possible to introduce different substituents into the 4-position of the oxazolidinones by means of an amidoalkylation reaction, with replacement of the 4-methoxy group (Scheme 3).



Scheme 3. Nucleophilic exchange reaction

These nucleophilic substitutions proceed with high *trans* selectivity, induced by the substituents in the 5-position of the oxazolidinone. The relative configurations of the synthesized products were determined with the aid of nuclear Overhauser effects or, in the case of known compounds, by comparison of coupling constants.

As we have shown elsewhere, organocopper reagents are able to react with oxazolidinones **2** and **3** under $BF_3{\cdot}OEt_2$ catalysis conditions.[12,14] The best results are obtained by the use of higher order cuprates, which permit the introduction of a phenyl group in 62% yield and with 92% *ds* (Table 1, entry 1) and of an *n*-butyl group in 59% yield and with 95% *ds* (Table 1, entry 2).

Table 1. Reactions between **2** and organocopper reagents

product	nucleophile	R	isolated yield (%)	*ds* for **4a** − **5a** (%)
4ab	Ph_3Cu_2Li	Ph	62	92
5ab	nBu_3Cu_2Li	*n*Bu	59	95
5ab	*n*BuCu/BF_3	*n*Bu	52	88

One disadvantage is the fact that only one of the three alkyl groups of the organocopper reagent can be transferred. From this point of view, the use of RCu·DMS complexes as reported by Wistrand et al. is more economical,[17] but − as shown for the example of the *n*-butyl copper DMS complex − the yield and diastereoselectivity are not as high (Table 1, entry 3).

Grignard reagents are well-known as good nucleophiles.[18] They are convenient to handle and many reagents are commercially available. To determine the scope of the applicability of Grignard reagents in amidoalkylations with oxazolidinone **2,** three electronically different nucleophiles were chosen.

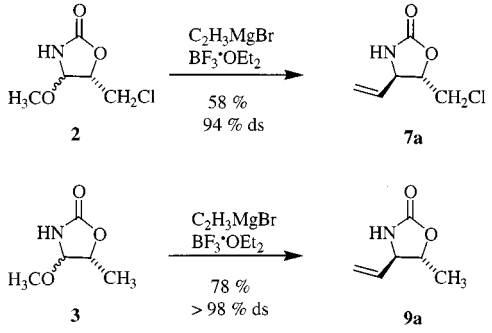
Under $BF_3{\cdot}OEt_2$ catalysis conditions, the reactive phenyl Grignard reagent reacted to give oxazolidinones **14ab** in good yield (Table 2, entry 1). Similarly, the *n*-butyl and allyl Grignard reagents, which are known to be less reactive, also give good yields (Table 2, entries 2,3 and 5). Introduction of the phenyl and the *n*-butyl group by this method proceeds with high *trans* selectivity, but the allyl Grignard surprisingly displays lower diastereoselectivity.

Table 2. Reactions between **2** and **3** and Grignard reagents

starting material	product	nucleophile	R	isolated yield (%)	ds for **4a** - **9a** (%)
2	**4ab**	PhMgBr	Ph	64	96
2	**5ab**	*n*BuMgCl	*n*Bu	64	95
2	**6ab**		allyl	66	82
2	**7ab**		vinyl	58	94
3	**8ab**		allyl	67	80
3	**9a**		vinyl	78	> 98

The use of Grignard reagents also makes it possible to introduce the vinyl function into the 4-position of the ox-

azolidinone with very good diastereoselectivity and in good yield (Scheme 4). This thus establishes an easy way to obtain derivatives of vinyl glycine.

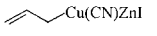


Scheme 4. Synthesis of derivatives of vinylglycine

Many organocopper reagents are prepared from the corresponding magnesium or lithium organometallics. Unfortunately, this approach is not compatible with the presence of most functional groups. However, copper zinc organometallics of the RCu(CN)ZnX type can be prepared from organozinc reagents by performing a transmetallation using the soluble copper salt CuCN·2LiCl as reported by Knochel.[19] Since organozinc reagents tolerate a wide range of functionalities, this method offers general access to polyfunctional reagents.

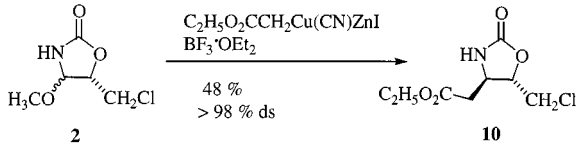
Aliphatic organozincs may conveniently be obtained by the direct insertion of activated zinc (dust) into alkyl iodides in THF. It is thus possible to introduce the *n*-butyl and the allyl group into the 4-position of the oxazolidinone in good yields and with very good diastereoselectivities, starting from *n*-butyl iodide or from allyl iodide (Table 3, entries 2−3).

Table 3. Reactions between **2** and copper zinc reagents

product	nucleophile	R	isolated yield (%)	ds for **4a** - **6a** (%)
4ab	PhCu(CN)ZnI	Ph	72	95
5ab	*n*BuCu(CN)ZnI	*n*Bu	57	98
6ab		allyl	62	94

Aryl halides do not readily undergo a zinc insertion in THF, but they may be prepared by a lithium-iodine exchange reaction.[19] Using this method, it is possible to form the 4-phenyl-substituted oxazolidinone **4a** in 72% yield and with 95% *ds* (Table 3, entry 1).

In order to introduce functionalized alkyl groups, we generated a copper-zinc reagent starting from ICH_2COOEt. The reagent was obtained by insertion of zinc into the alkyl-iodine bond. The desired product **10** was obtained in 48% yield and with excellent diastereoselectivity (Scheme 5). We thus established easy access to derivatives of β-amino acids in one step.



Scheme 5. Synthesis of β-amino acid derivatives with Knochel reagent

Another way to obtain β-amino acid derivatives is based on the Reformatsky reaction. Other Reformatsky reactions with *N*-acyliminium ions and *N*-acylimines have already been described.[20] Accordingly, oxazolidinone **2** was treated with $BrCH_2COOEt$ in the presence of activated zinc, with catalysis using TMSCl and $BF_3{\cdot}OEt_2$. Again, the diastereoselectivity was excellent and the yield was similar to that in the case of the copper zinc organometallics. This approach to compound **10** is easier than the use of copper zinc organometallics but not as flexible.

A comparison between the different organometallic nucleophiles with respect to their reaction with the oxazolidinone **2** is given in Table 4.

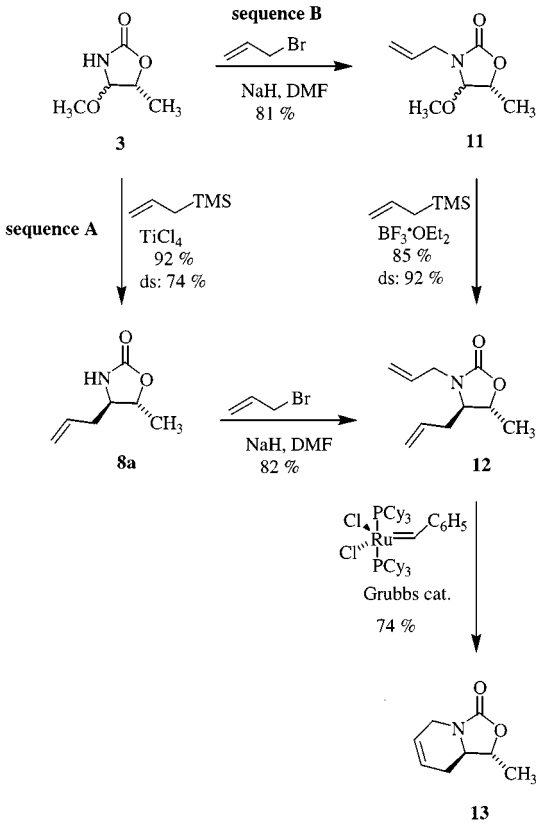
Table 4. Comparison of the different nucleophiles in amidoalkylation reactions with **2**

type of reagent	R = phenyl, **4a**		R = *n*-butyl, **5a**		R = allyl, **6a**	
	yield (%)	*ds* (%)	yield (%)	*ds* (%)	yield (%)	*ds* (%)
R_3Cu_2Li	62	92	59	95		
RCu/BF_3			52	88		
RMgX	64	96	64	95	66	82
RCu(CN)ZnI	72	95	57	98	62	94

Several trends in yield and stereoselectivity are obvious. Higher order cuprates give good results. Unfortunately, they are not very economical, as only one of the three alkyl groups is transferred. Wistrand cuprates are more effective, but the yields and selectivities are lower. Use of copper zinc organometallics enables good yields and very good diastereoselectivities to be achieved. These reagents can also be used to introduce substituents with functional groups into the 4-position of the oxazolidinones **2** and **3**. In general, Grignard reagents work quite well, many of them are commercially available and they are quite easy to handle. In the case of the allyl Grignard, however, the diastereoselectivity is surprisingly lower.

4-Substituted oxazolidinones are excellent starting materials for construction of bicyclic piperidine structures using the ring-closing metathesis (RCM) strategy or the Heck reaction. It is thus possible to produce precursors for azasugar structures, which play an important role as inhibitors of glycosidases.[21]

The metathesis reaction is widely used in ring constructions, especially for pharmacologically important compounds such as epothilone.[22] Grubbs'[23] catalyst (see



Scheme 6. Metathesis reaction

Scheme 6) shows the best results.[24] We used this RCM approach starting from oxazolidinone **3** to synthesize compound **13** (Scheme 6).

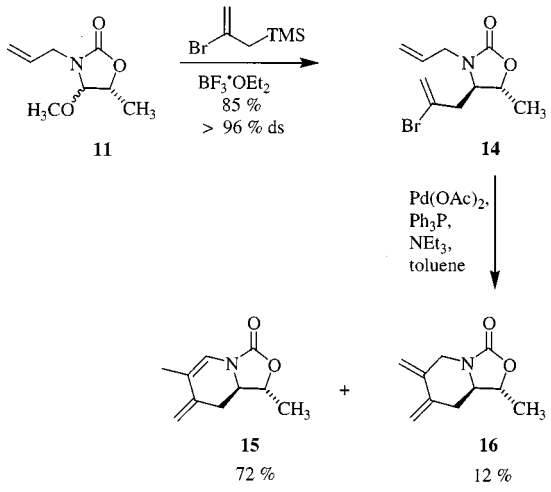
It is first necessary to synthesize compound **12**. We therefore introduced the allyl group into the 4-position of the oxazolidinone by amidoalkylation with allyltrimethylsilane as we have described elsewhere,[12] followed by *N*-alkylation (Scheme 6, sequence A). Inversion of the reaction sequence − *N*-alkylation in the first step and amidoalkylation in the second − resulted in a decisive increase in the diastereoselectivity of the amidoalkylation (sequence B).

Cyclization took place with the aid of Grubbs' catalyst, and **13** was obtained in 74% yield.[25]

Another route to piperidine structures uses the Heck reaction.[26] The reaction sequence is shown in Scheme 7. Starting once more from the *N*-alkylated oxazolidinone **11**, a diastereoselective amidoalkylation reaction was used to synthesize **14**. In this case, 2-bromo trimethylallylsilane was the nucleophile. Subsequent Heck reaction in the presence of triethylamine and palladium acetate resulted in the formation of compounds **15** and **16** (Scheme 7).

Conclusion

In conclusion, we have demonstrated that the readily available enantiopure 4-methoxy-2-oxazolidinones **2** and **3** are very effective chiral amidoalkylation reagents, which can be substituted in the 4-position with good to excellent *trans* selectivities by the use of organometallic nucleophiles



Scheme 7. Heck reaction

in an extremely flexible way. We have thus established a method that allows a broad variety of substituents to be introduced diastereoselectively into the 4-position of 2-oxazolidinones. This is a prerequisite for targeted syntheses of biologically active β-amino alcohol derivatives or azasugar precursors based on chiral oxazolidinones **2** and **3**.

Experimental Section

General Methods: Nuclear magnetic resonance (^{1}H NMR) spectra were determined in the reported solvent using Bruker AC 200 (200 MHz), Bruker WM 250 (250 MHz) and Bruker AC 400 (400 MHz) spectrometers. The same instruments were also used for the measurement of ^{13}C spectra (50.3 MHz; 62.9 MHz; 100.6 MHz). Chemical shifts are given in ppm downfield from tetramethylsilane. − R_f values were obtained by thin layer chromatography (TLC) on aluminium sheets coated with silica gel (Merck silica gel F_{254}). − Optical rotations were measured with a Perkin−Elmer P241 machine. − Elemental analyses were performed by the central service of our Institute. Melting points are uncorrected. All solvents were dried before use. − The relative configurations were determined by comparison of ^{1}H NMR coupling constants with those of known compounds and by measurement of difference NOE spectra.

Compound ***S*-2** was obtained in 76% yield by anodic oxidation of ***S*-1** according to the previously described method.[11b,12] Compound **3** was prepared starting from L-threonine, by cyclization to oxazolidinone followed by electrochemical methoxylative decarboxylation.[12]

(*S*)- and (*R*)-5-Chloromethyl-1,3-oxazolidin-2-one (1): In an alternative to the previously described procedure,[11a] potassium cyanate (0.81 g, 10 mmol) was dissolved in water (40 mL) and epichlorohydrin (0.46 g) was slowly added. The solution was refluxed for 15 h and cooled to room temp. The reaction mixture was extracted with ethyl acetate until no product remained in the water phase. The organic phase was dried with sodium sulfate and concentrated in vacuo. The crude product was used for further transformations. For analytical purposes, the product was purified by flash chromatography on silica gel (ethyl acetate/cyclohexane 2:1), resulting in 0.68 g (100%) of **1** as a colourless solid. − R_f = 0.20 (ethyl acetate/cyclohexane, 2:1); m.p. 65 °C.

Compound *S*-1: $[\alpha]_D^{20} = +18$ ($c = 2$, dichloromethane). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.52 (ddd, $J = 9.1, 5.5, 1.3$ Hz, 1 H), 3.68 (d, $J = 6.1$ Hz, 2 H), 3.75 (dd, $J = 9.1, 9.1$ Hz, 1 H), 4.76–4.92 (m, 1 H), 6.13 (br, NH, 1 H). – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 43.6, 44.5, 74.7, 159.2. – MS (70 eV, EI): *m*/*z* = 135 (13.44) [M^+], 86 (100), 42 (45), 36 (11). – HRMS calcd. for $C_4H_6ClNO_2$ [M^+]: 135.0087, found 135.0081. – $C_4H_6ClNO_2$ (135.0): calcd. C 35.44, H 4.46, N 10.33; found C 35.60, H 4.57, N 10.38.

Compound *R*-1: $[\alpha]_D^{20} = -18$ ($c = 3$, dichloromethane).

Nucleophilic Exchange with Organocopper Reagents of R_3Cu_2Li Stoichiometry. – General Procedure I: In a dry Schlenk tube, the organolithium compound was added to a suspension of CuI in dry THF at −50 °C under argon atmosphere. After stirring for 15 min at this temperature, the reaction mixture was cooled to −78 °C and $BF_3{\cdot}OEt_2$ was added slowly. The mixture was stirred for 5 min and **2** was added as a solution in dry THF. The mixture was stirred for several hours and heated to room temp. The mixture was extracted three times with 30 mL conc. NH_3/aq. NH_4Cl (1:1) until a clear solution was formed. The organic phase was dried with sodium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (ethyl acetate/cyclohexane).

Nucleophilic Exchange with Organocopper Reagents of RCu/BF_3 Stoichiometry. – General Procedure II: In a dry Schlenk tube, $Cu^IBr{\cdot}DMS$ was suspended in dry diethyl ether under argon atmosphere and cooled to −40 °C. The organolithium compound was added slowly at the same temperature and the reaction mixture was stirred for 30 min. After the mixture had been cooled to −78 °C, $BF_3{\cdot}OEt_2$ was added dropwise. The reaction mixture was stirred for 5 min and oxaxolidinone **2** in dry diethyl ether was added. The mixture was stirred for several hours and heated to room temp. The reaction mixture was quenched by the addition of 30 mL conc. NH_3/aq. NH_4Cl (1:1) and the solids were filtered off. The water phase was extracted three times with diethyl ether and the combined organic phases were dried with sodium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (ethyl acetate/cyclohexane).

Nucleophilic Exchange with Grignard Reagents. – General Procedure III: The Grignard compound was dissolved in dry THF and cooled to −78 °C in a dry Schlenk tube under argon atmosphere. $BF_3{\cdot}OEt_2$ was slowly added at the same temperature, and the reaction mixture was stirred for 10 min. Oxazolidinone **2** or **3**, dissolved in dry THF, was added slowly and the reaction mixture was stirred for 15 h at −78 °C. After heating to room temp., the reaction was stopped by the addition of a conc. aq. $NaHCO_3$ solution and the solids were filtered off. The phases were separated and the water phase was extracted three times with diethyl ether. The combined organic phases were dried with sodium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (ethyl acetate/cyclohexane).

Nucleophilic Exchange with Alkyl Copper Zinc Reagents. – General Procedure IV: Zinc powder was suspended in dry THF (1 mL) in a dry Schlenk tube under argon atmosphere, and 1,2-dibromoethane was added. The suspension was heated to 65 °C for 1 min and cooled to room temp. TMSCl was then added dropwise and the suspension was stirred for 15 min. The alkyl iodide, in dry THF (4 mL), was added slowly and the reaction mixture was stirred for 4 h at room temp. In a second dry Schlenk tube, dry lithium chloride and dry copper(I) cyanide were dissolved in dry THF (11 mL) and cooled to −20 °C. The organozinc compound was slowly added at this temperature and the reaction mixture was stirred for 5 min. The solution was cooled to −78 °C and $BF_3{\cdot}OEt_2$ was added. After the mixture had been stirred for 5 min, oxazolidinone **2** or **3** in dry THF (5 mL) was added. After stirring for 15 h at this temperature, the mixture was heated to room temp., the reaction was stopped by addition of 30 mL conc. NH_3/aq. NH_4Cl (1:1) and the solids were filtered off. The water phase was extracted three times with diethyl ether, while the combined organic phases were washed with 30 mL conc. NH_3/NH_4Cl (1:1), dried with sodium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (ethyl acetate/cyclohexane).

Nucleophilic Exchange with Aryl Copper Zinc Reagents. – General Procedure V: The aryl iodide was dissolved in dry THF (6 mL) in a dry Schlenk tube under argon atmosphere and cooled to −100 °C. *n*-Butyllithium was added dropwise at the same temperature, and the solution was stirred for 3 min. A solution of dry zinc iodide (dried for 1 h at 140 °C) in dry THF (2.5 mL) was added and the reaction mixture was stirred for 5 min. A solution of lithium chloride and copper(I) cyanide in dry THF (5 mL) was added, the reaction mixture was heated to −60 °C and the solution was stirred for 5 min. After the mixture had been cooled to −78 °C, $BF_3{\cdot}OEt_2$ was added. After the mixture had been stirred for 5 min the oxazolidinone **2** in dry THF (5 mL) was added. After stirring for 15 h at this temperature, the solution was heated to room temp., the mixture was quenched by the addition of 30 mL conc. NH_3/aq. NH_4Cl (1:1) and the solids were filtered off. The water phase was extracted three times with diethyl ether, while the combined organic phases were washed with 30 mL conc. NH_3/NH_4Cl (1:1), dried with sodium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (ethyl acetate/cyclohexane).

(4*R*,5*S*)-5-Chloromethyl-4-phenyl-1,3-oxazolidin-2-one (4a): General procedure I was used. Oxazolidinone **2** (0.5 g, 3 mmol) was treated with CuI (3.43 g, 18 mmol), phenyllithium in cyclohexane/diethyl ether (1.8 M, 15 mL 27 mmol) and $BF_3{\cdot}OEt_2$ (0.4 mL, 3 mmol) in 40 mL of THF. The reaction was complete after 10 h. Purification of the crude product on silica gel (1. ethyl acetate/cyclohexane 1:5; 2. ethyl acetate) resulted in 0.39 g (62%) of **4a** as a colourless solid. The (4*R*,5*S*) product ***trans*-4a** was obtained in 92% *ds*.

General procedure III was also used. Oxazolidinone **2** (0.1 g, 0.6 mmol) was treated with PhMgBr in THF (3 M, 0.5 mL, 1.5 mmol) and $BF_3{\cdot}OEt_2$ (0.2 mL, 1.5 mmol) in 8 mL of THF. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:3) afforded 0.08 g (64%) of **4a** as a colourless solid. The (4*R*,5*S*) product ***trans*-4a** was obtained in 96% *ds*.

General procedure V was also used. Oxazolidinone **2** (0.1 g, 0.6 mmol) was treated with PhI (0.51 g, 2.5 mmol), *n*-butyllithium in hexane (15%, 1.6 mL, 2.6 mmol), CuCN (0.23 g, 2.6 mmol), LiCl (0.22 g, 5.2 mmol) and $BF_3{\cdot}OEt_2$ (0.6 mL, 4.5 mmol) in 18.5 mL of THF. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:3) afforded 0.091 g (72%) of **4a** as a colourless solid. The (4*R*,5*S*) product ***trans*-4a** was obtained in 95% *ds*. – $R_f = 0.67$ (ethyl acetate/cyclohexane 1:1); m.p. 104 °C; $[\alpha]_D^{25} = +28$ ($c = 1$, dichloromethane). – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.70 (dd, $J = 10.0, 3.8$ Hz, 1 H), 3.78 (dd, $J = 10.0, 4.8$ Hz, 1 H), 4.52 (ddd, $J = 5.3, 4.8, 3.8$ Hz, 1 H), 4.82 (dd, $J = 5.3, 0.3$ Hz, 1 H), 6.75 (br, NH, 1 H), 7.47–7.22 (m, 5 H). – ^{13}C NMR (50.2 MHz, $CDCl_3$): δ = 39.2, 59.1, 82.7, 126.1, 128.9, 129.2, 139.1, 158.6. – MS (70 eV, EI): *m*/*z* = 211 (10) [M^+], 176 (100), 133 (18), 105 (55), 104 (68), 91 (28), 77 (37). – HRMS calcd. for $C_{10}H_{10}ClNO_2$ [M^+]: 211.0401, found 211.0399.

(4*RS*,5*S*)-4-*n*-Butyl-5-chloromethyl-1,3-oxazolidin-2-one (5ab): General procedure I was used. Oxazolidinone **2** (0.5 g, 3 mmol) was

treated with CuI (3.43 g, 18 mmol), *n*-butyllithium in hexane (15%, 16.5 mL, 27 mmol) and $BF_3{\cdot}OEt_2$ (0.4 mL, 3 mmol) in 40 mL of THF. The reaction was complete after 12 h. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:2) afforded 0.34 g (59%) of **5a** as a colourless oil. The (4*R*,5*S*) product ***trans*-5a** was obtained in 95% *ds.*

General procedure II was also used. The oxazolidinone **2** (0.25 g, 1.5 mmol) was treated with CuBr·DMS (0.68 g, 3 mmol), *n*-butyllithium in hexane (15%, 1.8 mL, 3 mmol) and $BF_3{\cdot}OEt_2$ (0.4 mL, 3 mmol) in 17 mL of diethyl ether. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:2) afforded 0.15 g (52%) of **5ab** as a colourless oil. The (4*R*,5*S*) product ***trans*-5a** was obtained in 88% *ds.*

General procedure III was also used. Oxazolidinone **2** (0.1 g, 0.6 mmol) was treated with *n*BuMgCl in THF (2 M, 1 mL, 2 mmol) and $BF_3{\cdot}OEt_2$ (0.3 mL, 2.25 mmol) in 8 mL of THF. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:2) afforded 0.07 g (64%) of **5a** as a colourless oil. The (4*R*,5*S*) product ***trans*-5a** was obtained in 95% *ds.*

General procedure IV was also used. Oxazolidinone **2** (0.13 g, 0.75 mmol) was treated with *n*BuI (0.92 g, 5 mmol), 1,2-dibromoethane (0.04 mL, 0.2 mmol), TMSCl (0.02 mL, 0.16 mmol), CuCN (0.4 g, 4.0 mmol), LiCl (0.38 g, 8.8 mmol) and $BF_3{\cdot}OEt_2$ (0.6 mL, 4.5 mmol) in 21 mL of THF. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:2) afforded 0.08 g (57%) of **5a** as a colourless oil. The (4*R*,5*S*) product ***trans*-5a** was obtained in 98% *ds.* − R_f = 0.31 (ethyl acetate/cyclohexane 1:2).

Compound *trans*-5a: $[\alpha]_D^{25}$ = +21 (*c* = 1, chloroform). − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.89 Hz, 3 H), 1.28 (m, 4 H), 1.53 (m, 2 H), 3.57 (dd, *J* = 11., 6.4 Hz, 1 H), 3.61 (dd, *J* = 11.6, 4.7 Hz, 1 H), 3.65 (m. 1 H), 4.29 (ddd, *J* = 6.4, 4.7, 4.4 Hz, 1 H), 6.27 (br, NH, 1 H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.9, 22.4, 27.1, 35.4, 44.2, 55.7, 80.2, 158.5. − MS (70 eV, EI): *m*/*z* = 191 (2), 156 (6), 136 (30), 134 (100), 90 (11), 63 (13). − HRMS calcd. for $C_8H_{14}ClNO_2$ [M^+]: 191.0713, found 191.0713. − $C_4H_6ClNO_2$ (191.1): calcd. C 50.14, H 7.36, N 7.31; found C 50.30, H 7.42, N 7.19.

Compound *cis*-5b: ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.9, 22.4, 28.1, 28.7, 40.4, 55.0, 78.4, 158.5.

(4*RS*,5*S*)-4-Allyl-5-chloromethyl-1,3-oxazolidin-2-one (6ab): General procedure III was used. Oxazolidinone **2** (0.16 g, 0.75 mmol) was treated with C_3H_5MgBr in THF (1 M, 2 mL, 2 mmol) and $BF_3{\cdot}OEt_2$ (0.3 mL, 2.25 mmol) in 8 mL of THF. Purification of the crude product on silica gel (ethyl acetate/cyclohexane, 1:2) afforded 0.09 g (66%) of **6ab** as a colourless oil. The (4*R*,5*S*) product ***trans*-6a** was obtained in 82% *ds.*

General procedure IV was also used. Oxazolidinone **2** (0.13 g, 0.75 mmol) was treated with C_3H_5I (0.84 g, 5 mmol), 1,2-dibromoethane (0.04 mL, 0.2 mmol), TMSCl (0.02 mL, 0.16 mmol), CuCN (0.4 g, 4. mmol), LiCl (0.38 g, 8.8 mmol) and $BF_3{\cdot}OEt_2$ (0.6 mL, 4.5 mmol) in 21 mL of THF. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:2) afforded 0.08 g (62%) of **6a** as a colourless oil. The (4*R*,5*S*) product ***trans*-6a** was obtained in 95% *ds.* − R_f = 0.18 (ethyl acetate/cyclohexane, 1:2).

Compound *trans*-6a: $[\alpha]_D^{25}$ = +88 (*c* = 1, methanol). − ^{1}H NMR (200 MHz): δ = 2.38 (m, 2 H), 3.60 (d, *J* = 4.7 Hz, 2 H), 3.75 (dt, *J* = 5.6, 5.0 Hz, 1 H), 4.38 (dt, *J* = 5.6, 4.7 Hz, 1 H), 5.13 (ddt, *J* = 7.5, 1.2, 1.2 Hz, 1 H), 5.17 (d, *J* = 1.2 Hz, 1 H), 5.67 (m, 1 H), 6.73 (br, NH, 1 H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 39.7, 44.2, 54.8, 79.3, 120.1, 131.5, 158.5. − MS (70 eV, EI): *m*/*z* = 176 (1.84), 175 (0.95), 148 (17), 136 (40), 134 (100), 90 (26). − HRMS calcd. for $C_7H_{10}ClNO_2$ [M^+]: 175.0400, found 175.0399.

Compound *cis*-6b: ^{1}H NMR (200 MHz): δ = 2.38 (m, 2 H), 3.60 (d, *J* = 5.1 Hz, 2 H), 3.67 (m, 1 H), 4.38 (m, 1 H), 5.14 (m, 1 H), 5.17 (d, *J* = 1.2 Hz, 1 H), 5.67 (m, 1 H), 6.51 (br, NH, 1 H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 40.3, 42.5, 54.1, 80.8, 119.7, 132.3, 158.4.

(4*RS*,5*R*)-4-Allyl-5-methyl-1,3-oxazolidin-2-one (8ab): General procedure III was used. Oxazolidinone **3** (0.13 g, 1.02 mmol) was treated with C_3H_5MgBr in THF (1 M, 4.1 mL, 4.1 mmol) and $BF_3{\cdot}OEt_2$ (0.51 mL, 4.1 mmol) in 7 mL THF. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:1) afforded 0.10 g (67%) of **8ab** as a colourless oil. The (4*R*,5*R*) product ***trans*-8a** was obtained in 80% *ds.* − R_f = 0.32 (ethyl acetate 1:1).

Compound *trans*-8a: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.33 (d, *J* = 6.7 Hz, 3 H), 2.28 (m, 2 H), 3.41 (ddd, *J* = 6.4, 6.4, 6.4 Hz, 1 H), 4.38 (qd, *J* = 6.7, 6.4 Hz, 1 H), 5.14 (m, 2 H), 5.57 (m, 1 H), 6.52 (br, NH, 1 H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.92, 39.11, 58.77, 78.33, 119.43, 132.18, 159.19. − MS (70 eV, EI): *m*/*z* = 142 (17.8), 100 (100), 56 (84.3). − HRMS calcd. for $C_7H_{11}NO_2$ [M^+] 141.0782, found 141.0786; for $C_7H_{12}NO_2$ [M^+ + H] 142.0864, found 142.0866.

Compound *cis*-8a: ^{1}H NMR (250 MHz, $CDCl_3$): δ =1.30 (d, *J* = 6.5 Hz, 3 H), 2.28 (m, 2 H), 3.78 (ddd, *J* = 6.4, 6.4, 6.4 Hz, 1 H), 4.38 (qd, *J* = 6.5 Hz, 6.4 Hz, 1 H), 5.14 (m, 2 H), 5.57 (m, 1 H), 6.52 (br, NH, 1 H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.88, 34.60, 54.93, 75.95, 119.35, 132.98, 159.19.

(4*RS*,5*S*)-5-Chloromethyl-4-vinyl-1,3-oxazolidin-2-one (7ab): General procedure III was used. Oxazolidinone **2** (0.125 g, 0.75 mmol) was treated with C_2H_3MgBr in THF (1 M, 2 mL, 2 mmol) and $BF_3{\cdot}OEt_2$ (0.3 mL, 2.25 mmol) in 8 mL of THF. Purification of the crude product on silica gel (ethyl acetate/cyclohexane, 1:3) afforded 0.07 g (58%) of **7a** as a colourless oil. The (4*R*,5*S*) product ***trans*-7a** was obtained in 94% *ds.*

Compound *trans*-7a: ^{1}H NMR (400 MHz): δ = 3.64 (dd, *J* = 11.9, 4.4 Hz, 1 H), 3.68 (dd, *J* = 11.9, 5.7 Hz, 1 H), 4.21 (dd, *J* = 7.1, 5.7 Hz, 1 H), 4.38 (ddd, *J* = 5.7, 5.7, 4.4 Hz, 1 H), 5.23 (d, *J* = 10.1 Hz, 1 H), 5.31 (d, *J* = 17.0 Hz, 1 H), 5.79 (ddd, *J* = 17.0, 10.1, 7.1 Hz, 1 H), 6.69 (br, NH, 1 H);

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 43.7, 58.2, 80.3, 120.7, 140.2, 158.6. − MS (70 eV, EI): *m*/*z* = 162 (6), 161 (5.6), 134 (17), 126 (22), 112 (100), 83 (52), 55 (96). − HRMS calcd. for $C_6H_{18}ClNO_2$ [M^+]: 161.0243, found 161.0243.

(4*R*,5*R*)-5-Methyl-4-vinyl-1,3-oxazolidin-2-one (9a): General procedure III was used. Oxazolidinone **3** (0.137 g, 1.04 mmol) was treated with C_3H_5MgBr in THF (1 M, 4.2 mL, 4.2 mmol) and $BF_3{\cdot}OEt_2$ (0.52 mL, 4.2 mmol) in 7 mL THF. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:1) afforded 0.10 g (67%) of **8ab** as a colourless oil. The (4*R*,5*R*) product ***trans*-8a w**as obtained in > 98% *ds.* − R_f = 0.29 (ethyl acetate/cyclohexane, 1:1).

Compound *trans*-9a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (d, *J* = 6.2 Hz, 3 H), 3.75 (dd, *J* = 7.2, 7.1 Hz, 1 H), 4.26 (dq, *J* = 7.1, 6.2 Hz, 1 H), 5.21 (d, *J* = 17.0 Hz,1 H), 5.27 (d, *J* = 10.1 Hz, 1 H), 5.79 (ddd, *J* = 17.0 Hz, 10.1 Hz, 7.2 Hz, 1 H), 6.52 (br, NH, 1 H). − ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.92, 62.83, 78.81,

118.82, 135.23, 159.55. − $C_6H_9NO_2$·1/5H_2O (130.6) calcd. C 56.68; H 7.13, N 11.02; found C 56.12, H 7.09, N 10.72.

Ethyl (4*R*,5*S*)-5-Chloromethyl-1,3-oxazolidin-2-one-4-carboxylate (10): General procedure IV was used. Oxazolidinone **2** (0.13 g, 0.75 mmol) was treated with EtO_2CCH_2I (1.07 g, 5 mmol), 1,2-dibromoethane (0.04 mL, 0.2 mmol), TMSCl (0.02 mL; 0.16 mmol), CuCN (0.4 g, 4. mmol), LiCl (0.38 g, 8.8 mmol) and BF_3·OEt_2 (0.6 mL, 4.5 mmol) in 21 mL of THF. Purification of the crude product on silica gel (ethyl acetate/cyclohexane, 1:2) afforded 0.08 g (48%) of **10** as a colourless oil. The (4*R*,5*S*) product **10** was obtained in >98% *ds.*

Reformatsky Reaction: Zinc powder was suspended in dry THF (2 mL) in a dry Schlenk tube under argon atmosphere, and TMSCl (0.1 mL, 0.16 mmol) was added. After the mixture had been stirred for 5 min, EtO_2CCH_2Br (0.30 g, 5 mmol) in dry THF (2 mL) was added dropwise and the mixture was stirred for 10 min. The mixture was cooled to −20 °C, BF_3·OEt_2 (0.6 mL, 4.5 mmol) was slowly added and the solution was stirred for 5 min. The oxazolidinone **2** (0.1 g, 0.6 mmol), in dry THF (5 mL), was added. After stirring for 15 h at this temperature, the solution was heated to room temp., the mixture was quenched by the addition of conc. aq. $NaHCO_3$ and the solids were filtered off. The phases were separated and the water phase was extracted three times with diethyl ether, which was dried with sodium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (ethyl acetate/cyclohexane, 1:2). The reaction afforded 0.08 g (58%) of **10** as a colourless oil. The (4*R*,5*S*) product **10** was obtained in >98% *ds.* − R_f = 0.10 (ethyl acetate/cyclohexane, 1:2); $[\alpha]_D^{25}$ = +13 (*c* = 0.5, dichloromethane). − ^{1}H NMR (400 MHz): δ = 1.22 (t, *J* = 7.2 Hz, 3 H), 3.38 (m, 2 H), 3.66 (dd, *J* = 11.6, 5.9 Hz, 1 H), 3.71 (dd, *J* = 11.6, 4.4 Hz, 1 H), 4.04 (dt, *J* = 6.7, 4.6 Hz, 1 H), 4.12 (q, *J* = 7.2 Hz, 2 H), 4.42 (ddd, *J* = 5.9, 4.6, 4.4 Hz, 1 H), 6.44 (br, NH, 1 H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 14.9, 39.9, 44.4, 52.0, 62.7, 79.5, 157.9, 170.3. − MS (70 eV, EI): *m*/*z* = 142 (100), 136 (23), 134 (79), 88 (39), 71 (100). − MS (FAB): *m*/*z* = 222 [M^+ + H].

Nucleophile Exchange with Allylsilane Reagents. − General Procedure VI:[12] Oxazolidinone **3** or **11** was dissolved in dry dichloromethane in a dry Schlenk tube under argon atmosphere and cooled to −78 °C. At the same temperature, BF_3.OEt_2 or $TiCl_4$ was added slowly and the reaction mixture was stirred for 20 min. The allylsilane reagent was added slowly and the reaction mixture was stirred for 18 h at −78 °C. After heating to room temp., the reaction was stopped by the addition of saturated aq. $NaHCO_3$ solution and the solids were filtered off. The layers were separated and the water phase was extracted four times with dichloromethane. The combined organic phases were dried with magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (ethyl acetate/cyclohexane).

(4*RS*,5*R*)-3,4-Diallyl-5-methyl-1,3-oxazolidin-2-one (12ab): General procedure VI was used. The oxazolidinone **11** (0.13 g, 0.78 mmol) was treated with allyltrimethylsilane (0.16 mL, 1.02 mmol) and BF_3.OEt_2 (0.13 mL, 1.02 mmol) in 6 mL dichloromethane. Purification of the crude product on silica gel (ethyl acetate/cyclohexane, 1:4) afforded 0.11 g (85%) of **12ab** as a colourless oil. The (4*R*,5*R*) product ***trans*-12a** was obtained in > 92% *ds.* − R_f = 0.27 (ethyl acetate/cyclohexane, 1:4).

Compound *trans*-12a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (d, *J* = 6.3 Hz, 3 H), 2.20 (dddt, *J* = 14.3, 7.6, 6.7, 1.2 Hz, 1 H), 2.36 (dddt, *J* = 14.3, 6.7, 3.7, 1.5 Hz, 1 H), 3.30 (ddd, *J* = 9.4, 7.6, 3.7 Hz, 1 H), 3.54 (ddt, *J* = 15.5, 7.4, 1.0 Hz, 1 H), 4.09 (ddt, *J* = 15.5, 4.9, 1.5, 1 H), 4.21 (dq, *J* = 9.4, 6.3 Hz, 1 H), 5.65 (m, 2 H), 5.15 (m, 4 H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.47, 35.92, 44.57, 60.66, 74.71, 118.52, 119.70, 131.50, 132.17, 157.37. − MS (70 eV, EI): *m*/*z*: 181 (0.4), 140 (100), 112 (22.1), 96 (10.7). − HRMS calcd. for $C_{10}H_{15}NO_2$ [M^+ − C_3H_5) 140.0711, found 140.0710;

Compound *cis*-12b: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (d, *J* = 6.3 Hz, 3 H), 2.28 (dddt, *J* = 14.3, 7.6, 6.7, 1.2 Hz, 1 H), 2.36 (dddt, *J* = 14.3, 6.7, 3.7, *J* = 1.5 Hz, 1 H), 3.30 (ddd, *J* = 9.4, 7.6, 3.7 Hz, 1 H), 3.73 (ddt, *J* = 15.5, 7.4, 1.0 Hz, 1 H), 4.21 (dq, *J* = 9.4, 6.3 Hz, 1 H), 4.60 (ddt, *J* = 15.5, 4.9, 1.5 Hz, 1 H), 5.65 (m, 2 H), 5.15 (m, 4 H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.94, 31.82, 44.83, 57.04, 73.86, 118.24, 118.76, 132.29, 132.89, 157.37.

(4*RS*,5*R*)-3-Allyl-4-(2-bromoallyl)-5-methyl-1,3-oxazolidin-2-one (14ab): General procedure VI was used. Oxazolidinone **11** (0.09 g, 0.50 mmol) was treated with (2-bromoallyl)trimethylsilane (0.25 mL, 1.51 mmol) and BF_3·OEt_2 (0.10 mL, 0.70 mmol) in 5 mL dichloromethane. Purification of the crude product on silica gel (ethyl acetate/cyclohexane, 1:4) afforded 0.11 g (85%) of **14ab** as a colourless oil. The (4*R*,5*R*) product ***trans*-14a** was obtained in > 96% *ds.* − R_f = 0.18 (ethyl acetate/cyclohexane 1:4); $[\alpha]_D^{25}$ = +43.2 (*c* = 0.54, dichloromethane).

Compound *trans*-14a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (d, *J* = 6.3 Hz, 3 H), 2.42 (dd, *J* = 14.3, 8.9 Hz, 1 H), 2.81 (ddd, *J* = 14.3, 4.3, 0.7 Hz, 1 H), 3.54 (ddt, *J* = 15.5, 7.4, 1.0 Hz, 1 H), 3.59 (dt, *J* = 8.9, 4.4 Hz, 1 H), 4.08 (ddt, *J* = 15.5, 4.9, 1.5 Hz, 1 H), 4.23 (qd, *J* = 6.4, 4.4 Hz, 1 H), 5.20 (dd, *J* = 17.3, 1.2 Hz, 1 H), 5.23 (dd, *J* = 10.1, 1.2 Hz, 1 H), 5.52 (d, *J* = 1.7 Hz, 1 H), 5.70 (d, *J* = 1.7 Hz, 1 H), 5.72 (dddd, *J* = 17.3, 10.1, 7.6, 4.9 Hz, 1 H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.86, 44.18, 44.94, 59.43, 74.85, 119.01, 120.90, 127.57, 131.97, 157.04. − MS (70 eV, EI): *m*/*z* = 259 (0.4), 180 (0.4), 140 (100), 112 (22.7), 96 (12.8). − HRMS calcd. for $C_{10}H_{14}NO_2Br$ [M^+] 259.0194; found 259.0200. − $C_{10}H_{14}NO_2Br$ (259.0) calcd. C 46.17; H 5.42, N 5.38; found C 46.18, H 5.29, N 5.29.

***N*-Allylation. − General Procedure VII:** Oxazolidinone **3, 8a** or **9a** was dissolved in *N,N*-dimethylformamide and cooled to 0 °C. After the mixture had been stirred for 3 h at this temperature, allyl bromide was added. After stirring for 24 h at room temp. the reaction mixture was quenched by the addition of an aqueous solution of citric acid (5%). The mixture was extracted repeatedly with ethyl acetate. The organic phase was dried with sodium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (ethyl acetate/cyclohexane).

(4*RS*,5*R*)-3-Allyl-4-methoxy-5-methyl-1,3-oxazolidin-2-one (11ab): General procedure VII was used. Oxazolidinone **3** (0.67 g, 5.10 mmol) was treated with sodium hydride (spatula tip) and allyl bromide (1.10 mL, 12.75 mmol) in 20 mL *N,N*-dimethylformamide. Purification of the crude product on silica gel (ethyl acetate/cyclohexane, 1:4) afforded 0.70 g (81%) of **11ab** as a yellow oil. The (4*R*,5*R*) product ***trans*-11a** was obtained in 80% *ds.* − R_f = 0.27 (ethyl acetate/cyclohexane, 1:4).

Compound *trans*-11a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (d, *J* = 6.6 Hz, 3 H), 3.20 (s, 3 H), 3.62 (ddt, *J* = 15.5, 7.4, 1.0 Hz, 1 H), 4.37 (qd, *J* = 6.6, 1.7 Hz, 1 H), 4.53 (d, *J* = 1.7 Hz, 1 H), 4.57 (ddt, *J* = 15.5, 4.7, 1.5 Hz, 1 H), 5.19 (dddd, *J* = 17.0, 10.0, 1.5, 1.0 Hz, 2 H), 5.65 (dddd, *J* = 17.0, 10.0, 7.4, 4.7 Hz, 1 H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 19.24, 43.86, 52.81, 74.96, 90.99, 118.49, 131.87, 156.58. − MS (70 eV, EI): *m*/*z* = 171 (10.7), 156

(2.0), 140 (23.7), 112 (16.7), 99 (100), 84 (22.2). − HRMS calcd. for $C_8H_{13}NO_3$ [M^+] 171.0893; found 171.0895.

Compound *cis*-11b: ^{1}H NMR (400 MHz, $CDCl_3$): δ =1.35 (d, J = 6.6 Hz, 3 H), 3.38 (s, 3 H), 3.62 (ddt, J = 15.5, 7.4, 1.0 Hz, 1 H), 4.48 (qd, J = 6.6, 1.7 Hz, 1 H), 4.57 (ddt, J = 15.5, 4.7, 1.5 Hz, 1 H), 4.70 (d, J = 1.7 Hz, 1 H), 5.19 (dddd, J = 17.0, 10.0, 1.5, 1.0 Hz, 2 H), 5.65 (dddd, J = 17.0, 10.0, 7.4, 4.7 Hz, 1 H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.74, 44.31, 57.46, 74.96, 88.26, 118.33, 132.40, 156.85.

(4*RS*,5*R*)-3,4-Diallyl-5-methyl-1,3-oxazolidin-2-one (12ab): General procedure VII was used. Oxazolidinone **8a** (0.220 g, 1.21 mmol) was treated with sodium hydride (spatula tip) and allyl bromide (0.26 mL, 3.03 mmol) in 20 mL dimethylformamide. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:4) afforded 0.13 g (58%) of **11ab** as a yellow oil. − R_f = 0.27 (ethyl acetate/cyclohexane, 1:4).

(4*RS*,5*R*)-3-Allyl-5-methyl-4-vinyl-1,3-oxazolidin-2-one (14): General procedure VI was used. Oxazolidinone **9a** (0.08 g, 0.59 mmol) was treated with sodium hydride (spatula tip) and allyl bromide (0.12 mL, 1.48 mmol) in 6 mL dimethylformamide. Purification of the crude product on silica gel (ethyl acetate/cyclohexane 1:4) afforded 0.08 g (77%) of **14** as a colourless oil. − R_f = 0.21 (ethyl acetate/cyclohexane, 1:4). $[\alpha]_D^{25}$ = +33.2 (c = 0.85, dichloromethane).

Compound *trans*-14a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (d, J = 6.2 Hz, 3 H), 3.43 (ddt, J = 15.5, 7.6, 1.0 Hz, 1 H), 3.67 (dd, J = 7.6, 6.3 Hz, 1 H), 4.01 (ddt, J = 15.5, 4.9, 1.5 Hz, 1 H), 4.16 (dq, J = 6.3, 6.2 Hz, 1 H), 5.12 (m, 2 H), 5.27 (m, 2 H), 5.62 (m, 2 H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.80, 44.62, 66.16, 75.66, 118.73, 121.59, 131.72, 134.34, 157.42. − MS (70 eV, EI): m/z = 167 (51.4), 140 (44.3), 108 (25.3), 94 (82.1), 68 (100). − HRMS calcd. for $C_9H_{13}NO_2$ [M^+] 167.0944; found 167.0945. − $C_9H_{13}NO_2$ (167.1) calcd. C 64.65; H 7.84, N 8.38; found C 64.07, H 7.76, N 8.07.

Metathesis Reaction

(1*R*,8a*R*)-1-Methyl-1,5,8,8a-tetrahydro-oxazolo[3,4-*a*]pyridin-3-one (13): Oxazolidinone **12** (0.12 mg, 0.66 mmol) was dissolved in 4 mL of dried dichloromethane and Grubbs' catalyst (0.11 mg, 0.13 mmol), also dissolved in 8 mL of dried dichloromethane, was added. The violet solution was refluxed for 30 min. During this time a colour change of the solution from violet through red to brown took place. The reaction mixture was quenched by the addition of 6 mL of an aqueous solution of citric acid (5%). The water phase was extracted four times with dichloromethane and the combined organic phases were dried with magnesium sulfate and concentrated in vacuo. Purification of the crude product on silica gel (cyclohexane/ethyl acetate, 4:1) afforded 0.10 mg (74%) of **13** as a colourless oil. − R_f = 0.15 (cyclohexane/ethyl acetate, 4:1). $[\alpha]_D^{25}$ = +63.4 (c = 0.37, dichloromethane).

Compound *trans*-13: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (d, J = 6.2 Hz, 3 H), 2.20 (m, 1 H), 2.25 (m, 1 H), 3.28 (ddd, J = 10.3, 5.6, 4.9 Hz, 1 H), 3.61 (ddd, J = 18.2, 4.4, 2.2 Hz, 1 H), 4.02 (ddd, J = 18.2, 5.6, 2.8 Hz, 1 H), 4.23 (qd, J = 6.2, 5.6 Hz, 1 H), 5.68 (ddd, J = 10.3, 5.6, 4.4 Hz, 1 H), 5.76 (dddd, J = 10.3, 8.1, 4.2, 2.2 Hz, 1 H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 19.81, 29.37, 41.04, 57.06, 77.98, 123.07, 123.92, 157.17. − MS (70 eV, EI): m/z = 153 (17.3), 138 (4.3), 108 (25.3), 94.1 (18.8), 54 (100). − HRMS calcd. for $C_8H_{11}NO_2$ [M^+] 153.0798; found 153.0794. − $C_8H_{11}NO_2$ (153.1) calcd. C 62.73; H 7.24, N 9.14; found C 63.00, H 7.72; N 9.29.

Heck Reaction

Palladium diacetate (0.01 g, 0.37 mmol), triphenylphosphane (0.03 g, 0.04 mmol) and triethylamine (0.1 mL, 0.11 mmol) were added to a solution of oxazolidinone **14** in 2 mL toluene in a dry Schlenk tube. The reaction mixture was refluxed for 16 h. Purification of the crude product on silica gel (cyclohexane/ethyl acetate 4:1) afforded 0.05 g (72%) of **15** and 0.01 g (12%) of **16.** Both products are solids.

(1*R*,8a*R*)-1,6-Dimethyl-7-methylene-1,7,8,8a-tetrahydro-oxazolo-[3,4-*a*]pyridin-3-one (15): R_f = 0.40 (cyclohexane/ethyl acetate, 4:1)**;** $[\alpha]_D^{25}$ = +5.3 (c = 0.33, dichloromethane).

Compound *trans*-15: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (d, J = 6.2 Hz, 3 H), 1.75 (d, J = 1.2 Hz, 3 H), 2.20 (ddt, J = 14.6, 10.8, 2.2 Hz, 1 H), 2.60 (dd, J = 4.6, 3.4 Hz, 1 H), 3.49 (ddd, J = 10.8, 9.1, 3.4 Hz, 1 H), 4.24 (dq, J = 9.1, 6.4 Hz, 1 H), 4.78 (m, 1 H), 4.93 (m, 1 H), 6.50 (d, J = 1.2 Hz, 1 H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.30, 18.51, 34.59, 53.63, 78.43, 110.65, 119.31, 123.45, 137.68, 153.14. − MS (70 eV, EI): m/z = 179 (60.7), 164 (90.7), 134 (18.6), 107 (100), 91 (18.6), 79 (50.7). − HRMS calcd. for $C_{10}H_{13}NO_2$ [M^+] 179.0946; found 179.0946, for $C_{10}H_{14}NO_2$ [M^+ − H]178.0869; found 178.0867.

(1*R*,8a*R*)-1-Methyl-6,7-dimethylene-1,7,8,8a-tetrahydro-oxazolo-[3,4-*a*]pyridin-3-one (16): R_f = 0.35 (cyclohexane/ethyl acetate, 4:1). M.p. 100 °C; $[\alpha]_D^{25}$ = −35 (c = 0.25, dichloromethane);

Compound *trans*-16: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (d, J = 6.3 Hz, 3 H), 2.17 (ddt, J = 13.3, 11.3, 2.2 Hz, 1 H), 2.47 (dd, J = 13.3, 3.7 Hz, 1 H), 3.49 (ddd, J = 11.3, 5.8, 3.7 Hz, 1 H), 3.54 (dt, J = 14.6, 2.2 Hz, 1 H), 4.18 (dq, J = 6.3, 5.8 Hz, 1 H), 4.30 (d, J = 14.6 Hz, 1 H), 4.85 and 5.12 (m, 4 H). − ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 19.70, 38.30, 46.30, 60.73, 77.36, 110.74, 111.97, 140.91, 142.14, 156.48. − MS (70 eV, EI): m/z = 179 (62.1), 164 (14.3), 134 (28.6), 120 (32.1), 107 (100), 92 (20.0), 79 (100). − HRMS calcd. for $C_{10}H_{13}NO_2$ [M^+] 179.0946; found 179.0946.

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