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1,2-Diastereoselective C–C Bond-Forming Reactions for the Synthesis of Chiral β-Branched α-Amino Acids

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S_N2' sequences have been employed for the synthesis of β-branched α-amino acids using 1,2-diastereocontrol for forming C–C bonds. An oxazolidine fragment derived from Garner's aldehyde provides the handle for facial discrimination and acts as a masked amino acid functionality. This study encompasses directed and non-directed allylic substitution reactions. The stereocontrol of the oxazolidine appendage during terminal olefin hydroformylation was also studied. Efforts to understand the diastereochemical outcome of the reactions as well as synthetic applications are disclosed.

Introduction

Stereocontrol in the course of carbon–carbon bond-forming reactions can be achieved either by reagent or substrate control. The latter strategy is attractive if the substrate is readily accessible in a few productive steps from the chiral pool and amenable to diastereoselective transformations.[1–3] Following our interest in non-proteinogenic amino acids, we envisaged the construction of β-substituted α-amino acids from D- or L-serine using a suitable C–C bond-forming reaction. Indeed, β-substituted α-amino acids are employed as building blocks for the synthesis of wide ranges of natural products and biomolecules or as probes to identify the mechanism of biological reactions.[4] In addition, they have played a crucial role in the development of therapeutic agents such as peptides and peptidomimetics, especially by inducing conformational constraints or metabolic stability.[5]

Some years ago our group reported that α,β-unsaturated esters **2** and **3** (the *E* and *Z* stereoisomers), obtained from Garner's aldehyde **1**, were suitable substrates for the 1,4-addition of organo-cuprates.[6] Indeed, the conjugate addition was high-yielding and the diastereoselectivity excellent, favouring the formation of the *syn* adduct (*syn*/*anti*, 95:5) [see Equation (1) in Figure 1]. Interestingly, the *E* and *Z* stereoisomers of enoate **2** both gave the *syn* adduct. At the time these results were explained by a vinylogous Felkin–Anh model. Then, after a few chemical manipulations, the *syn* adducts were transformed into stereodefined 3-alkylated glutamic acids. The work culminated in the synthesis of *seco*-kainic acid. Another pathway that has been explored employed chiral bromoallenes that underwent S_N2' alkylation to produce *anti*-β-branched alkynyl amino alcohol derivatives [Equation (2) in Figure 1].[7] More recently, we applied the concept of "reagent-directing group" to a 1,2-diastereoselective copper-mediated allylic substitution using the oxazolidine group derived from Garner's aldehyde as a handle for facial discrimination and as a masked amino acid functionality.[8–10] Indeed, hydrolytic deprotections and oxidation of the primary alcohol function of the *N*-Boc-oxazolidine could restore the α-amino acid function and therefore represent a new synthesis of β-branched α-amino acids. Herein we disclose a full account

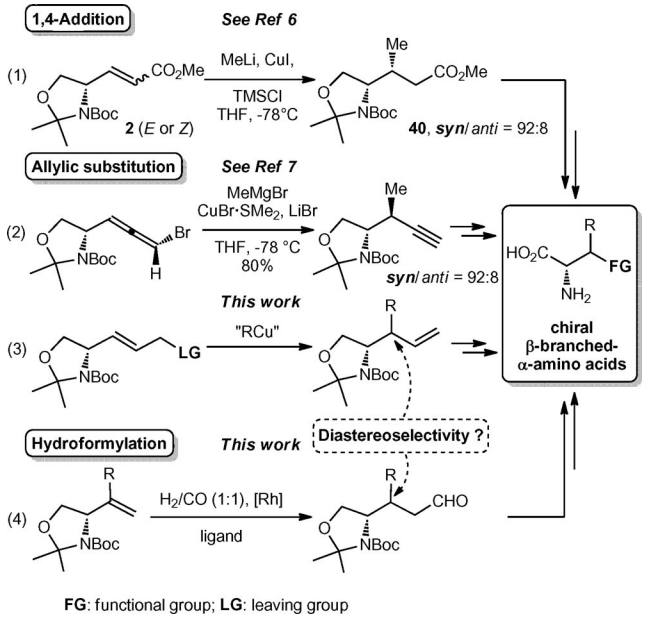

Figure 1. Diastereoselective approaches to β-branched α-amino acids.

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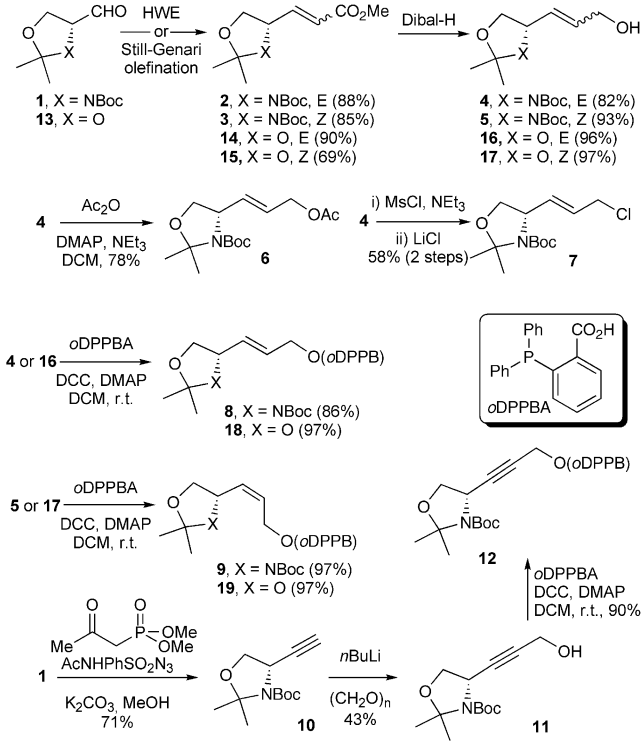
focusing on the unique capability of the oxazolidine moiety to drive the stereochemical outcome of the directed allylic substitution with organometallic reagents [see Equation (3) in Figure 1]. In addition, a methallyl adduct of Garner's aldehyde was submitted to hydroformylation to delineate the influence of the oxazolidine fragment in hydrometallation and a subsequent carbonylative sequence which would deliver a valuable glutamate analogue possessing a terminal aldehyde ready for further manipulations [Equations (3) and (4) in Figure 1].

Results and Discussion

Synthesis of the Starting Substrates for S_N2' Reactions

For the exhaustive study of the S_N2' reaction, several strategic substrates were prepared by cognate chemistry. Garner's aldehyde **1** or the dioxolane **13**, as starting materials, underwent *E*- or *Z*-selective olefination reactions to yield the enoates **2** or **3** and **14** or **15**, respectively, as separable stereoisomers. Then DIBAl-H reduction afforded the allylic alcohols **4** or **5** and **16** or **17**, respectively. At first the alcohol functions in **4** and **5** were converted into leaving groups such as OAc (**6**) or Cl (**7**) and the directing/leaving group *ortho*-(dihenylphosphanyl)benzoate (*o*DPPB) by Steglich esterification (**8** and **9**). Also, starting from **1**, alkyne derivative **12** was obtained by Bestmann–Ohira reaction followed by alkylation[11] and Steglich esterification. The substrates **18** and **19** were prepared to compare the diastereochemical bias of the oxazolidine function with a dioxolane function in the course of the S_N2' reaction. The chemical steps towards the starting substrates **6**–**9**, **12**, **18** and **19** for the copper-mediated allylic substitution reaction are depicted in Scheme 1. When *E* or *Z* stereoisomers were involved the geometric purity of the compounds was ensured by HPLC.

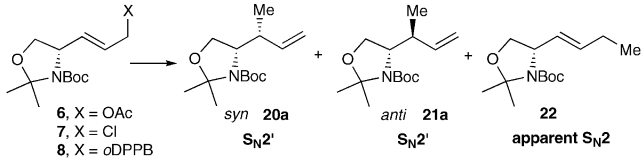


Scheme 1. Preparation of substrates for the copper-mediated allylic substitution reaction.

Results of the Studies of the S_N2' Substitution Reaction

Under standard conditions with leaving groups such as OAc or Cl, the regioselectivity of the reaction was a concern. Indeed, the sterically demanding oxazolidine group in substrates **6** and **7** favoured the apparent S_N2 pathway over the S_N2' pathway (Table 1, entries 1–4). The reaction mixture with several organometallic reagents (Mg, Cu or Zn) gave **22**, the S_N2 substitution product, and a mixture of **20a** and **21a**, the S_N2' products. But the S_N2 pathway was by far the major one whereas in the minor S_N2' pathway a trend for the *syn* adduct was still notable. This poor regioselectivity could be overcome with a "reagent-directing/leaving group", *ortho*-(dihenylphosphanyl)benzoate (*o*DPPB), which has the capability of precoordinating the copper reagent to allow for intramolecular delivery of the organometallic nucleophile. Under these conditions the desired regiocontrol was nearly perfect for substrate **8**; the S_N2' pathway was predominant and gave an excellent diastereomeric ratio in favour of the *anti* adduct **20a** (entry 5) using an organo-copper reagent.

Table 1. Initial conditions for the S_N2' reaction with substrates **6**, **7** and **8**.



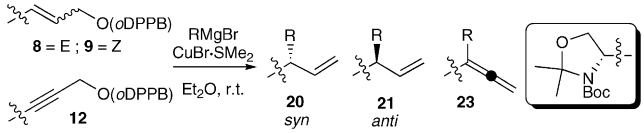
Entry		Conditions[a]	*syn*/*anti*	S_N2'/S_N2
1	**6**	MeMgBr, 50 mol-% CuCN, Et_2O, –78 °C	51:49	18:82
2	**6**	Me_2Zn, CuCN·2LiCl, THF, –30 °C	–	–
3	**7**	MeLi, CuI, BF_3·Et_2O, THF, –30 °C	86:14	28:71
4	**7**	MeLi, CuBr·SMe_2, $ZnCl_2$, THF, –70 °C	74:26	4:96
5	**8**	0.5 equiv. CuBr·SMe_2/1.6 equiv. MeMgBr, Et_2O, room temp.	15:85	98:2

[a] Full conversions were observed for entries 1 and 3–5. Regioselectivities and diastereoselectivities were determined by GC analysis.

Next, the chiral substrates **8** and **9** possessing opposite alkene geometries were treated with different organometallic reagents (Table 2, entries 1–9). With alkyl Grignard reagents, the regioselectivity was controlled by the directing group and the diastereochemical outcome was found to be stereodivergent after correlation with the corresponding isoleucines.[9] The *E* isomer gave rise to the valuable *anti*

adducts in good diastereomeric ratios more or less independently of the steric demand of the nucleophile (entries 1–4). Conversely, the *Z* isomer led to *syn* diastereomers with excellent diastereomeric excesses (entries 6–9). As a result of a slower reductive elimination pathway, the phenyl Grignard gave poor regioselectivity although the diastereoselectivity seems consistent with alkyl Grignard reagents (entry 5).

Table 2. Copper-mediated *o*DPPB-directed S_N2' reactions with substrates **8**, **9** and **12**.

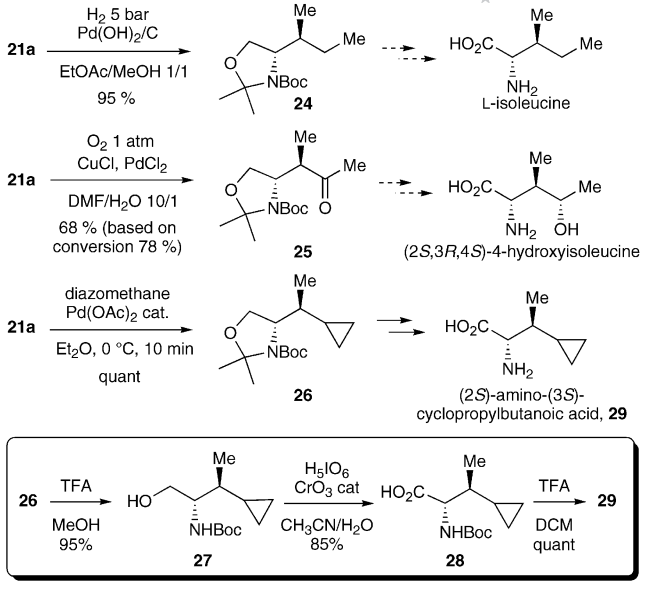


Entry[a]		R	S_N2'/S_N2	*syn*/*anti*[b] (products)	Yield [%][c]
1	**8**	Me	98:2	15:85 (**20a/21a**)	78
2	**8**	Et	96:4	15:85 (**20b/21b**)	91
3	**8**	*n*Bu	98:2	17:83 (**20c/21c**)	97
4	**8**	*i*Pr	98:2	7:93 (**20d/21d**)	97
5	**8**	Ph	44:56	17:83	–
6	**9**	Me	96:4	97:3 (**20a/21a**)	86
7	**9**	Et	99:1	97:3 (**20b/21b**)	98
8	**9**	Bu	98:2	98:2 (**20c/21c**)	96
9	**9**	*i*Pr	95:5	95:5 (**20d/21d**)	98
10	**12**	Me	95:5	**23**	75

[a] 0.1 M RMgBr (2 equiv.) was added at a rate of 3 mL/h to a solution of **8** or **9** precomplexed with 0.01 M $CuBr·SMe_2$ (0.5 equiv.) in Et_2O at room temp. [b] The configurations of **20b–d** and **21b–d** were assigned by analogy with **20a** and **21a**. [c] Isolated yield after silica gel chromatography.

Note, detection of the formal S_N2 products in small but traceable quantities arising from the starting *Z* olefin resulted predominantly in the *E* isomer **22**, which suggests that the S_N2-type products do not result from a simple substitution pathway but probably from a copper–π-allyl complex.[12,13] Next, to investigate the influence of the oxazolidine group with respect to the geometry of the electrophile, an S_N2' reaction was performed using propargylic substrate **12** (Scheme 1). It was found that allene **23** was formed in a good yield with an excellent regioselectivity. To the best of our knowledge, the *o*DPPB-directed S_N2' reaction with primary alkynes has no precedents (Table 2, entry 10).

The newly prepared adducts feature a terminal olefin function that allows for several chemical transformations such as reduction, cyclopropanation or oxidation. Exemplarily, **21a** was transformed into different amino acid precursors. Thus, hydrogenation produced **24** in 95% yield, a precursor for isoleucine, Wacker oxidation yielded **25** in 68% yield, a precursor for the fenugreek[14a,14b] amino acid hydroxyisoleucine and cyclopropanation[14b] furnished **26** quantitatively, a precursor for the synthesis of the naturally occurring β-branched α-amino acid **29** (Scheme 2). Cleavage of the acetonide with TFA in methanol produced **27** and subsequent oxidation of the primary alcohol to the carboxylic acid with periodic acid and chromium(VI) oxide furnished the Boc-protected amino acid **28** in good overall yield. Cleavage of the Boc group under standard conditions yielded the desired **29** quantitatively (*dr* 9:1).



Scheme 2. Functionalization of the terminal olefin for the preparation of β-branched α-amino acids.

An interesting feature of the *o*DPPB leaving group is the manipulation of the oxidation state of the phosphorus atom. It has been shown that by switching the directing group to the "off state" (oxidation of the phosphorus atom) the opposite diastereomer could be obtained from the same substrate.[15] Therefore stereodivergency may be possible with little chemical effort (Figure 2). These results are based on the following rational explanation: the entering nucleophile approaches the phosphane oxide in an antiperiplanar fashion rather than by *syn* attack as is the case for the directed S_N2' reaction. However, owing to the enhanced leaving-group ability of the *o*DPPB oxide in substrates **30** and **31**, the less nucleophilic dialkylzinc-derived copper reagent was required to achieve good regiocontrol.[16]

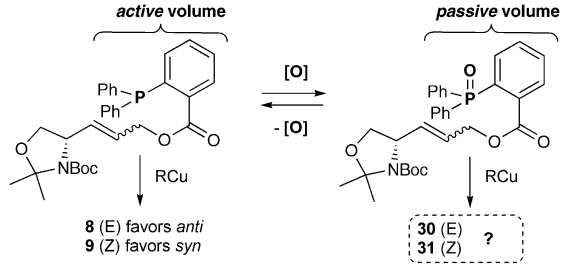
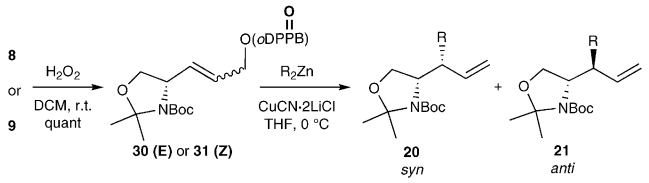


Figure 2. *o*DPPB on/off switch for S_N2' stereodivergency.

Indeed, for **30** (the *E* isomer), a reversal of diastereoselectivity (*syn* >> *anti*) was observed with alkylzinc reagents (Table 3, entries 1–3). This inversion of diastereoselectivity in **30** with respect to **8** confirms our expectations, and although Zn instead of Mg was used, a trend in the *syn*/*anti* ratio similar to that for the *o*DPPB-directed reaction was observed. These data suggest that the incoming nucleophile indeed enters *anti* with respect to the leaving group. In con-

trast, for substrate **31** (the *Z* isomer), the *syn* diastereomer was formed as the major product even though the *anti* diastereomer was expected (Table 3, entry 4).

Table 3. "Nondirected" S_N2' reaction with substrates **30** and **31**.[a]



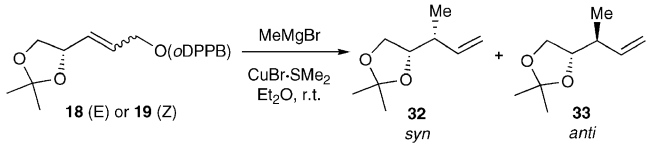
Entry		R	*syn*/*anti* (products)[b]	S_N2'/ S_N2	Yield [%][c]
1	**30**	Me	77:23 (**20a/21a**)	95:5	75
2	**30**	*n*Bu	85:15 (**20c/21c**)	99:1	61
3	**30**	*i*Pr	85:15 (**20d/21d**)	86:14	88
4	**31**	*n*Bu	99:1 (**20c/21c**)	99:1	40

[a] Conditions: In a dry flask under argon, CuCN·2LiCl (13 mg, 74.7 μmol) in anhydrous THF (0.5 mL) was introduced. The solution was stirred until the copper salt had dissolved and then it was cooled to –30 °C by mean of a cryostat. A solution of alkylzinc in toluene (2.4 equiv.) was added dropwise. The mixture was stirred for 30 min at –30 °C (light yellow) and a solution of **30** or **31** (35 mg, 62.2 μmol) in THF (0.9 mL) was then added with a syringe pump (rate 0.5 mL/h) at 0 °C. The mixture was stirred for 5 h at 0 °C and then overnight at room temp. (black solution). [b] The configurations of **20b–d** and **21b–d** were assigned by analogy with **20a** and **21a**. [c] Isolated yield after silica gel chromatography.

At present we do not have convincing arguments to explain why, under substrate control, there is a discrepancy between *syn* and *anti* attack of the directed and non-directed allylic substitutions. Nonetheless, intrigued by this divergence, we speculated that the *N*-Boc group could exert a neighbouring-group participation effect.[17] To probe this hypothesis, dioxolane analogues **18** and **19** were prepared in isomerically pure form starting from D-mannitol (see above; Scheme 1). By using our previously optimized conditions for the directed S_N2' reactions of **8** and **9**, we subjected **18** and **19** to the directed allylic substitution, as summarized in Table 4. Strikingly, isomer *E* (**18**) shows a profile virtually identical to that of the *N*-Boc derivative with an *anti*/*syn* ratio of 85:15 and a regioselectivity of 95:5. However, for the *Z* isomer (**19**), the allylic substitution reaction was completely non-selective both regio- and diastereoselectively (entry 2). From this result it would appear that the *N*-Boc group plays an essential role during the allylic substitution of the *Z*-*o*DPPB ester **9**.

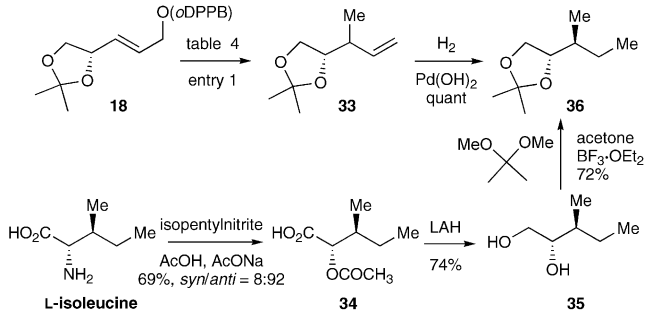
The pronounced $A^{1,3}$ strain expected for a *cis*-disubstituted alkene could be responsible for the higher diastereoselectivities observed for **9** but also a destabilizing effect of the transient π-copper–allyl complex, as was the case for **19**. From this result it may be possible that the oxygen atoms in the *N*-Boc group coordinate the copper atom thereby allowing extra stabilization in the transition state. The relative configuration of the major adduct **32** was unambiguously assigned by GC comparison of the hydrogenated adduct **33** with the synthetic material **36** obtained from L-isoleucine. Indeed, the latter underwent diazotization with isoamyl nitrite in acetic acid to yield the corresponding (2*S*,3*S*)-2-acetoxy-3-methylvaleric acid (**34**) as the major diastereomer (*syn*/*anti*, 8:92).[18] The mixture of diastereomers was reduced with lithium aluminium hydride and acetonide formation with 2,2-dimethoxypropane gave **36** in the same diastereomeric ratio thereby enabling the relative assignment of both *syn* and *anti* adducts (Scheme 3).[19]

Table 4. *o*DPPB-directed S_N2' reactions of substrates **18** and **19**.[a]



	syn/*anti* (products)	S_N2'/S_N2	Yield [%][b]
18	15:85 (**32**/**33**)	95:5	75
19	43:57	65:35	ND

[a] Conditions: 2 equiv. of 0.1 M MeMgBr were added at 3 mL/h to a solution of 0.01 M **18** or **19** and 0.5 equiv. of CuBr·SMe_2 in Et_2O at room temp. [b] Isolated yield after silica gel chromatography.



Scheme 3. Correlation of the relative stereochemistry of the dioxolane derivatives.

Rationale for the Observed Results[20]

In the case of substrates **8** and **9**, a directing/leaving group was used. For stereoelectronic reasons the reactive conformation should allow efficient overlap of the σ* orbital of the C–O bond to be broken and the π* orbital of the alkene, that is, a dihedral angle of about 0°. Thus, for the *E* substrate **8** it is plausible that reactive conformations **A** or **A′** account for the observed stereochemical outcome. Both conformations are in agreement with the stereoelectronic requirements for the S_N2' reaction and minimize allylic $A^{1,2}$ and $A^{1,3}$ strains. Directed attack from the least hindered *Si* alkene face provides the *anti* diastereomer preferentially for both conformations **A** and **A′** (Figure 3). In the case of the *Z* substrate **9**, conformation **B** with delivery of the alkyl nucleophile to the sterically less-hindered *Re* face could explain the preferred formation of the *syn* diastereomer. The pronounced $A^{1,3}$ strain expected for a *cis*-disubstituted alkene could be responsible for the higher diastereoselectivities observed for the *Z*-*o*DPPB ester **9**. Moreover, the fact that the *Z*-oxo derivative **19** displayed poor regio- and diastereoselectivity indicates that the more pronounced $A^{1,3}$ strain affected the course of the reaction. But,

as highlighted, the Boc group functioning as an additional ligand for the copper atom during the reaction cannot be excluded (Figure 3).

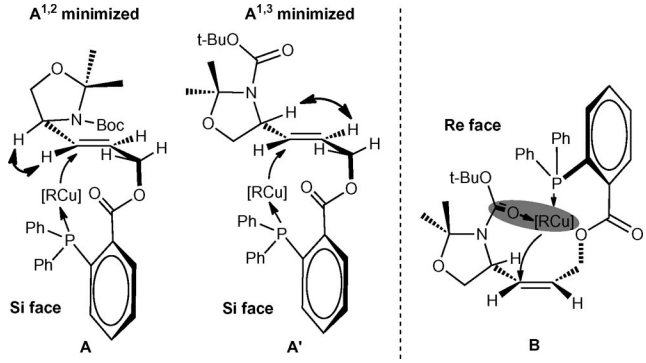


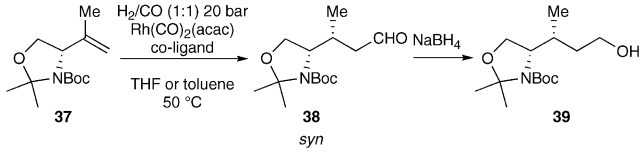
Figure 3. Rationale for the diastereochemical outcome.

Finally, the oxazolidine residue has demonstrated its capability to induce good-to-very-good 1,2-diastereocontrol in the course of C–C bond-forming reactions. Whereas the 1,4-addition of cuprates gave only the *syn* product independently of double-bond geometry, the directed copper-mediated allylic substitution (S_N2') allowed the preparation of both diastereomers selectively at the β-carbon next to the oxazolidine. Accordingly, other C–C bond-forming reactions were explored.

Stereocontrol During the Hydroformylation of 37

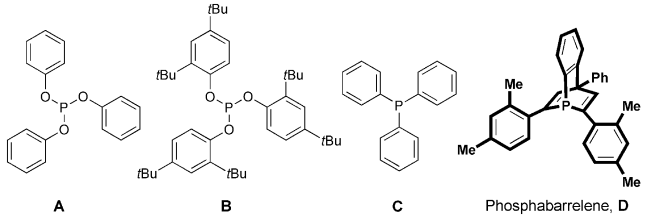
The influence of the oxazolidine appendage on diastereocontrol was further evaluated with the methallylic substrate **37** under hydroformylative conditions. Indeed, the methallylic substrate **37** should undergo hydroformylation exclusively at the less substituted C-terminus of the 1,1-disubstituted alkene (Keulemans' rule) and deliver solely the linear aldehyde **38**, but the influence of the stereogenic centre of the oxazolidine with respect to 1,2-stereoinduction was unknown.[21] If successful, this sequence would secure the introduction of the commonly encountered methyl group at the β-carbon and deliver the valuable aldehyde **38**.[22,23] Although it has been demonstrated that neighbouring stereogenic centres generated moderate-to-good 1,2-diastereoselectivity in passive substrate control during hydroformylation, the use of a proximal nitrogen-containing group has never been reported.[24] Olefin **37**, the substrate for hydroformylation, was obtained in five steps from D-serine by using known methods.[25] The most active hydroformylation catalysts are phosphane-modified rhodium(I) complexes. The activity and selectivity of these catalysts depends largely on the selected P-donor ligands. For this reason different types of phosphorus-containing ligands were screened. The results of our experiments are disclosed in Table 5. The hydroformylation was conducted in toluene or THF at 50 °C, the syngas pressure being fixed at 20 bar. By employing $[Rh(CO)_2(acac)]$ without a co-ligand, moderate diastereoselectivity was observed (*syn*/*anti* = 83:17, Table 5, entry 1). Addition of triphenyl phosphite (**A**) led to a significant increase in diastereoselectivity (entries 2 and 3), however, the use of the more bulky phosphite **B** gave disappointing results with a lower diastereoselectivity (entries 4 and 5). Switching to phosphane ligands and starting with triphenylphosphane (**C**) gave similar results as ligand A (entry 6). Finally, the bulky phosphane ligand phosphabarrelene[26] (**D**) was found to give the best diastereocontrol and yield favouring the *syn* isomer **38** (*syn*/*anti* = 94:6, Table 5, entries 7 and 8). The relative configuration was determined by correlation with the known *syn* product formed by the addition of methyl cuprate to **2** (Scheme 1). Reduction of the latter ester with lithium aluminium hydride and **38** with sodium borohydride gave the same primary alcohol **39**.[27]

Table 5. Diastereoselective hydroformylation of *N*-Boc-oxazolidine **37**.



Entry	Ligand	Solvent	*syn*/*anti*	Yield [%]
1[c]	none	toluene	83:17	63
2[a]	**A**	toluene	91:9	71[d]
3[c]	**A**	THF	89:11	78
4[a]	**B**	toluene	87:13	91,[c] 75[d]
5[c]	**B**	THF	87:13	93
6[c]	**C**	toluene	90:10	65
7[b]	**D**	toluene	94:6	76[d]
8[c]	**D**	THF	93:7	90

[a] Reactions were performed with 0.1 M, 0.9 mol-% $[Rh(CO)_2(acac)]$ and 4 mol-% co-ligand. [b] Reactions were performed with 0.1 M, 2 mol-% $[Rh(CO)_2(acac)]$ and 8% co-ligand. [c] In a parallel autoclave: reactions were performed with 0.1 M, 1.5 mol-% $[Rh(CO)_2(acac)]$ and 6 mol-% co-ligand. [d] Isolated yield after silica gel chromatography.



To rationalize the formation of the *syn* preferred diastereomer, a model derived from the 1,2-diastereoselective Rh^I-catalyzed hydroboration of olefins is suggested.[28] Complexation of the double bond with the catalyst would take place from the less hindered face of a conformation in which the 1,3-allylic strain is minimized and the withdrawing group (*N*-Boc) is antiperiplanar to the double bond.

Furthermore, if 1,2-allylic strain is minimized, the coordination of the catalyst to the Boc residue may also contribute for the observed *syn* diastereocontrol. This sequence accounts for the substrate-directed hydroformylation (Figure 4) and enables the preparation after some chemical

transformations of the *threo*-3-methyl glutamate [e.g., (2*S*,3*R*)-3TMG from D-serine], a synthon present in numerous natural products.[29–31]

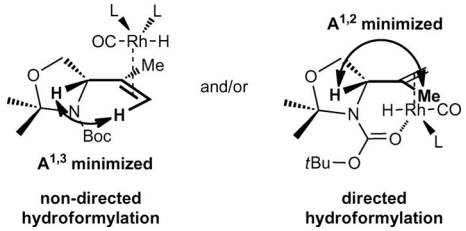


Figure 4. Proposed rationale for the observed *syn* diastereoselectivity.

Conclusions

A comprehensive study of 1,2-diastereoselective C–C bond-forming reactions in the synthesis of chiral β-branched α-amino acids has been performed. Copper-mediated 1,2-diastereoselective *o*DPPB-directed allylic substitution with an oxazolidine group as the chiral auxiliary on an open-chain substrate and primary leaving group readily obtained from Garner's aldehyde has been successfully performed. By using this strategy very-good-to-excellent regioselectivities in favour of the S_N2' product were observed. Notably, the geometry of the alkene is directly related to the stereochemical outcome of the S_N2' reaction. Thus, the *E* stereoisomer led preferentially to the *anti* diastereomer in good-to-very-good *dr* values and yields. Conversely, the *Z* isomer furnished the *syn* S_N2' product in very-good-to-excellent *dr* values and yields. The resulting substitution products could be used for the preparation of naturally occurring β-branched α-amino acids in a straightforward manner. The selectivity of our substrates may be explained by a model that involves a reactive conformation as a result of minimization of allylic strain combined with an intramolecular *o*DPPB-directed organometallic nucleophile delivery. From non-directed allylic substitutions and reactions of dioxolane analogues it appears that the Boc group coordinates the copper atom, enhancing the conformational stability of the *Z* substrate. Finally, a methallyl derivative of Garner's aldehyde underwent regio- and diastereoselective hydroformylation to yield a useful orthogonally protected glutamic acid derivative. From this detailed study it is clear that the preparation of *anti* diastereomers of β-branched α-amino acids still remains a challenging task.

Experimental Section

General: All reagents were used as purchased from commercial suppliers without further purification. The reactions were carried out in oven- or flame-dried vessels and performed under argon. Solvents were dried and purified by conventional methods prior to use. Et_2O and THF were freshly distilled from sodium/benzophenone and dichloromethane was distilled from CaH_2. Flash column chromatography was performed with Merck silica gel 60 (0.040–0.063 mm, 230–400 mesh). Merck aluminium-backed plates pre-coated with silica gel 60 (UV_{254}) were used for thin-layer chromatography and were visualized by staining with $KMnO_4$.

^1H, ^{13}C and ^{31}P NMR spectra were recorded with Bruker 400/300/200 spectrometers. Conditions are specified for each spectrum (temperature of 25 °C unless specified). Chemical shifts (δ) are given in ppm relative to the resonance of the solvent peak. Infrared spectra were recorded with a Nicolet 380 FT-IR spectrometer. GC analyses were conducted with a 6890N chromatograph from Agilent Technologies™ using a SUPLECOWAX™-10 fused silica capillary column (30 m × 0.25 mm × 0.25 μm film thickness). The inlet temperature was set at 200 °C, gas carrier He (53.6 mL/min), pressure 12.04 psi, flow 1 mL/min, detector FID 250 °C, H_2 flow 30 mL/min, air flow 406 mL/min, He 1 mL/min (see below for retention times and gradients). Elemental analyses were performed at the Institut für Organische Chemie, Freiburg in Breisgau. High- and low-resolution mass spectroscopy was conducted at the University of Strasbourg. Melting points were determined on a Gallenkamp melting point apparatus. Specific rotations were measured with a Perkin–Elmer apparatus: values are given in 10^{-1} deg cm^2 g^{-1}.

***tert*-Butyl (4*S*)-4-[(1*E*)-3-Methoxy-3-oxoprop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (2):**[6b] A mixture of (*R*)-Garner's aldehyde **1** (3.8 g, 16.6 mmol), trimethyl phosphonoacetate (6.6 mL, 33.2 mmol), tetrabutylammonium iodide (613 mg, 1.66 mmol) and 3 M aqueous K_2CO_3 (8 mL, 23 mmol) was stirred at room temp. for 16 h. The mixture was diluted with water (40 mL) and extracted with EtOAc (3×). The organic layer was washed with brine and dried with Na_2SO_4. The solvents were removed under reduced pressure and the residue was purified over silica gel chromatography (heptane/EtOAc, 7:3) to yield the desired *E* isomer in a pure form (4.87 g, 88%). R_f = 0.59 (hexane/Et_2O, 7:3). ^1H NMR (200 MHz, 60 °C, C_6D_6): δ = 6.88 (dd, *J* = 15, 7 Hz, 1 H), 5.95 (br. t, *J* = 15 Hz, 1 H), 4.63–4.49 (m, 0.5 H), 4.49–4.36 (m, 0.5 H), 4.10 (dd, *J* = 9, 6 Hz, 1 H), 3.80 (dd, *J* = 9, 2 Hz, 1 H), 3.76 (s, 3 H), 1.56 (s, 3 H), 1.50 (s, 3 H), 1.42 (s, 9 H) ppm.

***tert*-Butyl (4*S*)-4-[(1*Z*)-3-Methoxy-3-oxoprop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (3):**[32] Into a dry flask under argon was introduced successively bis(2,2,2-trifluoroethyl) (methoxycarbonyl)methylphosphonate (1.00 g, 3.14 mmol), 18-crown-6 complexed with acetonitrile (6.6 g, 5.5 equiv.) and anhydrous THF (48 mL). The mixture was cooled to –78 °C and a 0.5 M solution of KHMDS (6.36 mL, 5.18 mmol) in toluene was added dropwise. After 15 min of stirring at –78 °C a solution of **1** (600 mg, 2.62 mmol) in anhydrous THF (6 mL) was added dropwise and the reaction mixture was allowed to gradually reach 0 °C. The reaction was quenched with a solution of saturated aqueous NH_4Cl and extracted with Et_2O several times. The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (heptane/EtOAc, 8:2) to yield the desired product (638 mg, 85%) as a white solid. ^1H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 6.27 (br. m, 1 H), 5.84 (br. d, *J* = 11.2 Hz, 1 H), (br. t, *J* = 6.6 Hz, 1 H), 4.27 (br. t, *J* = 7.8 Hz, 1 H), 3.77 (dd, *J* = 3.1, 8.7 Hz, 1 H), 3.71 (s, 3 H, Me), 1.62 (s, 3 H, Me), 1.55 (s, 3 H, Me), 1.43 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.60 (CO), 152.60/151.60 (rotamers, CO), 120.0 (CH), 119.4 (CH), 94.8 (C_{quat}), 80.3 (C_{quat}), 69.4/69.1 (rotamers, CH_2), 57.0/55.9 (rotamers, CH), 51.7 (CH_3), 28.7 (*t*Bu), 27.7/26.9 (rotamers, CH_3), 25.2/24.1 (rotamers, CH_3) ppm.

***tert*-Butyl (4*S*)-4-[(1*E*)-3-Hydroxyprop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (4):**[9] Into a dry round-bottomed flask under argon was introduced the unsaturated ester **2** (300 mg, 1.05 mmol) and anhydrous THF (3 mL). The solution was cooled to 0 °C using an ice bath and a solution of DIBAL-H (2.48 mL,

1.0 M in THF) was added dropwise with stirring. After 1.5 h at 0 °C the mixture was poured into MeOH (15 mL) followed after a few minutes by a solution of sodium potassium tartrate (10 mL), water and EtOAc. The heterogeneous mixture was stirred overnight. The mixture was extracted with EtOAc and the organic layer was washed with brine before being dried with $MgSO_4$. The solvent was removed under reduced pressure. Purification by flash chromatography (heptane/EtOAc, 6:4) yielded **4** as a colourless oil (82%). R_f = 0.40 (cyclohexane/EtOAc, 6:4). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.78–5.72 (m, 2 H), 4.41/4.31 (rotamers, br. m, 1 H), 4.16 (br. d, J = 4.7 Hz, 2 H), 4.05 (dd, J = 8.9, 6.2 Hz, 1 H), 3.75 (dd, J = 8.8, 2.2 Hz, 1 H), 1.60 (s, 3 H), 1.51 (s, 3 H), 1.46 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.4/152.1 (rotamers, CO), 131.5/131.2 (rotamers, CH), 130.0/129.5 (rotamers, CH), 94.0 (C_{quat}), 80.6/79.8 (rotamers, C_{quat}), 68.33 (CH_2), 62.7 (CH_2), 58.9 (CH), 28.6 (*t*Bu), 27.4/26.8 (rotamers, CH_3), 25.0/23.9 (rotamers, CH_3) ppm.

***tert*-Butyl (4*S*)-4-[(1*Z*)-3-Hydroxyprop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (5):**[9] Into a dry round-bottomed flask under argon was introduced the unsaturated ester **3** (300 mg, 1.05 mmol) and anhydrous THF (3 mL). The solution was cooled to 0 °C using an ice bath and a solution of DIBAL-H (2.48 mL, 1.0 M in THF) was added dropwise with stirring. After 1.5 h at 0 °C the mixture was poured into MeOH (15 mL) followed after a few minutes by a solution of sodium potassium tartrate (10 mL), water and EtOAc. The heterogeneous mixture was stirred overnight. The mixture was extracted with EtOAc and the organic layer was washed with brine before being dried with $MgSO_4$. The solvent was removed under reduced pressure. Purification by flash chromatography (heptane/EtOAc, 1:1) yielded **5** as a colourless oil (251 mg, 93%). R_f = 0.55 (cyclohexane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.85 (ddd, J = 10.5, 8.5, 6.5 Hz, 1 H), 5.53 (t, J = 10.5 Hz, 1 H), 4.90 (br. dd, J = 10.0, 6.5 Hz, 1 H), 4.42 (br. dd, J = 12.0, 8.5 Hz, 1 H), 4.23 (br. s, 0.5 H), 4.14 (br. s, 0.5 H), 4.04 (dd, J = 6.0, 9.0 Hz, 1 H), 3.88 (m, 1 H), 3.69 (dd, J = 9.0, 1.5 Hz, 1 H), 1.57 (s, 3 H), 1.48 (s, 3 H), 1.45 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.5 (CO), 130.9 (CH), 130.2 (CH), 93.5 (C_{quat}), 81.0 (C_{quat}), 68.0 (CH_2), 57.6 (CH_2), 53.7 (CH), 28.4 (*t*Bu), 27.6 (CH_3), 24.8 (CH_3) ppm.

***tert*-Butyl (4*S*)-4-[(1*E*)-3-(Acetyloxy)prop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (6):** Into a dry flask under argon was introduced **4** (200 mg, 0.78 mmol), anhydrous dichloromethane (7.6 mL), NEt_3 (0.32 mL, 2.33 mmol) and acetic anhydride (0.22 mL, 2.33 mmol) at room temp. DMAP was added (10 mg, 0.10 mmol) and the reaction mixture was stirred overnight at room temp. The solvent was removed under reduced pressure and the residue was taken up in water and extracted with EtOAc (3×). The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The residual oil was purified over a silica gel column (heptane/EtOAc, 8:2) to yield a colourless liquid (0.175 mg, 78%). R_f = 0.26 (cyclohexane/EtOAc, 8:2). $[\alpha]_D^{20}$ = +11.7 (c = 1, $CHCl_3$). ^{1}H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 5.68 (br. d, J = 4.3 Hz, 2 H), 4.51 (br. d, J = 4.1 Hz, 2 H), 4.27 (br. m, 1 H), 4.10–3.96 (m, 1 H), 3.68 (dd, J = 8.9, 2.4 Hz, 1 H), 1.99 (s, 3 H), 1.54 (s, 3 H), 1.45 (s, 3 H), 1.39 (s, 9 H) ppm. ^{13}C NMR (300 MHz, $CDCl_3$): δ = 170 (CO), 151.9 (CO), 133.7 (CH), 126.0 (CH), 94.0 (C_{quat}), 79.9 (C_{quat}), 68.1 (CH_2), 64.1 (CH_2), 58.6 (CH), 28.4 (*t*Bu), 26.9 (CH_3), 24.1 (CH_3), 20.8 (CH_3) ppm. HRMS (ESI positive, HCOOLi): calcd. for $[M + Li]^+$ 306.1887; found 306.1893.

***tert*-Butyl (4*S*)-4-[(1*E*)-3-Chloroprop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (7):** Into a dry flask under argon was introduced **4** (0.53 g, 2 mmol) in anhydrous dichloromethane (32 mL). The solution was stirred at room temp. and NEt_3 (0.56 mL, 4 mmol) followed by MsCl (0.31 mL, 4 mmol) were added. The mixture was stirred overnight and the organic layer was washed successively with water and brine. The organic layer was removed under reduced pressure. DMF (5 mL) and LiCl (340 mg, 8 mmol) were added to the dry oily residue (0.66 g, 2 mmol). The mixture was stirred at room temp. until no more starting material could be detected by TLC (ca. 3 h). The solvent was removed under reduced pressure and the residue was taken up in water and extracted several times with Et_2O. The ethereal layer was washed with brine before being dried with $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (heptane/Et_2O, **7**:**3**) to yield 320 mg (58%) of the desired product as a light-yellow solid. R_f = 0.27 (cyclohexane/EtOAc, 8:2). Mp 62 °C. $[\alpha]_D^{20}$ = +16.1 (c = 1, $CHCl_3$). ^{1}H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 5.75 (br. d, J = 3.8 Hz, 2 H), 4.33 (br. s, 1 H), 4.03 (m, 3 H), 3.73 (dd, J = 9.1, 2.2 Hz, 1 H), 1.60 (s, 3 H, Me), 1.51 (s, 3 H, Me), 1.46 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (300 MHz, 50 °C, $CDCl_3$): δ = 152.2 (CO), 134.1 (CH), 128.1 (CH), 94.4 (C_{quat}), 80.4 (C_{quat}), 68.3 (CH_2), 58.7 (CH), 44.5 (CH_2), 28.8 (*t*Bu), 27.2 (CH_3), 24.4 (CH_3) ppm. LRMS: m/z = 298.166 [M + Na]$^+$. HRMS (ESI + HCOOLi): calcd. for $[M + Li]^+$ 282.1443; found 282.1438.

Experimental Conditions for Table 1

Entry 1: Into a dry round-bottomed flask under argon was introduced **6** (50 mg, 0.167 mmol) with CuCN (7.5 mg, 0.084 mmol) in anhydrous diethyl ether (5 mL). The mixture was placed at –78 °C and then a solution of 3.0 M of MeMgBr (0.111 mL, 0.334 mmol) was added dropwise. The colourless solution was allowed to reach room temp. over a period of 2 h (the mixture goes yellow at 0 °C). The reaction was quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted three times with EtOAc. The organic layer was dried with $MgSO_4$ and evaporated under reduced pressure. The crude mixture was directly injected into a GC apparatus.

Entry 3: Into a dry round-bottomed flask under argon was introduced CuI (35 mg, 0.181 mmol) and anhydrous THF (0.9 mL). The mixture was cooled to –30 °C and a 1.3 M solution of MeLi in diethyl ether (0.140 mL, 0.181 mmol) was added dropwise (colourless solution). After 5 min of stirring at this temperature the mixture was cooled to –70 °C and $BF_3{\cdot}OEt_2$ was added (23 μL, 0.181 mmol). The solution turned yellow. Finally, after a few minutes of stirring at –70 °C a solution of **7** (50 mg, 0.181 mmol) in anhydrous THF (0.9 mL) was added dropwise. The mixture was allowed to reach room temp. The reaction was quenched with saturated aqueous NH_4Cl and the aqueous layer was extracted three times with EtOAc. The organic layer was dried with $MgSO_4$ and evaporated under reduced pressure. The crude mixture was directly injected into a GC apparatus.

Entry 4: Into a dry flask under argon was introduced $CuBr{\cdot}SMe_2$ (37.2 mg, 0.181 mmol) and anhydrous THF (0.36 mL). The suspension was cooled to –70 °C and a solution of 1.3 M of MeLi in Et_2O (280 μL, 0.362 mmol) was added dropwise. The solution was then allowed to reach 0 °C and was stirred for an additional 10 min before cooling again to –70 °C. A 1 M solution of $ZnCl_2$ (181 μL, 0.181 mmol) was added dropwise. The mixture was stirred for 10 min at this temperature and **7** (50 mg, 0.181 mmol) was added. The reaction was kept at –70 °C for 15 h and then 2 h at –40 °C. The reaction was diluted with heptane and washed with saturated aqueous $NaHCO_3$. The organic layer was dried with $MgSO_4$ and evaporated under reduced pressure. The crude mixture was directly injected into a GC apparatus.

General Procedure for the Coupling of the Directing Group with the Unsaturated Alcohols 4 and 5 to Form the Corresponding Esters 8 and 9: Into a dry round-bottomed flask under argon was introduced the unsaturated alcohol **4** or **5** (285 mg, 1.11 mmol), *o*DPPBA (340 mg, 1.11 mmol), DMAP (136 mg, 1.11 mmol), DCC (229 mg, 1.11 mmol) and dry dichloromethane (5.6 mL, 0.2 M). The cloudy mixture was stirred at room temp. overnight. Brine was added and the mixture was extracted three times with dichloromethane. The organic layer was dried with $MgSO_4$, filtered and removed under reduced pressure. The residue was purified by flash chromatography (heptane/EtOAc, 9:1).

***tert*-Butyl (4*S*)-4-[(1*E*)-3-{[2-(Diphenylphosphanyl)benzoyl]oxy}-prop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (8):** White solid (86%). R_f = 0.78 (heptane/EtOAc, 6:4); m.p. 102 °C. $[\alpha]_D^{20}$ = +10.7 (*c* = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2981, 1688, 1361, 1248, 1098, 1057, 961, 943, 758, 744, 521, 501 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07 (m, 1 H), 7.44–7.25 (m, 12 H), 6.95 (m, 1 H), 5.71 (br. s, 2 H), 4.65 (d, *J* = 4.8 Hz, 2 H), 4.26–4.30 (2 br. s, 1 H), 4.03 (dd, *J* = 9.0, 6.3 Hz, 1 H), 3.72 (dd, *J* = 8.8, 2.6 Hz, 1 H), 1.6 (s, 3 H), 1.51 (s, 3 H), 1.42 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5 (CO), 151.9 (CO), 140.7 (d, $J_{C,P}$ = 25.4 Hz, C_{quat}), 138.0 (d, $J_{C,P}$ = 12.4 Hz, C_{quat}), 134.4 (br. s, CH), 133.99 (d, $J_{C,P}$ = 20.7 Hz, CH_{Ar}), 133.97 (d, $J_{C,P}$ = 20.7 Hz, CH_{Ar}), 132.1 (br. s, CH_{Ar}), 130.7 (br. s, CH_{Ar}), 128.7 (CH_{Ar}), 128.5 (d, $J_{C,P}$ = 7.6 Hz, CH_{Ar}), 128.2 (CH_{Ar}), 125.8 (CH), 94.1 (C_{quat}), 79.8 (C_{quat}), 68.0 (CH_2), 64.9 (CH_2), 58.7 (CH), 28.5 (*t*Bu), 26.7 (CH_3), 23.8 (CH_3) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = –4.53 ppm. $C_{32}H_{36}NO_5P$ (454.61): calcd. C 70.44, H 6.65, N 2.57; found C 70.6, H 6.94, N 2.38. Chiral HPLC: CHIRALCEL AD-H column 0.46 cm × 25 cm, flow rate 0.8 mL/min (*n*-heptane/EtOH, 95/5), UV 230 nm, R_t: (*S*)-*E* 10.25 min (100% *E*).

***tert*-Butyl (4*S*)-4-[(1*Z*)-3-{[2-(Diphenylphosphanyl)benzoyl]oxy}-prop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (9):** White solid (97%). R_f = 0.73 (cyclohexane/EtOAc, 1:1); m.p. 96 °C. $[\alpha]_D^{20}$ = –70.0 (*c* = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2970, 1712, 1681, 1388, 1377, 1268, 1253, 1105, 1065, 757, 744, 696, 526, 400 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07 (m, 1 H), 7.44–7.25 (m, 12 H), 6.95 (m, 1 H), 5.58 (m, 2 H), 4.89–5.00 (2 br. s, 1 H), 4.68 (m, 2 H), 3.98 (dd, *J* = 6.3, 9.0 Hz, 2 H), 3.55 (br. s, 1 H), 1.60 (s, 3 H), 1.52 (s, 3 H), 1.43 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 151.8, 140.6 (d, $J_{C,P}$ = 27.0 Hz), 138.0 (d, $J_{C,P}$ = 10.4 Hz), 132.1 (br. s), 134.4, 134.0 (d, $J_{C,P}$ = 20.8 Hz) 133.8 (d, $J_{C,P}$ = 20.6 Hz), 132.1 (br. s), 130.7 (br. s), 128.7 (d, $J_{C,P}$ = 4.1 Hz), 128.50 (d, $J_{C,P}$ = 6.5 Hz), 128.48 (d, $J_{C,P}$ = 7.1 Hz), 128.2, 125.2, 123.6, 94.2/93.5 (rotamers, C_{quat}), 80.1/79.9 (rotamers, C_{quat}), 68.6/68.3 (rotamers), 61.0/60.6 (rotamers), 54.5/54.3 (rotamers), 28.5 (*t*Bu), 27.5/26.6 (rotamers), 25.0/23.9 (rotamers) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = –4.53 ppm. $C_{32}H_{36}NO_5P$ (454.61): calcd. C 70.44, H 6.65, N 2.57; found C 70.21, H 6.67, N 2.53. Chiral HPLC: CHIRALCEL AD-H column, 0.46 cm × 25 cm, flow rate 0.8 mL/min (*n*-heptane/EtOH, 95:5), UV 230 nm, R_t: (*S*)-*E* 8.18 min (100% Z).

General Procedure for Allylic Substitution Reactions: Into a dry round-bottomed flask under argon was introduced **8** or **9** (80 mg, 0.146 mmol) in anhydrous Et_2O (14.6 mL, 0.01 M) followed by $CuBr{\cdot}SMe_2$ (15 mg, 0.073 mmol). The mixture was stirred at room temp. until the copper salt had completely dissolved (ca. 10 min) to yield a clear light-yellow solution. Then the alkylmagnesium bromide in diethyl ether at 0.1 M (3 mL) was added through a syringe pump (rate 3 mL/h) at room temp. The mixture was stirred for an additional 1 h and saturated aqueous NH_4Cl was added and extraction with EtOAc was performed. The organic layer was dried with $MgSO_4$, filtered and the solvent removed under reduced pressure. The residue was purified by flash chromatography (heptane/EtOAc, 9:1).

***tert*-Butyl (4*S*)-2,2-Dimethyl-4-[(1*R*)-1-methylprop-2-enyl]-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 20a):** Light-yellow oil. R_f = 0.62 (heptane/EtOAc, 7:3). IR (neat): $\tilde{\nu}$ = 2926, 1694, 1384, 1364, 1254, 1175, 1085, 1056, 543 cm^{-1}. ^1H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 5.78 (m, 1 H), 5.04 (m, 2 H), 3.87 (m, 3 H), 2.75 (br. m, 1 H), 1.61 (s, 3 H), 1.55 (s, 3 H), 1.49 (s, 9 H), 1.01 (d, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 152.9 (CO), 140.1 (CH), 115.8 (CH_2), 94.3/93.8 (rotamers, C_{quat}), 80.1/79.7 (rotamers, C_{quat}), 64.7/64.3 (rotamers, CH_2), 61.7/61.5 (CH), 40.8/39.9 (rotamers, CH), 28.7 (*t*Bu), 27.0/26.5 (rotamers, CH_3), 24.7/23.2 (rotamers, CH_3), 17.2/17.0 (rotamers, CH_3) ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 256.1907; found 256.1901.

***tert*-Butyl (4*S*)-2,2-Dimethyl-4-[(1*S*)-1-methylprop-2-enyl]-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 21a):** Light-yellow oil. R_f = 0.61 (heptane/EtOAc, 7:3). IR (neat): $\tilde{\nu}$ = 2926, 1695, 1374, 1364, 1254, 1175, 1084, 1054, 849 cm^{-1}. ^1H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 5.82 (m, 1 H), 5.08–5.02 (m, 2 H), 3.94–3.81 (m, 3 H), 2.75 (br. m, 1 H), 1.60 (s, 3 H), 1.49 (s, 9 H, *t*Bu), 1.46 (s, 3 H), 1.01 (d, *J* = 7.18 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, 50 °C, $CDCl_3$): δ = 152.6 (CO), 141.1 (CH), 114.7 (CH_2), 94.1 (C_{quat}), 79.8 (C_{quat}), 68.7 (CH_2), 61.1 (CH), 39.9 (CH), 28.6 (*t*Bu), 26.7 (br. s, CH_3), 24.0 (br. s, CH_3), 14.2 (CH_3) ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 256.1907; found 256.1903.

***tert*-Butyl (4*S*)-4-[(1*R*)-1-Ethylprop-2-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 20b):** Light-yellow oil. R_f = 0.29 (cyclohexane/EtOAc, 8:2). IR (neat): $\tilde{\nu}$ = 2928, 1698, 1387, 1365, 1259, 1176, 1091 cm^{-1}. ^1H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 5.67–5.55 (m, 1 H), 5.13–5.00 (m, 2 H), 3.87–3.80 (m, 3 H), 2.46 (br. m, 1 H), 1.55 (s, 3 H), 1.48 (s, 9 H), 1.46 (s, 3 H), 1.26 (m, 2 H), 0.89 (t, *J* = 7.49 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.8/152.4 (rotamers, CO), 138.7 (CH), 117.7 (CH_2), 94.2/93.2 (rotamers, C_{quat}), 80.0/79.7 (rotamers, C_{quat}), 64.7/64.3 (rotamers, CH_2), 61.1/60.5 (rotamers, CH), 49.0/47.9 (rotamers, CH), 28.6 (*t*Bu), 26.9/26.3 (rotamers, CH_3), 24.8 (CH_2), 24.5/24.3 (rotamers, CH_3), 12.3 (CH_3) ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 270.2064; found 270.2052.

***tert*-Butyl (4*S*)-4-[(1*S*)-1-Ethylprop-2-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 21b):** Light-yellow oil. R_f = 0.41 (cyclohexane/EtOAc, 8:2). IR (neat): $\tilde{\nu}$ = 2930, 1694, 1384, 1363, 1255, 1174, 1089, 847, 767 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.65 (m, 1 H), 5.14–5.00 (m, 2 H), 3.92–3.81 (m, 3 H), 2.39 (m, 1 H), 1.59 (s, 3 H), 1.53 (s, 9 H), 1.46 (s, 3 H), 1.18 (m, 2 H), 0.88 (t, *J* = 7.49 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.9/152.4 (rotamers, CO), 139.5 (CH), 117.2/116.7 (rotamers, CH_2), 94.2/93.6 (rotamers, C_{quat}), 80.0/79.7 (rotamers, C_{quat}), 65.7 (CH_2), 61.0/60.9 (rotamers, CH), 49.73/49.66 (rotamers, CH), 29.6 (*t*Bu), 27.2/26.4 (rotamers, CH_3), 24.6 (CH_2), 23.1/22.7 (rotamers, CH_3), 12.2 (CH_3) ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 270.2064; found 270.2053.

***tert*-Butyl (4*S*)-4-[(1*R*)-1-Butylprop-2-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 20c):** Light-yellow oil. R_f = 0.50 (heptane/EtOAc, 7:3). IR (neat): $\tilde{\nu}$ = 2929, 1694, 1384, 1363, 1254, 1174, 1090, 913, 847, 767 cm^{-1}. ^1H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 5.64 (ddd, *J* = 16.8, 10.3, 9.6 Hz, 1 H), 5.11 (dd, *J* = 10.3, 2.1 Hz, 1 H), 4.98 (dd, *J* = 16.8, 2.1 Hz, 1 H), 3.87 (m, 3 H), 2.55 (br. m, 1 H), 1.54 (s, 3 H), 1.48 (s, 9 H), 1.46 (s, 3 H), 1.33–1.26 (m, 6 H), 0.90 (t, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 152.8/152.3 (rotamers, CO), 139.1 (CH), 117.5 (CH_2), 94.2/93.7 (rotamers, C_{quat}), 80.0/79.7 (rotamers, C_{quat}), 64.7/64.3

(rotamers, CH_2), 61.2/60.8 (rotamers, CH), 46.9/46.1 (rotamers, CH), 31.3/31.1 (rotamers, CH_2), 30.9, 28.6 (*t*Bu), 26.9/26.3 (rotamers, CH_3), 24.8/23.2 (rotamers, CH_3), 22.8 (CH_2), 14.1 (CH_3) ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 298.2377; found 298.2375.

***tert*-Butyl (4*S*)-4-[(1*S*)-1-Butylprop-2-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 21c):** Light-yellow oil. R_f = 0.63 (heptane/EtOAc, 7:3). IR (neat): $\tilde{\nu}$ = 2928, 1694, 1385, 1363, 1252, 1175, 1087, 912, 848, 767, 544 cm^{-1}. ^1H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 5.64–5.55 (m, 1 H), 5.10–4.98 (m, 2 H), 3.91–3.79 (m, 3 H), 2.42 (m, 1 H), 1.58 (s, 3 H), 1.48 (s, 12 H), 1.34–1.26 (m, 6 H), 0.87 (t, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 152.4 (CO), 139.9 (CH), 117.0/116.4 (rotamers, CH_2), 94.2/93.6 (rotamers, C_{quat}), 80.0/79.7 (rotamers, C_{quat}), 65.6 (CH_2), 61.1 (CH), 47.5 (CH), 30.8 (CH_2), 29.8/29.7 (rotamers, CH_2), 28.6 (*t*Bu), 27.2/26.4 (rotamers, CH_3), 24.7/23.1 (rotamers, CH_3), 22.8 (CH_2), 14.1 (CH_3) ppm. HRMS (ESI positive): calcd. for $[M + Na]^+$ 320.2196; found 320.2209.

***tert*-Butyl (4*S*)-4-[(1*R*)-1-Isopropylprop-2-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 20d):** Light-yellow oil. R_f = 0.65 (heptane/EtOAc, 7:3). IR (neat): $\tilde{\nu}$ = 2930, 1695, 1382, 1253, 1175, 1098, 1054, 963, 850, 768 cm^{-1}. ^1H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 5.64 (ddd, *J* = 16.8, 10.3, 10.1 Hz, 1 H), 5.12 (dd, *J* = 10.3, 2.4 Hz, 1 H), 5.00 Hz (dd, *J* = 16.8, 2.2 Hz, 1 H), 4.10 (br. m, 1 H), 3.92 (m, 2 H), 2.34 (br. m, 1 H), 1.56 (s, 3 H), 1.48 (s, 9 H), 1.45 (s, 3 H), 0.94 (d, *J* = 6.8 Hz, 3 H), 0.89 (d, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 152.2 (CO), 137.5/137.2 (rotamers, CH), 118.4 (CH_2), 94.2/93.7 (rotamers, C_{quat}), 79.9/79.7 (rotamers, C_{quat}), 64.3/64.2 (rotamers, CH_2), 59.3/59.1 (rotamers, CH), 53.5/52.3 (rotamers, CH), 29.8, 29.2/28.8 (rotamers, *t*Bu), 26.7/26.0 (rotamers, CH_3), 24.8, 23.2, 22.3 (CH_3), 21.2 (CH_3) ppm. HRMS (ESI positive): calcd. for $[M + Na]^+$ 306.2040; found 306.2033.

***tert*-Butyl (4*S*)-4-[(1*S*)-1-Isopropylprop-2-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 21d):** Light-yellow oil. R_f = 0.62 (heptane/EtOAc, 7:3). IR (neat): $\tilde{\nu}$ = 2929, 1694, 1384, 1364, 1253, 1173, 1089, 912, 848, 767, 545 cm^{-1}. ^1H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 5.81 (m, 1 H), 5.14–4.87 (m, 2 H), 4.14–3.70 (m, 3 H), 2.11 (m, 1 H), 1.69 (m, 1 H), 1.55 (s, 3 H), 1.50 (s, 3 H), 1.49 (s, 9 H), 0.89 (d, *J* = 7.0 Hz, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.1 (CO), 136.3/135.6 (rotamers, CH), 118.7/117.6 (rotamers, CH_2), 94.0/93.4 (rotamers, C_{quat}), 79.8 (C_{quat}), 67.6/67.1 (rotamers, CH_2), 59.0/58.9 (rotamers, CH), 55.8/55.2 (rotamers, CH), 29.8 (CH), 29.0/28.6 (rotamers, *t*Bu), 27.5/26.8 (rotamers, CH_3), 24.8, 23.3, 22.3, 21.3, 17.0 (CH_3), 16.6 (CH_3) ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 284.2220; found 284.2215.

(*S*)-2,2-Dimethyl-3-(*tert*-butoxycarbonyl)-4-ethynyloxazolidine (10):[33] Into a dry flask under argon was introduced dimethyl (2-oxopropyl)phosphonate (2.13 mL, 14.8 mmol) in anhydrous chloroform (36 mL). The solution was cooled to 0 °C and under vigorous stirring 4-acetamidobenzenesulfonyl azide (3.67 g, 15.3 mmol) and potassium carbonate (2.1 g, 15.2 mmol) were added. The solution was stirred between 0 and 10 °C for 48 h. Then a solution of **1** (1.0 g, 4.46 mmol) in anhydrous methanol (36 mL) was added dropwise at 0 °C. The mixture was stirred for 24 h at 0 °C with additional potassium carbonate (0.96 g, 7.0 mmol). Saturated aqueous NH_4Cl was then added and the mixture was extracted with chloroform. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The residue was purified over silica gel column (pentane/Et_2O, 9:1) to yield the desired alkyne as a colourless oil (697 mg, 71%). R_f = 0.40 (heptane/EtOAc, 7:3). $[\alpha]_D^{20}$ = +96.6 (*c* = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 50 °C): δ = 4.46 (br. m, 1 H), 3.99–3.90 (m, 2 H), 2.21 (d, *J* = 1.7 Hz, 1 H), 1.55 (br. s, 3 H), 1.42 (br. s, 12 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 50 °C): δ = 151.5 (CO), 94.3 (C_{quat}), 82.8 (C_{quat}), 80.4 (C_{quat}), 70.3 (CH), 68.7 (CH_2), 48.4 (CH), 28.4 (*t*Bu), 26.1 (CH_3), 24.7 (CH_3) ppm.

***tert*-Butyl (*S*)-4-(3-Hydroxyprop-1-ynyl)-2,2-dimethyloxazolidine-3-carboxylate (11):**[34] Into a dry flask under argon was introduced alkyne **10** (205 mg, 0.910 mmol) in anhydrous THF (5 mL). The solution was cooled to –78 °C and a 1.42 M solution of *n*BuLi in hexanes (673 μL, 0.955 mmol) was added dropwise. The mixture was stirred at –78 °C for 30 min and paraformaldehyde (273 mg, 9.100 mmol) was added in one portion. The mixture was allowed to reach room temp. Saturated aqueous NH_4Cl was added and the mixture was extracted with DCM (3×). The organic layer was dried with Na_2SO_4 and removed under reduced pressure. The residue was purified by silica gel chromatography (heptane/EtOAc, 7:3) to yield a colourless oil (101 mg, 43%). R_f = 0.12 (heptane/EtOAc, 7:3). $[\alpha]_D^{20}$ = +100.4 (*c* = 1, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$, 50 °C): δ = 4.57 (br. m, 1 H), 4.25 (br. d, *J* = 1.3 Hz, 2 H), 4.07–3.93 (m, 2 H), 2.21 (br. s, 1 H, OH), 1.60 (br. s, 3 H), 1.49 (br. s, 12 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 50 °C): δ = 151.8 (CO), 94.43 (C_{quat}), 84.5 (C_{quat}), 80.9 (C_{quat}), 80.7 (C_{quat}), 68.9 (CH_2), 51.1 (CH_2), 48.8 (CH), 28.6 (*t*Bu), 26.5 (CH_3), 25.0 (CH_3) ppm.

***tert*-Butyl (*S*)-4-{3-[2-(Diphenylphosphanyl)phenylcarbonyloxy]prop-1-ynyl}-2,2-dimethyloxazolidine-3-carboxylate (12):** Into a dry flask under argon was introduced alcohol **11** (99 mg, 0.388 mmol) in DCM (2 mL). *o*DPPBA (119 mg, 0.388 mmol), DCC (80 mg, 0.388 mmol) and DMAP (48 mg, 0.388 mmol) were added at room temp. The mixture was stirred overnight and brine was added and the mixture was extracted with DCM (3×). The organic layer was dried with Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by silica gel chromatography (heptane/EtOAc, 8:2) to yield the desired product as a white solid (187 mg, 90%); m.p. 110 °C. $[\alpha]_D^{20}$ = +37.6 (*c* = 1, $CHCl_3$). R_f = 0.32 (petroleum ether/Et_2O, 7:3). IR (neat): $\tilde{\nu}$ = 2985, 2360, 1707, 1689, 1364, 1250, 1092, 1057, 756, 695 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 50 °C): δ = 8.12–8.06 (m, 1 H), 7.43–7.26 (m, 12 H), 7.01–6.97 (m, 1 H), 4.78 (d, *J* = 1.8 Hz, 2 H), 4.59 (br. s, 1 H), 4.07–3.97 (m, 2 H), 1.64 (br. s, 3 H), 1.52 (br. s, 3 H), 1.50 (br. s, 9 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 50 °C): δ = 165.9 (CO), 151.6 (CO), 141.2 (d, $J_{C,P}$ = 28.0 Hz, C_{quat}), 138.1 (d, $J_{C,P}$ = 12.7 Hz, C_{quat}), 134.5 (CH_{Ar}), 134.5 (CH_{Ar}), 134.3 (CH_{Ar}), 133.9 (CH_{Ar}), 132.2 (CH_{Ar}), 130.9 (CH_{Ar}), 128.7 (CH_{Ar}), 128.6 (CH_{Ar}), 128.5 (CH_{Ar}), 128.2 (CH_{Ar}), 94.5 (C_{quat}), 86.0 (C_{quat}), 76.2 (C_{quat}), 68.7 (CH_2), 53.0 (CH_2), 48.8 (CH), 28.6 (*t*Bu), 26.4 (br., CH_3), 24.9 (br., CH_3) ppm. ^{31}P NMR (121 MHz, $CDCl_3$): δ = –3.8 ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 544.2247; found 544.2224.

***tert*-Butyl (*S*)-4-(Buta-2,3-dien-2-yl)-2,2-dimethyloxazolidine-3-carboxylate (23):** Prepared by using the general procedure for the directed allylic substitution. Colourless oil. R_f = 0.59 (heptane/Et_2O, 7:3). IR (neat): $\tilde{\nu}$ = 2925, 1698, 1375, 1364, 1088, 848 cm^{-1}. ^1H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 4.74 (br. s, 2 H), 4.30 (br. m, 1 H), 4.06 (dd, *J* = 8.8, 6.6 Hz, 1 H), 3.88 (dd, *J* = 8.8, 2.1 Hz, 1 H), 1.7 (t, *J* = 3.0 Hz, 3 H), 1.62 (br. s, 3 H), 1.50 (br. s, 3 H), 1.47 (br. s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.3/206.1 (C_{quat}), 152.2 (CO), 99.6/99.1 (C_{quat}), 94.3/93.8 (C_{quat}), 80.2/79.6 (C_{quat}), 77.5/77.0 (CH_2), 67.7/67.1 (CH_2), 59.9 (CH), 28.5 (*t*Bu), 26.7/25.9 (CH_3), 23.5/22.9 (CH_3), 15.7/15.2 (CH_3) ppm. HMRS (ESI positive + HCOOLi): calcd. for $[M + Li]^+$ 260.1833; found 260.1825.

***tert*-Butyl (4*S*)-2,2-Dimethyl-4-[(1*S*)-1-methylpropyl]-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 24):** Into a suitable flask

was introduced **21a** (80 mg, 0.31 mmol) and EtOAc/MeOH (9 mL, 1:1). Then $Pd(OH)_2/C$ 20% (62 mg) was added. The flask was purged with H_2 before setting a pressure of 5 bar for 2 h at room temp. The mixture was filtered through a plug of Celite. The solvent was removed under reduced pressure and the residue was purified through a silica gel column (heptane/EtOAc, 9:1) to yield a colourless oil (75 mg, 95%). ^{1}H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 4.40–4.27 (m, 3 H), 2.08 (br. m, 1 H), 1.63 (s, 3 H), 1.49 (s, 12 H), 1.33–1.24 (m, 1 H), 1.14–1.05 (m, 1 H), 0.83 (t, J = 8.9 Hz, 3 H), 0.75 (d, J = 8.3 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 152.8 (CO), 94.0/93.5 (rotamers, C_{quat}), 79.9/79.6 (rotamers, C_{quat}), 63.9 (CH_2), 61.6/60.8 (rotamers, CH), 37.0/35.9 (rotamers, CH), 28.6 (*t*Bu), 26.8 (CH_2), 26.8/26.2 (rotamers, CH_3), 24.5/22.9 (rotamers, CH_3), 14.2/13.8 (rotamers, CH_3), 12.3 (CH_3) ppm. HRMS (ESI positive): calcd. for $[M + 1]^+$ 258.2037; found 258.2060.

***tert*-Butyl (4*S*)-2,2-Dimethyl-4-[(1*R*)-1-methyl-2-oxopropyl]-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 25):** Into a round-bottomed flask was introduced CuCl (33 mg, 0.329 mmol), $PdCl_2$ (12 mg, 0.066 mmol) and DMF/H_2O (0.4 mL, 10:1). The mixture was stirred at room temp. for 2 h under O_2 (the mixture turned black). Then a solution of **21a** (84 mg, 0.329 mmol) in DMF/H_2O (0.4 mL, 10:1) was added. The mixture was stirred overnight. A solution of saturated aqueous NH_4Cl was added and the mixture was extracted with diethyl ether (3×). The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The resulting oil was purified through a silica gel column (heptane/EtOAc, 9:1) to yield 60 mg of the desired product (68%) and 11 mg of starting material (78% brsm). R_f = 0.52 (heptane/EtOAc, 6:4). IR (neat): $\tilde{\nu}$ = 2978, 2933, 1694, 1365, 1169 cm^{-1}. ^{1}H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 4.20 (br. m, 1 H), 3.99–3.78 (m, 2 H), 3.26 (br. m, 1 H), 2.16 (s, 3 H), 1.59 (s, 3 H), 1.47 (s, 9 H), 1.45 (s, 3 H), 1.12 (d, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 211.3 (CO), 153.0 (CO, *t*Bu), 94.3/93.7 (C_{quat}), 80.7 (C_{quat}), 64.6 (CH_2), 57.8 (CH), 48.1 (CH), 30.0 (CH_3), 28.7 (*t*Bu), 27.1 (CH_3), 24.3 (CH_3), 10.7 (CH_3) ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 272.1856; found 272.1869.

***tert*-Butyl (4*S*)-4-[(1*S*)-1-Cyclopropylethyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (Major Diastereomer, 26):** Into a dry flask containing **21a** (118 mg, 0.462 mmol) was added at 0 °C a dry solution of diazomethane (2.7 mmol, 12 mL) in Et_2O. Then $Pd(OAc)_2$ (1.5 mg) was added at 0 °C in one portion and gas evolution was observed. After 10 min at 0 °C the solvent was removed under reduced pressure and the residue was purified through a silica gel column (heptane/EtOAc, 9:1) to yield the desired product (124 mg, quant.). R_f = 0.61 (heptane/EtOAc, 7:3). ^{1}H NMR (300 MHz, 50 °C, $CDCl_3$): δ = 4.07–3.88 (m, 3 H), 1.70 (m, 1 H), 1.61 (rotamers, 3 H), 1.49 (rotamers, 12 H), 0.98 (d, J = 7.0 Hz, 3 H), 0.87 (m, 1 H), 0.55–0.38 (m, 2 H), 0.24 (m, 1 H), 0.06 (m, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 152.8/152.6 (rotamers, CO), 94.1/93.6 (rotamers, C_{quat}), 79.9/79.5 (rotamers, C_{quat}), 64.2 (CH_2), 61.5/61.0 (rotamers, CH), 41.0/40.0 (rotamers, CH), 28.6 (*t*Bu), 26.9/26.1 (rotamers, CH_3), 24.6/22.9 (rotamers, CH_3), 15.2/14.9 (rotamers, CH_3), 14.4 (CH), 4.2 (CH_2), 3.7 (CH_2) ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 270.2064; found 270.2064.

***tert*-Butyl (1*S*,2*S*)-2-Cyclopropyl-1-(hydroxymethyl)propylcarbamate (Major Diastereomer, 27):** Compound **26** (111 mg, 0.412 mmol) was dissolved in dry MeOH (2 mL) and TFA (0.4 mL, 5.15 mmol) was added at 0 °C. The mixture was stirred for 3 h at room temp. and DCM and saturated aqueous Na_2CO_3. were added to the mixture. The aqueous layer was extracted with DCM (3×). The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The desired product was obtained as a white solid (90 mg, 95%) and needed no further purification. R_f = 0.29 (heptane/EtOAc, 7:3). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.94 (br. d, J = 6.9 Hz, 1 H), 3.70–3.43 (m, 3 H), 2.90 (br. s, 1 H), 1.41 (s, 9 H), 0.97 (br. s, 3 H), 0.60–0.30 (m, 3 H), 0.20–0.16 (m, 1 H), 0.03–0.04 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.9 (CO), 79.5 (C_{quat}), 64.1 (CH_2), 58.0 (CH), 39.9 (CH), 28.5 (*t*Bu), 17.1 (CH_3), 14.4 (CH), 5.3 (CH_2), 2.8 (CH_2) ppm. HRMS (ESI positive): calcd. for $[M + Na]^+$ 252.1570; found 252.1557.

(2*S*,3*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-cyclopropylbutanoic Acid (Major Diastereomer, 28): A stock solution of H_5IO_6/CrO_3 (1.25 mL; H_5IO_6, 5 g, 0.22 mmol, CrO_3, 10 mg, 0.1 mmol, MeCN 49.6 mL, H_2O, 0.4 mL) was added dropwise to a solution of **27** (50 mg, 0.218 mmol) in MeCN (containing 0.75% of H_2O; 2.75 mL) at 0 °C. After 2 h no further starting material could be detected by TLC. The crude mixture was diluted in toluene and a phosphate buffer (pH 5.8) was added. The organic phase was separated and dried with $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (100% EtOAc) to yield the desired compound (90 mg, 85%). R_f = 0.30 (heptane/EtOAc, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51 (br. s, 1 H), 5.22 (br. d, J = 8.7 Hz, 1 H), 4.40 (m, 1 H), 1.46 (s, 9 H), 1.07 (d, J = 6.9 Hz, 3 H), 0.67 (m, 1 H), 0.46 (m, 2 H), 0.25 (m, 1 H), 0.08 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.1 (CO), 155.9 (CO), 80.1 (C_{quat}), 58.1 (CH), 41.6 (CH), 28.8 (*t*Bu), 16.9 (CH_3), 13.4 (CH), 4.4 (CH_2), 3.2 (CH_2) ppm. HRMS (ESI positive): calcd. for $[M + Na]^+$ 266.1363; found 266.1439.

(2*S*,3*S*)-2-Amino-3-cyclopropylbutanoic Acid (Major Diastereomer, 29):[14c] Into a dry flask under argon was introduced **28** (33 mg, 0.136 mmol) and anhydrous DCM (2.5 mL). Then trifluoroacetic acid (188 μL, 2.448 mmol) was added at room temp. The mixture was stirred overnight and then it was evaporated under reduced pressure to yield the desired product as a TFA salt in a quantitative yield (*syn*/*anti*, 10:90). ^{1}H NMR (400 MHz, D_2O/DMSO): δ = 3.87 (d, J = 4.7 Hz, 1 H), 1.28 (m, 1 H), 0.97 (d, J = 6.7 Hz, 3 H), 0.55 (m, 1 H), 0.36 (m, 2 H), 0.08 (m, 1 H), 0.00 (m, 1 H) ppm. ^{13}C NMR (100 MHz, D_2O/DMSO): δ = 173.3 (CO), 59.7 (CH), 41.0 (CH), 17.3 (CH_3), 14.4 (CH), 5.6 (CH_2), 4.4 (CH_2) ppm. LRMS (ESI positive): calcd. for $[M + H]^+$ 144.1; found 144.1.

Oxidation of the *o*DPPB Esters 8 and 9: Into a round-bottomed flask equipped with a magnetic stirring bar was introduced **8** or **9** (179 mg, 0.327 mmol) and dichloromethane (3.5 mL). Then at room temp. a solution of hydrogen peroxide (35% in water, 313 μL, 3.275 mmol) was added. The mixture was stirred for 3 h and then extracted with EtOAc. A spatula edge of manganese oxide was added to the organic layer to eliminate any residual peroxide. The organic was then dried with $MgSO_4$ and removed under reduced pressure. The residue was taken up in EtOAc and passed through a silica gel column (EtOAc, 100%) to yield a waxy solid in quantitative yields.

***tert*-Butyl (4*S*)-4-[(1*E*)-3-{[2-(Diphenylphosphoryl)benzoyl]oxy}prop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (30):** Waxy solid. R_f = 0.41 (EtOAc). $[\alpha]_D^{20}$ = +20.2 (c = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2980, 1728, 1689, 1386, 1253, 1117, 722, 694, 538 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (br. dd, J = 7.5, 3.6 Hz, 1 H), 7.64–7.55 (m, 5 H), 7.50–7.46 (m, 4 H), 7.42–7.39 (m, 4 H), 5.52 (m, 2 H), 4.37 (m, 2.5 H), 4.16 (br. m, 0.5 H), 3.95 (dd, J = 8.7, 6.2 Hz, 1 H), 3.64 (dd, J = 8.9, 2.1 Hz, 1 H), 1.54 (br. s, 3 H), 1.46 (br. s, 3 H), 1.35 (br. s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.8 (CO), 151.8 (CO), 136 (d, $J_{C,P}$ = 6.0 Hz, C_{quat}), 134.8 (d, $J_{C,P}$ = 10.9 Hz, CH_{Ar}), 134.1 (CH), 133.9 (CH_{Ar}), 133.9 (CH_{Ar}), 132.8/

132.80 (rotamers, C_{quat}), 131.9 (CH_{Ar}), 131.8 (CH_{Ar}), 131.8 (CH_{Ar}), 131.6 (CH_{Ar}), 130.9 (d, $J_{C,P}$ = 11.6 Hz, CH_{Ar}), 130.2 (d, $J_{C,P}$ = 8.6 Hz, CH_{Ar}), 128.3 (d, $J_{C,P}$ = 12.5 Hz, CH_{Ar}), 125.4 (CH), 94.0/93.7 (rotamers, C_{quat}), 80.2/79.7 (rotamers, C_{quat}), 67.9 (CH_2), 65.3 (CH_2), 58.5 (CH), 28.4 (*t*Bu), 27.4/26.6 (rotamers, CH_3), 24.8/23.7 (rotamers, CH_3) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 30.99 ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 562.2353; found 562.2328.

***tert*-Butyl (4*S*)-4-[(1*Z*)-3-{[2-(Diphenylphosphoryl)benzoyl]oxy}-prop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (31):** Waxy solid. R_f = 0.32 (EtOAc). $[\alpha]_D^{20}$ = +56.0 (c = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2957, 1722, 1694, 1283, 1254, 1191, 1121, 724, 693, 532 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.88 (br. m, 1 H), 7.66–7.58 (m, 5 H), 7.55–7.48 (m, 4 H), 7.45 (m, 4 H), 5.48 (t, J = 10.2 Hz, 1 H), 5.32 (br. m, 1 H), 4.69/4.64 (rotamers, br. m, 1 H), 4.49 (br. m, 2 H), 3.93 (dd, J = 8.7, 6.5 Hz, 1 H), 3.53 (br. m, 1 H), 1.56 (br. s, 3 H), 1.48 (br. s, 3 H), 1.37 (br. s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.9 (CO), 151.9 (CO), 136.1 (C_{quat}), 134.9 (CH_{Ar}), 134.8 (CH_{Ar}), 134.0/133.5 (rotamers, CH), 132.9 (C_{quat}), 132.0 (CH_{Ar}), 131.9 (CH_{Ar}), 131.8 (CH_{Ar}), 131.7 (CH_{Ar}), 131.0 (d, $J_{C,P}$ = 11.4 Hz, CH_{Ar}), 130.5 (CH_{Ar}), 128.4 (d, $J_{C,P}$ = 12.0 Hz, CH_{Ar}), 125.0/123.5 (rotamers, CH), 94.2/93.5 (rotamers, C_{quat}), 80.0 (C_{quat}), 68.6/68.4 (rotamers, CH_2), 61.5/61.2 (rotamers, CH_2), 54.3 (CH), 28.52 (*t*Bu), 27.5/26.6 (CH_3), 25.1/24.0 (CH_3) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 31.22 ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 562.2353; found 562.2328.

General Procedure for Allylic Substitution Reactions with *o*DPPB Oxides 30 and 31: Into a dry flask under argon was introduced CuCN·2LiCl[34] (13 mg, 74.7 μmol) in anhydrous THF (0.5 mL). The solution was stirred until the copper salt had dissolved and then cooled to –30 °C by means of a cryostat. A solution of dialkylzinc in toluene (2.4 equiv.) was added dropwise. The mixture was stirred for 30 min at –30 °C (light yellow) and a solution of **30** or **31** (35 mg, 62.2 μmol) in THF (0.9 mL) was added through a syringe pump (rate 0.5 mL/h) at 0 °C. The mixture was stirred for 5 h at 0 °C and then overnight at room temp. (black solution). Saturated aqueous NH_4Cl was added and the mixture was extracted with EtOAc (3×). The organic layer was dried with $MgSO_4$ and the solvents removed under reduced pressure. The residue was purified by silica gel chromatography (heptane/EtOAc, 9:1).

Methyl (2*E*)-3-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]acrylate (14):[35] A solution of sodium periodate (3.88 g, 18.12 mmol) in water (40 mL) was added dropwise to a suspension of 1,2:5,6-di-*O*-isopropylidene-D-mannitol[36] (3.66 g, 13.94 mmol) in saturated aqueous $NaHCO_3$ (60 mL) cooled to 0 °C. After 10 min at 0 °C the ice bath was removed and the reaction was stirred for 2.5 h at room temp. (TLC monitored). The mixture was cooled again to 0 °C and potassium carbonate (78 g, 560 mmol) was added followed by diethyl ethylphosphonate ester (10.2 mL, 57.2 mmol). After 10 min at 0 °C the ice bath was removed and the mixture was stirred for 12 h at room temp. Water was added and the aqueous layer was extracted with Et_2O (5×). The organic layer was dried with $MgSO_4$ and removed under reduced pressure. The colourless oil was purified through a silica gel column (cyclohexane/EtOAc, 10:1) to yield 5.02 g of **14** as a colourless liquid (90%, *E*/*Z* = 95:5). R_f = 0.79 (cyclohexane/EtOAc, 1:1). ^1H NMR (300 MHz, C_6D_6): δ = 6.84 (ddd, J = 15.5, 5.3, 1.4 Hz, 1 H), 6.13 (ddd, J = 15.5, 2.4, 1.5 Hz, 1 H), 4.21 (m, 1 H), 3.99 (q, J = 7.1 Hz, 2 H), 3.65 (m, 1 H), 3.25 (ddd, J = 7.2, 2.3, 1.0 Hz, 1 H), 1.27 (s, 3 H), 1.23 (s, 3 H), 0.96 (td, J = 7.1, 1.3 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 165.7 (CO), 145.2 (CH), 122.3 (CH), 110.0 (C_{quat}), 75.1 (CH), 68.8 (CH_2), 60.3 (CH_2), 26.5 (CH_3), 25.8 (CH_3), 14.2 (CH_3) ppm.

Methyl (2*Z*)-3-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]acrylate (15):[37] A solution of sodium periodate (4.3 g, 20.13 mmol, 30 mL) in MeOH/H_2O (2:1) was added dropwise to a slurry of 1,2:5,6-di-*O*-isopropylidene-D-mannitol (4.00 g, 15.25 mmol) in MeOH/H_2O (73 mL, 4:1) and 5% aqueous $NaHCO_3$ at 0 °C. The mixture was stirred for 2 h at this temperature and a solution of $Ph_3PCH_2CO_2Me$ (14.78 g, 44.23 mmol, 34 mL) in MeOH was added dropwise at 0 °C. The mixture was stirred for 24 h at 0 °C and then extracted with DCM. The organic layer was dried with $MgSO_4$. The solvent was removed under reduced pressure and the residue was taken up with a mixture of heptane/Et_2O (4:1) and the white solid was filtered off (triphenylphosphane oxide). The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (heptane/EtOAc, 9:1) to yield 3.93 g (69%) of the desired product and 0.54 g (9%) of the *E* isomer (*Z*/*E* = 88:12). R_f = 0.50 (heptane/EtOAc, 7:3). ^1H NMR (300 MHz, $CDCl_3$): δ = 6.24 (dd, J = 11.6, 6.6 Hz, 1 H), 5.72 (dd, J = 11.6, 1.6 Hz, 1 H), 5.35 (dq, J = 7.8, 1.6 Hz, 1 H), 4.24 (dd, J = 8.1, 6.9 Hz, 1 H), 3.58 (s, 3 H), 3.47 (dd, J = 8.1, 6.9 Hz, 1 H), 1.30 (s, 3 H), 1.25 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.0 (CO), 149.8 (CH), 120.3 (CH), 109.7 (C_{quat}), 73.7 (CH), 69.4 (CH_2), 51.5 (CH_3), 26.6 (CH_3), 25.5 (CH_3) ppm.

(2*E*)-3-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]prop-2-en-1-ol (16):[37] Into a dry flask under argon was introduced **14** (500 mg, 2.5 mmol) and anhydrous DCM (12.5 mL). The solution was cooled to –78 °C and a 1.0 M solution of DIBAL-H in hexanes (6.25 mL, 6.25 mmol) was added over a period of 30 min through a syringe pump. The mixture was stirred for 2 h at –78 °C and quenched with water (0.41 mL) at –78 °C. A saturated solution of sodium potassium tartrate (12.5 mL) was added, the mixture was allowed to reach room temp. and then extracted with DCM (3×). The organic layer was dried with $MgSO_4$ and removed under reduced pressure. The oily residue was purified through a silica gel column (heptane/EtOAc, 1:1) to yield 380 mg (96%) of the desired product as a colourless oil. R_f = 0.32 (cyclohexane/EtOAc, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.93 (dt, J = 15.5, 4.9 Hz, 1 H), 5.69 (ddt, J = 15.4, 7.5, 1.5 Hz, 1 H), 4.51 (q, J = 7.2 Hz, 1 H), 4.13 (br. d, J = 4.5 Hz, 2 H), 4. 08 (dd, J = 8.3, 6.4 Hz, 1 H), 3.58 (t, J = 7.9 Hz, 1 H), 2.19 (br. s, 1 H), 1.41 (s, 3 H), 1.37 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 133.8 (CH), 128.3 (CH), 109.5 (C_{quat}), 76.7 (CH), 69.5 (CH_2), 62.5 (CH_2), 26.8 (CH_3), 26.0 (CH_3) ppm.

(2*Z*)-3-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]prop-2-en-1-ol (17):[37] Into a dry flask under argon was introduced **15** (1.00 g, 5.37 mmol) and anhydrous DCM (27 mL). The solution was cooled to – 78 °C and a 1.0 M solution of DIBAL-H (13.42 mL, 13.42 mmol) in DCM was added over 30 min through a syringe pump. The mixture was stirred for 2 h at –78 °C and quenched with water (0.89 mL) at –78 °C. A saturated solution of sodium potassium tartrate (27 mL) was added and the mixture was allowed to reach room temp. and then extracted with DCM (3×). The organic layer was dried with $MgSO_4$ and evaporated under reduced pressure. The oily residue was purified through a silica gel column (heptane/EtOAc, 1:1) to yield 822 mg (97%) of the desired product as a colourless oil. R_f = 0.29 (heptane/EtOAc, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.73 (m, 1 H), 5.48 (m, 1 H), 4.79 (q, J = 7.2 Hz, 1 H), 4.10 (m, 2 H), 4.02 (dd, J = 8.1, 5.9 Hz, 1 H), 3.49 (t, J = 7.8 Hz, 1 H), 3.01 (br. s, 1 H), 1.36 (s, 3 H), 1.33 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 133.5 (CH), 129.2 (CH), 109.5 (C_{quat}), 72.0 (CH), 69.6 (CH_2), 58.3 (CH_2), 26.8 (CH_3), 26.0 (CH_3) ppm.

(2*E*)-3-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]prop-2-enyl 2-(Diphenylphosphanyl)benzoate (18): The procedure was duplicated as mentioned in ref.[38] Colourless oil (97%). R_f = 0.66 (cyclohexane/

EtOAc, 1:1). $[\alpha]_D^{20}$ = +22.1 (*c* = 1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07 (m, 1 H), 7.41–7.25 (m, 12 H), 6.93 (m, 1 H), 5.76 (m, 2 H), 4.66 (dt, *J* = 5.9, 1.1 Hz, 2 H), 4.48 (q, *J* = 6.8 Hz, 1 H), 4.07 (dd, *J* = 8.2, 6.2 Hz, 1 H), 3.56 (t, *J* = 7.8 Hz, 1 H), 1.43 (s, 3 H), 1.39 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.44 (d, $J_{C,P}$ = 2.2 Hz, CO), 140.6 (d, $J_{C,P}$ = 26.8 Hz, C_{quat}), 138.0 (d, $J_{C,P}$ = 11.1 Hz, C_{quat}), 134.2 (CH_{Ar}), 134.3 (d, $J_{C,P}$ = 19.1 Hz, CH_{Ar}), 134.1 (d, $J_{C,P}$ = 2.7 Hz, CH_{Ar}), 133.9 (d, $J_{C,P}$ = 2.7 Hz, CH_{Ar}), 132.1 (CH), 130.8 (d, $J_{C,P}$ = 2.7 Hz, CH_{Ar}), 128.7 (CH_{Ar}), 128.6 (d, $J_{C,P}$ = 7.0 Hz), 128.3 (CH_{Ar}), 127.8 (CH), 109.5 (C_{quat}), 76.3 (CH), 69.3 (CH_2), 64.7 (CH_2), 26.8 (CH_3), 25.9 (CH_3) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = –4.45 ppm. $C_{27}H_{27}O_4P$ (446.47): calcd. C 72.63, H 6.1; found C 72.62, H 6.2.

(2*Z*)-3-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]prop-2-enyl 2-(Diphenylphosphanyl)benzoate (19): The procedure was duplicated as mentioned in ref.[37] Colourless oil. R_f = 0.57 (heptane/EtOAc, 1:1). $[\alpha]_D^{20}$ = –22.1 (*c* = 1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.06 (m, 1 H), 7.39–7.26 (m, 12 H), 6.94 (m, 1 H), 5.63 (m, 2 H), 4.84 (m, 2 H), 4.71 (m, 1 H), 4.04 (dd, *J* = 6.3, 1.9 Hz, 1 H), 3.49 (t, *J* = 7.7 Hz, 1 H), 1.42 (s, 3 H), 1.38 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.28 (d, $J_{C,P}$ = 2.2 Hz, CO), 140.4 (d, $J_{C,P}$ = 27.0 Hz, C_{quat}), 137.7 (d, $J_{C,P}$ = 11.6 Hz, C_{quat}), 134.2 (CH_{Ar}), 134.0 (d, $J_{C,P}$ = 19.1 Hz, CH_{Ar}), 133.9 (d, $J_{C,P}$ = 11.6 Hz, CH_{Ar}), 133.7 (d, $J_{C,P}$ = 11.6 Hz, CH_{Ar}), 132.1 (CH), 131.9 (CH_{Ar}), 130.6 (d, $J_{C,P}$ = 2.7 Hz, CH_{Ar}), 128.5 (d, $J_{C,P}$ = 3.6 Hz, CH_{Ar}), 128.4 (d, $J_{C,P}$ = 7.2 Hz, CH_{Ar}), 128.1 (CH_{Ar}), 127.2 (CH), 109.3 (C_{quat}), 71.7 (CH), 69.2 (CH_2), 60.6 (CH_2), 26.6 (CH_3), 25.7 (CH_3) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = –4.34 ppm. HRMS (ESI positive): calcd. for $[M + H]^+$ 447.1720; found 447.1712.

(4*S*)-2,2-Dimethyl-4-[(1*S*)-1-methylprop-2-enyl]-1,3-dioxolane (Major Diastereomer, 33): The procedure was duplicated as mentioned in ref.[37] Major diastereomer: R_f = 0.63 (heptane/Et_2O, 9:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.82 (ddd, *J* = 7.5, 7.2, 2.8 Hz, 1 H), 5.09 (d, *J* = 4.1 Hz, 1 H), 5.06 (s, 1 H), 3.99 (m, 2 H), 3.64 (m, 1 H), 2.31 (m, 1 H), 1.40 (s, 3 H), 1.34 (s, 3 H), 1.01 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.3 (CH), 115.3 (CH_2), 109.2 (C_{quat}), 79.6 (CH), 67.6 (CH_2), 41.1 (CH), 26.8 (CH_3), 25.8 (CH_3), 15.8 (CH_3) ppm.

(2*S*,3*S*)-2-(Acetyloxy)-3-methylpentanoic Acid (34):[39] Isopentyl nitrite (1.51 mL, 11.3 mmol) was added dropwise to a solution of L-isoleucine (1.31 g, 10 mmol) and sodium acetate (820 mg, 10 mmol) in acetic acid (14.3 mL) at 15 °C. The mixture was stirred for 2.5 d at 15 °C. Acetic acid was removed under reduced pressure. Water and Et_2O were added. The aqueous layer was acidified with concentrated HCl to pH 1. The organic layer was separated and washed with water. Then saturated aqueous $NaHCO_3$ was added and the aqueous layer was separated and acidified with concentrated HCl to pH 1. The aqueous layer was extracted with Et_2O (3×), the organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure to give a colourless oil (1.208 g, 69%, *syn*/*anti* = 8:92). ^1H NMR (300 MHz, $CDCl_3$): δ = 10.31 (br. s, 1 H, OH), 4.91 (d, *J* = 4.4 Hz, 1 H), 2.11 (s, 3 H), 1.98 (m, 1 H), 1.54 (m, 1 H), 1.30 (m, 1 H), 0.97 (d, *J* = 6.9 Hz, 3 H), 0.90 (t, *J* = 7.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.4 (CO), 171.3 (CO), 76.3 (CH), 36.7 (CH), 24.7 (CH_2), 20.8 (CH_3), 15.5 (CH_3), 11.8 (CH_3) ppm.

(2*S*,3*S*)-3-Methylpentane-1,2-diol (35):[40] Into a dry flask under argon was introduced LAH (828 mg, 21.8 mmol) and anhydrous THF (10.9 mL). The mixture was placed at 0 °C and a solution of **34** (950 mg, 5.45 mg) in anhydrous THF (5.5 mL) was added dropwise. The ice bath was removed and the mixture was heated at reflux for 5 h and then cooled to 0 °C. The work-up involved adding dropwise water (0.8 mL) and then 15% aqueous NaOH (2.4 mL) followed by water (0.8 mL). The white-yellow solid was filtered off and washed with DCM. The solvent was removed under reduced pressure and the residue was purified through a silica gel column (heptane/EtOAc, 1:1) to yield 475 mg (74%) as a pale-yellow oil. R_f = 0.50 (EtOAc, 100%). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.67 (m, 1 H), 3. 49 (br. d, *J* = 7.5 Hz, 2 H), 3.28 (br. s, 2 H), 1.58 (m, 1 H), 1.50 (m, 1 H), 1.20 (m, 1 H), 0.92 (d, *J* = 7.5 Hz, 3 H), 0.87 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 76.3 (CH), 65.0 (CH_2), 37.9 (CH), 25.4 (CH_2), 15.0 (CH_3), 11.5 (CH_3) ppm. HRMS (ESI positive): calcd. for $[M + Li]^+$ 125.1148; found 125.1146.

(4*S*)-2,2-Dimethyl-4-[(1*S*)-1-methylpropyl]-1,3-dioxolane (36): Into a dry flask under argon was introduced **35** (415 mg, 3.51 mmol), 2,2-dimethoxypropane (5.2 mL, 42.14 mmol) and acetone (15 mL). The mixture was stirred at room temp. and $BF_3{\cdot}Et_2O$ was added (40 mL, 0.32 mmol). The yellow solution was stirred overnight at room temp. NEt_3 (1.5 equiv.) was added until the yellow colour disappeared (ca. 0.5 mL). The solvent was removed under reduced pressure and the residue was purified by column chromatography (pentane/Et_2O, 9:1) to yield the desired product (402 mg, 72%) as a clear yellow liquid. R_f = 0.50 (heptane/EtOAc, 7:3). $[\alpha]_D^{20}$ = +13.1 (*c* = 1, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 4.00–3.80 (m, 2 H), 3.56 (t, *J* = 7.4 Hz, 1 H), 1.62 (m, 2 H), 1.38 (s, 3 H, Me), 1.34 (s, 3 H, Me), 1.15 (m, 1 H), 0.90 (t, *J* = 6.9 Hz, 3 H), 0.82 (d, *J* = 6.7 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 108.9 (C_{quat}), 80.4 (CH), 67.9 (CH_2), 38.3 (CH), 27.0 (CH_3), 26.2 (CH_2), 26.0 (CH_3), 14.6 (CH_3), 11.4 (CH_3) ppm. Elemental analysis and HRMS were not possible due to the very high volatility and non-ionization of the compound. GC method (Table 4): Column: initially 50 °C for 3 min, 15 °C/min until 200 °C, isotherm for 5 min, 20 °C/min until 250 °C, isotherm for 10 min. For the S_N2' reaction (Table 4, entry 1) *syn*: 7.033 min (**33**), *anti*: 7.387 min; S_N2 (*E*): 8.410 min; S_N2 (*Z*): 8.200 min. After reduction: *syn*: 7.012 min, *anti*: 6.962 min (**36**); S_N2-reduced: 7.528 min. From L-*i*Leu: *syn*: 7.027, *anti* 6.975 min (**36**).

***tert*-Butyl 2,2-Dimethyl-4-(1-methyl-3-oxopropyl)oxazolidine-3-carboxylate (38):** Major diastereomer: R_f = 0.43 (cyclohexane/EtOAc, 7:3). IR (neat): $\tilde{\nu}$ = 2976, 2935, 1692, 1363, 1170, 1082 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.72 (br. s, 1 H), 3.90 (m, 2 H), 3.76 (d, *J* = 7.7 Hz, 1 H), 2.66 (m, 1 H), 2.60 (dd, *J* = 16.2, 3.7 Hz, 1 H), 2.20 (m, 1 H), 1.55 (s, 3 H), 1.46 (s, 9 H), 1.44 (s, 3 H), 0.92 (d, *J* = 7.32 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.5/202.0 (rotamers, CO), 153.3 (CO), 94.5/94.1 (rotamers, C_{quat}), 80.5/80.3 (rotamers, C_{quat}), 64.2 (CH_2), 61.1 (CH), 46.2/45.8 (rotamers, CH_2), 30.1 (CH), 28.5 (*t*Bu), 26.8/26.4 (rotamers, CH_3), 24.1/22.6 (rotamers, CH_3), 17.2/16.9 (CH_3) ppm. $C_{14}H_{25}NO_4$ (271.35): calcd. C 61.97, H 9.29, N 5.16; found C 61.69, H 9.39, N 4.99.

***tert*-Butyl 4-(3-Hydroxy-1-methylpropyl)-2,2-dimethyloxazolidine-3-carboxylate (39)**

Method A: Sodium borohydride (52 mg, 1.387 mmol) was added in one portion to a solution of **38** (80 mg, 0.295 mmol) in ethanol (p.a.; 3 mL) at 0 °C. The mixture was stirred at this temperature until the starting material disappeared (30 min). The solvent was removed under reduced pressure and brine was added. Extraction with EtOAc was performed and the organic layer was dried with $MgSO_4$. The solvent was removed under vacuum. Purification through a silica gel column (cyclohexane/EtOAc, 7:3) afforded 35 mg (spot to spot reaction) of the desired products. R_f = 0.20 (cyclohexane/EtOAc, 7:3). ^1H NMR ($CDCl_3$): δ = 3.94–3.58 (m, 5 H), 2.17–2.10 (m, 2 H), 1.82–1.71 (m, 1 H), 1.59 (br., s, 3 H), 1.44

(s, 12 H), 1.40–1.27 (br. s, 1 H), 0.91 (d, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 153.0, 152.8, 90.0, 79.6, 64.9, 61.8, 61.4, 37.7, 32.4, 26.8, 26.3, 24.3, 22.8, 16.5 (Me) ppm.

Method B: Into a dry flask under argon were introduced CuI (801.7 mg, 4.21 mmol) and anhydrous THF (10 mL). The suspension was cooled to 0 °C before adding dropwise a 1.6 M solution of methyllithium in diethyl ether (5.2 mL, 8.42 mmol). A clear solution was obtained and then cooled to –78 °C for 15 min. A solution of **2** (200 mg, 0.70 mmol) and TMSCl (0.538 mL, 4.21 mmol) in dry THF (4 mL) was added dropwise to the slurry. The mixture turned yellow and was allowed to reach room temp. A NH_4OH/NH_4Cl (1:9) pH 8 buffer was added carefully to the solution. The mixture was stirred for 15 min before extraction with Et_2O. The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The resulting oil was purified through a silica gel column (cyclohexane/EtOAc, 9:1) to yield 110 mg of **40**. R_f = 0.39 (cyclohexane/EtOAc, 7:3). ^1H NMR ($CDCl_3$): δ = 4.0–3.7 (m, 3 H), 3.66 (s, 3 H), 2.6–2.4 (m, 1 H), 2.51 (dd, J = 15.6, 3.7 Hz, 1 H), 2.07 (dd, J = 11.2, 15.6 Hz, 1 H), 1.7–1.5 (br. s, 3 H), 1.47 (s, 12 H), 0.93 (d, J = 7.1 Hz, 3 H) ppm. Into a dry flask under argon was introduced **40** (100 mg, 0.33 mmol) and anhydrous diethyl ether (3.3 m^3 L). The solution was placed in an ice bath and $LiAlH_4$ (14 mg, 0.36 mmol) was added. The mixture was stirred for 1.5 h at room temp. before adding sequentially H_2O (0.014 mL), 15% aqueous NaOH and H_2O (0.042 mL). The solution was filtered through a pad of Celite® and toluene was added. The solvent was removed under reduced pressure yielding quantitatively the desired product. ^1H NMR ($CDCl_3$): δ = 3.94–3.58 (m, 5 H), 2.17–2.10 (m, 2 H), 1.82–1.71 (m, 1 H), 1.59 (br. s, 3 H), 1.44 (s, 12 H), 1.40–1.27 (br. s, 1 H), 0.91 (d, J = 7.2 Hz, 3 H) ppm. GC method (Table 5): GC analyses were conducted with a 6890N chromatograph from Agilent Technologies™ using a SUPLECOWAX™-10 fused silica capillary column 30 m × 0.25 mm × 0.25 μm film thickness. The inlet temperature was set at 250 °C, gas carrier He (104 mL/min). Column: initially 140 °C for 10 min, 20 °C/min until 250 °C, isotherm for 8 min. Pressure 26.82 psi, flow 2 mL/min. Detector FID 250 °C, H_2 flow 30 mL/min, air flow 400 mL/min, He 25 mL/min.

Compound **39**: From method A: R_t = 15.803 min (*anti* product: R_t = 15.887 min). From method B: R_t = 15.798 min (*anti* product: R_t = 15.884 min). Compound **38**: R_t = 13.896 min (*syn*)/14.070 min (*anti*).

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