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Diastereospecific carbonylation of π-allylpalladium complexes to give 3,6-disubstituted 3,6-dihydro-1*H*-pyridin-2-ones

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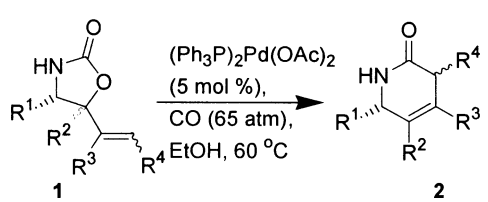
Abstract—$(Ph_3P)_2PdCl_2$ was found to be the most effective of a range of catalysts for decarboxylative carbonylation of (4*S*,5*RS*)-5-ethenyl-4-(2-propyl)oxazolidin-2-one to give the δ-lactam, (6*S*)-3,6-dihydro-6-(2-propyl)-1*H*-pyridin-2-one. In a similar way, diastereoisomerically pure (4*S*,5*S*)-4-benzyl-5-((*Z*)alk-1-enyl)oxazolidin-2-ones undergo stereospecific carbonylation to give (3*R*,6*S*)-6-benzyl-3-alkyl-3,6-dihydro-1*H*-pyridin-2-ones. The diastereoisomeric (4*S*,5*R*)-4-benzyl-5-((*Z*)alk-1-enyl)oxazolidin-2-ones give rise to a separable mixture of the corresponding (3*S*,6*S*)-6-benzyl-3-alkyl-3,6-dihydro-1*H*-pyridin-2-one and (4*S*,5*S*)-4-benzyl-5-((*E*)alk-1-enyl)oxazolidin-2-one. Under more forcing conditions, the latter oxazolidinone is carbonylated to the 3,6-*anti*-pyridinone. The stereochemical course of the reactions can be rationalized by formation of a π-allyl palladium cation with inversion of configuration followed by carbonylation with retention. The stereospecificity observed in our system precludes metal–metal exchange of the π-allyl complexes by a Pd(0) displacement process.

1. Introduction

The piperidine ring system is found in a large number of naturally occurring alkaloids and synthetic products of biological interest.[1] We recently reported the decarboxylative carbonylation of 5-vinyloxazolidin-2-ones **1** (R^4=H) to give 3,6-dihydro-1*H*-pyridin-2-ones **2** in which the stereochemistry at the 6-position was derived from a naturally occurring α-amino acid (Scheme 1).[2]

Several classes of naturally occurring piperidine, most notably the ergot alkaloids[3] and aminosteroids,[4] possess 3,6-disubstituted piperidine rings. We were therefore interested in exploring the carbonylation of substituted 5-alkenyloxazolidin-2-ones (**1**, $R^4 \neq$H) to give 3,6-disubstituted pyridinones (**2**, $R^4 \neq$H). Unlike our previous work, in which the product (**2**) possesses only the stereocenter at the 6-position, the carbonylation of alkenyloxazolidinones (**1**, $R^4 \neq$H) leads to a product with an additional stereocenter at the 3-position of the pyridinone ring. In order to investigate



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Scheme 1. Carbonylation of 5-vinyloxazolidinones **1**.

Keywords: oxazolidinone; diastereospecific carbonylation; aminosteroids.

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the relationship between the stereochemistry of the oxazolidinone **1** and that of the product **2**, we chose to study the carbonylation of single diastereoisomers of the oxazolidinones (**1**) in which both the alkene geometry and the relative stereochemistry at the 4- and 5-positions of the oxazolidinone ring were defined. The stereoselectivity of reactions involving cationic π-allylpalladium complexes has been extensively investigated, mostly in the context of allylic alkylation of nucleophiles.[5] While there are examples in which the stereochemistry of 1,3-disubstituted allyl electrophiles is transferred with control,[6] there are many examples in which the stereochemistry of the intermediate allyl complex is completely scrambled.[7] One mechanism which has been proposed to explain such scrambling is metal–metal exchange by attack of a free Pd(0) species onto a π-allyl complex.[8] It was not clear, therefore, what would be the stereochemical outcome of the carbonylation shown in Scheme 1.

2. Results and discussion

Before attempting the carbonylation of these more substituted species, several catalytic systems were investigated for the carbonylation of the simple valine-derived oxazolidinone (**1a**, R^1=^{i}Pr, R^2=R^3=R^4=H; used as a 1:3 mixture of 4,5-*syn*/4,5-*anti* diastereoisomers) in order to reduce the reaction times (5 days in our original work)[2] (Table 1).

Reducing the reaction time from 5 days to 3 days resulted in a reduction in the yield of the pyridinone **2a** (R^1=^{i}Pr,

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Table 1. Effect of different catalyst systems on the carbonylation of 5-vinyloxazolidinone **1a**

	Catalyst precursor	Time	Yield[a] of **2a** (%)	Yield[a] of recovered **1a** (%)
1	$Pd(OAc)_2(PPh_3)_2$	5 days	87	–
2	$Pd(OAc)_2(PPh_3)_2$	3 days	40	36[b]
3	$Pd(PPh_3)_4$	3 days	12	72[b]
4	$PdCl_2(PPh_3)_2$	24 h	87	–
5	$Pd(OAc)_2(PPh_3)_2$[c]	24 h	68	–

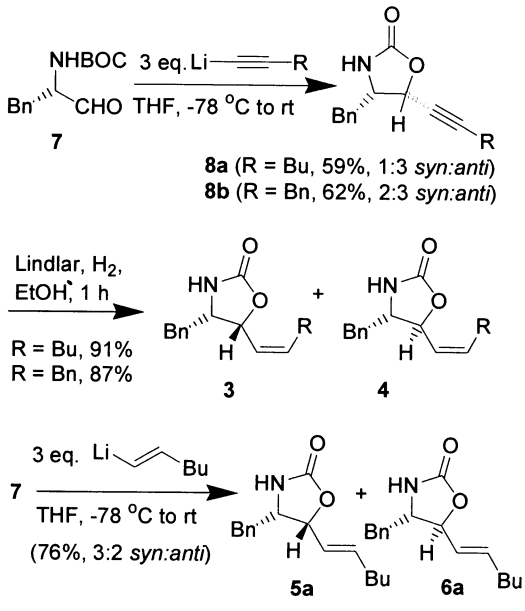
Pd catalyst (10 mol%), CO (65 atm), EtOH, 60°C.
[a] Isolated yield.
[b] Recovered as the single 4,5-*anti* diastereoisomer.
[c] 20 mol% HCl (1 M solution in Et_2O) was added to the reaction mixture.

R^2=R^3=R^4=H) from 87% (entry 1) to 40% (entry 2) and recovery of the oxazolidinone **1a** in 36% yield as the single 4,5-*anti* diastereoisomer. Using $Pd(PPh_3)_4$ as catalyst gave only 12% of the pyridinone (entry 3). We were pleased to find that using $PdCl_2(PPh_3)_2$ led to complete consumption of **1a** after 24 h to give the pyridinone in 87% yield (entry 4). Since reduction of the PdX_2 catalyst precursor to the active Pd(0) catalyst probably involves the liberation of HX, the rate increase observed in entry 4 might be due to the presence of a stronger acid (HCl vs HOAc) which could assist in the decarboxylation of nitrogen. The addition of 20 mol% HCl to the carbonylation catalyzed by $Pd(OAc)_2$-$(PPh_3)_2$ did indeed lead to an increase in the rate of reaction (entry 5). However, the 19% reduction in yield (compare entries 4 and 5) almost exactly equals the amount of HCl added. It seems likely that the increase in rate is due to the presence of chloride (which presumably displaces acetate from palladium) and that the addition of H^+ leads to a decrease in the isolated yield of pyridinone (perhaps due to formation of an ammonium salt which is unable to cyclize).

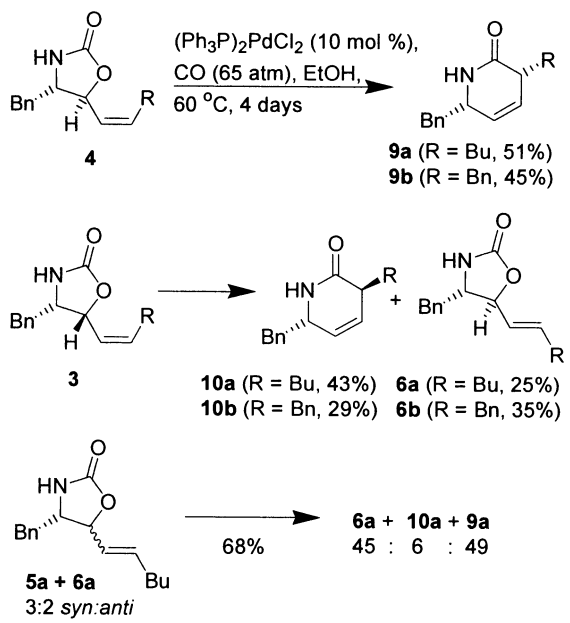
In order to investigate the stereochemical course of the carbonylation of substituted alkenyloxazolidinones, the diastereoisomeric oxazolidinones *Z-syn* **3**, *Z-anti* **4**, *E-syn* **5**, and *E-anti* **6** were prepared (Scheme 2). Addition of alkynyl lithium to BOC-protected phenylalaninal **7** proceeded with subsequent cyclization to give the 5-alkynyl-oxazolidinones **8** directly as mixtures of diastereoisomers. Lindlar hydrogenation gave the corresponding *Z*-alkenyl-oxazolidinones in excellent yield. The major *Z-anti* **4** and minor *Z-syn* **3** isomers could be separated by column chromatography at this point. Addition of *E*-hexenyl lithium (prepared by treatment of *E*-1-iodohexene with BuLi) to **7** also proceeded with subsequent cyclization to give a 3:2 mixture of the oxazolidinones **5a** and **6a** which could not be separated.[9]

We were pleased to discover that both *Z*-isomers, **3** and **4**, underwent carbonylation to give dihydropyridones (Scheme 3) although longer reaction times were required for these more highly substituted alkenes in comparison to the simple vinyl-substituted oxazolidinone **1a**. In the case of the *Z-anti* isomers **4** a single pyridinone **9** was isolated. The *Z-syn* oxazolidonones **3** appeared to be less reactive, and the products of reaction were an isomeric pyridinone **10** together with the *E-anti* oxazolidinone **6**. This result suggests that the carbonylation of the *E-anti* oxazolidinone **6** is more difficult than that of the *Z-anti* **4** and *E-syn* **5** diastereoisomers. The *E-anti* isomer **6** is expected to be the most stable of the oxazolidinone diastereoisomers and this extra stability is presumably reflected in a higher barrier to carbonylation. In accord with this, the mixture of *E*-isomers **5a** and **6a** gave rise to a 46:6:49 ratio of *E-anti* **6a** and pyridinones **10** and **9**, respectively. The pure *E-anti* isomer **6a** could be separated from this mixture and was carbonylated at 100°C to give the pyridinone **10a** albeit in low yield (35%). It seems likely that the *E-syn*-oxazolidinone **5a** gives rise to **9a** and that, at 70°C, the *E-anti* isomer **6a** reacts slowly to form the small amount of **10a** observed.

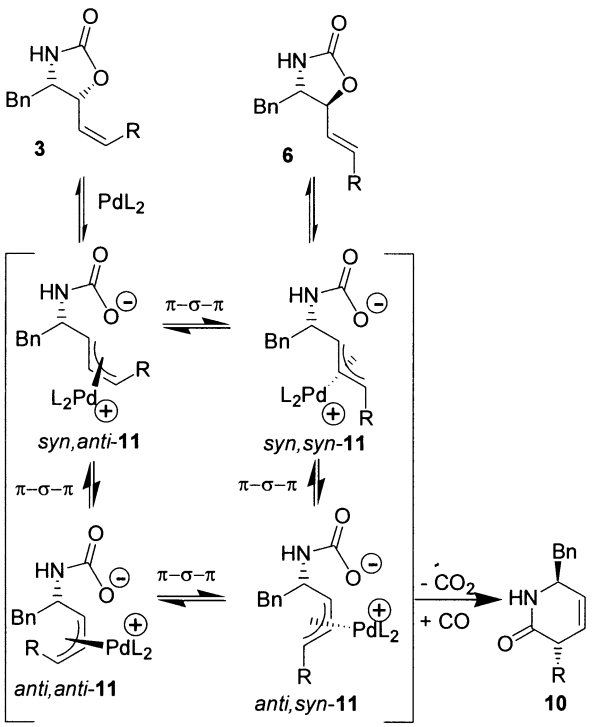
Although we had hoped to determine the relative stereochemistry of the pyridinone products by nOe experiments, there was no observable nOe between the protons on the 3- and 6-positions of the pyridinones **9a** or **10a**. Compounds **9b**



Scheme 2. Synthesis of stereoisomerically pure 5-alkenyloxazolidin-2-ones.



Scheme 3. Carbonylation of diastereoisomeric 5-alkenyloxazolidinones.



Scheme 4. Proposed catalytic cycle for carbonylation reaction.

and **10b** have been prepared previously by ring-closing metathesis.[10] Comparison of the ^{1}H NMR spectra of the pyridinone **9b** (obtained from *Z-anti* isomer **4**) and **10b** (from *Z-syn* isomer **3**) with those reported by Guibé enabled the stereochemistry of the pyridinones to be assigned as shown in Scheme 3.

A mechanism which is consistent with all of the stereochemical observations is shown in Scheme 4 for the *Z-syn* isomer **3** and *E-anti* isomer **6**.

Formation of the π-allyl palladium cation **11** is expected to occur with inversion of configuration to give the *syn*,*anti* species.[11] This is in equilibrium, via π–σ–π rearrangements, with the three other π-allyl cations shown in Scheme 4. The *syn*,*syn* isomer may ring-close, again with inversion of configuration to give the *E*,*anti*-oxazolidinone **6**, as observed experimentally. Ring closure to a pyridinone is only possible from the *anti*,*anti* and *anti*,*syn* isomers, since only these have the cisoid geometry necessary to form a six-membered ring. Carbonylation is expected to occur with retention of configuration and hence will lead to the *anti*-disubstituted pyridinone **10** as observed experimentally. A similar mechanism leads from the *Z-anti*-oxazolidinone **4** and the *E-syn* isomer **5** to the *syn*-disubstituted pyridinone **9**.

Presumably, the equilibration between *Z-anti*-**4** and *E-syn*-**5** oxazolidinones does not adversely affect the carbonylation since both of these diastereoisomers suffer one sterically destabilizing influence (*Z*-alkene geometry or *syn*-oxazolidinone substitution). The stereoselectivity observed in our system precludes metal–metal exchange of the π-allyl complexes by a Pd(0) displacement process.[8]

3. Conclusion

In conclusion, we have succeeded in demonstrating the stereospecific synthesis of 3,6-dihydro-1*H*-pyridin-2-ones by palladium catalyzed decarboxylative carbonylation of diastereoisomerically pure 5-alkenyloxazolidin-2-ones. This reaction is most efficient from the *E-syn*- and *Z-anti*-oxazolidinones which are unable to isomerize to the rather less reactive *E-anti*-isomer.

4. Experimental

4.1. General

Melting points were determined on a Linkham TC92 hot stage and are uncorrected. Optical rotations were measured on a polAAr 2001 digital polarimeter at ambient temperature and are reported as follows $[\alpha]_D^T$ (*c* g/100 ml, solvent). Infrared spectra were recorded on a Nicolet 20 PCIR instrument. Mass spectra were recorded on Micromass autospec M and Kratos MS80 RF spectrometers in electron impact (EI) mode. ^{1}H NMR spectra were recorded on Bruker AC 200 (200 MHz), Bruker WM 300 (300 MHz), JEOL LA 500 (500 MHz) and Bruker AMX 500 (500 MHz) spectrometers at ambient temperature. ^{13}C NMR were recorded on Bruker AC 200 (50 MHz) and JEOL LA 500 (125 MHz) spectrometers at ambient temperature. Thin layer chromatography was performed on EM reagent 0.25 mm silica gel 60-F plates. Flash column chromatography[1] was performed on Fluorochem LC3025 silica gel (40–63 μm). All reactions were carried out under an atmosphere of nitrogen in pre-dried glassware unless otherwise stated. Where necessary, solvents were dried prior to use. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride under nitrogen immediately prior to use. Ethanol was distilled from magnesium under nitrogen and stored over 4 Å molecular sieves. Ether and tetrahydrofuran (THF) were distilled from sodium/benzophenone ketyl immediately prior to use. All chemicals were purchased from the Aldrich, Fluka, Sigma or Lancaster chemical companies and were used as supplied except where indicated. 5-Vinyloxazolidinone **1a**[2] and *N*-Boc-phenylalaninal[12] were synthesized according to the previously published procedures.

4.2. General procedure for synthesis of 5-alkynyloxazolidinones 8

To a stirred solution of the 1-alkyne (15 mmol) in THF (60 ml) was added *n*-BuLi (7.4 mmol, 2.0 M solution in hexanes, 14.8 mmol) dropwise at −78°C. Stirring was continued for an additional 1 h and a solution of *N*-Boc-phenylalaninal (1.25 g, 5 mmol) in THF (20 ml) was added dropwise. The resulting solution was stirred for 30 min at −78°C, allowed to warm to 0°C, stirred for an additional 3 h and quenched with saturated aqueous NH_4Cl (10 ml). EtOAc (100 ml) was added and the aqueous phase was separated and extracted with additional EtOAc (2×20 ml). The combined organic extracts were dried ($MgSO_4$), evaporated, and the products were purified by chromatography (petrol/EtOAc, 3:1).

4.2.1. (4*S*,5*SR*)-4-Benzyl-5-(hex-1-ynyl)oxazolidin-2-one 8a. Hex-1-ynyllithium addition to *N*-Boc-phenylalaninal (1.25 g, 5 mmol) gave a mixture of diastereoisomeric oxazolidinones **8a** (758 mg, 59%) (*anti*/*syn*, 3:1); pale yellow oil; ν_{max} (cm^{-1}) (film) 3274 (br), 1756 (s), 1382 (m), 1336 (m), 1232 (s), 995 (s), 701 (s); δ_H (500 MHz, $CDCl_3$) 7.24–7.03 (5H, m, major and minor), 5.62 (1H, br s, major), 5.22 (1H, br s, minor), 5.20 (1H, dt, *J*=7.5 Hz, 1.5, minor), 4.72 (1H, dt, *J*=6.0, 1.0 Hz, major), 3.93–3.83 (1H, m, major and minor), 2.97 (1H, dd, *J*=13.5, 4.0 Hz, minor), 2.83 (1H, dd, *J*=14.0, 5.5 Hz, major), 2.74 (1H, dd, *J*=13.5, 10.0 Hz, minor), 2.68 (1H, dd, *J*=14.0, 8.5 Hz, major), 2.18 (2H, dt, *J*=7.0, 1.5 Hz, minor), 2.07 (2H, dt, *J*=7.0, 1.0 Hz, major), 1.45–1.19 (4H, m, major and minor), 0.77 (3H, t, *J*=6.0 Hz, minor), 0.76 (3H, t, *J*=7.5 Hz, major); δ_C (125 MHz, $CDCl_3$) (major and minor) 157.8, 157.6, 136.6, 135.6, 129.3, 129.1, 128.9, 128.5, 127.3, 127.1, 92.4, 89.9, 75.1, 72.5, 71.1, 70.4, 61.0, 56.5, 40.5, 38.3, 30.2, 30.1, 21.9, 21.8, 18.4, 18.3, 14.1, 13.5; *m*/*z* (EI^+) 257 (M^+, 20%), 196 (42), 166 (87), 91 (100); Found (M^+) 257.1406, $C_{16}H_{19}NO_2$ requires 257.1415.

4.2.2. (4*S*,5*SR*)-4-Benzyl-5-(3-phenylprop-1-ynyl)oxazolidin-2-one 8b. 3-Phenylprop-1-ynyllithium addition to *N*-Boc-phenylalaninal (1.25 g, 5 mmol) gave a mixture of diastereoisomeric oxazolidinones **8b** (902 mg, 62%) (*anti*/*syn*, 3:2) as a colorless oil; ν_{max} (cm^{-1}) (film) 3276 (br s), 1741 (s), 1494 (m), 1384 (m),1232 (m), 1029 (s), 745 (s), 700 (s); δ_H (500 MHz, $CDCl_3$) 7.24–7.04 (10H, m, major and minor), 6.42 (1H, br s, major), 5.9 (1H, br s, minor), 5.22 (1H, dt, *J*=9.5, 2.0 Hz, minor), 4.78 (1H, dt, *J*=6.0, 2.0 Hz, major), 3.98–3.86 (1H, m, major and minor), 3.49 (2H, d, *J*=2.0 Hz, minor), 3.48 (2H, d, *J*=2.0 Hz, major), 2.99 (1H, dd, *J*=14.0, 5.0 Hz, minor), 2.80 (1H, dd, *J*=14.0, 9.0 Hz, minor), 2.77 (2H, dd, *J*=6.5, 5.0 Hz, major); δ_C (125 MHz, $CDCl_3$) (major and minor) 158.1, 157.9, 136.4, 135.3, 135.2, 135.1, 129.0, 128.9, 128.8, 128.7, 128.5, 128.4, 127.7, 127.6, 127.0, 126.9, 126.7, 126.6, 89.5, 86.8, 77.3, 74.7, 70.6, 70.5, 70.2, 70.1, 60.6, 56.4, 40.2, 38.1; *m*/*z* (EI^+) 291 (M^+, 10%), 230 (25), 200 (55), 156 (47), 129 (60), 91 (100); Found (M^+) 291.1266, $C_{19}H_{17}NO_2$ requires 291.1259.

4.3. General procedure for synthesis of *Z*-vinyl-oxazolidinones (Lindlar reduction)

To a solution of alkynyl oxazolidinone **8** (1 mmol) and quinoline (100 μl, 0.008 mmol) in MeOH (50 ml) was added Lindlar catalyst (100 mg). The flask was flushed with H_2 and the reaction was stirred for 3 h under H_2 (1 atm) at ambient temperature. The mixture was then filtered through Celite, the combined filtrates were evaporated and the residue was purified by chromatography (petrol/EtOAc, 3:1) to give the *syn* and *anti Z*-vinyl oxazolidinones.

4.3.1. (4*S*,5*R*)-4-Benzyl-5-((*Z*)hex-1-enyl)oxazolidin-2-one 3a. Following the Lindlar reduction procedure, butynyloxazolidinones **8a** (500 mg, 1.9 mmol) gave: the vinyloxazolidinone **3a** (112 mg, 23%) as a colorless oil; $[\alpha]_D^{21}=-26.5$ (*c*=0.7, $CHCl_3$); ν_{max} (cm^{-1}) (film) 3291 (br), 1751 (s), 1456 (m), 1386 (m), 998 (m); δ_H (500 MHz, $CDCl_3$) 7.28–7.04 (5H, m), 5.75 (1H, dt, *J*=11.0, 8.0 Hz), 5.56 (1H, dd, *J*=11.0, 9.5 Hz), 5.40 (1H, dd, *J*=9.5, 9.0 Hz), 5.11 (1H, br s), 3.93 (1H, ddd, *J*=11.0, 9.0, 3.5 Hz), 2.74 (1H, dd, *J*=14.0, 3.5 Hz), 2.74 (1H, dd, *J*=14.0, 11.0 Hz), 2.12–2.07 (1H, m), 2.02–1.94 (1H, m), 1.35–1.22 (4H, m), 0.85 (3H, t, *J*=7.5 Hz); δ_C (125 MHz, $CDCl_3$) 158.6, 137.4, 136.8, 129.0, 128.9, 127.1, 122.4, 75.6, 57.3, 37.2, 31.4, 27.6, 22.2, 13.8; *m*/*z* (EI^+) 259 (M^+, 55%), 177 (62), 167 (78), 124 (53), 91 (100); Found (M^+) 259.1564, $C_{16}H_{21}NO_2$ requires 259.1572; and *(4S,5S)-4-benzyl-5-((Z)hex-1-enyl)-oxazolidin-2-one* **4a**: (335 mg, 68%) as a colorless oil; $[\alpha]_D^{21}=-2.4$ (*c*=0.6, $CHCl_3$); ν_{max} (cm^{-1}) (film) 3291 (br), 1751 (s), 1456 (m), 1386 (m), 998 (m); δ_H (500 MHz, $CDCl_3$) 7.28–7.09 (5H, m), 5.63 (1H, dt, *J*=11.0, 7.5 Hz), 5.42 (1H, ddt, *J*=11.0, 9.0, 1.5 Hz), 5.19 (1H, br s), 4.95 (1H, dd, *J*=9.0, 6.5 Hz), 3.66 (1H, ddd, *J*=8.5, 6.5, 5.0 Hz), 2.83 (1H, dd, *J*=13.5, 5.0 Hz), 2.74 (1H, dd, *J*=13.5, 8.5 Hz), 2.03–1.95 (1H, m), 1.92–1.84 (1H, m), 1.27–1.09 (4H, m), 0.81 (3H, t, *J*=7.0 Hz); δ_C (125 MHz, $CDCl_3$) 158.5, 137.4, 136.1, 129.0, 128.9, 127.2, 125.2, 77.4, 60.3, 40.6, 31.6, 27.4, 22.2, 13.9; *m*/*z* (EI^+) 259 (M^+, 55%), 177 (62), 167 (78), 124 (53), 91 (100); Found (M^+) 259.1564, $C_{16}H_{21}NO_2$ requires 259.1572.

4.3.2. (4*S*,5*R*)-4-Benzyl-5-(3-phenyl(*Z*)prop-1-enyl)oxazolidin-2-one 3b. Following the Lindlar reduction procedure, butynyloxazolidinones **8b** (450 mg, 1.55 mmol) gave: the vinyloxazolidinone **3b** (159 mg, 35%) as white needles; mp 95–98°C; $[\alpha]_D^{21}=+2.8$ (*c*=0.4, $CHCl_3$); ν_{max} (cm^{-1}) (KBr) 3276 (br s), 1741 (s), 1494 (m), 1384 (m),1232 (m), 1029 (s), 745 (s), 700 (s); δ_H (500 MHz, $CDCl_3$) 7.25–7.02 (10H, m), 5.97 (1H, dtd, *J*=10.0, 7.5, 1.0 Hz), 5.72 (1H, ddd, *J*=10.0, 9.0, 2.0 Hz), 5.48 (1H, ddd, *J*=9.0, 8.0, 1.0 Hz), 5.04 (1H, br s), 3.87 (1H, ddd, *J*=11.0, 8.0, 3.5 Hz), 3.47 (1H, dd, *J*=15.5, 7.5 Hz), 3.31 (1H, ddd, *J*=15.5, 7.5, 2.0 Hz), 2.69 (1H, dd, *J*=13.5, 3.5 Hz), 2.57 (1H, dd, *J*=13.5, 8.0 Hz); δ_C (125 MHz, $CDCl_3$) 158.4, 139.1, 136.7, 135.2, 129.0, 128.9, 128.7, 128.3, 127.1, 126.5, 123.7; 75.5, 57.3, 37.3, 33.9; *m*/*z* (EI^+) 293 (M^+, 18%), 281 (20), 265 (40), 231 (55), 202 (95), 158 (75), 91 (100); Found (M^+) 293.1403, $C_{19}H_{19}NO_2$ requires 293.1415; and *(4S,5S)-4-benzyl-5-(3-phenyl(Z)prop-1-enyl)oxazolidin-2-one* **4b**: (236 mg, 52%) as a colorless oil; $[\alpha]_D^{21}=+3.5$ (*c*=0.7, $CHCl_3$); ν_{max} (cm^{-1}) (film) 3276 (br s), 1741 (s), 1494 (m), 1384 (m),1232 (m), 1029 (s), 745 (s), 700 (s); δ_H (500 MHz, $CDCl_3$) 7.23–6.93 (10H, m), 6.33 (1H, br s), 5.7 (1H, dt, *J*=10.0, 8.0 Hz), 5.49 (1H, ddt, *J*=10.0, 9.0, 1.5 Hz), 5.01 (1H, dd, *J*=9.0, 5.5 Hz), 3.70 (1H, td, *J*=6.5, 5.5 Hz), 3.24 (1H, dd, *J*=15.5, 8.0 Hz), 3.07 (1H, dd, *J*=15.5, 8.0 Hz), 2.79 (1H, dd, *J*=6.5, 13.5 Hz), 2.72 (1H, dd, *J*=6.5, 13.5 Hz); δ_C (125 MHz, $CDCl_3$) 159.1, 139.2, 136.7, 134.8, 129.1, 128.8, 128.7, 128.5, 128.4, 127.1, 126.5, 75.5, 60.1, 40.6, 33.5; *m*/*z* (EI^+) 293 (M^+, 18%), 281 (20), 265 (40), 231 (55), 202 (95), 158 (75), 91 (100); Found (M^+) 293.1403, $C_{19}H_{19}NO_2$ requires 293.1415.

4.3.3. (4*S*,5*R*)-4-Benzyl-5-(*E*-1-hexenyl)oxazolidin-2-one 5a and (4*S*,5*S*)-4-benzyl-5-(*E*-1-hexenyl)oxazolidin-2-one 6a. To a stirred solution of (*E*)-1-iodo-1-hexene (3.15 g, 15 mmol) in THF (60 ml) was added *n*-BuLi (7.4 ml, 2.0 M solution in hexanes, 14.8 mmol) dropwise at −78°C. Stirring was continued for an additional 15 min and a solution of *N*-Boc-phenylalaninal (1.25 g, 5 mmol) in THF (20 ml) was added dropwise. The resulting solution was stirred for 3 h at −78°C, allowed to warm to 0°C, stirred

for additional 1 h and quenched with saturated aqueous NH_4Cl (10 ml). EtOAc (100 ml) was added and the aqueous phase was separated and extracted with additional EtOAc (2×20 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated to give the crude mixture of oxazolidinones. Column chromatography (petrol/EtOAc, 3:1) produced a mixture of *syn* and *anti* oxazolidinones (3:2) as a white solid (990 mg, 76%). The NMR signals of the minor diastereoisomer matched those for the (4*S*,5*S*) isomer **6a** (obtained from the carbonylation of **3a**, see below). In addition to those the following could be seen for the major (4*S*,5*R*) diastereoisomer **5a**: δ_H (500 MHz, $CDCl_3$) 7.28–7.09 (5H, m, Ph), 5.81 (1H, dt, *J*=15.3, 6.7 Hz, CH=C*H*Bu), 5.53 (1H, ddt, *J*=15.3, 7.6, 1.5 Hz, C*H*=CHBu), 5.20 (1H, br s, NH), 5.00 (1H, dd, *J*=7.6, 8.0 Hz, CHOCO), 3.95 (1H, ddd, *J*=11.0, 8.0, 4.0 Hz, CHNH), 2.75 (1H, dd, *J*=13.8, 4.0 Hz, one of PhCH_2), 2.57 (1H, dd, *J*=13.8, 11.0 Hz, one of PhCH_2), 2.09–2.06 (2H, m, =CHCH_2), 1.36–1.20 (4H, m, CH_2CH_2CH_3), 0.85 (3H, t, *J*=6.7 Hz, CH_3); δ_C (125 MHz, $CDCl_3$) 158.6, 137.3, 136.0, 128.9, 128.8, 127.1, 125.6, 82.7, 59.7, 40.5, 31.7, 30.7, 22.0, 13.8; *m/z* (EI^+) 259 (M^+, 80%), 177 (55), 167 (61), 124 (45), 91 (100).

4.4. General carbonylation procedure

A mixture of the vinyl oxazolidinone and $PdCl_2(PPh_3)_2$ (10 mol%) in EtOH (5 ml per mmol of oxazolidinone) was transferred to a 300 ml autoclave. The autoclave was pressurized with CO (60 atm) and heated to 60°C (the pressure increased to 65 atm) with stirring for 24 h in the case of terminal vinyl oxazolidinone **1a** or 96 h in the case of *E* or *Z* vinyl oxazolidinones. After cooling and depressurization, the crude reaction mixture was filtered through a short pad of Celite and the solvent was evaporated under reduced pressure. The products were purified by column chromatography (commonly eluted with EtOAc/petrol, 1:1).

4.4.1. (6*S*)-3,6-Dihydro-6-(2-propyl)-1*H*-pyridin-2-one (2a). Following the general carbonylation procedure, (4*S*,5*RS*)-5-ethenyl-4-(2-propyl)oxazolidin-2-one **1a** (200 mg, 1.3 mmol) gave the pyridinone **2a** (0.156 g, 87%) as a colorless oil. The analytical data were identical to those reported previously.[2]

4.4.2. (3*R*,6*S*)-6-Benzyl-3-butyl-3,6-dihydro-1*H*-pyridin-2-one 9a. Following the general carbonylation procedure, vinyloxazolidinone **4a** (150 mg, 0.58 mmol) gave the pyridinone **9a** (72 mg, 51%) as a colorless oil; $[\alpha]_D^{21}=-5.0$ (*c*=1.5, $CHCl_3$); ν_{max} (cm^{-1}) (film) 3226 (br), 1656 (s), 1089 (br), 1022 (br), 800 (s); δ_H (500 MHz, $CDCl_3$) 7.26–7.08 (5H, m), 6.01 (1H, br s), 5.65 (2H, s), 4.18–4.12 (1H, m), 2.86 (1H, dd, *J*=13.5, 5.0 Hz), 2.8 (1H, m), 2.63 (1H, dd, *J*=13.5, 8.5 Hz), 1.62–1.53 (1H, m), 1.5–1.4 (1H, m), 1.25–1.18 (4H, m), 0.82 (3H, t, *J*=7.5 Hz); δ_C (125 MHz, $CDCl_3$) 172.5, 136.5, 129.6, 128.9, 128.7, 127.2, 124.4, 55.3, 44.2, 40.6, 32.8, 28.3, 22.8, 14.1; *m/z* (EI^+) 243 (M^+, 60%), 199 (80), 152 (50), 91 (100); Found (M^+) 243.1612, $C_{16}H_{21}NO$ requires 243.1623.

4.4.3. (3*R*,6*S*)-3,6-Dibenzyl-3,6-dihydro-1*H*-pyridin-2-one 9b. Following the general carbonylation procedure, vinyloxazolidinone **4b** (180 mg, 0.61 mmol) gave the pyridinone **9b** (76 mg, 45%) as white needles; mp 82–85°C; $[\alpha]_D^{21}=-7.8$ (*c*=1.2, $CHCl_3$); ν_{max} (cm^{-1}) (KBr) 3461 (br), 1656 (s), 1494 (s), 1454 (s), 1078 (br), 1029 (br); Found (M^+) 277.1463, $C_{19}H_{19}NO$ requires 277.1466; ^1H and ^{13}C NMR spectra were identical to those reported.[10]

4.4.4. (3*S*,6*S*)-6-Benzyl-3-butyl-3,6-dihydro-1*H*-pyridin-2-one 10a. Following the general carbonylation procedure, vinyloxazolidinone **3a** (120 mg, 0.46 mmol) gave: the pyridinone **10a** (48 mg, 43%) as a colorless oil; $[\alpha]_D^{21}=+5.2$ (*c*=0.9, $CHCl_3$); ν_{max} (cm^{-1}) (film) 3289 (br), 1654 (s), 1089 (br), 1022 (br), 800 (s); δ_H (500 MHz, $CDCl_3$) 7.29–7.08 (5H, m), 5.74 (1H, br s), 5.71–5.64 (2H, m), 4.19–4.13 (1H, m), 2.88 (1H, dd, *J*=13.5, 5.0 Hz), 2.75 (1H, m), 2.59 (1H, dd, *J*=13.5, 9.0 Hz), 1.74–1.54 (2H, m), 1.26–1.14 (4H, m), 0.79 (3H, t, *J*=7.0 Hz); δ_C (125 MHz, $CDCl_3$) 172.3, 136.3, 129.4, 128.8, 127.1, 127.0, 124.7, 54.9, 43.8, 40.5, 32.3, 27.9, 22.7, 13.9; *m/z* (CI^+) 244 (MH^+, 65%), 199 (80), 152 (50), 96 (100); Found (MH^+) 244.1704, $C_{16}H_{22}NO$ requires 244.1714; and *(4S,5S)-4-benzyl-5-((E)hex-1-enyl)oxazolidin-2-one* **6a**: (30 mg, 25%) as a colorless oil; $[\alpha]_D^{21}=-10.0$ (*c*=0.2, $CHCl_3$), ν_{max} (cm^{-1}) (KBr) 3291 (br), 1751 (s), 1456 (m), 1386 (m), 998 (m); δ_H (500 MHz, $CDCl_3$) 7.28–7.09 (5H, m), 5.72 (1H, dt, *J*=15.5, 7.0 Hz), 5.42 (1H, ddt, *J*=15.5, 7.2, 1.5 Hz), 4.88 (1H, br s), 4.67 (1H, dd, *J*=7.2, 7.0 Hz), 3.66 (1H, ddd, *J*=9.0, 7.0, 5.0 Hz), 2.85 (1H, dd, *J*=13.5, 5.0 Hz), 2.70 (1H, dd, *J*=13.5, 9.0 Hz), 2.02–1.95 (2H, m), 1.32–1.18 (4H, m), 0.83 (3H, t, *J*=7.5 Hz); δ_C (125 MHz, $CDCl_3$) 158.5, 138.3, 136.9, 129.0, 128.8, 127.0, 122.4, 80.5, 57.4, 37.4, 31.9, 30.7, 22.1, 13.5; *m/z* (EI^+) 259 (M^+, 55%), 177 (62), 167 (78), 124 (53), 91 (100); Found (M^+) 259.1564, $C_{16}H_{21}NO_2$ requires 259.1572.

4.4.5. (3*S*,6*S*)-3,6-Dibenzyl-3,6-dihydro-1*H*-pyridin-2-one 10b. Following the general carbonylation procedure, vinyloxazolidinone **3b** (160 mg, 0.55 mmol) gave: the pyridinone **10b** (44 mg, 29%) as colorless oil; $[\alpha]_D^{21}=+35.4$ (*c*=0.3, $CHCl_3$); ν_{max} (cm^{-1}) (film) 3220 (br), 1656 (s), 1494 (s), 1454 (s), 1344 (s), 700 (s); *m/z* (EI^+) 277 (M^+, 35%), 202 (45), 91 (100); Found (M^+) 277.1450, $C_{16}H_{22}NO$ requires 277.1466; ^1H and ^{13}C NMR spectra were identical to those reported;[10] and *(4S,5S)-4-benzyl-5-(3-phenyl(E)prop-1-enyl)oxazolidin-2-one* **6b**: (56 mg, 35%) as white needles; mp 108–110°C; $[\alpha]_D^{21}=-8.6$ (*c*=0.8, $CHCl_3$), ν_{max} (cm^{-1}) (KBr) 3284 (br s), 1752 (s), 1454 (m), 1240 (br m), 993 (br s), 971 (br s), 700 (s); δ_H (500 MHz, $CDCl_3$) 7.26–7.00 (10H, m), 5.76 (1H, dt, *J*=15.0, 8.5 Hz), 5.75 (1H, br s), 5.40 (1H, dd, *J*=15.0, 7.5 Hz), 4.59 (1H, dd, *J*=7.5, 6.5 Hz), 3.62 (1H, dt, *J*=6.5, 6.0 Hz), 3.23 (2H, d, *J*=8.5 Hz), 2.79 (1H, dd, *J*=14.0, 6.0 Hz), 2.68 (1H, dd, *J*=14.0, 6.0 Hz); δ_C (125 MHz, $CDCl_3$) 158.3, 138.8, 135.9, 135.5, 129.0, 128.9, 128.6, 128.5, 127.2, 127.0, 126.4, 82.4, 59.7, 40.7, 38.4; *m/z* (EI^+) 293 (M^+, 55%), 277 (35), 202 (42), 91 (100); Found (M^+) 293.1423, $C_{19}H_{19}NO_2$ requires 293.1415.

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