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A simple and easy access to 3-*N*-alkyl-5-vinyloxazolidinones mediated by palladium–phosphine catalysts

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Abstract—A new entry for the synthesis of 3-alkyl substituted 5-vinyloxazolidin-2-one derivatives **2** from *cis*-2-butenylene-1,4-dicarbonate **1** and primary amines mediated by palladium–phosphine catalysts is described. The scope and limitation, a plausible mechanism, and an asymmetric version of the reaction are also discussed. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

In our previous report, we briefly communicated the palladium-catalyzed formation of 5-vinyloxazolidin-2-ones **2** starting from *cis*-2-butenylene dicarbonate **1** with mainly simple amines and also a plausible mechanism of the reaction pathway.[1] This paper deals with the full details of the work which involves the use of more complex amines such as diamines and amino alcohols for expanding the applicability of the reaction to the synthesis of biologically important class of compounds. We also describe the scope and limitations, another possible mechanism, and an asymmetric construction of 5-vinyloxazolidin-2-one mediated by chiral palladium–phosphine catalysts.

2. Results and discussion

Oxazolidinone is well known to be an important class of compounds for pharmaceutical usage[2] and a chiral building block for organic synthesis.[3] For instance, toloxatone **3** (Fig. 1) is known to be a reversible monoamine oxidase inhibitor.[2a] Some chiral oxazolidinones such as **4** are commercially available.[†] Although there is extensive literature concerning the synthesis of oxazolidinone derivatives,[2,4] for instance, derivation from epichlorohydrin,[5] most of the methods need multi-step manipulations.

As mentioned in our previous report,[1] the reaction of *cis*-2-butenylene dicarbonate **1** with simple amines in the presence of π-allylpalladium(II) chloride dimer and diphenylphosphinoferrocene (dppf) in THF, dichloromethane or chloroform at room temperature to 50°C gave 5-vinyloxazolidin-2-one **2** in moderate to good yield (Scheme 1).

Especially, the efficiency of the reaction depended on the ligand used (Table 1).

For instance, as shown in Table 1, though dppe, dppb, triphenylphosphine, and BINAP gave low yields of the product, dppf provided acceptable yields considering the fact the reaction proceeded via a tandem pathway. Both $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and $Pd_2(dba)_3 \cdot CHCl_3$ were good sources of palladium(0) for this reaction. Additives such as a base (carbonates, amines, metal hydrides, and alkoxides) had no effect on the efficiency of this reaction.

It was found that more complex amines such as diamines and amino alcohols were also acceptable for this reaction (Table 2). We believe that these materials obtained as shown in Table 2 would be new useful building blocks for the purpose of drug discovery because these materials have an easily functionalizable double bond.

Surprisingly, no diastereo-discrimination was observed in the reaction using chiral amines as nucleophiles (entry 5 and 6) to give the corresponding oxazolidinones **2f** and **2g** in

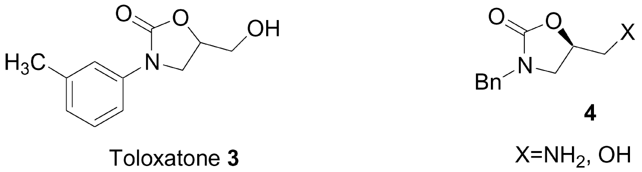

Figure 1.

Keywords: tandem allylic substitution; oxazolidinone; palladium catalyst; asymmetric synthesis.

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[†] Synthon Chiragenics.

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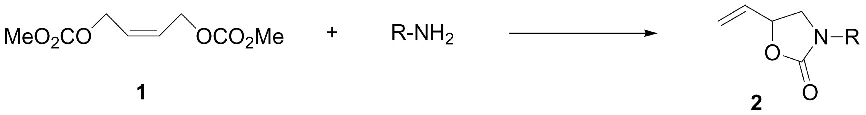
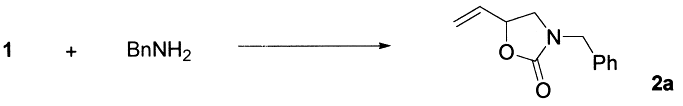


R=*n*-hexyl (67%), allyl (70%), *i*-butyl (55%), cyclohexyl (67%), benzyl (58%), (*R*)-1-phenylethyl (62%), (*S*)-2-hydroxy-1-phenylethyl (56%).

Scheme 1.

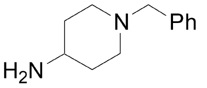
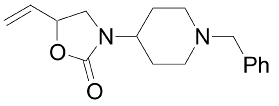
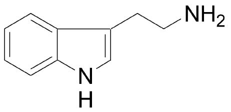
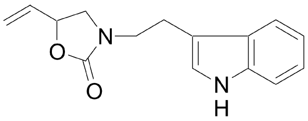
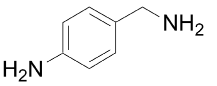
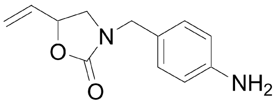
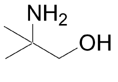
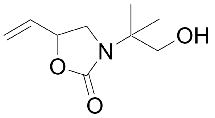
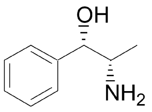
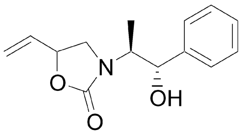
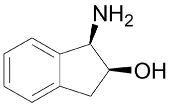
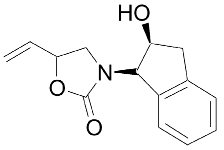
Table 1. Reaction of dicarbonate **1** with benzylamine under various conditions



Entry	**1** (equiv.)	Catalyst	Ligand	Solvent	Base	Temperature (°C)	Time (h)	Yield (%)[a]
1	1	$Pd_2dba_3 \cdot CHCl_3$	dppe	THF	Cs_2CO_3	50	O/N[b]	0
2	1	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	dppb	CH_2Cl_2	TMG[c]	Reflux	O/N[b]	17
3	2	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	PPh_3	CH_2Cl_2	None	RT	1.5	40
4	2	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	BINAP	CH_2Cl_2	None	RT	26	47
5	2	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	dppf	CH_2Cl_2	None	RT	3	58
6	1.5	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	dppf	THF	None	RT	20	60
7	1.5	$Pd_2dba_3 \cdot CHCl_3$	dppf	CH_2Cl_2	None	RT	32	61

[a] Isolated yield.
[b] O/N: overnight.
[c] TMG: tetramethylguanidine.

Table 2. Reaction of **1** with bifunctional and chiral amines

Entry	Amine	Product	Yields (%)[a]
1		 **2b**	61
2		 **2c**	74
3		 **2d**	26
4		 **2e**	16
5		 **2f**	57[b]
6		 **2g**	41[c]

[a] Isolated yield.
[b] A separable 1:1 mixture of diastereomers was obtained.
[c] An unseparable 1:1 mixture of diastereomers was obtained.

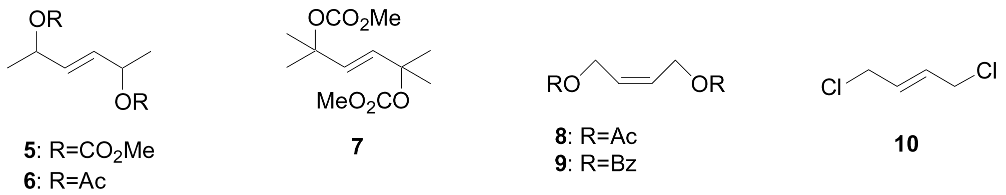
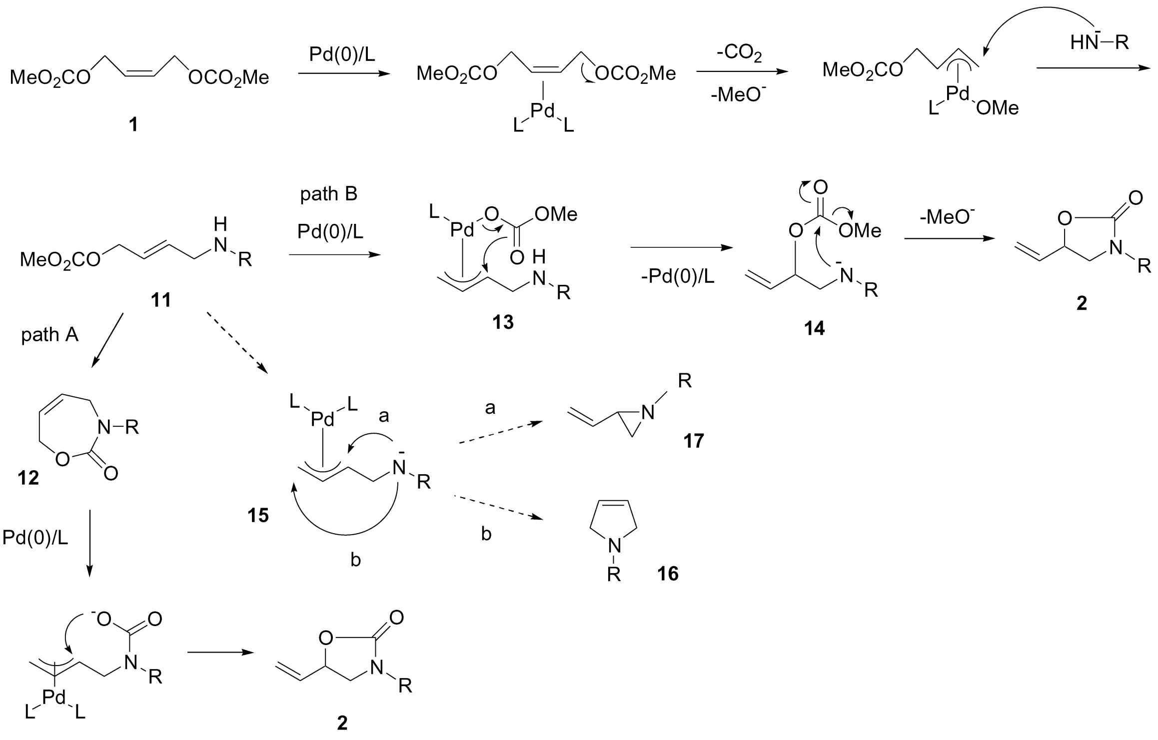


Figure 2.

almost 1:1 mixtures of diastereomers, respectively, under various conditions such as low temperature (0 and −20°C). Application of aromatic amines (aniline derivatives) to this process seems to be especially important because many pharmaceutically important oxazolidinones have an aromatic ring directly attached to the nitrogen atom such as toloxatone **3**[2a] and linezolide.[2b] Disappointingly, reaction of aniline and derivatives such as *p*-bromoaniline, *p*-nitroaniline, 1-aminonaphthalene, *p*-chloroaniline and *m*-toluidine with **1** under various conditions gave only the starting material recovered and/or a complex mixture. Moreno-Mañas et al. recently reported that a similar reaction catalyzed by Pd(dba)$_2$ and dppf employing *acidic* aniline such as 3,5-dinitroaniline as nucleophile in THF at room temperature produced *N*-aryl-4-vinyloxazolidin-2-ones,[4d] regioisomers of **2**. The mechanism of the process was explained by first amidation of the substrate with amines followed by intramolecular nucleophilic amination of the π-allyl intermediate.[4d]

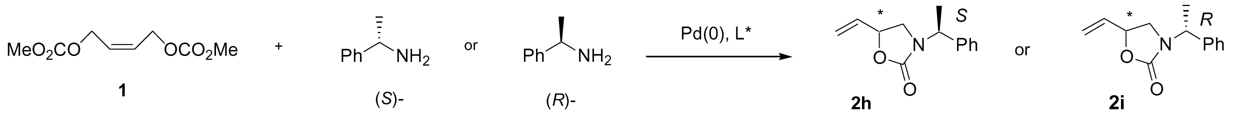
Other nucleophiles such as amino acids (e.g. phenylalanine), amino acid esters (e.g. phenylglycine methyl ester hydrochloride) and hydrazide (e.g. *p*-toluenesulfonhydrazide) gave no desired product in the same manner. Another diallylcarbonate ester such as **5** or **7** also gave no corresponding oxazolidinone, probably due to steric hindrance by the additional methyl group. Other symmetrical substrates possessing two reaction sites such as diacetates **6** and **8**, dibenzoate **9**, and dichloride **10** did not react with amines under the same reaction conditions and gave no noticeable product (Fig. 2).

In our previous report, we described the mechanistic consideration for the formation of oxazolidinone via seven-membered intermediate **12** (Scheme 2).[1] But, this pathway seems to be unlikely because of the formation of relatively unstable seven-membered ring and also olefinic *trans–cis* isomerization. The heat of formation of hypothetical intermediates **11**, **12**, and **14** (R=Me) was −120.6, −53.6 and −115.3 kcal/mol, respectively, by the AM1 calculations.[6] As mentioned above, the results of no enantio-selection observed in the reaction using chiral amine and amino alcohol as nucleophile suggests that the stage of nucleophilic attack is not an enantio-discrimination step. Allylic rearrangement of the π-allyl intermediate **13** generated from the first amination product **11** would produce secondary vinyl carbonate **14** (path B). The new C–O bond formation would occur by the attack of carbonyl oxygen of **13** to the more substituted terminus (electron deficient site) of allyl system to produce carbonate **14**. Intramolecular amide formation by nucleophilic attack of nitrogen to the carbonyl group should give oxazolidinone **2**.

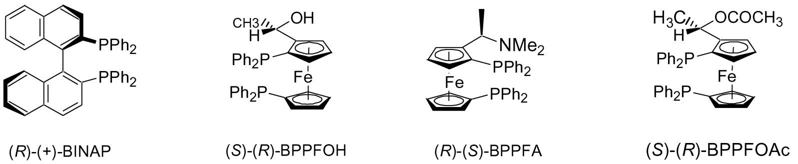


Scheme 2.

Table 3. Asymmetric synthesis of oxazolidinone using chiral ligands



Entry	Amine (equiv.)	Pd catalyst (mol%)	Ligand (mol%)	Solvent	Temperature (°C)	Time (h)	Recovery **1** (%)	Yield (%)[a]	Selectivity[b] (de. %)
1	*S* (1.5)	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.25)	(*R*)-(+)-BINAP (0.64)	THF	RT	3.5	0	52	56:46 (8)
2	*S* (1.5)	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.25)	(*S*)-(*R*)-BPPFOH (0.64)	CH_2Cl_2	RT	19.5	0	53	44:56 (12)
3	*S* (1.5)	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.5)	(*R*)-(*S*)-BPPFA (1.3)	CH_2Cl_2	RT	21.5	0	32	39:61 (22)
4	*R* (1.5)	$Pd_2dba_3\cdot CHCl_3$ (0.25)	(*S*)-(*R*)-BPPFOAc (0.64)	THF	40	20	0	67	83:17 (66)
5	*R* (1.5)	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.25)	(*S*)-(*R*)-BPPFOAc (0.64)	CH_2Cl_2	RT	1.5	68	13 (41)[c]	85:15 (70)
6	*R* (1.5)	$Pd_2dba_3\cdot CHCl_3$ (0.25)	(*S*)-(*R*)-BPPFOAc (0.64)	CH_2Cl_2	RT	1.5	80	13 (66)[c]	95:5 (90)
7	*S* (1.5)	$Pd_2dba_3\cdot CHCl_3$ (0.25)	(*S*)-(*R*)-BPPFOAc (0.64)	THF	40	39.5	0	23	8:92 (84)



(*R*)-(+)-BINAP (*S*)-(*R*)-BPPFOH (*R*)-(*S*)-BPPFA (*S*)-(*R*)-BPPFOAc

[a] Isolated yield.

[b] Less polar/more polar.

[c] Yield based on consumed starting material.

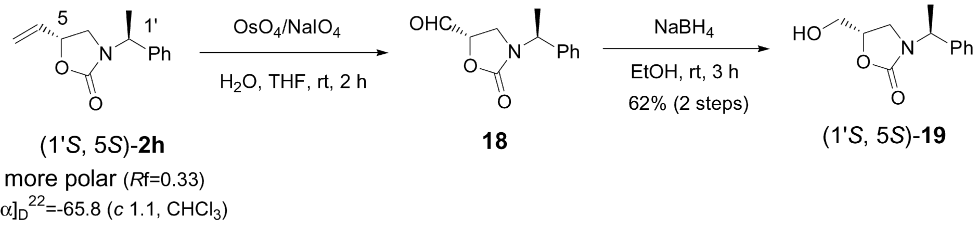
Formation of pyrrole **16** and aziridine **17** from π-allyl intermediate **15** would also be possible,[4d] but we could not detect such compounds. To determine the exact mechanism, it should be necessary to synthesize hypothetical intermediates such as **11**, **12** and **14** to subject them to the same reaction conditions. Such approach is now under investigation.

As described above, the reaction using chiral amine and achiral catalyst gave oxazolidinone as a 1:1 mixture of diastereomers (Table 2, entry 5 and 6). Fortunately, in the case using simple and inexpensive chiral 1-phenylethylamine, each diastereomer was easily separable on simple silica gel chromatography to give diastereomerically pure (which means enantiomerically pure) oxazolidinone, which would be advantageous for the practical production of optically pure materials in laboratory scale. The results prompted us to investigate the influence of chiral phosphine ligands in this reaction. The results using various chiral ligands are summarized in Table 3. (*S*)-*N*,*N*-Dimethyl-1-[(*R*)-2-(diphenylphosphino)ferrocenyl]ethylamine (PPFA), (1*R*, 2*R*)-(+)-1,2-diaminocyclohexane-*N*,*N*′-bis(2′-diphenylphosphinobenzoyl) (Trost ligand), and (*R*)-(+)-2-[2-(dihenylphosphino)phenyl]-4-(1-methylethyl)-4,5-dihydrooxazole gave no reaction product. As a result, BPPFOAc gave a good selectivity, though the yields were low (entry 4–7). Although elongation of the reaction time and also elevating the temperature provided a good yield, selectivity was decreased (entry 4 vs 5 and 6). Notable effect on the double stereo-differentiation of the chirality of the ligand and nucleophilic amines was observed (entry 4 vs 7).

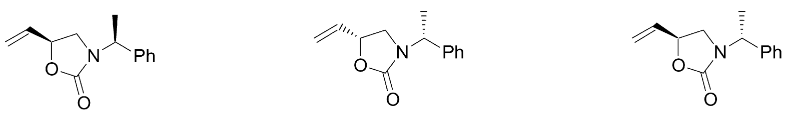
Determination of the absolute stereochemistry of products was conducted as follows (Scheme 3). Oxidative cleavage of the double bond of oxazolidinone **2h** from (*S*)-phenethylamine with $OsO_4/NaIO_4$ gave aldehyde **18** which was reduced with $NaBH_4$ to provide known alcohol (1′*S*,5*S*)-**19**[7] in 62% yield. The sign and absolute value of the optical rotation of **19** ($[\alpha]_D^{29}=-30.6$ (*c* 0.5, $CHCl_3$)) were nearly coincident with literature values ($[\alpha]_D=-28.4$ (*c* 5, $CHCl_3$)).[7] On the other hand, the more polar isomer of **2h** should be (1′*S*, 5*R*)-form and also oxazolidinone **2i** from (*R*)-phenethylamine possessimg the same R_f value with **2h** in the same solvent system (hexane/EtOAc=2.5:1) should be the enantiomer of **2h** (Fig. 3). Thus, all four stereoisomers of 3-(1′-phenylethy)-5-vinyloxazolidin-2-one **2 h** and **2i** have been assigned. To the best of our knowledge, this is the first example of catalytic asymmetric synthesis of 5-vinyloxazolidin-2-one.

3. Conclusion

In summary, we have developed a new simple protocol for the preparation of various functionalized 5-vinyl-2-oxazolidinone derivatives mediated by palladium-phosphine catalyst even in enantiomerically pure forms. Further work directed toward the synthesis of biologically active



Scheme 3.



(1'*S*, 5*R*)-**2h** less polar (*Rf*=0.43) $[\alpha]_D^{22}$=-34.0 (*c* 0.75, $CHCl_3$)

(1'*R*, 5*S*)-**2i** less polar (*Rf*=0.43) $[\alpha]_D^{22}$=+37.3 (*c* 1.84, $CHCl_3$)

(1'*R*, 5*R*)-**2i** more polar (*Rf*=0.33) $[\alpha]_D^{22}$=+78.4 (*c* 1.84, $CHCl_3$)

Figure 3.

compounds starting from the obtained products and mechanistic investigations including the asymmetric induction pathway are now in progress.

4. Experimental

4.1. General

Infrared (IR) spectra were recorded on a Perkin–Elmer FT-IR 1760X spectrometer. NMR spectra were recorded on a JEOL JNM-GX 270 spectrometer, operating at 270 MHz for ^1H NMR and 67.5 MHz for ^{13}C NMR. Chemical shifts in $CDCl_3$ are reported on the δ scale relative to $CHCl_3$ (7.26 ppm for ^1H NMR and 77.00 ppm for ^{13}C NMR) as an internal reference. The following abbreviations are used to multiplicities: 's' (singlet), 'd' (doublet), 't' (triplet), 'm' (multiplet), 'br' (broad). Optical rotations were measured on a JASCO DIP-360 polarimeter. Mass spectra were measured on a JEOL JNM-AX 500 mass spectrometer. Column chromatography were carried out with silica gel Merck 60 (230–400 mesh ASTM). Reactions were carried out in dry solvents under an argon atmosphere. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride. Other reagents were purified by usual methods.

4.2. General procedure for the synthesis of oxazolidones

A degassed solution of 2-butenylene dicarbonate **1** (0.27 g, 1.31 mmol, 1.5 equiv.), amine (0.88 mmol, 1 equiv.), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2 mg, 0.0054 mmol, 0.62 mol%), and dppf (7.6 mg, 0.014 mmol, 1.6 mol%) in dichloromethane (1.5 ml) was stirred at room temperature for 15 h. The mixture was filtered through a pad of silica gel and the solvent evaporated in vacuo. The residue was then subjected to preparative TLC.

4.2.1. 3-Benzyl-5-vinyl-1,3-oxazolidin-2-one (2a). Yield: 61%. Colorless oil. R_f=0.42 (hexane/EtOAc=2:1). IR (neat): 2922, 1752, 1426, 1253, 1025, 704 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 3.13 (1H, dd, *J*=7.3, 8.5 Hz, one of CH_2N), 3.55 (1H, dd, *J*=6.4, 8.5 Hz, one of CH_2N), 4.43 (2H, ABq, *J*=15.0, 24.1 Hz, CH_2Ph), 4.90 (1H, dd, *J*=6.4, 7.3 Hz, C*H*–O), 5.29 (1H, d, *J*=10.4 Hz, CH═C*H*H (*cis*)), 5.40 (1H, d, *J*=17.1 Hz, CH═C*H*H (*trans*)), 5.86 (1H, ddd, *J*=6.4, 10.4, 17.1 Hz, C*H*═CH_2), 7.20–7.43 (5H, m). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 48.2, 49.2, 73.8, 118.7, 127.8, 127.9, 128.6, 134.2, 135.4, 157.6. EI MS *m/z* (%) 203 (15, M^+), 153 (10), 136 (7), 120 (5), 104 (9), 91 (23), 85 (66), 83 (100), 77 (18), 54 (18). HRMS calcd for $C_{17}H_{22}O_2N_2$ (M^+) 203.0946; found 203.0742.

4.2.2. 3-[1-Benzyl(4-piperidyl)]-5-vinyl-1,3-oxazolidin-2-one (2b). Yield: 61%. Colorless oil. R_f=0.36 (hexane/EtOAc=1:1). IR (KBr): 3467, 2919, 1749, 1428, 1252, 1029, 737 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 1.57–1.83 (4H, m), 2.07 (2H, dt, *J*=3.9, 11.6 Hz), 2.94 (2H, d, *J*=11.6 Hz), 3.21 (1H, dd, *J*=7.0, 8.5 Hz), 3.50 (2H, s), 3.64 (1H, t, *J*=8.5 Hz), 3.60–3.82 (1H, m), 4.90 (1H, dd, *J*=7.0, 15.0 Hz), 5.30 (1H, d, *J*=10.4 Hz), 5.41 (1H, d, *J*=17.1 Hz), 5.88 (1H, ddd, *J*=7.0, 10.4, 17.1 Hz), 7.18–7.42 (5H, m). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 29.0, 29.4, 45.9, 50.8, 52.4, 52.5, 62.8, 73.9, 118.5, 126.9, 128.0, 128.9, 134.3, 137.9, 156.9. EI MS *m/z* (%) 286 (1, M^+), 195 (4), 149 (5), 132 (13), 91 (47), 82 (100). HRMS calcd for $C_{17}H_{22}O_2N_2$ (M^+) 286.3759; found 286.3741.

4.2.3. 3-(2-Indol-3-ylethyl)-5-vinyl-1,3-oxazolidin-2-one (2c). Yield: 74%. Colorless crystal. Mp: 88°C. R_f=0.57 (hexane/EtOAc=1:1.5). IR (KBr): 3241, 3059, 2924, 2863, 1729, 1486, 1438, 1335, 1251, 1099, 1016, 746 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 3.01 (1H, d, *J*=7.0 Hz), 3.11 (1H, dd, *J*=6.7, 8.5 Hz), 3.49 (2H, t, *J*=7.0 Hz), 3.55 (1H, dd, *J*=6.7, 7.0 Hz), 4.79 (1H, ddd, *J*=6.7, 7.0, 8.5 Hz), 5.21 (1H, d, *J*=10.4 Hz), 5.36 (1H, d, *J*=17.1 Hz), 5.75 (1H, ddd, *J*=6.7, 10.4, 17.1 Hz), 7.01–7.60 (5H, m), 8.39 (1H, s). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 23.5, 44.4, 50.3, 73.8, 111.3, 112.0, 118.3, 118.6, 119.2, 121.8, 121.9, 127.1, 134.3, 136.1, 157.7. EI MS *m/z* (%) 256 (8, M^+), 143 (100), 130 (95), 115 (5), 103 (10), 77 (13), 55 (24). HRMS calcd for $C_{17}H_{22}O_2N_2$ (M^+) 256.3060; found 256.3034.

4.2.4. 3-[(4-Aminophenyl)methyl]-5-vinyl-1,3-oxazolidin-2-one (2d). Yield: 26%. Colorless oil. R_f=0.15 (hexane/EtOAc=1:1). IR (neat): 3359, 2926, 1740, 1626, 1515, 1433, 1260 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 3.09 (1H, dd, *J*=7.8, 8.9 Hz), 3.51 (1H, dd, *J*=8.6, 8.9 Hz), 4.31 (2H, ABq, *J*=15.0, 24.1 Hz), 4.88 (1H, ddd, *J*=7.6, 7.8, 8.6 Hz), 5.29 (1H, d, *J*=10.4 Hz), 5.41 (1H, d, *J*=16.2 Hz), 5.81 (1H, ddd, *J*=7.6, 10.4, 16.2 Hz), 6.63–7.26 (4H, m). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 47.8, 49.1, 73.8, 115.1, 118.6, 125.2, 129.4, 134.4, 146.1, 162.0. EI MS *m/z* (%) 218 (20, M^+), 164 (100), 119 (70), 106 (71), 77 (23), 53 (19). HRMS calcd for $C_{17}H_{22}O_2N_2$ (M^+) 218.2568; found 218.2571.

4.2.5. 3-(2-Hydroxy-1,1-dimethylethyl)-5-vinyl-1,3-oxazolidin-2-one (2e). Yield: 16%. Colorless oil. R_f=0.46 (hexane/EtOAc=1:1). IR (neat): 3418, 2977, 1731, 1413, 1239, 1034, 768 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 1.30 (6H, s), 3.38 (1H, dd, *J*=7.3, 7.6 Hz), 3.77 (2H, s), 3.83–3.73 (1H, m), 4.90 (1H, dd, *J*=7.3, 7.6 Hz), 5.33 (1H, d, *J*=10.1 Hz), 5.43 (1H, d, *J*=17.4 Hz), 5.91 (1H, ddd, *J*=17.4, 10.1, 7.6 Hz). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 22.6, 23.3, 49.0, 57.8, 69.0, 73.9, 118.9, 134.1, 157.3.

4.2.6. 3-((1*S*,2*R*)-2-Hydroxy-1-methyl-2-phenylethyl)-5-vinyl-1,3-oxazolidin-2-one (2f). A 1:1 mixture of diastereomers. Yield: 57%. Colorless solid. R_f=0.32 (hexane/EtOAc=3:1). IR (KBr): 3411, 2939, 1720, 1448, 1260, 998, 762, 702 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 1.16 (3H, d, *J*=7.0 Hz), 1.18 (3H, d, *J*=7.0 Hz), 3.15 (1H, dd, *J*=7.3, 8.9 Hz), 3.27 (1H, dd, *J*=6.7, 8.9 Hz), 3.64 (1H, dt, *J*=8.9, 12.5 Hz), 3.89–4.04 (1H, m), 4.65–4.89 (1H, m), 4.93 (1H, dd, *J*=4.0, 5.8 Hz), 5.24–5.39 (2H, m), 5.70–5.85 (1H, m), 7.18–7.43 (5H, m). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 157.7, 141.2, 141.1, 134.3, 134.2, 128.2, 127.6, 126.0, 125.9, 118.7, 118.6, 76.5, 76.4, 74.5, 74.4, 55.1, 48.3, 48.1, 11.6, 11.4. EI MS *m/z* (%) 247 (2, M^+), 190 (11), 118 (44), 105 (100), 91 (17), 77 (16), 56 (25). HRMS calcd for $C_{17}H_{22}O_2N_2$ (M^+) 247.2955; found 247.2941.

4.2.7. 3-[(1*R*,2*S*)-2-Hydroxyindanyl]-5-vinyl-1,3-oxazolidin-2-one (2g). Yield: 41% (less polar 21%, more polar 20%). R_f=0.17 and 0.29 (hexane/EtOAc=2:1). Less polar: colorless needles. Mp. 127–128°C. R_f=0.29 (hexane/EtOAc=2:1). $[\alpha]_D^{22}=-47.1$ (*c* 1.2, $CHCl_3$). IR (neat): 3419, 2916, 1731, 1428, 1255, 757, 742 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 2.91 (1H, dd, *J*=6.1, 16.5 Hz), 3.21–3.42 (3H, m), 4.79–4.92 (2H, m), 5.43–5.23 (3H, m), 5.94 (1H, ddd, *J*=7.0, 10.4, 17.1 Hz), 7.13–7.37 (4H, m). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 39.9, 48.6, 60.1, 73.0, 75.4, 119.2, 125.3, 125.7, 127.3, 129.0, 134.4, 137.1, 140.7, 158.6. EI MS *m/z* (%) 245 (2, M^+), 188 (33), 176 (28), 144 (100), 115 (92), 103 (13), 91 (13), 77 (13), 56 (25). HRMS calcd for $C_{17}H_{22}O_2N_2$ (M^+) 245.2796; found 245.2818. More polar: colorless liquid. R_f=0.17 (hexane/EtOAc=2:1). $[\alpha]_D^{22}=+36.6$ (*c* 1.3, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$): δ 2.93 (1H, dd, *J*=5.8, 16.8 Hz), 3.00 (1H, dd, *J*=6.4, 8.9 Hz), 3.28 (1H, dd, *J*=7.0, 16.8 Hz), 3.75 (1H, t, *J*=8.9 Hz), 4.83 (1H, dt, *J*=5.8, 6.4 Hz), 4.99 (1H, dd, *J*=6.4, 15.3 Hz), 5.21–5.42 (3H, m), 5.84 (1H, ddd, *J*=6.4, 10.4, 17.1 Hz), 7.13–7.38 (4H, m). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 39.8, 48.4, 60.2, 72.8, 74.5, 118.5, 125.3, 125.5, 127.2, 128.9, 134.4, 136.9, 140.7, 158.6.

4.2.8. 3-(1-Phenyleth-1-yl)-5-vinyl-1,3-oxazolidin-2-one (2h and 2i). A degassed solution of 2-butenylene dicarbonate **1** (50 mg, 0.24 mmol), (*S*)-(−)-phenethylamine (0.046 mL, 0.36 mmol), $Pd_2(dba)_3\cdot CHCl_3$ (1.2 mg, 0.0012 mmol, 0.5 mol%), and DPPFOAc (2.0 mg, 0.0031 mmol, 1.3 mol%) in THF (1 ml) was stirred at 40°C for 20 h. The mixture was filtered through a pad of silica gel and the solvent evaporated in vacuo. The residue was then subjected to preparative TLC (50% EtOAc in hexane) to produce (1′*S*,5*R*)-**2h** (29.2 mg, 55%) and (1′*S*,5*S*)-**2h** (6 mg, 12%) as an oil.

Yield: 67% (less polar 55%, more polar 12%). Less polar isomer (1′*S*,5*R*)-**2h**: colorless liquid. R_f=0.43 (hexane/EtOAc=2.5:1). $[\alpha]_D^{22}=-34.0$ (*c* 0.75, $CHCl_3$). IR (KBr): 2980, 1750, 1420, 1244, 1024, 703 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 1.56 (3H, d, *J*=7.3 Hz, $-CH_3$), 3.20 (1H, t, *J*=8.6 Hz, one of CH_2N), 3.30 (1H, t, *J*=8.6 Hz, one of CH_2N), 4.82 (1H, dd, *J*=7.3, 7.6 Hz, *H*C–O), 5.22 (1H, q, *J*=7.3 Hz, −C*H*MePh), 5.30 (1H, d, *J*=10.6 Hz, CH═C*H*H (cis)), 5.39 (1H, d, *J*=17.2 Hz, CH═CH*H* (trans)), 5.89 (1H, ddd, *J*=7.6, 10.2, 17.2 Hz, C*H*═CH_2), 7.20–7.43 (5H, m). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 16.2, 45.5, 51.4, 73.9, 118.6, 126.8, 127.7, 128.5, 134.4, 139.3, 157.1. EI MS *m/z* (%) 217 (56, M^+), 202 (36), 163 (24), 153 (21), 131 (46), 105 (100), 77 (69). HRMS calcd for $C_{17}H_{22}O_2N_2$ (M^+) 217.1103; found 217.1074. More polar isomer (1′*S*,5*S*)-**2h**: colorless liquid. R_f=0.33 (hexane/EtOAc=2.5:1). $[\alpha]_D^{22}=-65.8$ (*c* 1.1, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$): δ 1.58 (1H, d, *J*=7.3 Hz), 2.85 (1H, dd, *J*=7.6, 8.5 Hz), 3.61 (1H, dd, *J*=7.6, 8.5 Hz), 4.90 (1H, dt, *J*=7.3, 7.6 Hz), 5.22 (1H, q, *J*=7.3 Hz), 5.23 (1H, d, *J*=10.7 Hz), 5.35 (1H, d, *J*=17.1 Hz), 5.75 (1H, ddd, *J*=7.6, 10.4, 17.1 Hz), 7.14–7.48 (5H, m). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 16.5, 45.3, 51.2, 73.9, 118.5, 126.8, 127.7, 128.5, 134.3, 139.1, 157.1.

(1′*R*, 5*S*)-**2i**: R_f=0.43 (hexane/EtOAc=2.5:1). $[\alpha]_D^{22}=+37.3$ (*c* 1.84, $CHCl_3$).

(1′*R*,5*R*)-**2i**: R_f=0.33 (hexane/EtOAc=2.5:1). $[\alpha]_D^{22}=+78.4$ (*c* 1.84, $CHCl_3$).

4.2.9. (1′*S*, 5*S*)-5-Hydroxymethyl-3-(1-phenylethyl)oxazolidin-2-one (19). To a solution of alkene (1′*S*,5*S*)-**2h** (50 mg, 0.23 mmol) in THF (4.2 mL) stirred under nitrogen atmosphere was added 1% aqueous osmium tetraoxide solution (1 mL). Then, sodium periodate (0.25 g, 1.15 mmol) in water (1.4 mL) was added to the solution and the resulting mixture was stirred for 2 h.

The above mixture was diluted with ethanol (1 mL), sodium borohydride (4.4 mg, 0.12 mmol) was added at 0°C, and the resulting mixture was stirred for 2.5 h at room temperature. Water (5 mL) was added and the mixture was extracted with ether. The combined organic phase was washed with water and brine, dried over $MgSO_4$, filtered, and evaporated in vacuo to yield crude alcohol, which was purified by silica gel chromatography (hexane/EtOAc=1:2) to give pure alcohol **19** (31 mg, 62%) as a white solid.

Yield: 62% (2 steps). R_f=0.6 (EtOAc). IR (KBr): 3392, 2897, 1733, 1444, 1406, 1257, 1074, 760 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 1.5 (3H, d, *J*=7.3 Hz, CH_3), 3.15 (1H, t, *J*=8.5, 9.2 Hz, one of CH_2N), 3.4 (1H, dd, *J*=8.5, 9.2 Hz, one of CH_2N), 3.7 (2H, m, CH_2OH), 3.8 (1H, br s, O*H*), 4.4–4.6 (1H, m, C*H*–O), 5.20 (1H, q, *J*=7.0 Hz, NCH_2Ph), 7.2–7.3 (5H, m, Ar*H*). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 16.2, 41.2, 51.5, 63.1, 73.4, 126.7, 127.8, 128.6, 139.3, 157.2. $[\alpha]_D^{29}=-30.6$ (*c* 0.5, $CHCl_3$) (lit.[7] −28.4 (*c* 5, $CHCl_3$)). Mp. 101°C (lit.[7] 102°C).

References

1. Tanimori, S.; Kirihata, M. *Tetrahedron Lett.* **2000**, *41*, 6785–6788.
2. (a) Mai, A.; Artico, M.; Esposito, M.; Sbardella, G.; Massa, S.; Befani, O.; Turini, P.; Giovannini, V.; Mondavì, B. *J. Med. Chem.* **2002**, *45*, 1180–1183. (b) Selvakumar, N.; Srinivas, D.; Khera, M. K.; Kumar, M. S.; Mamidi, R. N. V. S.; Sarnaik, H.; Charavaryamath, C.; Rao, B. S.; Raheem, M. A.; Das, J.; Iqbal, J.; Rajagopalan, R. *J. Med. Chem.* **2002**, *45*, 3953–3962, and references cited therein.
3. For recent examples, see: (a) Holden, K. G.; Mattson, M. N.;

Cha, K. H.; Rapoport, H. *J. Org. Chem.* **2002**, *67*, 5913–5918. (b) Shen, Y.; Friestad, G. K. *J. Org. Chem.* **2002**, *67*, 6236–6239.

4. (a) Trost, B. M.; Sudhakar, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 3792–3794. (b) Larksarp, C.; Alper, H. *J. Am. Chem. Soc.* **1997**, *119*, 3709–3715. (c) Larksarp, C.; Alper, H. *J. Org. Chem.* **1998**, *63*, 6229–6233. (d) Moreno-Mañas, M.; Morral, L.; Pleixats, R.; Villarroya, S. *Eur. J. Org. Chem.* **1999**, 181–186. (e) Trost, B. M.; Bunt, R. C.; Lemoine, R. C.; Calkins, T. L. *J. Am. Chem. Soc.* **2000**, *122*, 5968–5976, and references cited therein.
5. Feldman, K. S.; Saunders, J. C. *J. Am. Chem. Soc.* **2002**, *124*, 9060–9061.
6. All calculations were carried out using WinMOPAC V 2.0, Fujitsu Ltd.
7. Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *Tetrahedron* **1987**, *43*, 2505–2512.