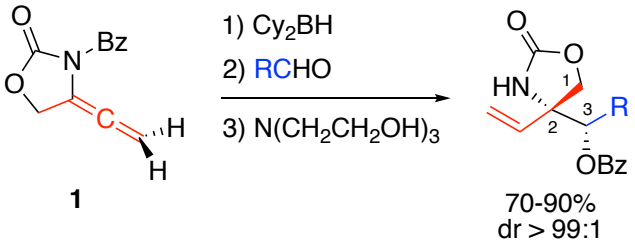
A Useful Allene for the Stereoselective Synthesis of Protected Quaternary 2-Amino-2-Vinyl-1,3-diols

Aleix Rodríguez,[†,‡] Xavier Ariza,*[,†,‡,§] Miguel A. Contreras,[†] Jordi Garcia,*[,†,‡,§] Paul Lloyd-Williams,[†,‡,§] Nerea Mercadal,[†] and Carolina Sánchez[†]

[†]*Departament de Química Inorgànica i Orgànica, Secció de Química Orgànica, Facultat de Química, Universitat de Barcelona, Martí i Franquès 1, 08028-Barcelona, Spain*

[‡]*Institut de Biomedicina de la Universitat de Barcelona (IBUB), Barcelona, Spain*

[§]*CIBER Fisiopatología de la Obesidad y la Nutrición (CIBERobn), Instituto de Salud Carlos III, Madrid, Spain*



ABSTRACT: Treatment of readily available allene **1** with Cy_2BH followed by addition of an aldehyde led to quaternary protected 2-amino-2-vinyl-1,3-diols in high yield and excellent stereochemical purity. The choice of benzoyl as *N*-protecting group is critical since the observed *N*- to *O*-Bz transfer during the process prevents later undesired isomerizations in the adducts and keeps all heteroatoms protected.

KEYWORDS: allene, crotylborane, hydroboration, quaternary carbon, sphingosine, substituted serine

Quaternary α amino acids bearing adjacent hydroxyl functionalities are structural features present in numerous metabolites of biological relevance including myriocin,[1]

the proteasome inhibitor lactacystin,[2] and the antitumor agent (–)-altemicidin (Fig. 1).[3] Even structurally simpler α-branched serines and threonines are also important synthetic targets.[4] Furthermore, (*S*)-α-vinyl serine and other α-vinyl amino acids show interesting biological activities as suicide inhibitors for enzymes of the amino acid decarboxylase class.[5]

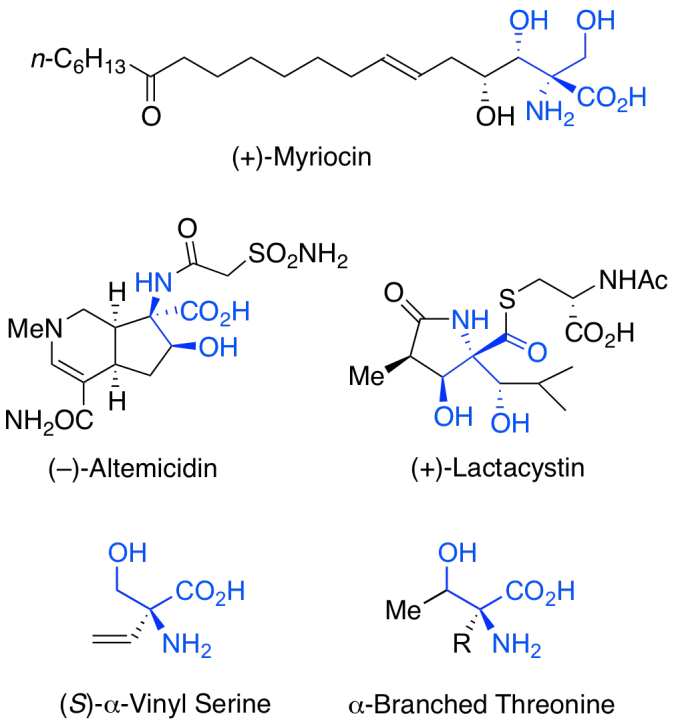


Figure 1. Compounds incorporating quaternary β-hydroxylated α-amino acids

Sphingolipids are a family of lipids that play essential roles as structural cell membrane components and also in cell signalling through a complex metabolism catalyzed by specific enzymes.[6] From a structural point of view, most mammalian sphingolipids share a common backbone incorporating (*E*)-2-amino-4-octadecen-1,3-diol (sphingosine). Interestingly, structural analogues of sphingosine such as quaternary 2-vinyl compound **2** might act as selective inhibitors of these enzymes.[6c]

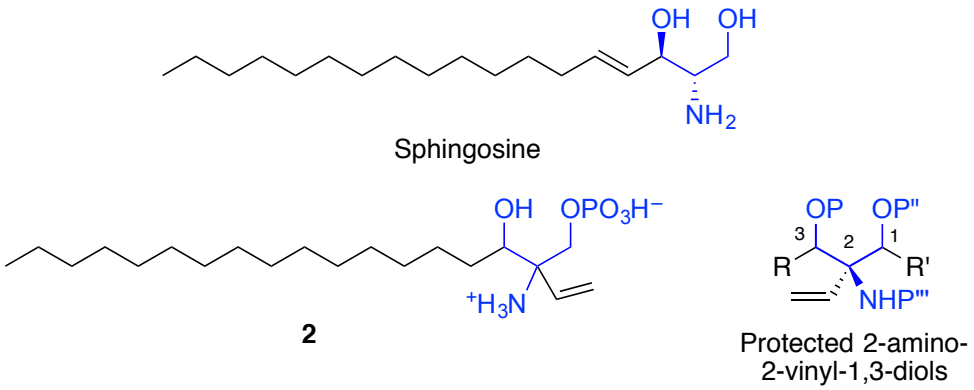
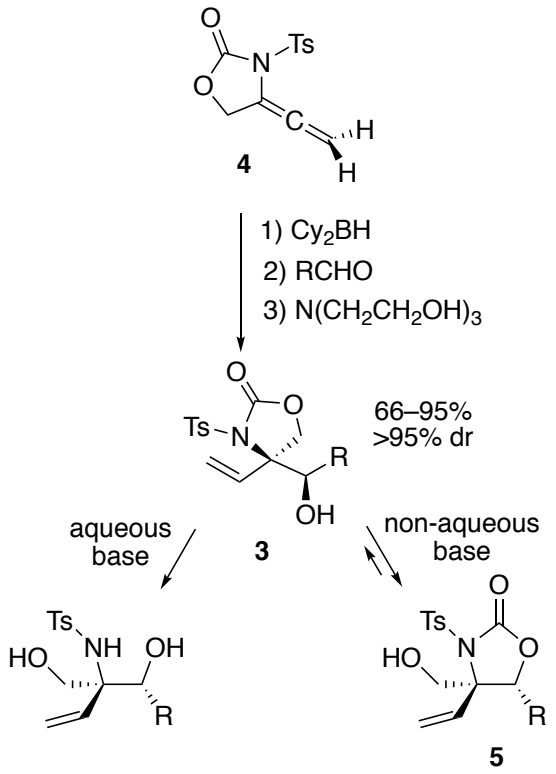


Figure 2. Sphingosine, compound **2** and its possible precursor

We envisaged that both β-hydroxylated α-amino acids such as (*S*)-α-vinyl serine and certain analogues of sphingolipids such as compound **2**, might be generated from protected 2-amino-2-vinyl-1,3-diols (Figure 2).[7]

As part of our studies aimed at the synthesis of polyhydroxylated α-amino acids,[8] we recently reported a new tandem reaction leading to protected tosylcarbamates **3** in high yields and excellent diastereoselectivities (Scheme 1).[9] This simple one-pot process was based on the hydroboration of tosyl allene **4** with Cy_2BH, followed by the addition of an aldehyde.

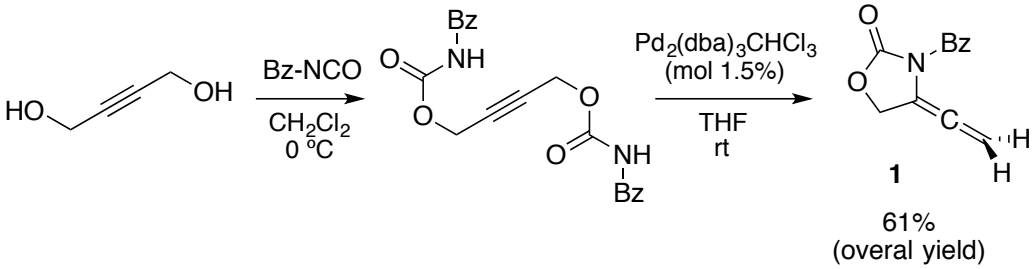


Scheme 1. Preparation of *N*-tosylcarbamates **3** and their hydrolysis and isomerization to **5**

However, in practice this procedure was hampered by drawbacks related to the use of the *N*-tosyl protecting group. This enhances the electrophilic character of the carbonyl group in **4** favoring hydrolysis of the carbamate or its isomerization to *N*-tosylcarbamates **5** in aqueous or dry basic media, respectively. Unfortunately, these deleterious side reactions have also been observed[10] occasionally during work-up and/or chromatographic purification of compounds **3**. On the other hand, removing the robust tosyl group in the final steps of a multi-step synthetic sequence could be troublesome limiting the synthetic utility of the methodology.

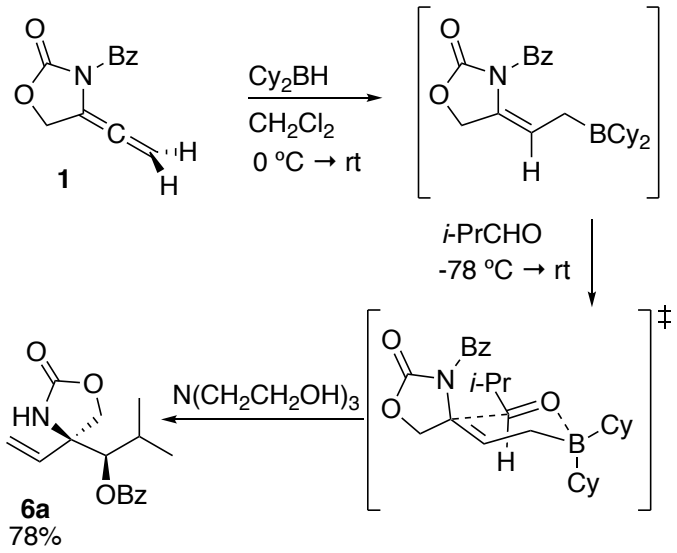
Some of these drawbacks were encountered in our approach to the synthesis of vinylsphinganines such as **2**, potential inhibitors of sphingosine-1-phosphate lyase. We envisaged that allene **1**, easily obtained from 2-butyn-1,4-diol in 61% yield (Scheme

2)[11] with the easily removable benzoyl N-protecting group, might be a better choice since it should be bulky enough to promote high stereoselectivity in the hydroboration step.



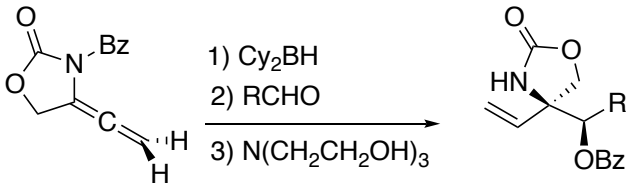
Scheme 2. Synthesis of allene **1** from 2-butyn-1,4-diol

When allene **1** was hydroborated with dicyclohexylborane in CH_2Cl_2 followed by addition of isobutyraldehyde and treatment with triethanolamine, carbamate **6a** was isolated in 78% yield (Scheme 3). As expected, a single diastereoisomer was obtained. Presumably, the relative stereochemistry of **6a** arises from the hydroboration of the less hindered face of allene **1** to afford the corresponding (Z)-2-alkenylborane that is added to the aldehyde through a six-membered transition state where 1,3-axial interactions are minimized. Surprisingly, N to O migration of the benzoyl group in carbamate **6a** had also occurred.[12] A corresponding migration was not observed when tosylated allene **4** was subjected to similar transformations. As expected, protected carbamate **6a** was stable under basic, non-nucleophilic conditions (DBU) and the ring isomerization observed in the case of tosylcarbamates **5** did not occur with the benzoyl derivative.



Scheme 3. Addition of allene **1** to isobutyraldehyde

The reaction was repeated with a variety of aldehydes (Table 1), in order to explore its scope. Carbamates **6** were obtained in good yields for aliphatic (entries 1 and 2), aromatic (entry 3), α,β-alkenyl (entries 4 and 5) and α,β-alkynyl aldehydes (entry 6). In all cases N to O migration of the benzoyl group was observed. Furthermore, a single diastereomer[13] was always obtained including in the cases of those carbamates that might be useful in the synthesis of SPL inhibitors (entries 2, 5 and 6).

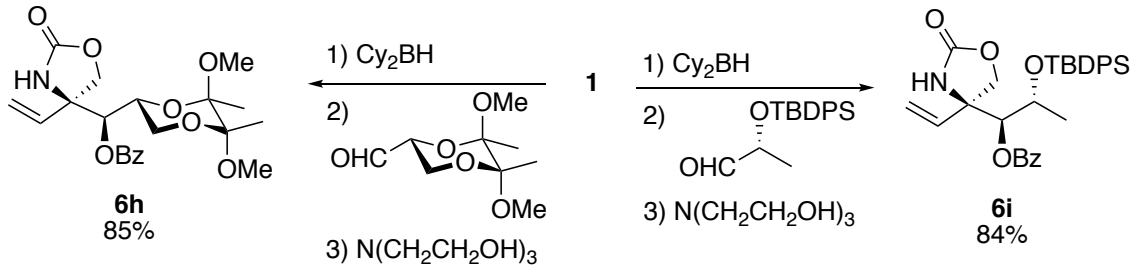


Entry	R	Product	Yield
1	ethyl	**6b**	81%
2	dodecanyl	**6c**	69%
3	phenyl	**6d**	82%
4	vinyl	**6e**	84%

5	(*E*)-1-undecenyl	**6f**	74%
6	1-heptynyl	**6g**	90%

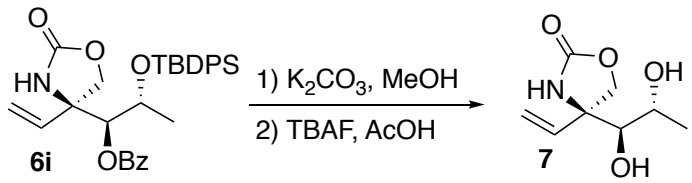
Table 1. Addition of allene **1** to aldehydes

Enantiopure carbamates were obtained when the reaction was performed with chiral aldehydes that exhibited strong stereofacial selectivity such as those derived from (*R*)-glyceraldehyde or (*R*)-lactaldehyde (Scheme 4). Again, only one stereoisomer of **6h** and **6i** were obtained in good yield with complete migration of the benzoyl group.



Scheme 4. Addition of allene **1** to enantiopure aldehydes.

Compound **6i** was used to check the deprotection steps in the synthesis of sphingosine derivatives such as myriocin (Figure 1) and we confirmed that this fully orthogonally protected carbamate can be partially deprotected (Scheme 5). Thus, treatment of carbamate **6i** with K_2CO_3 in MeOH removed the benzoyl group (86% yield) with only partial migration (10%) of the TBDPS group to the oxygen atom previously protected by the benzoyl group. Complete removal of the TBDPS group was achieved by treatment with TBAF and afforded carbamate **7** (78% yield). In the absence of the tosyl group, concomitant isomerization of the carbamate, as occurred when it was present (see Scheme 1), was minimized.



Scheme 5. Deprotection of **6i** to give **7**

In summary, allene **1** is a useful starting material for the synthesis of protected quaternary 2-amino-2-vinyl-1,3-diols by hydroboration followed by aldehyde addition since it avoids undesired migrations and affords a fully protected carbamate with complete stereoselectivity from a range of aldehydes in one step.

Experimental Section

All reactions involving moisture- or air-sensitive reagents were performed in oven-dried glassware under N_2. Chemical shifts (δ) are quoted in parts per million and in ^{1}H NMR are referenced to internal TMS (for $CDCl_3$). ^{13}C NMR are referenced to $CDCl_3$ (δ 77.0 ppm). Column chromatography was performed on silica gel (Merck 230-400 mesh). HRMS analyses were recorded on a LC/MSD-TOF mass spectrometer. Chiral aldehydes were prepared from D-mannitol[14] and (*R*)-methyl lactate.[15]

3-Benzoyl-4-vinylideneoxazolidin-2-one (1). A solution of benzoyl isocyanate (4.20 g, 25.6 mmol) in anhydrous CH_2Cl_2 (20 mL) was added to 2-butyn-1,4-diol (1.00 g, 11.6 mmol) at 0 ºC under N_2 atmosphere. The mixture was stirred for 5 hours at rt and the solvent was removed. A solution of $Pd_2(dba)_3{\cdot}CHCl_3$ (0.055 g, 0.05 mmol) in anhydrous THF (40 mL) and triethylamine (0.087 mL, 0.64 mmol) were added under N_2 atmosphere. The mixture was stirred for 16 h at rt and filtered through a pad of Celite. The solid was washed with EtOAc. The solvent was removed and the crude residue was

purified by column chromatography (hexanes/EtOAc 4:1) to afford 0.595 g (61%) of allene **1**: yellow solid; mp 102-103 ºC (lit.[11] 101.2-103 ºC); R_f (hexanes/EtOAc 2:1) = 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (m, 2H), 7.57 (m, 1H), 7.45 (m, 2H), 5.57 (t, *J* = 4.7 Hz, 2H), 5.04 (t, *J* = 4.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 167.3, 151.9, 132.8, 129.2, 128.1, 128.0, 103.9, 90.4, 63.9; IR (film): 1792, 1689, 1331, 1308, 1157, 1068 cm^{-1}; HRMS (ESI+) calculated for $C_{12}H_{10}NO_3$ $[M+H]^+$ = 216.0655, found = 216.0651.

General procedure for the allene hydroboration-aldehyde addition tandem process

A solution of the allene (1.00 equiv, 1.20 mM) in anhydrous CH_2Cl_2 was added to a suspension of Cy_2BH (1.20 equiv, 1.40 mM) in CH_2Cl_2 at 0 ºC and under nitrogen atmosphere. The resulting mixture was stirred for 10 min at 0 ºC and for 1 h at rt. The resulting solution was then cooled to – 78 ºC, and the aldehyde (1.40 equiv) was added. The reaction was stirred for 4 h at rt, and was then quenched by addition of triethanolamine (2.50 equiv). The resulting mixture was stirred for 1 h at rt. Solvent removal gave a crude that was purified by *flash* column cromatography yielding the following adducts:

(*RS*)-2-Methyl-1-[(*SR*)-2-oxo-4-vinyloxazolidin-4-yl]propyl benzoate (6a), 0.221 g (78%) from 0.210 g (0.98 mmol) of allene **1** as a colorless oil; R_f (hexanes/EtOAc 7:3) = 0.20; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 6.09 (dd, *J* = 17.3, 10.6 Hz, 1H), 5.96 (bs, 1H), 5.48 (d, *J* = 17.3 Hz, 1H), 5.40 (d, *J* = 10.6 Hz, 1H), 5.20 (d, *J* = 4.2 Hz, 1H), 4.53 (d, *J* = 8.6 Hz, 1H), 4.18 (d, *J* = 8.6 Hz, 1H), 2.13 (m, 1H), 1.00 (d, *J* = 7.4 Hz, 3H), 1.00 (d, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 158.7, 136.2, 133.5, 129.7, 129.2, 128.6, 116.6, 79.5, 72.3, 65.0, 29.3, 20.8, 17.5; IR (film): 3334, 2968, 2933, 1759, 1735 cm^{-1}; HRMS (ESI+) calculated for $C_{16}H_{20}NO_4$ $[M+H]^+$ = 290.1387, found = 290.1386.

(*RS*)-1-[(*SR*)-2-Oxo-4-vinyloxazolidin-4-yl]propyl benzoate (6b), 0.303 g (81%) from 0.293 g (1.37 mmol) of allene **1** as a colorless oil; R_f (hexanes/EtOAc 7:3) = 0.20; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (t, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.47 (bs, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 6.03 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.46 (d, *J* = 17.3 Hz, 1H), 5.33 (d, *J* = 10.7 Hz, 1H), 5.28 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.46 (d, *J* = 8.8 Hz, 1H), 4.16 (d, *J* = 8.8 Hz, 1H), 1.81-1.64 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 159.6, 135.6, 133.3, 129.7, 129.2, 128.5, 116.9, 77.8, 72.4, 64.8, 22.5, 10.1; IR (film): 3253, 2924, 2854, 1756, 1719, 1268, 1106 cm^{-1}; HRMS (ESI+) calculated for $C_{15}H_{18}NO_4$ $[M+H]^+$ = 276.1230, found = 276.1232.

(*RS*)-1-[(*SR*)-2-Oxo-4-vinyloxazolidin-4-yl]tridecyl benzoate (6c), 0.461 g (69%) from 0.348 g (1.62 mmol) of allene **1** as a colorless oil; R_f (hexanes/EtOAc 3:2) = 0.74; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-7.97 (m, 2H), 7.62-7.54 (m, 1H), 7.49-7.41 (m, 2H), 6.00 (dd, *J* = 17.2, 10.7 Hz, 1H), 5.83 (bs, 1H), 5.42 (d, *J* = 17.2 Hz, 1H), 5.35 (d, *J* = 10.7 Hz, 1H), 5.28 (dd, *J* = 8.9, 4.3 Hz, 1H), 4.45 (d, *J* = 8.7 Hz, 1H), 4.15 (d, *J* = 8.7 Hz, 1H), 1.70-1.58 (m, 2H), 1.37-1.16 (m, 20H), 0.86 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 158.7, 136.2, 133.6, 129.9, 129.4, 128.7, 117.2, 76.2, 72.0, 64.8, 35.7, 32.1, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 25.8, 25.6, 22.8, 14.3; IR (ATR): 3205, 2922, 2852, 1755, 1718, 1264, 1095, 709 cm^{-1}; HRMS (ESI+) calculated for $C_{25}H_{38}NO_4$ $[M+H]^+$ = 416.2795, found = 416.2789.

(*RS*)-[(*SR*)-2-Oxo-4-vinyloxazolidin-4-yl](phenyl)methyl benzoate (6d), 0.295 g (82%) from 0.240 g (1.11 mmol) of allene **1** as a colorless solid; mp = 72-74 °C; R_f (hexanes/EtOAc 7:3) = 0.18; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.0 Hz, 2H), 7.56-7.34 (m, 9H), 6.07 (dd, *J* = 18.0, 9.9 Hz, 1H), 6.06 (s, 1H), 5.38 (d, *J* = 18.0 Hz, 1H), 5.35 (d, *J* = 9.9 Hz, 1H), 4.57 (d, *J* = 8.8 Hz, 1H), 4.17 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 159.3, 135.9, 134.5, 133.4, 129.7, 129.1, 129.0,

128.4, 127.7, 117.1, 78.2, 71.8, 65.0; IR (KBr): 3462, 3215, 1753, 1712, 1269 cm^{-1}; HRMS (ESI+) calculated for $C_{19}H_{18}NO_4$ $[M+H]^+$ = 324.1230, found = 324.1230.

(*RS*)-1-[(*SR*)-2-Oxo-4-vinyloxazolidin-4-yl]allyl benzoate (6e), 0.282 g (84%) from 0.263 g (1.22 mmol) of allene **1** as a yellow oil; R_f (hexanes/EtOAc 7:3) = 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (t, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 2H), 6.41 (bs, 1H), 6.03 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.87 (ddd, *J* = 17.3, 10.7, 7.0 Hz, 1H), 5.57 (d, *J* = 7.0 Hz, 1H), 5.56 (d, *J* = 0.8 Hz, 1H), 5.54 (d, *J* = 17.3 Hz, 1H), 5.46 (d, *J* = 17.3 Hz, 1H), 5.46 (d, *J* = 10.7 Hz, 1H), 4.50 (d, *J* = 8.8 Hz, 1H), 4.17 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 159.4, 135.5, 133.4, 130.1, 129.7, 129.2, 128.5, 122.0, 117.4, 77.4, 71.8, 64.1; IR (film): 3250, 1756, 1721, 1266, 1070 cm^{-1}; HRMS (ESI+) calculated for $C_{14}H_{16}NO_2$ $[M+H]^+$ = 230.1176, found = 230.1176.

(*RS*,*E*)-1-[(*SR*)-2-Oxo-4-vinyloxazolidin-4-yl]dodec-2-en-1-yl benzoate (6f), 0.331 g (74%) from 0.243 g (1.13 mmol) of allene **1** as a colorless oil; R_f (hexanes/EtOAc 4:1) = 0.22; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04-7.98 (m, 2H), 7.59-7.53 (m, 1H), 7.46-7.41 (m, 2H), 6.30 (bs, 1H), 6.05-5.96 (m, 2H), 5.54-5.41 (m, 3H), 5.35 (d, *J* = 10.7 Hz, 1H), 4.46 (d, *J* = 8.7 Hz, 1H), 4.14 (d, *J* = 8.7 Hz, 1H), 2.05 (dt, *J* = 7.8, 4.0 Hz, =2H), 1.40-1.31 (m, 2H), 1.30-1.19 (m, 12H), 0.86 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 159.1, 140.7, 136.2, 133.5, 129.8, 129.7, 128.7, 121.8, 117.3, 77.8, 72.2, 64.3, 32.6, 32.0, 29.6, 29.5, 29.4, 29.3, 28.8, 22.8, 14.2; IR (ATR): 3240, 2923, 1755, 1707, 1263, 709 cm^{-1}; HRMS (ESI+) calculated for $C_{24}H_{37}N_2O_4$ $[M+NH_4]^+$ = 417.2748, found = 417.2747.

(*RS*)-1-[(*SR*)-2-Oxo-4-vinyloxazolidin-4-yl]oct-2-yn-1-yl benzoate (6g). 0.340 g (90%) from 0.237 g (1.10 mmol) of allene **1** as a colorless solid; mp = 122-124 °C; R_f (hexanes/EtOAc 4:1) = 0.22; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (m, 2H), 7.59 (m, 1H),

7.45 (m, 2H), 6.10 (dd, *J* = 17.2, 10.7 Hz, 1H), 5.79 (bs, 1H), 5.65 (t, *J* = 2.0 Hz, 1H), 5.50 (d, *J* = 17.2 Hz, 1H), 5.39 (d, *J* = 10.7 Hz, 1H), 4.70 (d, *J* = 8.8 Hz, 1H), 4.20 (d, *J* = 8.8 Hz, 1H), 2.21 (dt, *J* = 7.1, 2.0 Hz, 2H), 1.53-1.48 (m, 2H), 1.35-1.27 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 147.3, 135.2, 133.6, 130.9, 129.0, 128.5, 117.6, 89.7, 73.1, 72.0, 67.8, 64.4, 31.0, 27.8, 22.0, 18.6, 13.9; IR (KBr): 3243, 2932, 2860, 1760, 1684 cm^{-1}; HRMS (ESI+) calculated for $C_{20}H_{24}NO_4$ $[M+H]^+$ = 342.1700, found = 342.1696.

(*S*)-[(2*R*,5*R*,6*R*)-5,6-Dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl][(*S*)-2-oxo-4-vinyloxazolidin-4-yl]methyl benzoate (6h), 0.448 g (85%) from 0.269 g (1.25 mmol) of allene **1** as a colorless solid; mp = 69-71 °C; R_f (hexanes/EtOAc 7:3) = 0.16; $[\alpha]_D^{25}$ −81.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.9 Hz, 2H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.48 (d, *J* = 7.9 Hz, 2H), 6.27 (dd, *J* = 17.2, 10.6 Hz, 1H), 5.85 (bs, 1H), 5.59 (d, *J* = 17.2 Hz, 1H), 5.48 (d, *J* = 10.6 Hz, 1H), 5.33 (d, *J* = 8.7 Hz, 1H), 4.36 (d, *J* = 8.7 Hz, 1H), 4.31-4.23 (m, 1H), 4.05 (d, *J* = 8.7 Hz, 1H), 3.73 (t, *J* = 11.4 Hz, 1H), 3.40 (dd, *J* = 11.4, 3.4 Hz, 1H), 3.27 (s, 3H), 3.25 (s, 3H), 1.32 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 158.1, 135.6, 134.1, 129.8, 128.3, 127.6, 117.2, 99.6, 98.1, 74.7, 73.7, 67.5, 63.3, 60.8, 49.2, 48.2, 17.5, 17.5; IR (KBr): 3342, 2991, 2949, 1763, 1726 cm^{-1}; HRMS (ESI+) calculated for $C_{21}H_{28}NO_8$ $[M+H]^+$ = 422.1809, found = 422.1806.

(1*S*,2*R*)-2-[(*tert*-Butyldiphenylsilyl)oxy]-1-[(*S*)-2-oxo-4-vinyloxazolidin-4-yl]propyl benzoate (6i), 0.673 g (84%) from 0.324 g (1.51 mmol) of allene **1** as a colorless oil; R_f (hexanes/EtOAc 4:1) = 0.24; $[\alpha]_D^{25}$ +31.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (m, 2H), 7.60-7.71 (m, 5H), 7.35-7.50 (m, 8H), 6.05 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.59 (bs, 1H), 5.44 (d, *J* = 17.3 Hz, 1H), 5.39 (d, *J* = 10.7 Hz, 1H), 5.30 (m, 1H), 4.41 (d, *J* = 8.7 Hz, 1H), 4.15 (m, 1H), 4.07 (d, *J* = 8.7 Hz, 1H), 1.06 (s, 9H), 1.03 (d, *J* = 6.3

Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 135.9, 135.7, 135.6, 133.5, 132.7, 130.1, 129.9, 127.9, 127.7, 115.8, 78.7, 73.6, 70.7, 63.6, 27.0, 19.1, 18.9; IR (film): 3250, 3070, 2931, 2858, 1759, 1728 cm^{-1}; HRMS (ESI+) calculated for $C_{31}H_{36}NO_5Si$ $[M+H]^+$ = 530.2356, found = 530.2357.

(*S*)-4-[(1*S*,2*R*)-1,2-Dihydroxypropyl]-4-vinyloxazolidin-2-one (7). A solution of K_2CO_3 (0.154 g, 1.10 mmol) in MeOH (10 mL) was added to a solution of carbamate **6i** (0.389 g, 0.735 mmol) in MeOH (10 mL) at rt under N_2 atmosphere. The mixture was stirred for 2 h. Water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phase was dried over $MgSO_4$ and the solvent was evaporated under vacuum. The crude residue was purified by column chromatography (hexanes/EtOAc 3:2) to afford a mixture of debenzoylated products (0.224 g, 86% yield). A solution of TBAF·$3H_2O$ (0.201 g, 0.62 mmol) and acetic acid (35 μL, 0.6 mmol) in anhydrous THF (10 mL) was added via cannula to the mixture of debenzoylated products (0.175 g, 0.41 mmol) in anhydrous THF (10 mL). The solution was stirred at rt for 5 h. Phosphate buffer solution (pH = 7, 10 mL) was added and the aqueous layer was extracted with EtOAc (5 x 20 mL). The combined organic layer was dried over anhydrous $MgSO_4$, and the solvent was evaporated under vacuum. The crude residue was purified by column chromatography (CH_2Cl_2/MeOH, 95:5) to afford carbamate **7** (0.060 g, 0.32 mmol) in 78% yield: colorless oil; R_f (EtOAc) = 0.35; $[\alpha]_D^{25}$ +31.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.10 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.40 (d, *J* = 17.4, 1H), 5.35 (d, *J* = 10.7 Hz, 1H), 4.49 (d, *J* = 8.8 Hz, 1H), 4.14 (d, *J* = 8.8 Hz, 1H), 3.69-3.62 (m, 4H), 3.37 (d, *J* = 8.5 Hz, 1H), 1.25 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.2, 116.1, 78.4, 74.1, 69.2, 64.5, 20.9; IR (film): 3379, 2922, 1737, 1396, 933, 721 cm^{-1}; HRMS (ESI+) calculated for $C_8H_{14}NO_4$ $[M+H]^+$ = 188.0916, found = 188.0917.

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SUPPORTING INFORMATION

^{1}H NMR spectra of the prepared starting materials allene **1** and chiral aldehydes. ^{1}H and ^{13}C NMR spectra of products **6a-i**, and **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding authors

*Fax: +34 933397878. Tel: +34 934021248. E-mail: xariza@ub.edu.

*Fax: +34 933397878. Tel: +34 934034819. E-mail: jordigarciagomez@ub.edu.

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