JOC The Journal of Organic Chemistry

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pubs.acs.org/joc

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

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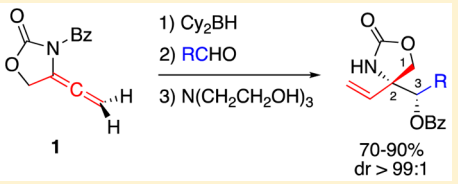
Supporting Information

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.



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 (Figure 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]

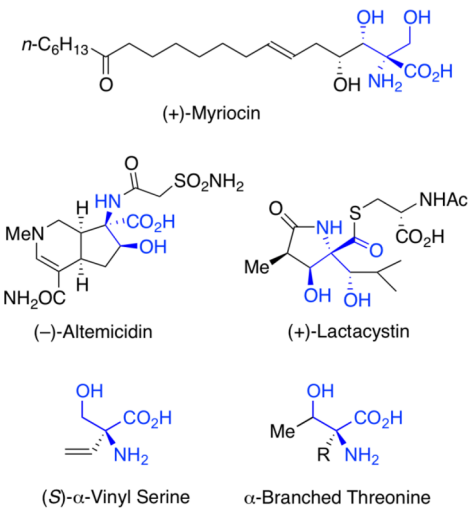


Figure 1. Compounds incorporating quaternary β-hydroxylated α-amino acids.

Sphingolipids are a family of lipids that play essential roles as structural cell membrane components and also in cell signaling 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]

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]

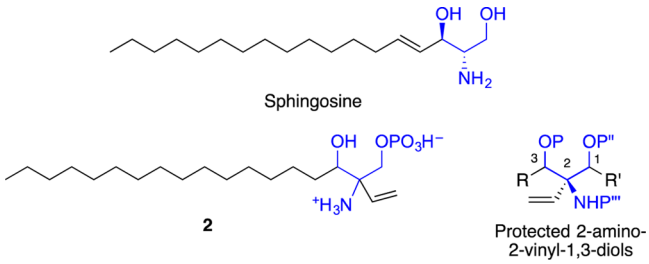


Figure 2. Sphingosine, compound **2**, and its possible precursor.

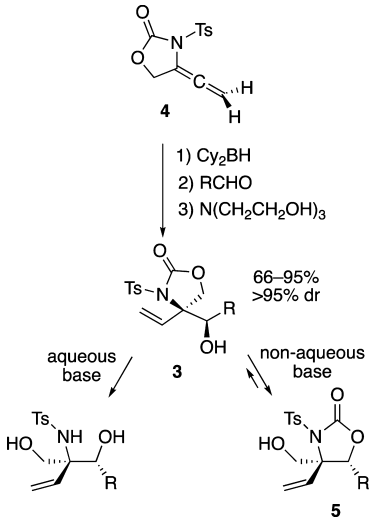
As part of our studies aimed at the synthesis of polyhydroxylated α-amino acids,[8] we recently reported a new tandem reaction leading to protected tosylcarbamates **3** in high yields and excellent diastereoselectivities (Scheme 1).[9] This simple one-pot process was based on the hydroboration of tosyl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

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,

Received: November 17, 2016
Published: January 13, 2017

DOI: 10.1021/acs.joc.6b02765
J. Org. Chem. 2017, 82, 1851−1855

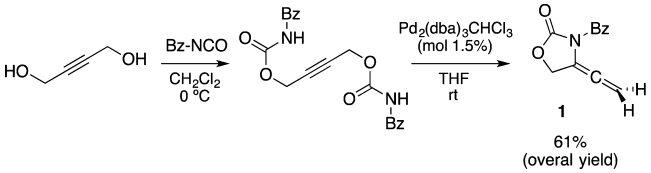
Scheme 1. Preparation of *N*-Tosylcarbamates 3 and Their Hydrolysis and Isomerization to 5



respectively. Unfortunately, these deleterious side reactions have also been observed[10] occasionally during workup and/or chromatographic purification of compounds **3**. On the other hand, removing the robust tosyl group in the final steps of a multistep 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.

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),

Scheme 3. Addition of Allene 1 to Isobutyraldehyde

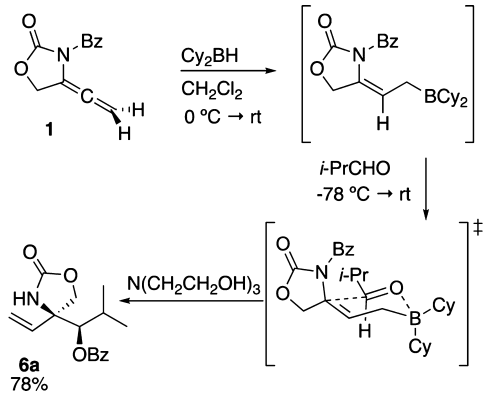
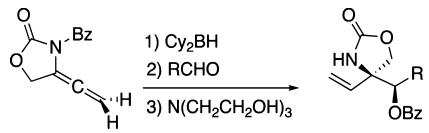


Table 1. Addition of Allene 1 to Aldehydes



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%

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).

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** was obtained in good yield with complete migration of the benzoyl group.

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.

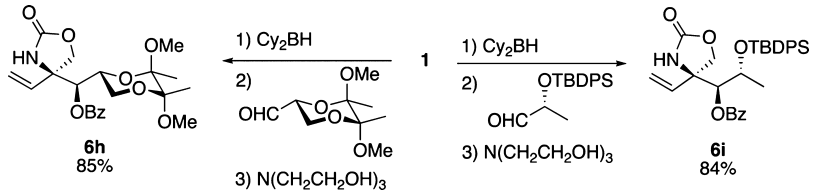
In summary, allene **1** is a useful starting material for the synthesis of protected quaternary 2-amino-2-vinyl-1,3-diols by hydroboration followed by aldehyde addition since it avoids undesired migrations and affords a fully protected carbamate with complete stereoselectivity from a range of aldehydes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

■ EXPERIMENTAL SECTION

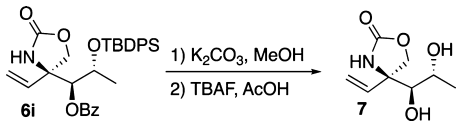
All reactions involving moisture- or air-sensitive reagents were performed in oven-dried glassware under N_2. Chemical shifts (*δ*) are

DOI: 10.1021/acs.joc.6b02765
J. Org. Chem. 2017, 82, 1851−1855

Scheme 4. Addition of Allene 1 to Enantiopure Aldehydes



Scheme 5. Deprotection of 6i To Give 7



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 °C under N_2 atmosphere. The mixture was stirred for 5 h 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 °C (lit.[11] 101.2−103 °C); 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+) calcd 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 °C and under nitrogen atmosphere. The resulting mixture was stirred for 10 min at 0 °C and for 1 h at rt. The resulting solution was then cooled to −78 °C, 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+) calcd 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+) calcd 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+) calcd 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+) calcd 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+) calcd 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+) calcd 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,

DOI: 10.1021/acs.joc.6b02765
J. Org. Chem. 2017, 82, 1851−1855

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+) calcd 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+) calcd 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+) calcd 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 × 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 × 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+) calcd for $C_8H_{14}NO_4$ $[M + H]^+$ = 188.0916, found = 188.0917.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02765.

^{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** (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Spanish Ministerio de Educación y Ciencia (CTQ2009-09692 and SAF2014-52223-C2-1-R), the University of Barcelona (fellowship to A.R.), and the Generalitat de Catalunya (2009SGR1037, 2014SGR107 and fellowship to C.S.)

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DOI: 10.1021/acs.joc.6b02765
J. Org. Chem. 2017, 82, 1851−1855

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