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Regioselective Base-Free Intermolecular Aminohydroxylations of Hindered and Functionalized Alkenes

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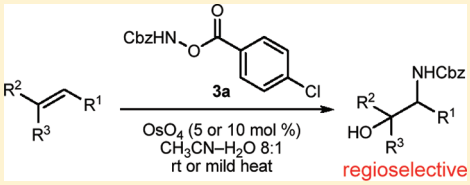
Supporting Information

ABSTRACT: Regioselective base-free intermolecular aminohydroxylations of functionalized trisubstituted and 1,1-disubstituted alkenes employing benzoyloxycarbamate **3a** and catalytic OsO_4 are described. In all cases, the more substituted alcohol isomer is favored. Sluggish reactions could be promoted by gentle heating, the use of amine ligands, or increased catalyst loadings. A competitive rearrangement was observed with a secondary allylic alcohol substrate. The adducts serve as useful precursors to dehydroamino acids.



The presence of 1,2-amino alcohols in several natural products, biologically active compounds, and chiral ligands has spurred the development of numerous methods for their construction.[1] The oxyamination of alkenes provides a straightforward route to this valuable structural motif.[2] In particular, the Os-catalyzed aminohydroxylation reaction[3] is attractive for its amenability to asymmetric catalysis.[4] Unfortunately, problems with regioselectivity have limited the scope of the Sharpless asymmetric aminohydroxylation.[5] Effective solutions for a few specific substrate types have been devised,[6] but a general remedy remains elusive. Donohoe's tethered aminohydroxylation of allylic and homoallylic alcohols[7] constitutes a major advance in this area. However, tethering of the nitrogen source to the substrate requires two synthetic steps, and cleavage of the cyclic carbamate product to reveal the amino alcohol involves strongly basic conditions. Hence, a need exists for practical and regioselective aminohydroxylation protocols.

Based on our interest in the synthesis of unusual amino acids,[8] we recognized the potential of regioselective intermolecular aminohydroxylations as a means of rapidly accessing β-hydroxy amino acids and dehydroamino acids. Although intermolecular aminohydroxylations of trisubstituted alkenes are rare, the isolated existing examples[9] indicate that regioselectivity is reliable and governed by steric effects. We were intrigued by the recent report of Luxenburger and coworkers describing base-free intermolecular aminohydroxylations of selected mono- and disubstituted alkenes with benzoyloxycarbamates as the nitrogen source reagents.[10] We recognized that these mild conditions should permit the aminohydroxylation of functionalized alkenes such as unprotected allylic alcohols, and we were hopeful that the method could be adapted to enable regioselective aminohydroxylations of sterically demanding trisubstituted alkenes. The products of these reactions would be useful precursors of β-hydroxy amino acids and dehydroamino acids. Herein, we disclose that simple modifications to the Luxenburger protocol facilitate efficient and regioselective aminohydroxylations of several types of hindered, functionalized alkenes. We also report an investigation of steric effects, electronic effects, and substrate-directed stereocontrol in base-free aminohydroxylations. Finally, we demonstrate the utility of this process by converting an aminohydroxylation adduct into a dehydrovaline-containing peptide.

At the outset, we elected to explore ligand-free, racemic aminohydroxylations. Our initial studies are summarized in Table 1. Prenol (**1**) was selected as a test substrate due to its ready availability and the utility of the expected product **4** as a precursor to the amino acids of interest. Aminohydroxylations of the isomeric 1,1-disubstituted alkene isoprenol (**2**)[11] were also examined. We were pleased to find that **1** afforded the anticipated adduct **4** in good yield upon exposure to 5 mol % of OsO_4 with benzyl 4-chlorobenzoyloxy carbamate (**3a**, R = Cbz) as the nitrogen source.[10] No traces of the regioisomeric amino diol were detected. *t*-BuOH$-H_2O$ and CH_3CN-H_2O mixtures were both effective solvent systems (entries 1 and 2), but the latter was preferred for the homogeneous reaction mixtures that resulted from its use. The Boc-based reagent **3b** was also effective in the aminohydroxylation of **1** (entry 3), but **3a** was employed in the remainder of our studies due to the convenience of isolating UV-active products.

In contrast, the aminohydroxylation of **2** was low-yielding, affording amino diol **5** in 30% yield, albeit as a single regioisomer (entry 4). Large quantities of benzyl carbamate ($CbzNH_2$) were obtained; similar results with tethered aminohydroxylations have been reported by Donohoe.[7d] This byproduct could presumably be derived from hydrolysis of an imidoosmium species, a process that might occur competitively with a slow aminohydroxylation. Fortunately, two strategies for increasing the yield of **5** were identified. The use of pyridine or DABCO as a ligand for Os gave improved results (entries 5 and 6). Interestingly, other amines (i.e., Et_3N, DMAP, imidazole) were not beneficial, demonstrating the subtleties of ligand-accelerated catalysis.[12] Ultimately, mild heating (35 °C) of the

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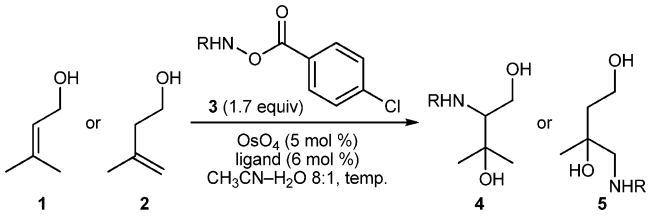
Table 1. Optimization of Reaction Conditions[a]



entry	alkene	R	ligand	temp (°C)	product	yield (%)
1[b]	**1**	Cbz	none	rt	**4a**	63
2	**1**	Cbz	none	rt	**4a**	62
3	**1**	Boc	none	rt	**4b**	75
4	**2**	Cbz	none	rt	**5**	30
5	**2**	Cbz	py	rt	**5**	61
6	**2**	Cbz	DABCO	rt	**5**	59
7	**2**	Cbz	none	35	**5**	85

[a]Reaction times were 20–24 h. [b]*t*-BuOH–H_2O 6:1 was used as solvent.

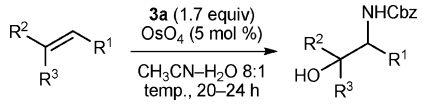
reaction mixture proved most effective, with an 85% yield of **5** obtained under these conditions (entry 7).

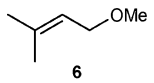
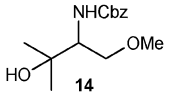
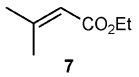
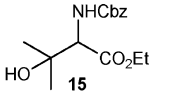
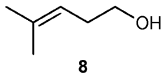
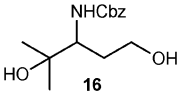
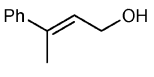
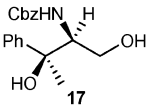
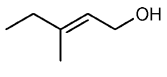
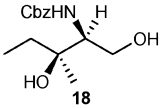
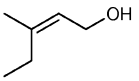
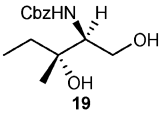
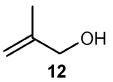
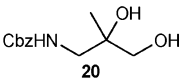
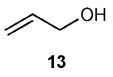
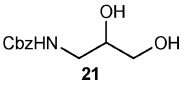
The scope of the base-free aminohydroxylation was then explored with allylic alcohols and other functionalized alkenes that were expected to afford high levels of regioselectivity. Allylic ether **6**, enoate **7**, and homoallylic alcohol **8** were each converted into a single amino alcohol in good yield, although gentle heating was required (Table 2, entries 1–3). Single regioisomers were also obtained from aminohydroxylations of bulkier allylic alcohols **9**–**11**, albeit in moderate yields (entries 4–6). As expected based on our studies with isoprenol, aminohydroxylation of methallyl alcohol (**12**) provided amino diol **20** in good yield, and heating was not required (entry 7). Allyl alcohol (**13**) also underwent a regioselective transformation into amino diol **21**, but a small amount of the meso isomer was produced in this case (entry 8). Some of the lower yielding reactions (i.e., entries 2, 5, and 6) could be improved significantly by doubling the OsO_4 loading. The aminohydroxylations shown in Table 2 were conducted on relatively small (0.3–1.0 mmol) scales, but the conversion of enoate **7** into amino alcohol **15** (entry 2) could be accomplished on a larger (2.9 mmol) scale with similar results.

To determine the role of steric and electronic effects in base-free aminohydroxylations, the reactions of *trans* allylic alcohols were investigated (Table 3). Poor regioselectivity was observed, but some interesting patterns emerged. Cinnamyl alcohols exhibited improved yields and regioselectivities as the electron-rich nature of the aryl ring was increased. With alkyl-substituted substrates, an increase in size from methyl to isopropyl caused a change in preference from the 1,2-diol to the 1,3-diol product, as well as a slight reduction in yield. These results demonstrate that both electronic and steric effects can impact the yields and regioselectivities of base-free aminohydroxylations.

To probe the degree of substrate-directed stereocontrol, we examined aminohydroxylations of chiral secondary allylic alcohols. The reaction of (±)-2-cyclohexen-1-ol (**32**) afforded regioisomers **33a** and **33b** as a 1.2:1 mixture in good yield (Scheme 1, eq 1). The stereoselective addition *anti* to the allylic hydroxyl group of **32** is consistent with Kishi's observations in related dihydroxylations,[13] and the poor regioselectivity is in harmony with the results shown in Table 3. Interestingly, the aminohydroxylation of racemic 4-methyl-3-penten-2-ol (**34**) produced a 4:1 mixture of diastereomers **35a** and **35b**, but the major product was unexpected regioisomer **35c** (Scheme 1, eq 2). Apparently, rearrangement of secondary allylic alcohol **34** is competitive with aminohydroxylation of this hindered sub-

Table 2. Regioselective Aminohydroxylations of Functionalized Alkenes



entry	alkene	product	temp., yield
1	 **6**	 **14**	35 °C, 54%
2	 **7**	 **15**	35 °C, 54% (79%)[a]
3	 **8**	 **16**	35 °C, 58%
4	 **9**	 **17**	35 °C, 46%
5	 **10**	 **18**	45 °C, 38% (55%)[b]
6	 **11**	 **19**	45 °C, 41% (59%)[b]
7	 **12**	 **20**	rt, 62%
8	 **13**	 **21**	rt, 70%[c]

[a]A 10 mol % loading of OsO_4 was used. [b]A 10 mol % loading of OsO_4 was used, and the reaction was conducted at 35 °C. [c]A 6.7:1 mixture of regioisomers was obtained.

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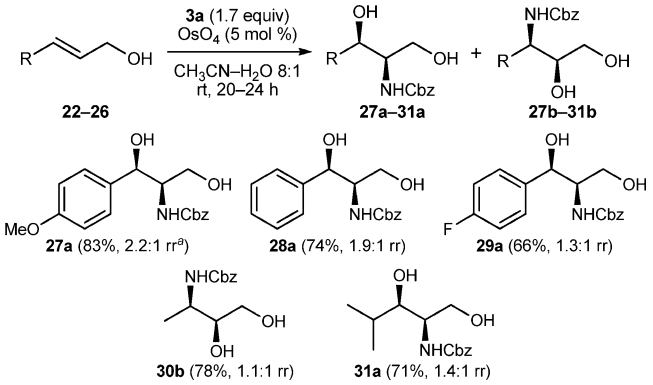
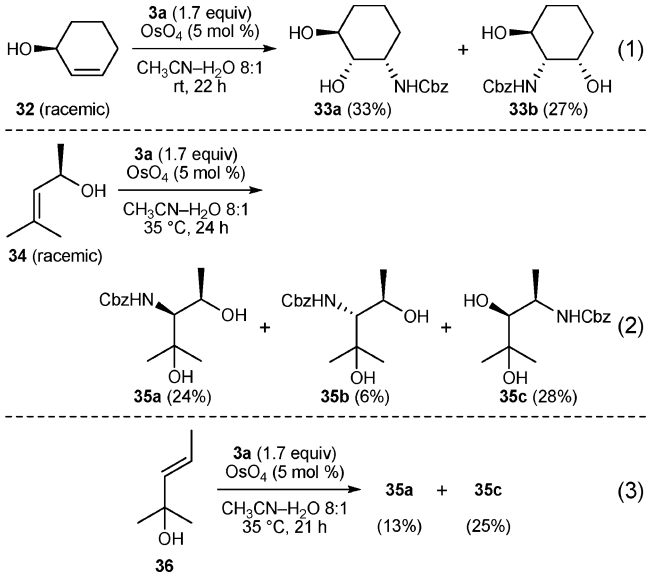
Table 3. Aminohydroxylations of *Trans* Allylic Alcohols



[a]Ratio of regioisomers. The major isomer is drawn in each case.

Scheme 1. Aminohydroxylations of Secondary Allylic Alcohols



strate. Isomerizations of allylic alcohols catalyzed by various metal–oxo species are known,[14] but we are unaware of any prior examples involving OsO_4.

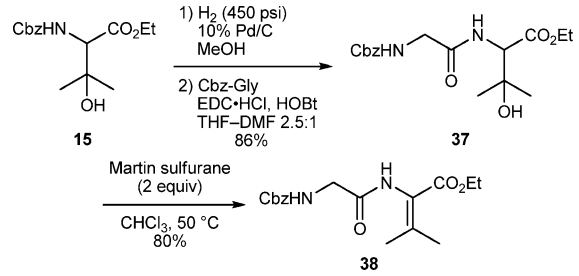
Intrigued by this result, we performed the aminohydroxylation of allylic alcohol **36**, which is presumably generated by the rearrangement of **34**. Regioisomers **35a** and **35c** were produced in a 1:2 ratio, and **35b** was not detected (Scheme 1, eq 3). Since **35b** could only be formed by rearrangement of **36** to **34** prior to aminohydroxylation, its absence suggests that **36** undergoes aminohydroxylation in preference to rearrangement. This is consistent with the fact that, in the absence of other factors such as conjugation,[14c] allylic alcohol rearrangements catalyzed by metal oxo species tend to proceed in the direction of the more substituted alcohol.[14a,b] Using the ratio of **35a** and **35c** obtained from aminohydroxylation of **36** (eq 3), we estimate that the majority (14%) of **35a** derived from **34** (eq 2) was produced by the rearrangement pathway, and the remainder (10%) originated from direct aminohydroxylation of this substrate. Thus, the rearrangement of **34** is approximately 2.6 times as fast as its aminohydroxylation, and the dr of the aminohydroxylation is modest (ca. 1.7:1). We are unsure why the aminohydroxylation of trisubstituted alkene **34** is higher yielding than that of disubstituted alkene **36**.

Heating solutions of **34** and **36** at 35 °C in $CD_3CN–D_2O$ 8:1 did not induce rearrangement or degradation of either allylic alcohol, indicating that an Os species is playing a role in the isomerization of **34**. Presumably, the mechanism of this Os-promoted rearrangement is analogous to the [3,3]-sigmatropic rearrangement pathway proposed for trioxorhenium catalysts.[15]

We were eager to explore the asymmetric aminohydroxylation of functionalized trisubstituted alkenes. Disappointingly and in contrast to Luxenburger's results with disubstituted alkenes,[10] reaction of prenol (**1**) with **3a** and OsO_4 in the presence of $(DHQD)_2PHAL$ afforded amino diol **4a** in low (18%) yield as a racemic mixture, and large amounts of benzyl carbamate were generated. A theoretical study has demonstrated the acceleration of Os-catalyzed aminohydroxylation by amine ligands,[16] and this finding is supported by our own work (see Table 1, entries 4–6). Thus, the sluggish and unselective asymmetric aminohydroxylation of **1** can presumably be attributed to steric rather than electronic effects, as the substrate, the dimeric chiral ligand, and the nitrogen source reagent combine to form a very congested Os center. The small amount of racemic product **4a** may actually be produced by a less-crowded unligated Os species.

To demonstrate the utility of the aminohydroxylation adducts, compound **15** was transformed into a dehydroamino acid as shown in Scheme 2. Hydrogenolysis of the Cbz group

Scheme 2. Conversion into Dehydroamino Acid



followed by coupling of the resulting amine with Cbz-Gly afforded dipeptide **37**. Exposure of **37** to the Martin sulfurane[17] facilitated the desired dehydration, producing α,β-dehydrovaline-containing dipeptide **38** in good yield. α,β-Dehydrovaline is present in a number of bioactive peptide natural products.[18]

In summary, we have found that the base-free aminohydroxylation protocol developed by Luxenburger[10] can be adapted to permit the use of functionalized trisubstituted and 1,1-disubstituted alkenes as substrates. Most of these hindered compounds reacted sluggishly under the original conditions, but three simple strategies (i.e., heating, use of amine ligands, and higher catalyst loadings) were developed to facilitate difficult transformations. The reactions are practical and regioselective, affording the more substituted alcohol isomers in good yields. We have also discovered an electronic effect in the aminohydroxylation of cinnamyl alcohols and an Os-mediated isomerization of a secondary allylic alcohol. The racemic amino alcohol products have good synthetic utility as evidenced by the transformation of adduct **15** into a dehydrovaline derivative. Efforts to expand the scope of this process and develop a viable enantioselective variant are in progress and will be disclosed in due course.

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EXPERIMENTAL SECTION

General Details. Dimethylformamide, methanol, and tetrahydrofuran were dried by passage through cylinders of activated alumina. Flash chromatography was conducted using 60−230 mesh silica gel. ^{1}H NMR spectra were acquired on a 500 MHz spectrometer with chloroform (7.27 ppm), methanol (3.34 ppm), or benzene (7.15 ppm) as internal reference. Signals are reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), td (triplet of doublets), br s (broad singlet), m (multiplet). ^{13}C NMR spectra were acquired on a spectrometer operating at 125 MHz with chloroform (77.23 ppm), methanol (49.86 ppm), or benzene (128.62 ppm) as internal reference. Infrared spectra were obtained on an FT-IR spectrometer. MS data were obtained using ESI techniques.

General Procedure for Base-Free Aminohydroxylations. *Caution: OsO_4 is toxic, and exposure to its vapors can cause damage to the eyes, respiratory tract, and skin. Solutions of this reagent should be handled with extreme care inside fume hoods using appropriate protective clothing. Aqueous waste containing Os should be collected with other hazardous heavy metals and disposed of in accordance with local environmental regulations.*. A solution of benzyl 4-chlorobenzoyloxy carbamate[10] (**3a**, 1.7 equiv) in CH_3CN (4 mL) at rt was treated with OsO_4 (4 wt % solution in H_2O, 100 μL, 0.0157 mmol, 0.05 equiv), stirred for 10 min, and then treated with the alkene (1 equiv) and H_2O (400 μL). A color change from clear to brown typically acccompanied alkene addition. The resulting mixture was stirred at either rt, 35 °C, or 45 °C for 20−24 h, treated with satd aq $K_2S_2O_5$ (400 μL), and stirred for an additional 5 min. It was then diluted with H_2O (15 mL) and extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with satd aq $NaHCO_3$ (2 × 15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography afforded the amino alcohol products.

Benzyl 1,3-Dihydroxy-3-methylbutan-2-ylcarbamate (4a). Prepared from **3a** (168.1 mg, 0.550 mmol) and **1** (32 μL, 27.1 mg, 0.315 mmol) according to the general procedure (rt, 23.5 h). Flash chromatography (SiO_2, 1.5 × 8.5 cm, 5−10% MeOH/CH_2Cl_2 elution) afforded **4a**[19] (49.6 mg, 0.196 mmol, 62%) as a colorless oil.

***tert*-Butyl 1,3-Dihydroxy-3-methylbutan-2-ylcarbamate (4b).** Prepared from *tert*-butyl 4-chlorobenzoyloxy carbamate[10] (**3b**, 147.1 mg, 0.541 mmol) and **1** (32 μL, 27.1 mg, 0.315 mmol) according to the general procedure (rt, 24 h). Flash chromatography (SiO_2, 1.5 × 8 cm, 5−10% MeOH/CH_2Cl_2 elution) afforded **4b**[20] (51.6 mg, 0.235 mmol, 75%) as a colorless oil.

Benzyl (2,4-Dihydroxy-2-methylbutyl)carbamate (5). Prepared from **3a** (167.9 mg, 0.549 mmol) and **2** (32 μL, 27.6 mg, 0.321 mmol) according to the general procedure (35 °C, 23 h). Flash chromatography (SiO_2, 1.5 × 10 cm, 2−5% MeOH/CH_2Cl_2 elution) afforded **5** (69.1 mg, 0.273 mmol, 85%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38−7.28 (m, 5H), 5.47 (s, 1H), 5.09 (s, 2H), 3.94−3.87 (m, 1H), 3.84−3.78 (m, 1H), 3.73 (br s, 1H), 3.24 (dd, *J* = 13.8, 6.1 Hz, 1H) 3.18 (dd, *J* = 13.8, 6.3 Hz, 1H), 3.11 (br s, 1H), 1.85−1.77 (m, 1H), 1.63−1.56 (m, 1H), 1.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.5, 136.4, 128.5 (2C), 128.2, 128.1 (2C), 73.3, 66.9, 59.3, 51.0, 39.4, 24.7; IR (film) ν_{max} 3346, 3066, 2935, 1701, 1535, 1455, 1257, 1144, 1042 cm^{-1}; HRMS (ESI) *m*/*z* 254.1406 (MH^+, $C_{13}H_{19}NO_4H^+$ requires 254.1387).

Benzyl (3-Hydroxy-1-methoxy-3-methylbutan-2-yl)-carbamate (14). Prepared from **3a** (163.5 mg, 0.535 mmol) and **6**[21] (34 μL, 31.6 mg, 0.315 mmol) according to the general procedure (35 °C, 23.5 h). Flash chromatography (SiO_2, 1.5 × 12 cm, 10−30% EtOAc/hexanes elution) afforded **14** (45.3 mg, 0.169 mmol, 54%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39−7.29 (m, 5H), 5.62 (d, *J* = 8.3 Hz, 1H), 5.12 (s, 2H), 3.82 (d, *J* = 7.2 Hz, 1H), 3.60−3.55 (m, 2H), 3.35 (s, 3H), 3.11 (s, 1H), 1.32 (s, 3H), 1.12 (3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.5, 136.5, 128.5 (2C), 128.1, 128.0 (2C), 73.7, 72.8, 66.8, 59.4, 57.0, 27.7, 26.9; IR (film) ν_{max} 3322, 2977, 1701, 1522, 1454, 1216, 1117, 1047 cm^{-1}; HRMS (ESI) *m*/*z* 268.1560 (MH^+, $C_{14}H_{21}NO_4H^+$ requires 268.1543).

Ethyl 2-(((Benzyloxy)carbonyl)amino)-3-hydroxy-3-methylbutanoate (15). Prepared from **3a** (492.8 mg, 1.61 mmol) and 7 (132 μL, 122 mg, 0.951 mmol) according to the general procedure with 600 μL of OsO_4 solution (0.0944 mmol, 0.10 equiv) and stirring at 35 °C for 10 h. Flash chromatography (SiO_2, 1.5 × 12 cm, 10−50% EtOAc/hexanes elution) afforded **15** (221.9 mg, 0.751 mmol, 79%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39−7.31 (m, 5H), 5.62 (br s, 1H), 5.13 (s, 2H), 4.31−4.19 (m, 3H), 2.50 (br s, 1H), 1.34−1.26 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.6, 156.5, 136.1, 128.5 (2C), 128.2, 128.1 (2C), 71.9, 67.2, 61.62, 61.56, 26.8, 26.3, 14.1; IR (film) ν_{max} 3406, 2978, 2922, 1720, 1709, 1512, 1501, 1467, 1452, 1211, 1051, 1027 cm^{-1}; HRMS (ESI) *m*/*z* 296.1497 (MH^+, $C_{15}H_{21}NO_5H^+$ requires 296.1492).

Benzyl (1,4-Dihydroxy-4-methylpentan-3-yl)carbamate (16). Prepared from **3a** (168.8 mg, 0.552 mmol) and **8** (37 μL, 31.7 mg, 0.317 mmol) according to the general procedure (35 °C, 23 h). Flash chromatography (SiO_2, 1.5 × 10 cm, 2−5% MeOH/CH_2Cl_2 elution) afforded **16** (49.5 mg, 0.185 mmol, 58%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37−7.28 (m, 5H), 5.33 (d, *J* = 9.4 Hz, 1H), 5.13 (d, *J* = 12.2 Hz, 1H), 5.08 (d, *J* = 12.2 Hz, 1H), 3.71−3.64 (m, 2H), 3.63−3.56 (m, 1H), 3.38 (br s, 1H), 2.78 (br s, 1H), 1.98−1.89 (m, 1H), 1.57−1.48 (m, 1H), 1.24 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.7, 136.3, 128.6 (2C), 128.2, 128.0 (2C), 72.2, 67.1, 58.6, 56.1, 32.2, 27.6, 27.0; IR (film) ν_{max} 3330, 2973, 1697, 1535, 1258, 1054 cm^{-1}; HRMS (ESI) *m*/*z* 268.1561 (MH^+, $C_{14}H_{21}NO_4H^+$ requires 268.1543).

Benzyl ((2*S,3*S**)-1,3-Dihydroxy-3-phenylbutan-2-yl)-carbamate (17).** Prepared from **3a** (116.4 mg, 0.381 mmol) and **9**[22] (33.2 mg, 0.224 mmol) according to the general procedure (35 °C, 18 h). Flash chromatography (SiO_2, 1.5 × 11 cm, 2−5% MeOH/CH_2Cl_2 elution) afforded **17** (32.4 mg, 0.103 mmol, 46%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.50−7.42 (m, 3H), 7.41−7.25 (m, 5H), 7.24−7.17 (m, 2H), 5.44 (d, *J* = 7.6 Hz, 1H), 4.98 (s, 2H), 4.18−4.07 (m, 1H), 4.03−3.91 (m, 2H), 3.37 (br s, 1H), 2.28 (br s, 1H), 1.71 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.4, 145.0, 136.3, 128.5 (2C), 128.3 (2C), 128.0, 127.7 (2C), 127.1, 124.7 (2C), 77.0 (obscured by $CDCl_3$), 66.6, 63.1, 58.9, 28.3; IR (film) ν_{max} 3404, 2977, 1701, 1517, 1447, 1251, 1072, 1048 cm^{-1}; HRMS (ESI) *m*/*z* 316.1558 (MH^+, $C_{18}H_{21}NO_4H^+$ requires 316.1543.

Benzyl ((2*S,3*S**)-1,3-Dihydroxy-3-methylpentan-2-yl)-carbamate (18).** Prepared from **3a** (164.2 mg, 0.537 mmol) and **10**[23] (37.5 μL, 27.2 mg, 0.316 mmol) according to the general procedure with 200 μL of OsO_4 solution (0.0315 mmol, 0.10 equiv) and stirring at 35 °C for 23 h. Flash chromatography (SiO_2, 1.5 × 11 cm, 0.1−2% MeOH/CH_2Cl_2 elution) afforded **18** (46.6 mg, 0.174 mmol, 55%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38−7.30 (m, 5H), 5.63 (d, *J* = 8.1 Hz, 1H), 5.12 (s, 2H), 4.06−4.00 (m, 1H), 3.88−3.82 (m, 1H), 3.62−3.57 (m, 1H), 2.63 (br s, 1H), 2.54 (br s, 1H), 1.63−1.55 (m, 1H), 1.54−1.45 (m, 1H), 1.29 (s, 3H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.7, 136.4, 128.5 (2C), 128.1, 128.0 (2C), 75.8, 66.9, 63.6, 56.0, 32.3, 23.9, 8.1; IR (film) ν_{max} 3400, 2970, 1701, 1529, 1455, 1250, 1061, cm^{-1}; HRMS (ESI) *m*/*z* 268.1557 (MH^+, $C_{14}H_{21}NO_4H^+$ requires 268.1543.

Benzyl ((2*S,3*R**)-1,3-Dihydroxy-3-methylpentan-2-yl)-carbamate (19).** Prepared from **3a** (163.7 mg, 0.536 mmol) and **11**[24] (37 μL, 31.3 mg, 0.312 mmol) according to the General Procedure with 200 μL of OsO_4 solution (0.0315 mmol, 0.10 equiv) and stirring at 35 °C for 23 h. Flash chromatography (SiO_2, 1.5 × 11 cm, 0.1−2% MeOH/CH_2Cl_2 elution) afforded **19** (48.9 mg, 0.183 mmol, 59%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40−7.30 (m, 5H), 5.69 (br s, 1H), 5.11 (s, 2H), 4.04−3.98 (m, 1H), 3.83−3.77 (m, 1H), 3.61−3.57 (m, 1H), 2.77−2.55 (m, 2H), 1.77−1.58 (m, 2H), 1.16 (s, 3H), 0.95 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.7, 136.4, 128.5 (2C), 128.2 (2C), 128.0, 76.1, 66.9, 63.1, 56.6, 32.8, 23.4, 8.3; IR (film) ν_{max} 3401, 2971, 1701, 1522, 1455, 1251, 1062 cm^{-1}; HRMS (ESI) *m*/*z* 268.1543 (MH^+, $C_{14}H_{21}NO_4H^+$ requires 268.1543).

Benzyl 2,3-Dihydroxy-2-methylpropylcarbamate (20). Prepared from **3a** (163.9 mg, 0.536 mmol) and **12** (27 μL, 23.0 mg, 0.319 mmol) according to the general procedure (rt, 23 h). Flash chromatography (SiO_2, 1.5 × 10 cm, 5−10% MeOH/CH_2Cl_2 elution) afforded **20**[25] (47.7 mg, 0.199 mmol, 62%) as a colorless oil.

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Benzyl 2,3-Dihydroxypropylcarbamate (21). Prepared from **3a** (164.5 mg, 0.538 mmol) and **13** (21.5 μL, 18.4 mg, 0.316 mmol) according to the general procedure (rt, 23.5 h). Flash chromatography (SiO_2, 1.5 × 9.5 cm, 5−10% MeOH/CH_2Cl_2 elution) afforded **21**[26] (49.6 mg, 0.220 mmol, 70%) as a colorless oil that was a 6.7:1 ratio of regioisomers.[27]

Benzyl ((1*R,2*R**)-1,3-Dihydroxy-1-(4-methoxyphenyl)-propan-2-yl)carbamate (27a).** Prepared from **3a** (81.4 mg, 0.266 mmol) and *p*-methoxycinnamyl alcohol (**22**,[28] 25.8 mg, 0.157 mmol) according to the general procedure, with 50 μL of OsO_4 solution (0.00787 mmol), 200 μL of H_2O, 2 mL of CH_3CN, and stirring at rt for 25 h. Flash chromatography (SiO_2, 1.5 × 9.0 cm, 2−5% MeOH/CH_2Cl_2 elution) afforded a 2.2:1 mixture of **27a** and its regioisomer **27b** (39.2 mg, 0.130 mmol, 83%). For **27a**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37−7.16 (m, 7H), 6.87−6.79 (m, 2H), 5.60 (d, *J* = 7.6 Hz, 1H), 4.99 (s, 2H), 4.85 (br s, 1H), 3.87−3.80 (m, 1H), 3.76 (s, 3H), 3.69−3.67 (m, 1H), 3.56 (br s, 1H), 3.53−3.43 (m, 1H), 3.13 (br s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.2, 157.0, 136.2, 133.2, 128.5 (2C), 128.1 (2C), 128.0, 127.2 (2C), 113.8 (2C), 73.3, 66.9, 63.7, 57.7, 55.2; IR (film, mixture of regioisomers) ν_{max} 3400, 3033, 2954, 1701, 1612, 1513, 1454, 1343, 1247, 1031, cm^{-1}; HRMS (ESI, mixture of regioisomers) *m*/*z* 332.1489 (MH^+, $C_{18}H_{21}NO_5H^+$ requires 332.1492). For **27b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37−7.16 (m, 7H), 6.87−6.79 (m, 2H), 5.81 (br s, 1H), 4.90 (s, 2H), 4.74 (br s, 1H), 3.87−3.80 (m, 1H), 3.73 (s, 3H), 3.67−3.65 (m, 1H), 3.53−3.43 (m, 1H), 3.35 (br s, 1H), 3.13 (br s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.1, 156.9, 136.4, 136.15, 128.6 (2C), 128.2, 128.0 (2C), 127.2 (2C), 114.1 (2C), 74.9, 67.1, 67.0, 63.5, 55.3.

Benzyl ((1*R,2*R**)-1,3-Dihydroxy-1-phenylpropan-2-yl)-carbamate (28a).** Prepared from **3a** (167.9 mg, 0.549 mmol) and cinnamyl alcohol (**23**, 42.3 mg, 0.315 mmol) according to the general procedure (rt, 24 h). Flash chromatography (SiO_2, 1.5 × 9.5 cm, 2−5% MeOH/CH_2Cl_2 elution) afforded a 1.9:1 mixture of **28a**[29] and its regioisomer **28b** (70.7 mg, 0.235 mmol, 74%). For **28b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38−7.24 (m, 10H), 5.87 (br s, 1H), 5.09−5.01 (m, 2H), 4.79 (br s, 1H), 3.70−3.65 (m, 2H), 3.56−3.44 (m, 2H), 3.17 (br s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.9, 139.6, 136.1, 128.8 (2C), 128.5 (2C), 128.2, 127.8, 126.8 (2C), 126.0 (2C), 74.7, 67.2, 63.6, 56.3; IR (film, mixture of regioisomers) ν_{max} 3400, 3032, 2950, 1691, 1429, 1347, 1061 cm^{-1}; HRMS (ESI, mixture of regioisomers) *m*/*z* 302.1391 (MH^+, $C_{17}H_{19}NO_4H^+$ requires 302.1387).

Benzyl ((1*R,2*R**)-1-(4-Fluorophenyl)-1,3-dihydroxypropan-2-yl)carbamate (29a).** Prepared from **3a** (83.9 mg, 0.274 mmol) and *p*-fluorocinnamyl alcohol (**24**,[30] 24.3 mg, 0.160 mmol) according to the general procedure, with 50 μL of OsO_4 solution (0.00787 mmol), 200 μL of H_2O, 2 mL of CH_3CN, and stirring at rt for 23 h. Flash chromatography (SiO_2, 1.5 × 9.5 cm, 2−5% MeOH/CH_2Cl_2 elution) afforded a 1.3:1 mixture of **29a** and its regioisomer **29b** (33.5 mg, 0.105 mmol, 66%). For **29a**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38−7.20 (m, 7H), 7.06−6.93 (m, 2H), 5.52 (d, *J* = 7.0 Hz, 1H), 5.04−4.93 (m, 3H), 3.93−3.72 (m, 2H), 3.61−3.49 (m, 1H), 3.44 (br s, 1H), 2.80 (br s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.3 (d, *J* = 246.0 Hz), 156.8, 136.7, 136.1, 128.5 (2C), 128.2 (2C), 128.0, 127.6 (d, *J* = 8.1 Hz, 2C), 115.3 (d, *J* = 21.4 Hz, 2C), 73.4, 67.0, 63.7, 57.4; IR (film, mixture of regioisomers) ν_{max} 3401, 3067, 2926, 1697, 1605, 1510, 1455, 1343, 1224, 1061 cm^{-1}; HRMS (ESI, mixture of regioisomers) *m*/*z* 342.1102 (MNa^+, $C_{17}H_{18}FNO_4Na^+$ requires 342.1112). For **29b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38−7.20 (m, 7H), 7.06−6.93 (m, 2H), 5.76 (br s, 1H), 5.10−5.04 (m, 2H), 4.80 (br s, 1H), 3.93−3.72 (m, 2H), 3.61−3.49 (m, 1H), 3.01 (br s, 1H), 1.83 (br s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.2 (d, *J* = 246.5 Hz), 156.78, 136.14, 136.0, 128.6 (2C), 128.4 (2C), 128.1, 127.6 (d, *J* = 8.1 Hz, 2C), 115.6 (d, *J* = 21.9 Hz, 2C), 74.6, 67.3, 63.8, 55.8.

Benzyl ((2*R,3*S**)-3,4-Dihydroxybutan-2-yl)carbamate (30b).** Prepared from **3a** (164.8 mg, 0.539 mmol) and crotyl alcohol (**25**, 27 μL, 22.8 mg, 0.316 mmol) according to the general procedure (rt, 24.5 h). Flash chromatography (SiO_2, 1.5 × 9.5 cm, 5−10% MeOH/CH_2Cl_2 elution) afforded a 1.1:1 mixture of **30b** and its regioisomer **30a**[31] (59.0 mg, 0.247 mmol, 78%). For **30b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36−7.29 (m, 5H), 5.18 (d, *J* = 7.9 Hz, 1H), 5.08 (s, 2H), 3.99−3.92 (m, 1H), 3.88−3.81 (m, 1H), 3.61−3.54 (m, 2H), 3.25 (br s, 1H), 2.07 (br s, 1H), 1.19 (d, *J* = 5.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.1, 136.3, 128.6 (2C), 128.2, 128.1 (2C), 74.5, 67.0, 63.8, 47.8, 17.7; IR (film, mixture of regioisomers) ν_{max} 3407, 3066, 2974, 1699, 1519, 1455, 1338, 1294, 1060, 910 cm^{-1}; HRMS (ESI, mixture of regioisomers) *m*/*z* 240.1248 (MH^+, $C_{12}H_{17}NO_4H^+$ requires 240.1230).

Benzyl ((2*R,3*R**)-1,3-Dihydroxy-4-methylpentan-2-yl)-carbamate (31a).** Prepared from **3a** (174.1 mg, 0.569 mmol) and (*E*)-4-methyl-2-penten-1-ol (**26**,[32] 42 μL, 35.0 mg, 0.350 mmol) according to the general procedure (rt, 26 h). Flash chromatography (SiO_2, 1.5 × 9.5 cm, 2−10% MeOH/CH_2Cl_2 elution) afforded a 1.4:1 mixture of regioisomers **31a**[33] and **31b** (66.0 mg, 0.247 mmol, 71%) as a colorless oil. For **31a**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36−7.31 (m, 5H), 5.59 (d, *J* = 8.6 Hz, 1H), 5.09 (s, 2H), 3.81−3.71 (m, 3H), 3.51 (d, *J* = 6.4 Hz, 1H), 3.06 (br s, 2H), 1.76−1.67 (m, 1H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.6, 136.3, 128.5 (2C), 128.2, 128.0 (2C), 71.0, 67.0, 64.3, 57.4, 29.8, 19.8, 18.8; IR (film, mixture of regioisomers) ν_{max} 3396, 3065, 2960, 1694, 1519, 1246, 1065 cm^{-1}; HRMS (ESI, mixture of regioisomers) *m*/*z* 268.1571 (MH^+, $C_{14}H_{21}NO_4H^+$ requires 268.1543). For **31b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36−7.31 (m, 5H), 5.20 (d, *J* = 9.8 Hz, 1H), 5.10 (s, 2H), 3.90−3.86 (m, 1H), 3.86−3.82 (m, 1H), 3.49−3.46 (m, 1H), 3.37 (td, *J* = 9.0, 1.9 Hz, 1H), 2.88 (br s, 1H), 2.01 (br s, 1H), 1.91−1.82 (m, 1H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.8, 136.3, 128.5 (2C), 128.2, 128.0 (2C), 77.9, 66.9, 65.2, 52.6, 30.9, 19.2, 19.0.

Benzyl ((1*S,2*S**,3*S**)-2,3-Dihydroxycyclohexyl)carbamate (33a) and Benzyl (2*S**,6*S**)-2,6-Dihydroxycyclohexylcarbamate (33b).** Prepared from **3a** (170.4 mg, 0.557 mmol) and (±)-cyclohex-2-enol (**32**, 30 μL, 28.8 mg, 0.293 mmol) according to the general procedure (45 °C, 21 h). Flash chromatography (SiO_2, 1.5 × 11 cm, 2−5% MeOH/CH_2Cl_2 elution) afforded **33a** (25.4 mg, 0.0957 mmol, 33%) and **33b** (20.7, 0.0780 mmol, 27%) as white solids. For **33a**: ^{1}H NMR (CD_3OD, 500 MHz) δ 7.40−7.24 (m, 5H), 5.07 (s, 2H), 3.93−3.88 (m, 1H), 3.79−3.75 (m, 1H), 3.65−3.61 (m, 1H), 1.82−1.72 (m, 1H), 1.71−1.58 (m, 2H), 1.57−1.40 (m, 3H); ^{13}C NMR (CD_3OD, 125 MHz) δ 156.9, 137.0, 128.0 (2C), 127.54, 127.45 (2C), 72.0, 69.8, 66.0, 49.8, 27.7, 26.8, 18.4; IR (film) ν_{max} 3402, 2938, 1694, 1531, 1455, 1242, 1075, 1047, 1005 cm^{-1}; HRMS (ESI) *m*/*z* 266.1397 (MH^+, $C_{14}H_{19}NO_4H^+$ requires 266.1387); 2D ^{1}H−^{1}H COSY NMR (CD_3OD, 500 MHz) δ 3.93−3.88/3.65−3.61 (m), 3.93−3.88/1.71−1.58 (s), 3.93−3.88/1.57−1.50 (s), 3.79−3.75/3.65−3.61 (s), 3.79−3.75/1.82−1.72 (m), 3.79−3.75/1.49−1.40 (s), 1.82−1.72/1.71−1.58 (m), 1.82−1.72/1.49−1.40 (s), 1.71−1.58/1.57−1.45 (s); 2D ^{1}H−^{13}C HSQC NMR (CD_3OD, 500 MHz) δ 7.40−7.24/128.0, 7.40−7.24/127.54, 7.40−7.24/127.45, 5.07/66.0, 3.93−3.88/49.8, 3.79−3.75/69.8, 3.65−3.61/72.0, 1.82−1.72/27.7, 1.71−1.58/26.8, 1.71−1.58/18.4, 1.57−1.48/26.8, 1.52−1.43/18.4, 1.49−1.40/27.7; NOE NMR (CD_3OD, 500 MHz): irradiation of the signal at 3.93−3.88 enhanced the signals at 3.65−3.61, 1.71−1.58, and 1.57−1.45; irradiation of the signal at 3.79−3.75 enhanced the signals at 1.82−1.72 and 1.52−1.43; irradiation of the signal at 3.65−3.61 enhanced the signal at 3.93−3.88.

For **33b**: ^{1}H NMR (4.5:1 mixture of rotamers, data for major rotamer, CD_3OD, 500 MHz) δ 7.39−7.25 (m, 5H), 5.09 (s, 2H), 4.06−4.00 (m, 1H), 3.67 (td, *J* = 9.9, 4.2 Hz, 1H), 3.40 (dd, *J* = 9.6, 2.2 Hz, 1H), 1.98−1.91 (m, 1H), 1.78−1.64 (m, 2H), 1.57−1.49 (m, 2H), 1.38−1.26 (m, 1H); ^{13}C NMR (CD_3OD, 125 MHz) δ 157.4, 136.9, 128.0 (2C), 127.53, 127.51 (2C), 68.7, 68.1, 66.1, 59.5, 33.2, 31.2, 18.0; IR (film) ν_{max} 3385, 2938, 1697, 1534, 1454, 1252, 1043 cm^{-1}; HRMS (ESI) *m*/*z* 266.1385 (MH^+, $C_{14}H_{19}NO_4H^+$ requires 266.1387); 2D ^{1}H−^{1}H COSY NMR (CD_3OD, 500 MHz) δ 4.06−4.00/3.40 (s), 4.06−4.00/1.78−1.64 (s), 4.06−4.00/1.57−1.49 (s), 3.67/3.40 (s), 3.67/1.98−1.91 (s), 3.67/1.38−1.26 (s), 1.98−1.91/1.78−1.64 (s), 1.98−1.91/1.57−1.49 (m), 1.98−1.91/1.38−1.26 (s), 1.78−1.64/1.57−1.49 (s), 1.78−1.64/1.38−1.26 (w), 1.57−1.49/1.38−1.26 (m); 2D ^{1}H−^{13}C HSQC NMR (CD_3OD, 500 MHz) δ

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7.39−7.25/128.0, 7.39−7.25/127.53, 7.39−7.25/127.51, 5.09/66.1, 4.06−4.00/68.7, 3.67/68.1, 3.40/59.5, 1.98−1.91/33.2, 1.57−1.49/31.2 1.57−1.49/18.0, 1.38−1.26/31.2, 1.38−1.26/18.0; NOE NMR (CD_3OD, 500 MHz): irradiation of the signal at 4.06−4.00 enhanced the signals at 3.40, 1.78−1.64, and 1.57−1.49; irradiation of the signal at 3.67 enhanced the signals at 1.98−1.91 and 1.78−1.64; irradiation of the signal at 3.40 enhanced the signals at 4.06−4.00, 1.57−1.49, and 1.38−1.26.

Benzyl ((3*S,4*R**)-2,4-Dihydroxy-2-methylpentan-3-yl)-carbamate (35a), Benzyl (3*R**,4*R**)-2,4-Dihydroxy-2-methylpentan-3-ylcarbamate (35b), and Benzyl (2*R**,3*S**)-3,4-Dihydroxy-4-methylpentan-2-ylcarbamate (35c).** Prepared from **3a** (170.4 mg, 0.557 mmol) and **34**[34] (37.7 μL, 31.7 mg, 0.317 mmol) according to the general procedure (45 °C, 25 h). Flash chromatography (SiO_2, 2 × 9.5 cm, 1.5−4% MeOH/CH_2Cl_2 elution) afforded **35a** (20.6 mg, 0.0771 mmol, 24%), **35b** (5.4 mg, 0.0202 mmol, 6%), and **35c** (23.9 mg, 0.0894, 28%) as white solids. For **35a**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39−7.29 (m, 5H), 5.57 (d, *J* = 9.4 Hz, 1H), 5.13 (s, 2H), 4.42 (q, *J* = 6.1 Hz, 1H), 3.37 (d, *J* = 9.8 Hz, 1H), 2.66 (br s, 2H), 1.38 (s, 3H), 1.24 (s, 3H), 1.18 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.4, 136.6, 128.5 (2C), 128.1, 127.9 (2C), 74.5, 67.1, 66.8, 60.6, 27.9, 27.7, 20.6; 2D ^{1}H−^{13}C HSQC NMR ($CDCl_3$, 500 MHz) δ 7.39−7.29/128.5, 7.39−7.29/128.1, 7.39−7.29/127.9, 5.13/66.8, 4.42/67.1, 3.37/60.6, 1.24/27.9, 1.34/27.7, 1.18/20.6; IR (film) ν_{max} 3407, 2976, 1699, 1515, 1455, 1226, 1056 cm^{-1}; HRMS (ESI) *m*/*z* 268.1567 (MH^+, $C_{14}H_{21}NO_4H^+$ requires 268.1543).

For **35b**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.41−7.30 (m, 5H), 5.12 (s, 2H), 4.91 (d, *J* = 9.5 Hz, 1H), 4.03−3.97 (m, 1H), 3.61 (dd, *J* = 9.9, 6.9 Hz, 1H), 3.13 (br s, 1H), 2.73 (br s, 1H), 1.33 (s, 3H), 1.27 (d, *J* = 6.2 Hz, 3H), 1.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.9, 136.3, 128.6 (2C), 128.3, 128.1 (2C), 73.6, 69.5, 67.1, 62.6, 28.5, 26.0, 20.8; 2D ^{1}H−^{13}C HSQC NMR ($CDCl_3$, 500 MHz) δ 7.41−7.30/128.6, 7.41−7.30/128.3, 7.41−7.30/128.1, 5.12/69.5, 4.03−3.97/67.1, 1.33/28.5, 1.27/20.8, 1.25/26.0; IR (film) ν_{max} 3416, 2976, 1698, 1544, 1455, 1244, 1027 cm^{-1}; HRMS (ESI) *m*/*z* 268.1569 (MH^+, $C_{14}H_{21}NO_4H^+$ requires 268.1543).

For **35c**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38−7.29 (m, 5H), 5.22 (br s, 1H), 5.13−5.07 (m, 2H), 4.02−3.92 (m, 1H), 3.27−3.24 (m, 1H), 2.81 (br s, 1H), 2.36 (br s, 1H), 1.27−1.22 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.4, 136.4, 128.5 (2C), 128.2, 128.0 (2C), 79.5, 72.9, 66.9, 46.6, 26.8, 24.9, 21.0; 2D ^{1}H−^{13}C HSQC NMR ($CDCl_3$, 500 MHz) δ 7.38−7.29/128.5, 7.38−7.29/128.2, 7.38−7.29/128.0, 5.13−5.07/66.9, 4.02−3.92/46.6, 3.27−3.24/79.5, 1.27/21.0, 1.25/26.8, 1.24/24.9; IR (film) ν_{max} 3421, 2973, 1697, 1512, 1454, 1246, 1100, 1050 cm^{-1}; HRMS (ESI) *m*/*z* 268.1560 (MH^+, $C_{14}H_{21}NO_4H^+$ requires 268.1543).

35a and **35c** were also prepared from **3a** (170.4 mg, 0.557 mmol) and **36** (38 μL, 31.7 mg, 0.316 mmol) according to the general procedure (35 °C, 21 h). Flash chromatography (SiO_2, 1.5 × 11 cm, 1.5−4% MeOH/CH_2Cl_2 elution) afforded **35a** (10.7 mg, 0.0400 mmol, 13%) and **35c** (21.3 mg, 0.0797 mmol, 25%) as white solids.

Ethyl 2-(2-(((Benzyloxy)carbonyl)amino)acetamido)-3-hydroxy-3-methylbutanoate (37). A suspension of **15** (280.4 mg, 0.949 mmol) and Pd/C (10 wt %, 42.6 mg) in MeOH (12 mL) was stirred at rt under H_2 (450 psi) for 23 h. The mixture was filtered through Celite, and the Celite pad was washed with MeOH (125 mL). The filtrate was concentrated in vacuo, and the crude amine was dissolved in THF/DMF (2.5:1, 42.5 mL), cooled to 0 °C under Ar, and treated with *N*-Cbz-glycine (370.0 mg, 1.769 mmol), HOBt (298.9 mg, 1.770 mmol), and EDC·HCl (338.5 mg, 1.766 mmol). The resulting mixture was allowed to warm to rt and stir for 24 h. The reaction was quenched with satd aq $NaHCO_3$ (15 mL), and the precipitate was filtered and washed with EtOAc (15 mL). The aqueous layer was extracted with EtOAc (3 × 15 mL), and the combined organic extracts were washed with brine (15 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. Flash chromatography (SiO_2, 2.3 × 17 cm, 1−7% MeOH/CH_2Cl_2 elution) afforded **37** (286.4 mg, 0.812 mmol, 86%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40−7.30 (m, 5H), 6.86 (d, *J* = 8.2 Hz, 1H), 5.48 (br s, 1H), 5.14 (s, 2H), 4.52 (d, *J* = 8.8 Hz, 1H), 4.30−4.15 (m, 2H), 3.94 (d, *J* = 5.4 Hz, 2H), 2.71 (br s, 1H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.28 (s, 3H), 1.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.2, 169.2, 156.6, 136.1, 128.6 (2C), 128.3, 128.1 (2C), 71.9, 67.3, 61.7, 59.8, 44.5, 26.7, 26.6, 14.1; IR (film) ν_{max} 3342, 2980, 1731, 1531, 1455, 1374, 1261, 1028 cm^{-1}; HRMS (ESI) *m*/*z* 353.1716 (MH^+, $C_{17}H_{24}N_2O_6H^+$ requires 353.1707).

Ethyl 2-(2-(Benzyloxycarbonylamino)acetamido)-3-methylbut-2-enoate (38). A solution of alcohol **37** (20.9 mg, 0.059 mmol) in $CHCl_3$ (stored over K_2CO_3, 250 μL) was treated with a solution of Martin sulfurane in $CHCl_3$ (0.23 M, 500 μL, 0.117 mmol). The mixture was stirred at 50 °C for 1 h, cooled to rt, and concentrated in vacuo. Flash chromatography (SiO_2, 1.5 × 7 cm, 0−1.6% MeOH/CH_2Cl_2 elution) afforded **38** (15.9 mg, 0.048 mmol, 80%) as a colorless oil: ^{1}H NMR (13.4:1 mixture of rotamers, data for major rotamer, $CDCl_3$, 500 MHz) δ 7.38−7.32 (m, 5H), 7.15 (br s, 1H), 5.42 (br s, 1H), 5.15 (s, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.96 (d, *J* = 5.7 Hz, 2H), 2.18 (s, 3H), 1.82 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 167.7, 164.6, 156.7, 146.5, 136.0, 128.6 (2C), 128.3, 128.1 (2C), 120.5, 67.3, 60.9, 44.7, 22.7, 21.4, 14.1; IR (film) ν_{max} 3316, 2923, 2853, 1714, 1514, 1457, 1309, 1237, 1093 cm^{-1}; HRMS (ESI) *m*/*z* 335.1592 (MH^+, $C_{17}H_{22}N_2O_5H^+$ requires 335.1601).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Structure proofs of **33a** and **33b**, stereochemical assignments of **35a−c**, and copies of ^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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