Imino Glycals via Ruthenium-Catalyzed RCM and Isomerization

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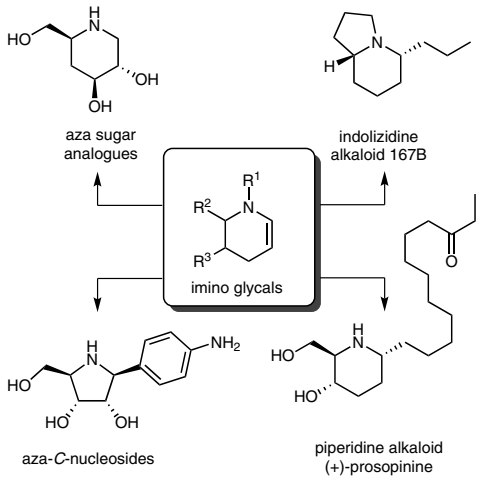
Received: 11.02.2014; Accepted after revision: 06.03.2014

Abstract: *N*-Allyl-*N*-homoallylamines were converted in one step into cyclic enamides via a ruthenium-catalyzed assisted tandem catalytic ring-closing metathesis–isomerization sequence. The sequence relies on the in situ transformation of a metathesis active Ru–carbene into an isomerization active Ru–hydride by addition of hydroxide as a chemical trigger.

Key words: heterocycles, isomerization, metathesis, ruthenium, tandem reaction

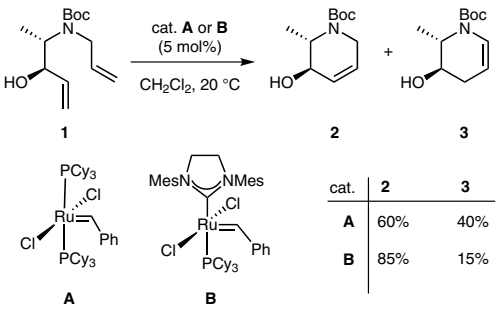
Glycals, 2,3-unsaturated carbohydrate derivatives with an enol ether structure,[1,2] are useful building blocks for the synthesis of glycosides and the assembly of oligosaccharide chains.[3,4] They have also been extensively used to synthesize non-carbohydrate natural products.[5] The aza analogues of glycals, sometimes referred to as imino glycals, have attracted less attention, although they are highly valuable intermediates in the synthesis of target molecules such as indolizidine alkaloids,[6] aza-*C*-nucleosides,[7] piperidine alkaloids,[8–10] and aza sugars (Scheme 1).[11]



Scheme 1 Selected synthetic applications of imino glycals

Methods for the synthesis of imino glycals include the reduction of lactams and subsequent elimination,[12] electrochemical oxidation of piperidines, followed by elimination,[13] addition of nucleophiles to pyridinium salts and subsequent partial reduction,[6] nucleophilic ring opening of aziridines followed by cyclization (formal [3+3]-annulation),[14] and hydroformylation of homoallyl amides.[15] Ring-closing olefin metathesis (RCM), although a well-established and commonly used method for the synthesis of piperidine and pyrrolidine derivatives via RCM of allyl amines or amides,[10,16,17] has scarcely been applied to enamines or enamides. Notable examples have been published by Rutjes and co-workers,[18] who reported the synthesis of five- and six-membered cyclic enamides and by Arisawa et al.,[19,20] who described the synthesis of indoles. There are two possible reasons for the reluctance of the synthetic community to use enamide-RCM reactions. Firstly, the required RCM precursors are less conveniently synthesized than allyl amides, which can be obtained by simple allylation of deprotonated amides. Secondly, precursors with electron-rich double bonds are notoriously difficult metathesis substrates that generally require less convenient reaction conditions, such as elevated temperatures, more expensive catalysts, or high dilution. A similarly reduced reactivity has also been observed for enol ethers[21–23] and was attributed to the formation of less active Fischer-type carbene complexes, resulting from initiation at the electron-rich double bond.[24]

To circumvent these obstacles in the metathesis-based synthesis of cyclic enol ethers, the group of Snapper[25] and one of us[26,27] have independently developed an assisted tandem catalytic RCM–isomerization sequence. Assisted tandem catalytic sequences[28] rely on the use of just one precatalyst (a Ru–carbene in the case of a metathesis reaction) which is converted into a catalyst for a different transformation (e.g., a Ru–hydride to mediate an isomerization). This organometallic transformation is triggered by the addition of an appropriate reagent after completion of the first transformation of the sequence. Apart from one example in Snapper's original contribution,[25] a cyclic enamide has so far only once, and inadvertently, been synthesized through RCM–isomerization (Scheme 2).[29]



cat.	2	3
A	60%	40%
B	85%	15%

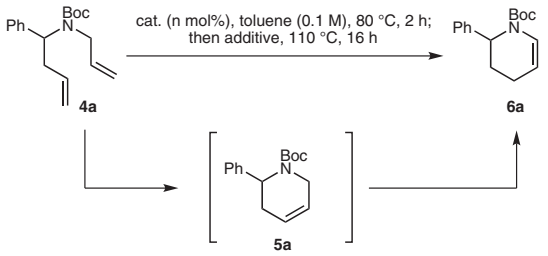
Scheme 2 Inadvertent and uncontrolled RCM–isomerization[29]

SYNTHESIS 2014, 46, 1648–1658
Advanced online publication: 28.03.2014
DOI: 10.1055/s-0033-1338615; Art ID: SS-2014-T0099-OP

Park and co-workers reported that allylamide **1** reacts under metathesis conditions to give a 3:2 mixture of the expected and desired product **2** and the undesired enamide **3** if the first-generation catalyst **A**[30] is used. The ratio is significantly improved with the second-generation catalyst **B**.[31] Undesired competing or subsequent isomerization reactions may be caused by contaminations of the precatalyst with Ru–hydrides (originating from washing the crude precatalyst with alcohols[32–34]) or by uncontrolled catalyst decomposition during the metathesis reaction. For first-generation catalyst **A**, Ru–hydrides have not been identified as products from thermal decomposition reactions.[35] This makes it more likely that the large amount of isomerization product **3** observed by Park and co-workers is either caused by a Ru–hydride impurity present in the precatalyst, or can be attributed to the specific structure of the metathesis substrate. In contrast, second-generation catalyst **B** is known to decompose thermally through a bimolecular pathway to a Ru–hydride.[36] However, it has recently been questioned that this particular decomposition product is catalytically competent in isomerization reactions,[37] which suggests that the formation of isomerized product **3** with precatalyst **B** may also be attributed to either a Ru–hydride impurity or the specific structure of the metathesis substrate. For these reasons we thought that a general, reliable, reproducible, and projectable RCM–isomerization sequence should rely on the use of a suitable additive to trigger the required conversion of the metathesis into an active isomerization catalyst. To identify suitable conditions, we chose the *N*-Boc-allyl amine **4a** as a test substrate (Table 1).

With first-generation catalyst **A**, the RCM step was complete within two hours at 80 °C. The crude reaction mixture contained only the expected RCM product **5a**, whereas the isomerized product **6a** was not observed by ^{1}H NMR spectroscopy. In the next experiment we checked if triggering the isomerization step requires an additive, or if the metathesis catalyst, contrary to previous literature reports for first-generation catalysts,[35] can be thermally converted into an isomerization catalyst. To this end, the reaction temperature was increased to 110 °C for 16 hours after completion of the RCM reaction (Table 1, entry 1). The ^{1}H NMR spectrum of the crude reaction mixture showed that no cyclic enamide **6a** was formed, which strongly underlines the necessity to use a chemical trigger

Table 1 Optimization of RCM–Isomerization Conditions



Entry	Catalyst	Catalyst loading (mol%)	Additive (equiv)	Yield(%) of **6a**
1	**A**	5.0	none	–[a]
2	**A**	5.0	$EtOCH{=}CH_2$ (5)	–[a]
3	**A**	5.0	NaH (0.5)	–[a]
4	**A**	5.0	$NaBH_4$ (0.5)	–[a]
5	**A**	5.0	Et_3SiH (1.0)	69[b]
6	**A**	5.0	PMHS (0.2)	31[c]
7	**A**	5.0	NaOH (1.5), *i*-PrOH (25%)	65
8	**A**	5.0	NaOH (1.5)	51
9	**B**	2.5	none	64[d]
10	**B**	2.5	Et_3SiH (1.0)	57
11	**B**	2.5	PMHS (0.2)	17
12	**B**	2.5	NaOH (1.5), *i*-PrOH (25%)	81
13	**B**	2.5	NaOH (1.5)	84

[a] Not detected, only RCM product **5a** was observed.
[b] RCM product **5a** (17%) was also isolated.
[c] Major amounts of **5a** were detected by NMR spectroscopy, but not isolated.
[d] RCM product **5a** (35%) was also isolated.

for the projected RCM–isomerization sequence. First, we tested three different additives that had previously proven useful in triggering the isomerization step. Ethyl vinyl ether (entry 2) is often used to terminate metathesis reactions, because it reacts with the alkylidene species to an inactive Fischer-type carbene complex. Upon heating, this complex is converted into a Ru–hydride[24] that is capable of isomerizing allyl ethers to enol ethers.[38] Sodium hydride and sodium borohydride (entries 3 and 4) have been discovered by one of us as suitable reagents for converting Ru–alkylidenes into isomerization catalysts with a Ru–hydride structure.[26] Unfortunately, all these additives, which were found to be highly successful for the analogous oxacycles, do not induce any isomerization of **4a**, as indicated by ^{1}H NMR spectroscopy of the crude reaction mixtures. The first successful RCM–isomerization was accomplished using triethylsilane,[27] which had also been previously established as an isomerization inducing additive by us (entry 5). The cyclic enamide **6a** was isolated in 69% yield, along with the RCM product **5a** (17%). The less expensive polymethylhydrosiloxane[39] was significantly less effective and furnished the isomerization product **6a** only in 31% yield, along with major amounts of **5a** (entry 6). Silanes (up to 5 equiv) have previously been used as hydrogen substitutes in tandem RCM–hydrogenation sequences,[40] which prompted us to check the ^{1}H NMR spectra for signals arising from the corresponding piperidine. However, no hydrogenation product could be detected in the crude reaction mixture, which can probably be explained by the lower amount of silane used in our experiments. Another successful reagent combination for inducing isomerization reactions is propan-2-ol as a co-solvent and sodium hydroxide as a base (entry 7).[41] We have previously discovered that under these conditions a Ru–hydride is formed,[27] and a thorough investigation of the pathways leading from first-generation catalyst **A** to a six-coordinate Ru–hydride complex upon treatment with alkoxides has recently been published by Fogg and co-workers.[42] Application of the propan-2-ol/sodium hydroxide combination to the RCM–isomerization of the test substrate **4a** furnished the isomerized product **6a** in a yield comparable to that obtained with triethylsilane (see entry 5 for comparison). Interestingly, with sodium hydroxide as a single additive the isomerization reaction still worked, but the isolated yield of **6a** was significantly lower (entry 8). At this point we thought that no further improvement could be achieved by testing other additives and therefore turned our attention to the precatalyst. The second-generation catalyst **B** has occasionally been reported to promote isomerization reactions, in particular at higher catalyst loadings and elevated temperatures, even in the absence of an additive.[43] For example, Fustero et al. discovered that geminally difluorinated unsaturated ε-caprolactams can be synthesized via RCM. Remarkably, the isomerization is completely suppressed with the first-generation catalyst **A**, but occurs quantitatively with second-generation catalyst **B**.[44] We started this part of the optimization study with a control experiment: the test substrate **4a** was subjected to the standard metathesis conditions (toluene, 80 °C, 2 h) in the presence of 2.5 mol% of **B**. Conversion to the RCM product **5a**, which could be isolated in 87% yield, was quantitative and isomerization was not observed. Next, this experiment was repeated, but upon completion of the metathesis reaction the temperature was raised to 110 °C for 16 hours (entry 9). These conditions led to the isolation of **6a** and **5a** in a ratio of ca. 2:1. While this experiment reveals that either **B**, its methylidene analogue (the propagating species of the metathesis reaction), or a degradation product show some isomerization activity, it also clearly demonstrates that triggering the isomerization exclusively by heating is insufficient for satisfactory rates of conversion. Therefore, **B** was tested in combination with the additives that were previously identified as suitable chemical triggers for the first-generation catalyst. With both silanes, triethylsilane (entry 10) and polymethylhydroxysilane (entry 11) the yield of **6a** was significantly lower than that for thermally induced isomerization. In particular polymethylhydrosiloxane might even be considered as an isomerization-preventing additive for second-generation catalysts, although its role is currently completely unclear. In contrast to the silanes, both sodium hydroxide (entry 13) and sodium hydroxide in combination with propan-2-ol as a co-solvent (entry 12) were highly successful additives, leading to a quantitative isomerization; isolated yields of **6a** were typically between 80% and 85%. For reasons of experimental simplicity, solid sodium hydroxide was used in the following experiments as a single isomerization-inducing additive.

To evaluate the scope of the method, we synthesized a set of precursors **4a**–**g** following a sequence previously reported by Aubé and co-workers.[45] The corresponding aldehydes **7** were condensed with allylamine (**8**), followed by addition of allylmagnesium bromide to give the intermediate *N*-allyl-*N*-homoallylamines **9**, which were eventually protected as Boc-amides **4a**–**g**. Subjecting these precursors to the optimized conditions (from Table 1, entry 13) furnished the cyclic enamides **6a**–**g** in most cases in good yields (Table 2). An exception is the cyclohexylidene-protected derivative **6e**, which was obtained in a moderate yield of 38%. We have no indication that the isomerization is incomplete or less selective in this particular case, suggesting that a considerable amount of product is lost during chromatographic purification.

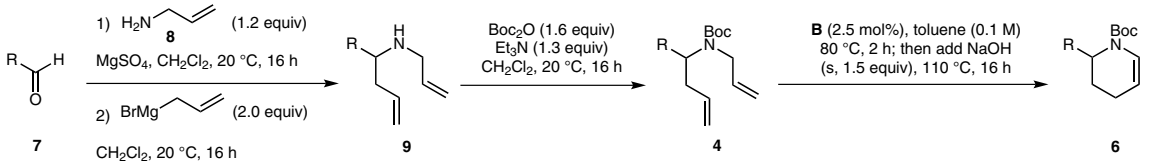
As an illustrative application of this RCM–isomerization sequence we investigated the synthesis of the imino glycals **6h**,**i** (Scheme 3). These imino glycals are fully protected aza analogues of L-rhodinal,[46] the glycal of the 2,3,6-tridesoxy sugar[47] L-rhodinose, and are potentially useful building blocks for the synthesis of azasugars or piperidine alkaloids, as outlined in the introduction.

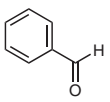
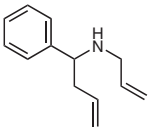
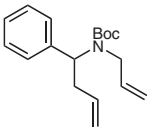
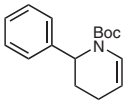
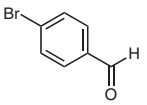
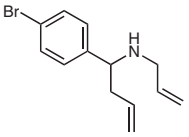
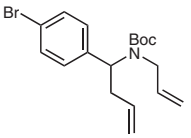
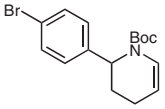
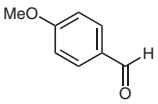
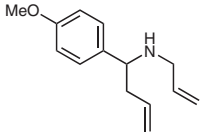
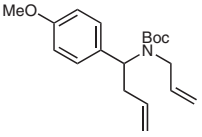
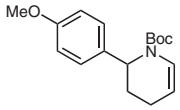
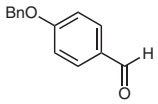
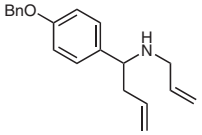
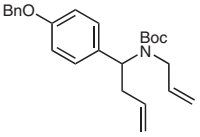
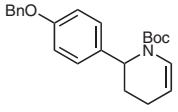
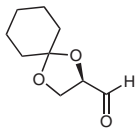
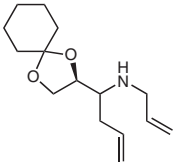
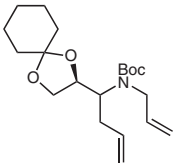
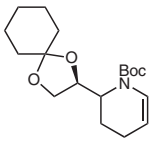
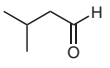
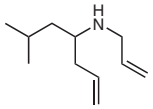
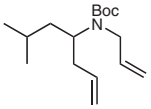
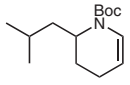
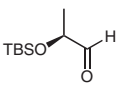
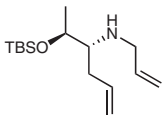
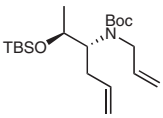
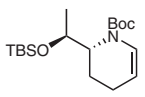
The synthesis starts from L-alanine (**10**), which was converted into the *N*-Boc-protected **11a** and *N*-Cbz-protected L-alanine methyl esters **11b**, respectively.[48] Their reduction with diisobutylaluminum hydride at low temperature furnished the respective aldehydes **12a** and **12b**,[48] which were then treated with vinylmagnesium chloride to give the allyl alcohols **13a** and **13b**. This reaction had previ-

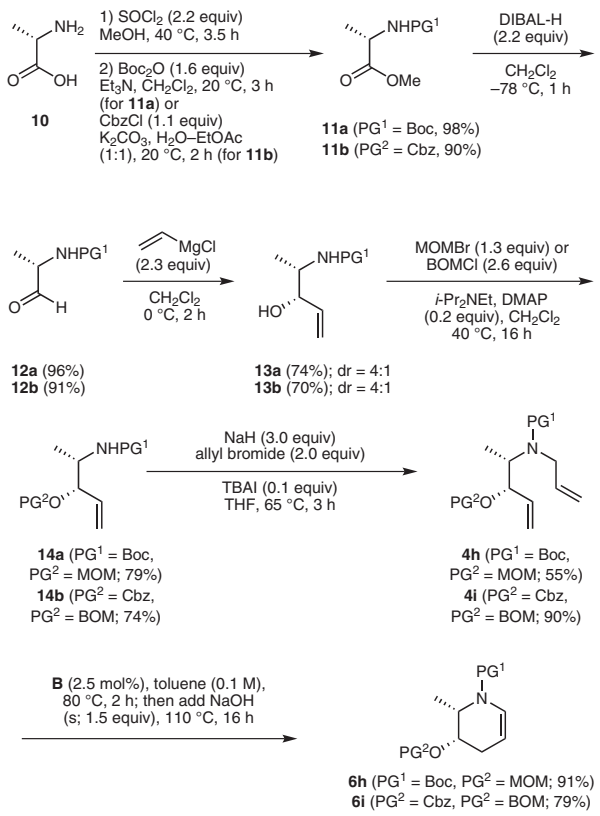
ously been investigated by Jurczak and co-workers,[49] who reported diastereomeric ratios of ca. 3:2 for **12a** and ca. 3:1 for **12b**, using tetrahydrofuran as a solvent at 0 °C. We repeated the Grignard reaction for the *N*-Boc derivative **12a** using Jurczak's conditions and obtained **13a** in an only marginally higher diastereomeric ratio. It had previously been reported that the diastereoselectivity of chelation-controlled addition reactions of organometallics to α-chiral aldehydes[50] can be improved by using less strongly coordinating solvents, such as dichloromethane.[51]

This led indeed to a diastereomeric ratio of 4:1 for both **13a** and **13b**, which could be isolated in comparable yields. In the following step the secondary alcohol was protected as a MOM ether **14a** or as a BOM ether **14b**, to allow for selective N-allylation after deprotonation of the

Table 2 Synthesis of Precursors **4a–g** and Yields of RCM–Isomerization Products **6a–g**



Entry	Aldehyde **7**	Amine **9**	Yield (%)	N-Boc amide **4**	Yield (%)	Cyclic enamide **6**	Yield (%)
1	 **7a**	 **9a**	40	 **4a**	85	 **6a**	84
2	 **7b**	 **9b**	56	 **4b**	69	 **6b**	80
3	 **7c**	 **9c**	90	 **4c**	70	 **6c**	64
4	 **7d**	 **9d**	39	 **4d**	66	 **6d**	83
5	 **7e**	 **9e**	32	 **4e**	92	 **6e**	39
6	 **7f**	 **9f**	10	 **4f**	95	 **6f**	77
7	 **7g**	 **9g**	47	 **4g**	54	 **6g**	83



Scheme 3 Application to the synthesis of 2,3,6-tridesoxy imino glycals **6h**,**i**

amide with sodium hydride. The resulting precursors **4h**,**i** were then subjected to the optimized RCM–isomerization conditions to give the desoxy imino glycals **6h**,**i**.

In summary, we have developed an assisted tandem catalytic RCM–isomerization reaction for the synthesis of cyclic enamides. The sequence requires only one catalyst, which mediates two independent transition-metal-catalyzed transformations in a defined order. The method has been applied to the synthesis of aza analogues of 2,3,6-tridesoxy glycals. Application to the synthesis of target molecules, in particular alkaloids, is currently under investigation in our laboratory.

All experiments were conducted in dry reaction vessels under an atmosphere of dry N_2. Solvents were purified using a commercial solvent purification system. ^{1}H NMR spectra were obtained at 300 MHz or at 500 MHz in $CDCl_3$ with $CHCl_3$ (δ = 7.26) as an internal standard. ^{13}C NMR spectra were recorded at 75 MHz or at 125 MHz in $CDCl_3$ with $CDCl_3$ (δ = 77.0) as an internal standard. The number of coupled protons was analyzed by DEPT or APT experiments and is denoted by a number in parentheses following the chemical shift value. In many cases signals are broad or split up due to hindered rotation of the Boc group or quadrupole broadening. FT-IR spectra were recorded on an ATR-crystal. Mass spectra were obtained using EI or ESI/TOF. N-Protected L-alanine methyl esters **11a**,**b** have been described previously.[48]

N-Allyl *N*-Homoallyl Amines 9; General Procedure

To a solution of the corresponding aldehyde **7** in CH_2Cl_2 (1.5 mL/mmol) was added allylamine (**8**, 1.2 equiv) and $MgSO_4$ (1.00 g per 10.0 mmol of aldehyde **7**). The suspension was stirred for 16 h at r.t., the mixture was filtered, and the filter cake washed several times with *t*-BuOMe. Evaporation of the solvent gave the crude imine, which was dissolved in anhyd CH_2Cl_2. Then, ca. 0.4 M allylmagnesium bromide in Et_2O (2.0 equiv) was added dropwise and the solution was stirred for 16 h at r.t. The reaction was quenched by the addition of sat. aq NH_4Cl soln, the organic layer was separated and the aqueous layer was extracted *t*-BuOMe (3 ×). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated. The residue was purified by column chromatography to yield the amine **9**.

N-Allyl-1-phenylbut-3-en-1-amine (9a)

Following the general procedure, **7a** (3.00 g, 28.3 mmol) was converted into **9a** (2.10 g, 11.2 mmol, 40%); colorless liquid.

IR (ATR): 3075 (w), 2911 (w), 1640 (w), 1454 (m), 933 (s), 914 (s), 699 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.20 (m, 5 H), 5.86 (dddd, *J* = 17.0, 10.2, 6.6, 5.5 Hz, 1 H), 5.73 (dddd, *J* = 16.9, 10.1, 7.5, 6.5 Hz, 1 H), 5.16–5.01 (m, 4 H), 3.70 (t, *J* = 7.2 Hz, 1 H), 3.13 (dddd, *J* = 14.1, 5.4, 1.5, 1.5 Hz, 1 H), 3.02 (dddd, *J* = 14.1, 6.6, 1.2, 1.2 Hz, 1 H), 2.47–2.36 (m, 2 H), 1.62 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.7 (0), 136.9 (1), 135.4 (1), 128.3 (1), 127.2 (1), 127.0 (1), 117.4 (2), 115.6 (2), 61.8 (1), 50.0 (2), 42.9 (2).

MS (EI): *m*/*z* (%) = 146 (40), 91 (21), 71 (22), 57 (38), 41 (100).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{18}N$: 188.1439; found: 188.1432.

N-Allyl-1-(4-bromphenyl)but-3-en-1-amine (9b)

Following the general procedure, **7b** (3.00 g, 16.2 mmol) was converted into **9b** (2.41 g, 9.1 mmol, 56%); colorless liquid.

IR (ATR): 3076 (w), 1640 (w), 1486 (m), 1010 (s), 915 (s), 820 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44 (dm, *J* = 8.4 Hz, 2 H), 7.19 (dm, *J* = 8.4 Hz, 2 H), 5.83 (ddt, *J* = 17.0, 10.2, 5.4 Hz, 1 H), 5.69 (ddt, *J* = 16.9, 10.1, 6.5 Hz, 1 H), 5.14–5.09 (m, 2 H), 5.09–5.02 (m, 2 H), 3.67 (t, *J* = 7.0 Hz, 1 H), 3.10 (dddd, *J* = 14.2, 5.4, 1.5, 1.5 Hz, 1 H), 2.98 (dddd, *J* = 14.1, 6.7, 1.1, 1.1 Hz, 1 H), 2.41–2.28 (m, 2 H), 1.66 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.8 (0), 136.7 (1), 134.9 (1), 131.4 (1), 129.0 (1), 120.6 (0), 117.8 (2), 115.8 (2), 61.2 (1), 49.9 (2), 42.8 (2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{17}NBr$: 266.0544; found: 266.0542.

Anal. Calcd for $C_{13}H_{16}NBr$ (266.18): C, 58.7; H, 6.1; N, 5.3. Found: C, 58.3; H, 6.4; N, 5.8.

N-Allyl-1-(4-methoxyphenyl)but-3-en-1-amine (9c)

Following the general procedure, **7c** (1.00 g, 7.30 mmol) was converted into **9c** (1.44 g, 6.60 mmol, 90%); colorless liquid.

IR (ATR): 3073 (w), 1609 (w), 1510 (s), 1459 (m), 1243 (s), 1034 (s), 914 (s), 830 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.22 (dm, *J* = 8.6 Hz, 2 H), 6.87 (dm, *J* = 8.7 Hz, 2 H), 5.85 (ddt, *J* = 17.0, 10.2, 5.5 Hz, 1 H), 5.71 (ddt, *J* = 17.1, 10.1, 7.1 Hz, 1 H), 5.15–5.09 (m, 1 H), 5.09–4.98 (m, 3 H), 3.80 (s, 3 H), 3.65 (t, *J* = 6.9 Hz, 1 H), 3.11 (dddd, *J* = 14.1, 5.4, 1.6, 1.5 Hz, 1 H), 3.00 (dddd, *J* = 14.1, 6.6, 1.2, 1.2 Hz, 1 H), 2.40 (ddm, *J* = 7.0, 6.5 Hz, 2 H), 1.66 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.7 (0), 137.0 (1), 135.7 (0), 135.5 (1), 128.2 (1), 117.3 (2), 115.6 (2), 113.7 (1), 61.1 (1), 55.2 (3), 49.9 (2), 42.9 (2).

MS (EI): *m*/*z* (%) = 176 (100), 161 (48), 134 (36), 121 (27), 91 (16), 57 (18), 41 (46).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{20}NO$: 218.1545; found: 218.1533.

_N_-Allyl-1-(4-benzyloxyphenyl)but-3-en-1-amine (9d)
Following the general procedure, **7d** (2.50 g, 11.8 mmol) was converted into **9d** (1.35 g, 4.6 mmol, 39%); colorless liquid.

IR (ATR): 3069 (w), 1608 (m), 1509 (s), 1235 (s), 916 (s), 736 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.30 (m, 5 H), 7.26 (d, *J* = 8.7 Hz, 2 H), 6.97 (d, *J* = 8.6 Hz, 2 H), 5.89 (ddt, *J* = 16.8, 10.3, 5.7 Hz, 1 H), 5.74 (ddt, *J* = 17.1, 10.0, 7.1 Hz, 1 H), 5.19–5.02 (m, 4 H), 5.07 (s, 2 H), 3.68 (t, *J* = 6.8 Hz, 1 H), 3.15 (ddm, *J* = 14.1, 5.4 Hz, 1 H), 3.04 (dd, *J* = 14.1, 6.6 Hz, 1 H), 2.43 (dd, *J* = 6.9, 6.7 Hz, 2 H), 1.69 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.0 (0), 137.2 (0), 137.0 (1), 136.0 (0), 135.5 (1), 128.5 (1), 128.3 (1), 127.9 (1), 127.5 (1), 117.3 (2), 115.6 (2), 114.7 (1), 70.1 (2), 61.1 (1), 49.9 (2), 42.9 (2).

MS (EI): *m*/*z* (%) = 253 (17), 254 (100), 161 (6), 91 (62), 41 (6).

HRMS (ESI) *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{24}NO$: 294.1858; found: 294.1832.

Anal. Calcd for $C_{20}H_{23}NO$ (293.40): C, 81.9; H, 7.9; N, 4.8. Found: C, 81.3; H, 7.9; N, 4.6.

_N_-Allyl-1-(1,4-dioxaspiro[4.5]decan-2-yl)but-3-en-1-amine (9e)
Following the general procedure, **7e** (4.00 g, 23.5 mmol) was converted into **9e** (1.90 g, 7.6 mmol, 32%) in a diastereomeric ratio of 3:1; colorless liquid. Analytical data of the major diastereomer were obtained from the mixture.

IR (ATR): 3075 (w), 2933 (s), 1640 (m), 1162 (m), 1100 (s), 913 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.94–5.71 (m, 2 H), 5.16 (ddd, *J* = 17.2, 3.3, 1.6 Hz, 1 H), 5.13–5.02 (m, 3 H), 4.05 (td, *J* = 6.8, 6.7 Hz, 1 H), 3.98 (td, *J* = 6.4, 6.3 Hz, 1 H), 3.68 (dd, *J* = 7.6, 7.1 Hz, 1 H), 3.33 (dddd, *J* = 14.1, 5.9, 1.4, 1.4 Hz, 1 H), 3.28 (dddd, *J* = 14.0, 6.2, 1.4, 1.3 Hz, 1 H), 2.68 (m, 1 H), 2.25 (m, 1 H), 2.07 (m, 1 H), 1.83 (br s, 1 H), 1.69–1.48 (m, 8 H), 1.43–1.31 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.1 (1), 134.9 (1), 117.5 (2), 115.7 (2), 109.4 (0), 77.8 (1), 66.4 (2), 58.7 (1), 50.3 (2), 36.3 (2), 35.2 (2), 34.9 (2), 25.2 (2), 24.0 (2), 23.8 (2).

MS (EI): *m*/*z* (%) = 251 (1, [M]$^+$), 210 (10), 112 (18), 110 (100), 41 (53).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{15}H_{25}NO_2$: 251.1885; found: 251.1897.

_N_-Allyl-6-methylhept-1-en-4-amine (9f)
Following the general procedure, **7f** (3.00 g, 34.8 mmol) was converted into **9f** (0.60 g, 3.6 mmol, 10%); colorless liquid.

IR (ATR): 3076 (m), 2955 (s), 1641 (m), 1463 (s), 994 (s), 912 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.86 (ddt, *J* = 16.9, 10.2, 6.1 Hz, 1 H), 5.76 (ddt, *J* = 16.8, 9.5, 7.1 Hz, 1 H), 5.13 (dtd, *J* = 17.2, 3.3, 1.6 Hz, 1 H), 5.09–5.01 (m, 3 H), 3.21 (ddd, *J* = 6.0, 2.6, 1.3 Hz, 2 H), 2.63 (tt, *J* = 6.5, 6.2 Hz, 1 H), 2.27–2.03 (m, 2 H), 1.66 (sept., *J* = 6.6 Hz, 1 H), 1.40 (br s, 1 H), 1.34–1.13 (m, 2 H), 0.87 (d, *J* = 6.6 Hz, 3 H), 0.87 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.2 (1), 135.5 (1), 117.1 (2), 115.6 (2), 54.0 (1), 49.6 (2), 43.7 (2), 38.5 (2), 24.8 (1), 22.9 (3), 22.8 (3).

MS (EI): *m*/*z* (%) = 163 (7), 126 (59), 105 (32), 91 (100), 77 (23), 55 (40), 41 (82).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{22}N$: 168.1752; found: 168.1768.

(2*S*,3*R*)-*N*-Allyl-2-(*tert*-butyldimethylsilyloxy)hex-5-en-3-amine (9g)
Following the general procedure, **7g** (1.80 g, 9.6 mmol) was converted into **9g** (1.20 g, 4.5 mmol, 47%, single diastereomer); colorless liquid.

$[\alpha]_D^{26}$ –2.8 (*c* 0.17, CH_2Cl_2).

IR (ATR): 3077 (w), 2931 (m), 1641 (w), 1466 (m), 1253 (m), 1094 (m), 913 (m), 832 (s), 773 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.95–5.74 (m, 2 H), 5.16 (dddd, *J* = 17.2, 1.7, 1.6, 1.6 Hz, 1 H), 5.11–4.98 (m, 3 H), 3.83 (qd, *J* = 6.2, 5.3 Hz, 1 H), 3.29 (dddd, *J* = 14.0, 5.9, 1.4, 1.3 Hz, 1 H), 3.20 (dddd, *J* = 14.0, 6.1, 1.4, 1.3 Hz, 1 H), 2.45 (ddd, *J* = 7.1, 7.1, 4.9 Hz, 1 H), 2.34 (m, 1 H), 2.03 (m, 1 H), 1.44 (br s, 1 H), 1.12 (d, *J* = 6.2 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.6 (1), 136.7 (1), 116.4 (2), 115.4 (2), 69.6 (1), 62.5 (1), 50.6 (2), 34.4 (2), 25.9 (3), 19.3 (3), 18.0 (0), –4.2 (3), –4.8 (3).

MS (EI): *m*/*z* (%) = 110 (100), 73 (9), 41 (13).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{32}NOSi$: 270.2253; found: 270.2270.

Anal. Calcd for $C_{15}H_{31}NOSi$ (269.50): C, 66.9; H, 11.6; N, 5.2. Found: C, 66.8; H, 11.7; N, 5.3.

Synthesis of N-Boc-Protected Amines 4; General Procedure
The corresponding secondary amine **9** (1.0 equiv) was dissolved in anhyd and degassed CH_2Cl_2 (6.0 mL/mmol). Et_3N (1.3 equiv) and Boc_2O (1.6 equiv) were added, and the solution was stirred at r.t. for 16 h. The reaction was quenched by the addition of sat. aq NH_4Cl, the organic layer was separated, and the aqueous layer was extracted with *t*-BuOMe. The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated. The residue was purified by chromatography (silica gel) to furnish the corresponding Boc-protected derivatives **4**.

***tert*-Butyl Allyl(1-phenylbut-3-enyl)carbamate (4a)**
Following the general procedure, **9a** (1.00 g, 5.3 mmol) was converted into **4a** (1.30 g, 4.5 mmol, 85%); colorless liquid.

IR (ATR): 3075 (w), 2976 (w), 1687 (s), 1395 (s), 1169 (s), 1141 (s), 913 (s), 699 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.25 (m, 5 H), 5.82 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H), 5.62 (br m, 1 H), 5.36 (br m, 1 H), 5.13 (ddt, *J* = 17.1, 1.7, 1.5 Hz, 1 H), 5.06 (dm, *J* = 10.2 Hz, 1 H), 5.01–4.85 (m, 2 H), 3.82–3.41 (m, 2 H), 2.81–2.65 (m, 2 H), 1.46 (br s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.7 (0), 140.4 (0), 135.8 (1), 135.2 (1), 128.2 (1), 127.9 (1), 127.3 (1), 117.1 (2), 115.6 (2), 79.7 (0), 58.0 (1), 46.5 (2), 35.6 (2), 28.4 (3).

MS (EI): *m*/*z* (%) = 246 (3), 190 (21), 146 (36), 57 (100), 41 (41).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{26}NO_2$: 288.1964; found: 288.1997.

Anal. Calcd for $C_{18}H_{25}NO_2$ (187.28): C, 75.2; H, 8.8; N, 4.9. Found: C, 75.2; H, 8.8; N, 4.8.

***tert*-Butyl Allyl[1-(4-bromophenyl)but-3-enyl]carbamate (4b)**
Following the general procedure, **9b** (2.32 g, 8.7 mmol) was converted into **4b** (2.21 g, 6.0 mmol, 69%); colorless liquid.

IR (ATR): 2975 (w), 1686 (s), 1395 (s), 1169 (s), 1142 (s), 915 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43 (dm, *J* = 8.5 Hz, 2 H), 7.19 (dm, *J* = 8.3 Hz, 2 H), 5.77 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H), 5.58 (br m, 1 H), 5.33 (br m, 1 H), 5.18–4.82 (m, 4 H), 3.83–3.35 (m, 2 H), 2.68 (dm, *J* = 6.8 Hz, 2 H), 1.44 (br s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.6, 139.5, 135.5, 134.7, 131.4, 129.6, 121.2, 117.4, 115.9, 79.9, 57.5, 46.6, 35.6, 28.4.

MS (EI): *m*/*z* (%) = 326 (14), 324 (15), 270 (55), 268 (61), 226 (45), 224 (52), 129 (19), 57 (100).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{25}NO_2Br$: 366.1069; found: 366.1086.

Anal. Calcd for $C_{18}H_{24}NO_2Br$ (366.29): C, 59.0; H, 6.6; N, 3.8. Found: C, 58.7; H, 7.0; N, 4.3.

***tert*-Butyl Allyl[1-(4-methoxyphenyl)but-3-enyl]carbamate (4c)**
Following the general procedure, **9c** (1.33 g, 6.1 mmol) was converted into **4c** (1.37 g, 4.3 mmol, 70%); colorless liquid.

IR (ATR): 2975 (w), 1684 (s), 1513 (s), 1395 (s), 1246 (s), 1171 (s), 1141 (s), 913 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 8.6 Hz, 2 H), 6.85 (dm, *J* = 8.8 Hz, 2 H), 5.79 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1 H), 5.59 (br m, 1 H), 5.33 (br m, 1 H), 5.11 (ddt, *J* = 17.2, 1.7, 1.4 Hz, 1 H), 5.04 (dm, *J* = 10.2 Hz, 1 H), 5.00–4.86 (m, 2 H), 3.79 (s, 3 H), 3.71–3.39 (m, 2 H), 2.68 (dm, *J* = 7.5 Hz, 2 H), 1.46 (br s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8, 155.7, 135.8, 135.3, 132.3, 129.1, 117.0, 115.5, 113.6, 79.6, 57.4, 55.2, 46.1, 35.8, 28.4.

MS (EI): *m*/*z* (%) = 276 (20), 220 (100), 176 (52), 161 (17), 134 (12), 57 (40).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{28}NO_3$: 318.2069; found: 318.2096.

***tert*-Butyl Allyl[1-(4-benzyloxyphenyl)but-3-enyl]carbamate (4d)**
Following the general procedure, **9d** (1.28 g, 4.4 mmol) was converted into **4d** (1.13 g, 2.9 mmol, 66%); colorless liquid.

IR (ATR): 2975 (w), 1684 (s), 1510 (s), 1394 (s), 1233 (s), 1170 (s), 1141 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48–7.29 (m, 5 H), 7.25 (d, *J* = 8.7 Hz, 2 H), 6.93 (dm, *J* = 8.8 Hz, 2 H), 5.81 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 2 H), 5.61 (br m, 1 H), 5.12 (ddt, *J* = 17.2, 1.7, 1.4 Hz, 1 H), 5.08–5.02 (m, 1 H), 5.06 (br s, 2 H), 5.01–4.87 (m, 2 H), 3.76–3.38 (m, 2 H), 2.69 (dm, *J* = 7.4 Hz, 2 H), 1.47 (br s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.0, 155.7, 137.0, 135.9, 135.3, 132.7, 129.1, 128.6, 127.9, 127.4, 117.0, 115.6, 114.6, 79.7, 70.0, 57.6, 46.2, 35.8, 28.5.

MS (EI): *m*/*z* (%) = 352 (18), 296 (92), 252 (26), 91 (100), 57 (77), 41 (20).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{31}NO_3Na$: 416.2202; found: 416.2227.

Anal. Calcd for $C_{25}H_{31}NO_3$ (393.52): C, 76.3; H, 7.9; N, 3.6. Found: C, 76.0; H, 8.3; N, 4.2.

***tert*-Butyl Allyl[1-(1,4-dioxaspiro[4.5]decan-2-yl)but-3-enyl]carbamate (4e)**
Following the general procedure, **9e** (0.62 g, 2.5 mmol) was converted into **4e** (0.80 g, 2.30 mmol, 92%); colorless liquid. Analytical data of the major diastereomer were obtained from the mixture.

IR (ATR): 3078 (w), 2934 (m), 1689 (s), 1365 (m), 1249 (m), 1162 (s), 1100 (s), 909 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.97–5.60 (m, 2 H), 5.07 (ddm, *J* = 18.2, 10.4 Hz, 2 H), 5.07 (ddm, *J* = 17.4, 9.5 Hz, 2 H), 4.23–4.02 (m, 2 H), 3.98 (dd, *J* = 8.1, 6.1 Hz, 1 H), 3.94–3.67 (m, 2 H), 3.58 (dd, *J* = 7.8, 7.8 Hz, 1 H), 2.42 (m, 1 H), 2.17 (m, 1 H), 1.67–1.48 (m, 8 H), 1.43 (br s, 9 H), 1.40–1.31 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.0, 136.5, 134.8, 117.2, 115.2, 109.3, 79.5, 76.2, 66.5, 56.9, 48.2, 36.2, 34.7, 34.2, 28.4, 25.2, 24.0, 23.8.

MS (EI): *m*/*z* (%) = 352 (1, [M + H]$^+$), 252 (17), 210 (43), 154 (100), 110 (49), 57 (58), 41 (24).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{34}NO_4$: 352.2488; found: 352.2482.

Anal. Calcd for $C_{20}H_{33}NO_4$ (351.48): C, 68.3; H, 9.5; N, 4.0. Found: C, 68.5; H, 9.8; N, 4.1.

***tert*-Butyl Allyl(6-methylhept-1-en-4-yl)carbamate (4f)**
Following the general procedure, **9f** (0.46 g, 2.7 mmol) was converted into **4f** (0.70 g, 2.6 mmol, 95%); colorless liquid.

IR (ATR): 3078 (w), 2925 (m), 1691 (s), 1364 (s), 1246 (s), 1157 (s), 914 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.97–5.60 (m, 2 H), 5.19–4.91 (m, 4 H), 4.13 (br m, 1 H), 3.81–3.49 (m, 2 H), 2.32–2.03 (m, 2 H), 1.60–1.49 (m, 2 H), 1.44 (br s, 9 H), 1.15 (m, 1 H), 0.90 (d, *J* = 6.5 Hz, 3 H), 0.86 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.8 (0), 136.5 (1), 136.1 (1), 135.8 (1), 135.6 (1), 116.6 (2), 116.5 (2), 115.6 (2), 115.4 (2), 79.1 (0), 54.4 (1), 53.2 (1), 45.4 (2), 42.3 (2), 41.8 (2), 38.6 (2), 38.4 (2), 28.4 (3), 23.2 (1).

MS (EI): *m*/*z* (%) = 226 (7), 170 (38), 126 (45), 57 (100), 41 (26).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{30}NO_2$: 268.2277; found: 268.2292.

***tert*-Butyl (*R*)-Allyl[(2*S*)-2-(*tert*-butyldimethylsiloxy)hex-5-en-3-yl]carbamate (4g)**
Following the general procedure, **9g** (1.10 g, 4.1 mmol) was converted into **4g** (0.83 g, 2.2 mmol, 54%); colorless liquid.

$[\alpha]_D^{25}$ +4.3 (*c* 0.25, CH_2Cl_2).

IR (ATR): 3078 (w), 2931 (w), 1692 (s), 1365 (s), 1251 (s), 1153 (s), 833 (s), 773 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.98–5.64 (m, 2 H), 5.16–4.96 (m, 4 H), 4.08–3.85 (m, 3 H), 3.77 (m, 1 H), 2.46 (m, 1 H), 2.25 (m, 1 H), 1.43 (br s, 9 H), 1.12 (d, *J* = 6.2 Hz, 3 H), 0.89 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.3, 155.9, 137.0, 135.9, 116.6, 115.1, 79.5, 79.2, 70.9, 70.7, 60.5, 48.3, 34.6, 34.4, 28.5, 27.5, 25.9, 21.0, 17.9, –4.2, –5.0.

MS (EI): *m*/*z* (%) = 256 (34), 210 (31), 154 (100), 110 (73), 73 (31), 57 (90), 41 (30).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{40}NO_3Si$: 370.2777; found: 370.2752.

Anal. Calcd for $C_{20}H_{39}NO_3Si$ (369.61): C, 65.0; H, 10.6; N, 3.8. Found: C, 64.9; H, 10.5; N, 3.8.

***tert*-Butyl 6-Phenyl-5,6-dihydropyridine-1(2*H*)-carboxylate (5a)**
To a solution of **4a** (200 mg, 0.70 mmol) in anhyd and degassed toluene (7 mL) was added 2nd generation Grubbs catalyst **B** (14.9 mg, 2.5 mol%). The mixture was heated to 80 °C for 2 h, cooled to r.t., and evaporated. The residue was chromatographed to furnish **5a** (157 mg, 0.61 mmol, 87%); colorless liquid.

IR (ATR): 3451 (w), 2974 (w), 1690 (s), 1407 (s), 1360 (s), 1165 (s), 1107 (s), 698 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.19 (m, 5 H), 5.88 (ddd, *J* = 10.1, 4.6, 2.2 Hz, 1 H), 5.64 (dm, *J* = 10.0 Hz, 1 H), 5.54 (dm, *J* = 5.3 Hz, 1 H), 4.22 (dm, *J* = 18.3 Hz, 1 H), 3.34 (ddm, *J* = 18.6, 4.8 Hz, 1 H), 2.71 (ddm, *J* = 17.6, 6.3 Hz, 1 H), 2.56 (ddm, *J* = 17.6, 4.5 Hz, 1 H), 1.50 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.1, 141.1, 128.2, 126.9, 126.7, 124.5, 123.2, 79.8, 50.7, 40.3, 28.4.

MS (EI): *m*/*z* = 259 (1, [M]$^+$), 158 (7), 104 (9), 77 (12), 57 (100), 41 (27).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{21}NO_2$: 259.1572; found: 259.1577.

Anal. Calcd for $C_{16}H_{21}NO_2$ (259.34): C, 74.1; H, 8.2; N, 5.4. Found: C, 73.9; H, 8.2; N, 5.5.

Cyclic Enamides 6; General Procedure

To a solution of the appropriate N-Boc-protected precursor **4** (1.0 equiv) in anhyd and degassed toluene (10 mL/mmol) was added 2nd generation Grubbs catalyst **B** (2.5 mol%). The solution was heated to 80 °C until the starting material was fully consumed (TLC, ca. 2 h). Solid NaOH 1.5 equiv) was then added, and the mixture was heated to reflux for 16 h. The mixture was cooled to r.t., H_2O was added, and the aqueous layer was separated and extracted with *t*-BuOMe (3 ×). The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated. The residue was purified by chromatography (silica gel) to furnish the cyclic enamides **6**.

***tert*-Butyl 2-Phenyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6a)**

Following the general procedure, **4a** (200 mg, 0.70 mmol) was converted into **6a** (153 mg, 0.59 mmol, 84%); colorless solid; mp 70–72 °C.

IR (ATR): 2975 (w), 1703 (s), 1653 (m), 1347 (s), 1168 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.13 (m, 5 H), 7.05 (br m, 1 H), 5.33 (br m, 1 H), 4.91 (br m, 1 H), 2.11–1.95 (m, 2 H), 1.88 (m, 1 H), 1.73 (m, 1 H), 1.60–1.13 (9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.8, 152.2, 142.8, 141.7, 128.2, 126.6, 125.4, 125.1, 105.5, 105.2, 80.8, 80.5, 55.1, 53.5, 28.3, 28.0, 27.6, 27.4, 17.2, 17.0.

MS (EI): *m*/*z* (%) = 259 (10, $[M]^+$), 203 (100), 186 (13), 158 (40), 142 (55), 104 (37), 57 (50).

HRMS (EI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{22}NO_2$: 260.1651; found: 260.1655.

Anal. Calcd for $C_{16}H_{21}NO_2$ (259.34): C, 74.1; H, 8.2; N, 5.4. Found: C, 74.0; H, 8.3; N, 5.4.

***tert*-Butyl 2-(4-Bromophenyl)-3,4-dihydropyridine-1(2*H*)-carboxylate (6b)**

Following the general procedure, **4b** (183 mg, 0.50 mmol) was converted into **6b** (135 mg, 0.40 mmol, 80%); colorless solid; mp 62–65 °C.

IR (ATR): 2977 (w), 1698 (s), 1366 (s), 1158 (s), 828 (w) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.41 (dm, *J* = 8.5 Hz, 2 H), 7.03 (dm, *J* = 8.3 Hz, 2 H), 6.94 (br m, 1 H), 5.26 (br m, 1 H), 4.89 (br m, 1 H), 2.10–1.58 (m, 4 H), 1.57–1.21 (m, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 131.4 (1), 127.3 (1), 125.2 (1), 120.4 (0), 105.4 (1), 80.9 (0), 28.2 (3), 27.4 (2), 17.0 (2).

MS (EI): *m*/*z* (%) = 286 (10), 284 (13), 228 (15), 184 (20), 85 (14), 83 (18), 57 (100), 41 (32).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{21}NO_2Br$: 338.0756; found: 338.0781.

Anal. Calcd for $C_{16}H_{20}NO_2Br$ (338.24): C, 56.8; H, 6.0; N, 4.1. Found: C, 56.8; H, 6.2; N, 4.1.

***tert*-Butyl 2-(4-Methoxyphenyl)-3,4-dihydropyridine-1(2*H*)-carboxylate (6c)**

Following the general procedure, **4c** (159 mg, 0.50 mmol) was converted into **6c** (93 mg, 0.32 mmol, 64%); colorless oil.

IR (ATR): 2975 (w), 1698 (s), 1513 (s), 1351 (s), 1247 (s), 1168 (s), 834 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.07 (d, *J* = 8.5 Hz, 2 H), 6.97 (br m, 1 H), 6.82 (d, *J* = 8.8 Hz, 2 H), 5.29 (br m, 1 H), 4.90 (br m, 1 H), 3.77 (s, 3 H), 2.10–1.63 (m, 4 H), 1.62–1.18 (m, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3, 152.7, 134.9, 126.5, 125.3, 113.6, 105.3, 80.6, 55.2, 54.5–53.0 (br), 28.1, 27.6, 17.1.

MS (EI): *m*/*z* (%) = 254 (22), 236 (26), 208 (40), 193 (54), 180 (74), 162 (67), 147 (72), 136 (92), 57 (100), 41 (57).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{24}NO_3$: 290.1756; found: 290.1768.

Anal. calcd for $C_{17}H_{23}NO_3$ (289.37): C, 70.6; H, 8.0; N, 4.8. Found: C, 70.5; H, 8.2; N, 4.9.

***tert*-Butyl 2-(4-Benzyloxyphenyl)-3,4-dihydropyridine-1(2*H*)-carboxylate (6d)**

Following the general procedure, **4d** (197 mg, 0.50 mmol) was converted into **6d** (151 mg, 0.41 mmol, 83%); colorless oil.

IR (ATR): 2975 (w), 1699 (s), 1509 (s), 1349 (s), 1238 (s), 1169 (s), 736 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.29 (m, 5 H), 7.12 (d, *J* = 8.5 Hz, 2 H), 7.03 (br m, 1 H), 6.94 (d, *J* = 8.8 Hz, 2 H), 5.34 (br m, 1 H), 5.05 (s, 2 H), 5.90 (br m, 1 H), 2.16–1.67 (m, 4 H), 1.64–1.20 (m, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.5, 152.6, 137.1, 134.7, 128.4, 127.8, 127.4, 126.5, 125.2, 114.6, 105.2, 80.5, 70.0, 53.8, 28.1, 27.6, 17.1.

MS (EI): *m*/*z* (%) = 365 (3, $[M]^+$), 309 (6), 256 (7), 174 (6), 91 (100), 57 (19), 41 (9).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{27}NO_3Na$: 388.1889; found: 388.1882.

Anal. Calcd for $C_{23}H_{27}NO_3$ (365.47): C, 75.6; H, 7.5; N, 3.8. Found: C, 75.2; H, 7.5; N, 3.9.

***tert*-Butyl 2-(1,4-Dioxaspiro[4.5]decan-2-yl)-3,4-dihydropyridine-1(2*H*)-carboxylate (6e)**

Following the general procedure, **4e** (246 mg, 0.70 mmol) was converted into **6e** (86 mg, 0.27 mmol, 39%); colorless oil.

IR (ATR): 2933 (s), 1700 (s), 1653 (m), 1361 (s), 1164 (s), 1115 (s), 927 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 6.83 (br m, 1 H), 4.83 (br m, 1 H), 4.40–4.15 (m, 2 H), 4.01 (dd, *J* = 8.0, 6.3 Hz, 1 H), 3.67 (br m, 1 H), 2.17–1.88 (m, 2 H), 1.88–1.69 (m, 2 H), 1.65–1.20 (m, 19 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.5, 124.8, 109.7, 104.8, 80.4, 75.2, 66.3, 51.6, 36.0, 35.1, 28.2, 25.2, 23.9, 23.9, 23.2, 18.5.

MS (EI): *m*/*z* (%) = 323 (16, $[M]^+$), 223 (58), 141 (19), 108 (20), 82 (100), 57 (39), 41 (15).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{29}NO_4$: 323.2097; found: 323.2093.

***tert*-Butyl 2-Isobutyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6f)**

Following the general procedure, **4f** (250 mg, 0.94 mmol) was converted into **6f** (174 mg, 0.73 mmol, 77%); colorless oil.

IR (ATR): 2956 (m), 1700 (s), 1651 (s), 1360 (s), 1171 (s), 1121 (s), 767 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 6.71 (d, *J* = 7.9 Hz, 1 H), 4.80 (br m, 1 H), 4.28 (br m, 1 H), 2.12–1.85 (m, 2 H), 1.85–1.51 (m, 3 H), 1.47 (br s, 9 H), 1.31 (m, 2 H), 0.94 (d, *J* = 6.6 Hz, 3 H), 0.89 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.6, 152.1, 124.4, 124.0, 105.1, 104.6, 80.2, 48.8, 47.7, 39.8, 39.3, 28.3, 24.5, 24.4, 24.1, 23.5, 22.0, 17.7, 17.5.

MS (EI): *m*/*z* (%) = 239 (2, $[M]^+$), 183 (5), 127 (12), 82 (34), 57 (100), 41 (42).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{25}NO_2$: 239.1885; found: 239.1875.

Anal. Calcd for $C_{14}H_{25}NO_2$ (239.35): C, 70.3; H, 10.5; N, 5.9. Found: C, 70.0; H, 10.5; N, 5.7.

***tert*-Butyl (*R*)-2-[(*S*)-1-(*tert*-Butyldimethylsiloxy)ethyl]-3,4-dihydropyridine-1(2*H*)-carboxylate (6g)**
Following the general procedure, **4g** (259 mg, 0.70 mmol) was converted into **6g** (198 mg, 0.58 mmol, 83%); colorless solid; mp 68 °C.

$[\alpha]_D^{24}$ –29.1 (*c* 0.78, CH_2Cl_2).

IR (ATR): 2930 (m), 2857 (m), 1703 (s), 1651 (m), 1349 (s), 1251 (s), 1174 (s), 1114 (s), 832 (s), 774 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 6.77 (br m, 1 H), 4.79 (br m, 1 H), 4.12 (br m, 1 H), 3.89 (dq, *J* = 8.4, 6.2 Hz, 1 H), 2.01–1.86 (m, 3 H), 1.78–1.59 (m, 1 H), 1.47 (br s, 9 H), 1.14 (d, *J* = 6.2 Hz, 3 H), 0.86 (s, 9 H), 0.01 (s, 3 H), –0.01 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.5, 125.3, 104.9, 80.2, 66.5, 55.0, 28.4, 25.9, 22.2, 20.6, 18.6, 18.0, –4.7, –4.9.

MS (EI): *m*/*z* (%) = 341 (2, $[M]^+$), 228 (75), 184 (17), 159 (16), 126 (21), 82 (100), 73 (46), 57 (52).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{35}NO_3Si$: 341.2386; found: 341.2393.

Anal. Calcd for $C_{18}H_{35}NO_3Si$ (341.56): C, 63.3; H, 10.3; N, 4.1. Found: C, 63.2; H, 10.3; N, 4.0.

***tert*-Butyl (*S*)-1-Oxopropan-2-ylcarbamate (12a)**
A solution of **11a** (406 mg, 2.00 mmol) in anhyd and degassed CH_2Cl_2 (50 mL) was cooled to –78 °C. 1.01 M DIBAL-H in cyclohexane (6.0 mL, 6.1 mmol) was added dropwise and the solution was stirred at –78 °C until the starting material was fully consumed (TLC, ca. 0.75 h). MeOH (5 mL) was added at –78 °C, the solution was then warmed to r.t., and poured into sat. aq sodium potassium tartrate solution. The aqueous layer was separated and extracted with Et_2O (3 ×), and the combined organic layers were dried ($MgSO_4$), filtered, and evaporated. The residue was purified by column chromatography to give **12a** (331 mg, 1.90 mmol, 96%); colorless solid; mp 84–85 °C.

$[\alpha]_D^{23}$ +14.2 (*c* 0.46, CH_2Cl_2).

IR (ATR): 3331 (m), 2980 (m), 1728 (s), 1681 (s), 1528 (s), 1366 (s), 1249 (s), 1164 (s), 1057 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 9.55 (s, 1 H), 5.10 (br s, 1 H), 4.22 (br s, 1 H), 1.45 (s, 9 H), 1.33 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.7, 155.2, 80.1, 55.5, 28.3, 14.8.

MS (EI): *m*/*z* (%) = 174 (6, $[M + H]^+$), 161 (7), 144 (40), 118 (16), 88 (49), 74 (13), 57 (100), 44 (42).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_8H_{15}NO_3Na$: 196.0950; found: 196.0961.

Anal. Calcd for $C_8H_{15}NO_3$ (173.21): C, 55.5; H, 8.7; N, 8.1. Found: C, 55.9; H, 8.4; N, 7.9.

Benzyl (*S*)-1-Oxopropan-2-ylcarbamate (12b)
A solution of **11b** (12.30 g, 51.7 mmol) in anhyd and degassed CH_2Cl_2 (200 mL) was cooled to –78 °C. 1.01 M DIBAL-H in cyclohexane (103 mL, 114 mmol) was added dropwise and the solution was stirred for 0.75 h (TLC control). The reaction was quenched at –78 °C by addition of MeOH (50 mL), warmed to r.t., and poured into sat. aq sodium potassium tartrate solution. Workup and purification as described for **12a** furnished **12b** (9.70 g, 46.8 mmol, 91%); colorless liquid.

$[\alpha]_D^{23}$ +9.9 (*c* 0.75, CH_2Cl_2).

IR (ATR): 3327 (m), 2940 (w), 1693 (s), 1517 (s), 1454 (m), 1239 (s), 1051 (s), 737 (s), 696 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 9.45 (s, 1 H), 7.42–7.26 (m, 5 H), 5.50 (br s, 1 H), 5.11 (s, 2 H), 4.26 (q, *J* = 7.1 Hz, 1 H), 1.35 (d, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.1, 155.8, 136.1, 128.5, 128.2, 128.0, 67.0, 55.8, 14.7.

MS (EI): *m*/*z* (%) = 208 (4, $[M + H]^+$), 178 (21), 134 (12), 91 (100), 65 (9).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{14}NO_3$: 208.0974; found: 208.0953.

Anal. Calcd for $C_{11}H_{13}NO_3$ (207.23): C, 63.8; H, 6.3; N, 6.8. Found: C, 63.5; H, 6.2; N, 6.7.

***tert*-Butyl (2*S*)-3-Hydroxypent-4-en-2-ylcarbamate (13a)**
A solution of **12a** (240 mg, 1.40 mmol) in anhyd and degassed CH_2Cl_2 (50 mL) was cooled to 0 °C. 1.6 M Vinylmagnesium chloride in THF (2.00 mL, 3.2 mmol) was added and the mixture was stirred at 0 °C for 2 h. The mixture was quenched by the addition of sat. aq NH_4Cl. The aqueous layer was separated and extracted *t*-BuOMe (2 ×), the combined organic extracts were dried ($MgSO_4$), filtered, and evaporated. The residue was purified by column chromatography (silica gel) to give **13a** (207 mg, 1.00 mmol, 74%); 4:1 mixture of diastereomers; colorless liquid.

IR (ATR): 3353 (m), 2977 (m), 1684 (s), 1504 (s), 1366 (s), 1246 (s), 1165 (s), 1050 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 5.86 (ddd, *J* = 17.0, 10.4, 6.1 Hz, 1 H), 5.29 (ddd, *J* = 17.2, 1.3, 1.2 Hz, 1 H), 5.18 (dm, *J* = 10.4 Hz, 1 H), 4.72 (d, *J* = 3.9 Hz, 1 H), 4.00 (dm, *J* = 5.9 Hz, 1 H), 3.68 (qm, *J* = 6.8 Hz, 1 H), 2.71 (br s, 1 H), 1.42 (s, 9 H), 1.15 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 184.5 (0), 138.0 (1), 116.5 (2), 79.5 (0), 76.2 (1), 50.7 (1), 28.4 (3), 17.5 (3).

MS (EI): *m*/*z* (%) = 202 (11, $[M + H]^+$), 146 (39), 144 (47), 128 (17), 88 (33), 57 (100), 44 (49).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{10}H_{20}NO_3$: 202.1443; found: 202.1447.

Anal. Calcd for $C_{10}H_{19}NO_3$ (201.26): C, 59.7; H, 9.5; N, 7.0. Found: C, 59.4; H, 9.3; N, 7.0.

Benzyl (2*S*)-3-Hydroxypent-4-en-2-ylcarbamate (13b)
Following the procedure for the synthesis of **13a**, aldehyde **12b** (900 mg, 4.30 mmol) was converted into **13b** (705 mg, 3.00 mmol, 70%); 4:1 mixture of diastereomers; colorless liquid.

IR (ATR): 3442 (m), 2932 (w), 1694 (s), 1513 (s), 1218 (s), 1051 (s), 750 (s), 696 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.28 (m, 5 H), 5.88 (ddd, *J* = 16.9, 10.4, 6.1 Hz, 1 H), 5.30 (ddd, *J* = 17.2, 1.3, 1.3 Hz, 1 H), 5.20 (ddd, *J* = 10.4, 1.2, 1.2 Hz, 1 H), 5.09 (m, 1 H), 5.10 (s, 2 H), 4.05 (m, 1 H), 3.80 (qm, *J* = 6.8 Hz, 1 H), 2.63 (br s, 1 H), 1.20 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.5, 137.7, 136.4, 128.4, 128.0, 128.0, 116.7, 75.6, 66.7, 51.0, 17.5.

MS (EI): *m*/*z* (%) = 236 (5, $[M + H]^+$), 178 (15), 134 (17), 91 (100), 65 (10).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{18}NO_3$: 236.1287; found: 236.1272.

***tert*-Butyl (2*S*)-3-(Methoxymethoxy)pent-4-en-2-ylcarbamate (14a)**
To a solution of **13a** (201 mg, 1.00 mmol) in anhyd and degassed CH_2Cl_2 (10 mL) was added *i*-Pr_2NEt (0.26 mL, 1.50 mmol), MOMBr (technical grade, 90%, 0.12 mL, 1.30 mmol), and DMAP (24 mg, 0.20 mmol). The mixture was stirred for 16 h at 40 °C, cooled to r.t., and hydrolyzed by addition of a sat. aq NH_4Cl. The aqueous layer was separated and repeatedly extracted with *t*-BuOMe, and the combined organic extracts were dried ($MgSO_4$), filtered, and evaporated. Purification by column chromatography

(silica gel) furnished **14a** (192 mg, 0.80 mmol, 79%); colorless liquid.

IR (ATR): 2976 (m), 1707 (s), 1158 (s), 1028 (s), 920 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 5.70 (ddd, *J* = 16.9, 12.0, 7.5 Hz, 1 H), 5.32–5.19 (m, 2 H), 4.66 (d, *J* = 6.7 Hz, 1 H), 4.52 (d, *J* = 6.7 Hz, 1 H), 3.94 (qd, *J* = 7.5, 3.7 Hz, 1 H), 3.78 (m, 1 H), 3.36 (s, 3 H), 1.41 (s, 9 H), 1.15 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.4 (0), 134.9 (1), 118.9 (2), 94.0 (2), 79.4 (1), 55.6 (3), 49.5 (1), 28.3 (3), 17.6 (3).

MS (EI): *m*/*z* (%) = 202 (50), 158 (19), 88 (53), 57 (100), 44 (74).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{24}NO_4$: 246.1705; found: 246.1686.

Anal. Calcd for $C_{12}H_{23}NO_4$ (245.32): C, 58.8; H, 9.5; N, 5.7. Found: C, 58.7; H, 9.4; N, 5.7.

Benzyl (2*S*)-3-(Benzyloxymethoxy)pent-4-en-2-ylcarbamate (14b)

Following the procedure for the synthesis of **14a**, the alcohol **13b** (650 mg, 2.80 mmol) and BOMCl (technical grade 90%, 1.0 mL, 7.20 mmol) were converted into **14b** (725 mg, 2.04 mmol, 74%); colorless liquid.

IR (ATR): 3337 (w), 2940 (w), 1706 (s), 1498 (s), 1228 (s), 1025 (s), 737 (s), 697 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.27 (m, 10 H), 5.75 (ddd, *J* = 17.6, 9.9, 7.7 Hz, 1 H), 5.40–5.25 (m, 2 H), 5.12 (s, 2 H), 4.97 (m, 1 H), 4.79 (d, *J* = 6.7 Hz, 1 H), 4.72 (d, *J* = 6.8 Hz, 1 H), 4.71 (dm, *J* = 11.5 Hz, 1 H), 4.53 (dd, *J* = 11.8, 1.5 Hz, 1 H), 4.07 (dd, *J* = 7.1, 2.9 Hz, 1 H), 3.93 (m, 1 H), 1.24 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.9, 137.6, 136.6, 134.7, 128.5, 128.4, 128.0, 127.8, 127.7, 119.4, 91.9, 79.5, 69.7, 66.6, 50.2, 17.9.

MS (EI): *m*/*z* (%) = 281 (3), 127 (12), 99 (25), 91 (100), 85 (52), 71 (82), 57 (99), 43 (47).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{26}NO_4$: 356.1862; found: 356.1835.

***tert*-Butyl Allyl[(2*S*,3*S*)-3-(methoxymethoxy)pent-4-en-2-yl]carbamate (4h)**

To a solution of **14a** (1.95 g, 8.0 mmol) in anhyd and degassed THF (100 mL) was added NaH (dispersion in mineral oil 60 wt%, 0.95 mg, 23.9 mmol), allyl bromide (1.37 mL, 15.9 mmol), and TBAI (294 mg, 0.80 mmol). The mixture was heated to reflux and stirred for 3 h and then cooled to r.t. The mixture was carefully poured into H_2O, and the aqueous layer was separated and repeatedly extracted with *t*-BuOMe. The combined organic layers were dried ($MgSO_4$), filtered, and evaporated. The residue was purified by chromatography (silica gel) to give **4h** (1.24 g, 4.4 mmol, 55%); single diastereomer; colorless liquid.

$[\alpha]_D^{24}$ +44.1 (*c* 0.33, CH_2Cl_2).

IR (ATR): 2977 (m), 1690 (s), 1365 (s), 1155 (s), 1029 (s), 919 (s), 773 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 5.80 (m, 1 H), 5.62 (m, 1 H), 5.30–5.19 (m, 2 H), 5.18–4.98 (m, 2 H), 4.63 (d, *J* = 6.8 Hz, 1 H), 4.48 (m, 1 H), 4.25–3.89 (m, 2 H), 3.89–3.62 (m, 2 H), 3.33 (s, 3 H), 1.44 (br s, 9 H), 1.14 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.5, 136.2, 135.9, 135.7, 119.0, 115.5, 115.1, 93.9, 79.4, 79.2, 55.6, 55.5, 54.5, 48.7, 47.4, 28.4, 16.1, 15.5.

MS (EI): *m*/*z* (%) = 267 (19), 184 (30), 128 (82), 98 (73), 84 (100), 71 (73), 56 (94), 41 (45).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{28}NO_4$: 286.2018; found: 286.1998.

Anal. Calcd for $C_{15}H_{27}NO_4$ (285.38): C, 63.1; H, 9.5; N, 4.9. Found: C, 63.2; H, 9.5; N, 5.0.

Benzyl Allyl[(2*S*,3*S*)-3-(benzyloxymethoxy)pent-4-en-2-yl]carbamate (4i)

Following the procedure for the synthesis of **4h**, the Cbz-protected amine **14b** (178 mg, 0.50 mmol) was converted into **4i** (176 mg, 0.45 mmol, 90%); colorless liquid.

IR (ATR): 2942 (w), 1695 (s), 1408 (m), 1242 (m), 1025 (s), 734 (s), 696 cm^{-1} (s).

^1H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.27 (m, 10 H), 5.86 (m, 1 H), 5.64 (m, 1 H), 5.37–5.03 (m, 6 H), 4.80–4.57 (m, 3 H), 4.45 (d, *J* = 11.9 Hz, 1 H), 4.30–4.02 (m, 2 H), 4.02–3.74 (m, 2 H), 1.22 (d, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.1, 137.8, 136.8, 135.6, 135.3, 128.4, 127.8, 127.7, 127.6, 119.6, 115.8, 91.7, 79.3, 69.4, 66.9, 55.7, 47.6, 15.5.

MS (EI): *m*/*z* (%) = 396 (4, $[M + H]^+$), 288 (6), 218 (30), 174 (28), 91 (100).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{29}NO_4Na$: 418.1994; found: 418.2007.

***tert*-Butyl (2*S*,3*S*)-3-(Methoxymethoxy)-2-methyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6h)**

Following the general procedure for the RCM–isomerization sequence, **4h** (483 mg, 1.69 mmol) was converted into **6h** (395 mg, 1.54 mmol, 91%); colorless liquid.

$[\alpha]_D^{23}$ +13.3 (*c* 0.42, CH_2Cl_2).

IR (ATR): 2929 (m), 1702 (s), 1345 (s), 1270 (s), 1102 (s), 1045 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 6.63 (d, *J* = 7.6 Hz, 1 H), 4.74 (m, 1 H), 4.68 (s, 2 H), 4.35 (m, 1 H), 3.84 (qd, *J* = 5.7, 4.9 Hz, 1 H), 3.37 (s, 3 H), 2.26 (ddd, *J* = 16.9, 5.9, 5.7 Hz, 1 H), 2.08 (dddd, *J* = 16.8, 10.6, 2.5, 2.4 Hz, 1 H), 1.47 (s, 9 H), 1.04 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.2, 151.6, 123.9, 123.6, 101.4, 95.4, 95.3, 80.7, 80.7, 72.4, 72.1, 55.4, 49.7, 48.3, 28.3, 25.1, 10.7.

MS (EI): *m*/*z* (%) = 257 (33, $[M]^+$), 201 (16), 141 (62), 124 (43), 112 (39), 97 (100), 82 (70), 57 (81), 45 (38).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{23}NO_4$: 257.1622; found: 257.1633.

Benzyl (2*S*,3*S*)-3-(Benzyloxymethoxy)-2-methyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6i)

Following the general procedure for the RCM–isomerization sequence, **4i** (277 mg, 0.70 mmol) was converted into **6i** (203 mg, 0.56 mmol, 79%); colorless liquid.

$[\alpha]_D^{25}$ –2.1 (*c* 0.30, CH_2Cl_2).

IR (ATR): 2890 (w), 1702 (s), 1654 (m), 1408 (s), 1337 (s), 1260 (s), 1038 (s), 732 (s), 696 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.27 (m, 10 H), 6.72 (d, *J* = 8.0 Hz, 1 H), 5.31–5.11 (m, 2 H), 4.83 (s, 2 H), 4.75 (ddd, *J* = 7.7, 5.7, 5.3 Hz, 1 H), 4.64 (s, 2 H), 4.51 (dt, *J* = 6.0, 5.6 Hz, 1 H), 3.96 (m, 1 H), 2.31 (ddd, *J* = 17.1, 5.6, 5.4 Hz, 1 H), 2.13 (dddd, *J* = 17.1, 10.6, 2.5, 2.4 Hz, 1 H), 1.12 (d, *J* = 6.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.6, 137.6, 136.2, 128.5, 128.4, 128.1, 128.0, 127.8, 123.6, 123.2, 102.8, 93.7, 93.2, 72.4, 71.8, 69.8, 69.7, 67.6, 67.5, 49.6, 49.0, 25.0, 24.8, 11.3, 10.7.

MS (EI): *m*/*z* (%) = 396 (2, $[M]^+$), 232 (8), 170 (6), 91 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{22}H_{25}NO_4$: 367.1784; found: 367.1773.

Acknowledgment

Generous financial support of this work by the Deutsche Forschungsgemeinschaft (DFG grant Schm1095/6-2) is gratefully acknowledged. We thank Evonik oxeno for donations of solvents.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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