ChemPubSoc Europe

DOI: 10.1002/ejoc.201901520

EurJOC European Journal of Organic Chemistry

Full Paper

Tetrahydropyridine Synthesis

Diastereoselective Synthesis of 2,6-Disubstituted-1,2,3,6-Tetrahydropyridines through a Palladium-Catalyzed Intramolecular Allylic Amination

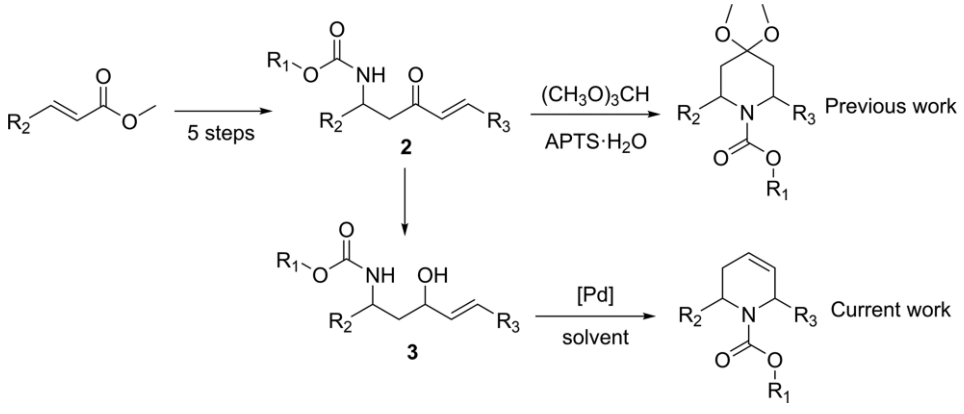
Alexia Visseq,[a] Thibaut Boibessot,[a] Lionel Nauton,[a] Vincent Théry,[a] Fabrice Anizon,*[a] and Isabelle Abrunhosa-Thomas*[a]

Abstract: An efficient synthesis of 2,6-disubstituted-1,2,3,6-tetrahydropyridines is reported, featuring a highly diastereoselective palladium-catalyzed intramolecular allylic amination from non-activated alcohols. This method allowed a straightforward access to 2,6-*trans*-1,2,3,6-tetrahydropyridines with de up to 100 % under mild conditions, in moderate to good yields.

Introduction

1,2,3,6-Tetrahydropyridines (TP) are important heterocycles found in numerous alkaloids and pharmaceutical compounds[1] that also could be used as intermediates in polysubstituted piperidines or imino sugars synthesis, with possible double bond reduction or functionalization.[2] Consequently, many strategies for TP synthesis have been proposed.[1b,1c,3] Among these approaches, the synthesis of 2,6-disubstituted-TP/piperidines have attracted much attention because these heterocycles are found in many interesting products with a wide range of pharmacological activities.[1a,1b,3a] Various methods have been described for the preparation of *cis*- or *trans*-2,6-disubstituted-TP[4] including cationic cyclization,[3a] nucleophilic substitution,[5] ring-closing metathesis,[6] aza-Diels–Alder[1b] and Mitsunobu[1c] reactions, allyl nitrone cyclization,[7] aza-[2,3]-Wittig rearragements of vinylaziridines[8] or diastereoselective C–H functionalization.[9] However, methods leading to *trans*-2,6-disubstituted-TP/piperidines are less reported, because the *trans* relative configuration is thermodynamically disfavored.[10] For example, *trans*-2,6-disubstituted-TP/piperidines can be obtained by C–N bond formation and ring closure, the TP substituents at 2- and 6-positions being already present in the structure. These methods employed allylic alcohols or their activated counterparts as precursors, and used Brønsted acid conditions, S_N2 or Mitsunobu reactions affording nitrogen attack, to form the unsaturated 6-membered ring.

Knowing the importance of stereocenter configuration for biological activities, the development of new stereoselective syntheses of *trans*-2,6-disubstituted-TP/piperidines remains an important challenge. During our previous studies, we developed a methodology to prepare stereoselectively either 2,6-*cis* or 2,6-*trans*-disubstituted-piperidines via a Michael-type cyclization.[11] This methodology used β'-carbamate-α,β-unsaturated ketone[3a] as a key precursor. We further envisioned that 2,6-disubstituted-TP could be formed via a palladium-catalyzed



Scheme 1. Previous work toward the synthesis of 2,6-disubstituted-piperidines. Current methodology toward the preparation of 2,6-disubstituted-TP.

[a] *Université Clermont Auvergne,CNRS, SIGMA Clermont, Institut de Chimie de Clermont-Ferrand, 63000 Clermont-Ferrand, France*
E-mail: fabrice.anizon@uca.fr (FA)
isabelle.thomas@sigma-clermont.fr (IAT)
https://iccf.uca.fr/

Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under https://doi.org/10.1002/ejoc.201901520.

intramolecular allylic amination. Key precursor allylic alcohols would be prepared by reduction of the corresponding ketones, as already described in previous work (Scheme 1).

Results and Discussion

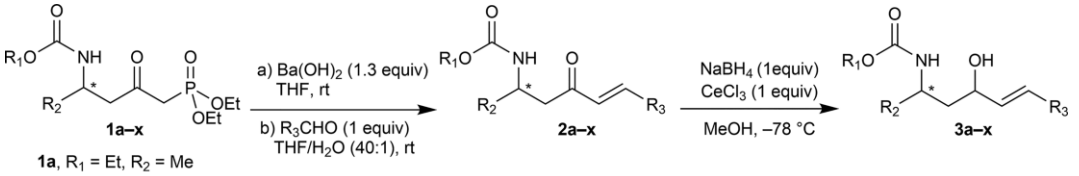
We have previously shown that β′-carbamate-α,β-unsaturated ketone **2**, starting material for this study, could be easily obtained from the corresponding methyl ester in 5 steps with an overall yield of about 30 % (Scheme 1).[11,12] This methodology allows the preparation of various precursors needed for the current work. Ketones **2a–x** were prepared in good to excellent yields via Horner–Wadsworth-Emmons reaction between phosphonates **1a**–**g** and various aldehydes (Table 1). The double bond configuration was (*E*) in all cases, except for **2x** (entry 24) obtained in a 1:1 ratio of both stereoisomers. Starting material **3a**–**x** for our current study were obtained in excellent yields from **2a**–**x** via a reduction step according to Luche procedure,[13] in MeOH at –78 °C by using 1 equivalent of both $NaBH_4$ and $CeCl_3$. The major diastereoisomer obtained was *syn* with a ratio up to 8:2, both *anti* and *syn* diastereoisomers being separable by column chromatography.

According to the literature reporting catalyzed allylic amination to form the six-membered ring of piperidines,[3c,14] dihydroquinolines[15] or substituted amines,[16] the alcohol function can be free or activated as a carbonate or an acetate. In order to optimize the reaction conditions for our TP synthesis, we decided to start from either alcohol **3a** or methyl carbonate **4a** (Table 2). Carbonates **4a-*syn*** and **4a-*anti*** were prepared in the presence of methyl chloroformate and pyridine in dichloromethane in 80 % and 67 % yields, respectively.

With precursor **4a-*syn*** in hand, the cyclization reaction was investigated. First, and based on Unenishi transformation,[3c] 30 mol-% of $PdCl_2(CH_3CN)_2$ was used to validate the feasibility of the cyclization to **5a** and determine the best solvent (Table 2, entries 1–4). At room temperature, DCE gave faster total conversion in favor of a diastereoisomer with a 82:18 ratio. More polar solvent such as THF or CH_3CN were also efficient with better diastereoisomeric ratio but with much slower reaction. Other palladium sources were tested in DCE, but did not yield the desired product (entries 5–8).

Then, we have pursued our investigation using $PdCl_2(CH_3CN)_2$ to see how the diastereoisomeric ratio could be improved in DCE. First, three tests using 30 mol-% of

Table 1. Preparation of allylic alcohols.

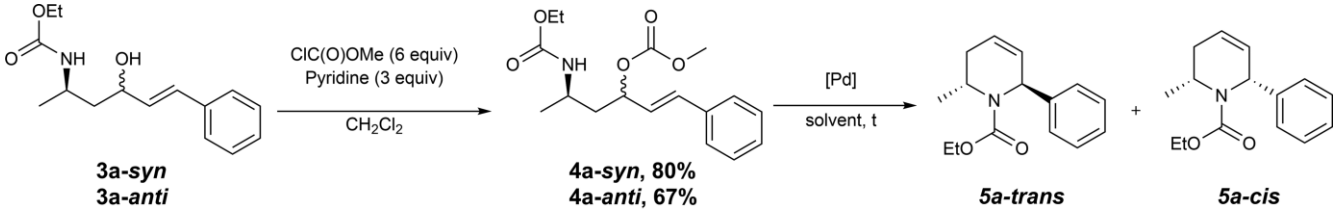


1a, R_1 = Et, R_2 = Me
1b, R_1 = Et, R_2 = Pr
1c, R_1 = Et, R_2 = Ph
1d, R_1 = Bn, R_2 = Me
1e, R_1 = Bn, R_2 = Pr
1f, R_1 = Bn, R_2 = Ph
1g, R_1 = *t*-Bu, R_2 = Me

Entry	**1** (*R* or *S*)	R_3	Yield **2** [%][a]	Yield **3** [%][a] (*syn*/*anti*)[b]
1	**1a** (*R*)	Ph	**2a** (95)	**3a** (85) (90:10)
2	**1d** (*R*)	Ph	**2b** (96)	**3b** (94) (83:17)
3	**1g** (*R*)	Ph	**2c** (90)	**3c** (68) (75:25)
4	**1b** (*R*)	Ph	**2d** (91)	**3d** (79) (88:12)
5	**1e** (*R*)	Ph	**2e** (91)	**3e** (87) (87:13)
6	**1f** (*S*)	Ph	**2f** (81)	**3f** (93) (81:19)
7	**1a** (*S*)	2-naphthalenyl	**2g** (71)	**3g** (99) (89:11)
8	**1c** (*S*)	4-bromophenyl	**2h** (97)	**3h** (94) (85:15)
9	**1a** (*R*)	2-bromophenyl	**2i** (91)	**3i** (72) (80:20)
10	**1a** (*R*)	3-bromophenyl	**2j** (71)	**3j** (90) (85:15)
11	**1a** (*R*)	4-bromophenyl	**2k** (89)	**3k** (93) (85:15)
12	**1a** (*S*)	4-fluorophenyl	**2l** (76)	**3l** (92) (87:13)
13	**1a** (*R*)	3-pyridinyl	**2m** (87)	**3m** (78) (80:20)
14	**1a** (*R*)	2-nitrophenyl	**2n** (89)	**3n** (99) (80:20)
15	**1a** (*S*)	3-nitrophenyl	**2o** (73)	**3o** (quant) (90:10)
16	**1a** (*R*)	4-nitrophenyl	**2p** (91)	**3p** (93) (82:18)
17	**1a** (*S*)	4-methoxy-3-nitrophenyl	**2q** (70)	**3q** (98) (90:10)
18	**1a** (*S*)	2-fluoro-5-nitrophenyl	**2r** (65)	**3r** (98) (85:15)
19	**1a** (*R*)	4-methoxyphenyl	**2s** (79)	**3s** (90) (87:13)
20	**1a** (*S*)	3-phenoxyphenyl	**2t** (81)	**3t** (83) (84:16)
21	**1a** (*S*)	4-acetamidophenyl	**2u** (60)	**3u** (89) (88:12)
22	**1a** (*R*)	$C_{11}H_{23}$	**2v** (90)	**3v** (93) (84:16)
23	**1f** (*S*)	Me	**2w** (96)	**3w** (80) (69:31)
24	**1d** (*R*)	COOEt	**2x** (28)[c]	**3x** (69) (100:0)

[a] Isolated yield. [b] Calculated from ^1H NMR. [c] Yield of the (*E*) isomer.

Table 2. Reaction condition optimization.



3a-*syn*
3a-*anti*

4a-*syn*, 80%
4a-*anti*, 67%

5a-trans

5a-cis

Entry	solvent	compd	cat [mol-%]	*Time [h]*	*t* [°C]	Conv. **5a** [%][a] (*trans*/*cis*)
1	DCE	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (30)	0.3	r.t.	100 (82:18)
2	THF	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (30)	48	r.t.	100 (94:6)
3	CH_3CN	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (30)	96	r.t.	90 (95:5)
4	DCM	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (30)	1.25	r.t.	100 (47:53)
5	DCE	**4a-*syn***	$Pd(OAc)_2$ (30)	48	r.t.	SM
6	DCE	**4a-*syn***	$Pd_2(dba)_3{\cdot}CHCl_3$ (30)	48	r.t.	SM
7	DCE	**4a-*syn***	$[PdCl(allyl)]_2$ (30)	48	r.t.	SM
8	DCE	**4a-*syn***	$Pd(OAc)_2$ (30)	48	r.t.	SM
9	DCE	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (30)	1.5	r.t.	100 (46:54)
10	DCE	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (30)	48	r.t.	100 (29:71)
11	DCE	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (30)	16	0	100 (94:6)
12	DCE	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (30)	0.02	80	100 (28:72)
13	DCE	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (20)	0.58	r.t.	100 (77:23)
14	DCE	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (10)	1.25	r.t.	100 (90:10)
15	DCE	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (5)	6	r.t.	100 (93:7)
16	DCE	**4a-*syn***	$PdCl_2(CH_3CN)_2$ (2)	72	r.t.	54 (98:2)
17	DCE	**4a-*anti***	$PdCl_2(CH_3CN)_2$ (5)	7	r.t.	100 (97:3)
18	DCE	**3a-*syn***	$PdCl_2(CH_3CN)_2$ (5)	4.5	r.t.	100 (97:3)
19	DCE	**3a-*syn***	$PdCl_2(CH_3CN)_2$ (5)	3.3	40	100 (95:5)
20	DCE	**3a-*anti***	$PdCl_2(CH_3CN)_2$ (5)	6	r.t.	100 (95:5)
21	DCE	**3a-*anti***	$PdCl_2(CH_3CN)_2$ (5)	3	40	97 (95:5)

[a] Conversion and ratio were calculated from ^1H NMR.

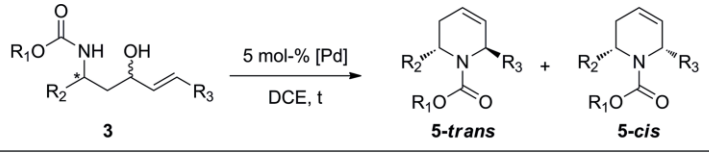
$PdCl_2(CH_3CN)_2$ were carried out at room temperature to establish if the ratio varied over the time or if it remained stable (Table 2, entries 1, 9–12). We observed an epimerization of **5a** for a prolonged reaction time. Actually, reaction mixture tended to an equilibrium between kinetic and thermodynamic 2,6-disubstituted-TP diastereoisomers. We can suppose that thermodynamically favored stereoisomer would be **5a-*cis***. Therefore, after 20 min at room temperature or 16 h at 0 °C (Table 2, entries 1 and 11) the major product was certainly **5a-*trans*** and, conversely, after 48 h at room temperature or less than 5 min at 80 °C (entries 10 and 12), the major product was **5a-*cis***. After separation by chromatography of the two diastereoisomers, a NOESY analysis was performed on **5a-*trans*** and **5a-*cis***, and validated our hypothesis on the relative configuration of both 2,6-TP stereoisomers. In order to reduce epimerization and access to higher proportion of the *trans*-TP in a minimum of time with a total conversion, we tested different amounts of palladium catalyst (Table 2, entries 14–16). For a total conversion, the best conditions were the use of 5 mol-% of $PdCl_2(CH_3CN)_2$, for 6 h at room temperature, leading to **5a** with a 93:7 *trans*/*cis* ratio. The next step was to determine if this ratio could be influenced by the stereochemistry of carbonate **4a**. Surprisingly, cyclization of **4a-*anti*** resulted in the same major diastereoisomer **5a-*trans*** (entry 17) in the same proportion after 7 h, with a total conversion.

Because the derivatization step of **3** into the corresponding carbonate **4** generated waste and lowered atom economy, we also investigated to carry out the cyclization directly on the alcohol derivatives **3a-*anti*** and **3a-*syn***, using 5 mol-% of palladium (entries 18–21). The transformation was even more efficient with total conversion after 4.5 h at room temperature. Interestingly, starting alcohols **3a-*syn*** and **3a-*anti*** led to the same major diastereoisomer, with a 97:3 *trans*/*cis* ratio. Moreover, increasing the temperature to 40 °C allowed to reduce the reaction time without affecting diastereoisomeric ratio. To study the scope of this methodology, the preferred conditions were fixed at 5 mol-% of palladium, in DCE.

According to Table 3, for the defined conditions, the selectivity observed for the cyclization reaction was in favor of the *trans*-isomer of **5**. However, the rate of the reaction was markedly dependent on some factors, mainly, steric hindrance (R_1, R_2, R_3), electronic effects and nature of R_3. On the one hand, when R_2 and R_3 were fixed (R_2 = Me, R_3 = Ph), a strong steric hindrance of the carbamate imposed a longer time to complete the reaction, even with a larger catalytic load, and reflux temperature to obtain the desired product (see **5a–c-*trans***). Similarly, when R_2 was a propyl group (**5d-*trans***, **5e-*trans***), the smaller ethyl substituent on the carbamate was preferable to afford the best conversion. No significant difference was observed when the phenyl was replaced by a naphthalene moiety (**5g-*trans***). On the other hand, when R_3 was an aromatic ring, electronic effects also played on the cyclization rate. When the phenyl was substituted by deactivating substituents such as halogens at *para*-position (Br, F), a positive effect on the reac-

tion rate was observed (**5h-*trans***, **5k-*trans,* 5l-*trans***). Conversely, a bromine atom at *ortho*- or *meta*-position (**5i-*trans,* 5j-*trans***), disfavored the conversion, even at reflux with, however, a diasteroisomeric ratio up to 95:5. Electron-withdrawing group with strong –M effect such as nitro group slowed down the transformation and requested a more important load of palladium at reflux, or even prevented the reaction. For example, when a nitro was substituted at *ortho*- or *para*-position on the phenyl ring, only the starting material was recovered after 24 h at reflux (**5n, 5p**). When the nitro was at the *meta*-position (**5o-*trans***), the TP was obtained in 27 % yield after 24 h at reflux and 30 mol-% of catalyst. Adding a methoxy group at *para*-

Table 3. Scope of allyl alcohols.



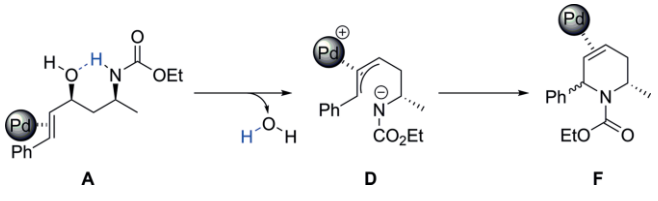
3 **5-*trans*** **5-*cis***

5a-*trans* conv. 100%, *dr* = 95:5 40 °C, 3 h 20 min Yield = 61%	**5b-*trans*** conv. 100%, *dr* = 96:4 40 °C, 6 h Yield = 56%	**5c-*trans*** conv. 46%, *dr* = 98:2 reflux 90 h, [Pd] (30 mol-%) Yield = 20%	**5d-*trans*** conv. 100%, *dr* = 96:4 reflux 2 h 30 min Yield = 81%
5e-*trans*[a] conv. 15%, *dr* > 96:4 8 h reflux	**5f-*trans*** conv. 100%, *dr* = 90:10 2 h 30 min reflux Yield = 62%	**5g-*trans*** conv. 100%, *dr* = 94:6 rt, 3 h Yield = 58%	**5h-trans** conv. 100%, *dr* = 95:5 40 °C, 24 h Yield = 74%
5i-*trans* conv. 66%, *dr* = 98:2 reflux, 30 h Yield = 38%	**5j-*trans*** conv. 86%, *dr* = 95:5 reflux 6 h Yield = 36%	**5k-*trans*** conv. 100%, *dr* = 97:3 40 °C, 1 h 45 min Yield = 84%	**5l-*trans*** conv. 100%, *dr* = 97:3 rt, 1 h 30 min Yield = 67%
5m[b] conv. 0% reflux 24 h	**5n[b]** conv. 0% reflux 24 h	**5o-*trans*** conv. 100%, *dr* = 100:0 reflux 24 h, [Pd] (30 mol-%) Yield = 27%	**5p[b]** conv. 0% reflux 24 h
5q-*trans* conv. 100%, *dr* = 96:4 rt, 22 h Yield = 89%	**5r[b]** conv. 0% reflux 24 h	**5s-*cis*** conv. 100%, *dr* = 79:21 40 °C 1 min or rt 25 min Yield = 75%	**5t-*trans*** conv. 100%, *dr* = 98:2 rt, 23 h Yield = 78%
5u-*trans* conv. 100%, *dr* = 74:26 rt, 1 h Yield = 72%	**5v[b]** conv. 0% reflux 24 h	**5w[b]** conv. 0% reflux 24 h	**5x[b]** conv. 0% reflux 24 h

Diastereoisomeric ratios are given for the crude products. [a] Not purified. [b] No conversion was observed, even with 30 mol-% of palladium, only the starting material was recovered without any decomposition.

position (**5q-*trans***) allowed to offset the deactivating nature of the nitro group at the *meta*-position, with a total conversion after 22 h at room temperature and 89 % yield. Electron-donating groups at the *para*-position (**5s-*cis*, 5u-*trans***) greatly accelerated the conversion, but also the epimerization rate, even with 5 mol-% of palladium. At the *meta*-position (**5t-*trans***), phenoxy electron-donating group, only slowed down the reaction and led to a 98:2 *trans*/*cis* ratio. When R_3 was an alkyl group (**5v, 5w**), or ethoxycarbonyl and pyridin-3-yl electron-withdrawing groups (**5m**, **5x**), no conversion was observed, only starting material alcohols were recovered. All these results suggested that in order to access the desired TP, the allylic alcohol system had to be connected to an aromatic ring and that electronic effects played an important role in the cyclization. This led us to suppose that the C–OH bond cleavage, initiated the transformation to the η^3-π-allyl palladium complex was influenced by the nature on the resonance on R_3.

According to the literature,[16b,17] the first step in nucleophilic allylic substitution using an unactivated allylic substrate, such as allylic alcohol, is an activation of the alcohol function. This activation can be performed by addition of Lewis or Brønsted acid or using a protic solvent, with or without catalyst. In our case, there was no activation by the solvent or acidic additives. However, the carbamate NH hydrogen could play this activation role by promoting the departure of a water molecule, leading to the formation of an η^3-π-allylic palladium complex and subsequent nitrogen nucleophilic attack and TP cycle formation (Scheme 2).



Scheme 2. Proposed mechanisms for the C-O bond cleavage.

To validate our proposal, we conducted theoretical calculations. The intramolecular allylic amination of compound **3a** catalyzed by $Pd(CH_3CN)_2$, was studied with Gaussian software[18] using Density Functional Theory (DFT) using B3LYP hybrid functional and LANL2DZ basis set for Pd and 6-31g+(d,p) basis set for all other atoms. During the optimization, dichloroethane was taken into account as solvent, by using the polarizable continuum model (PCM). All energies are given in kcal/mol, after thermodynamic corrections, corresponding to Gibbs free energies. This study is based on the work of Oshima[17b] who showed that the activation energy for the water molecule removal on the allylic alcohol system, and the subsequent formation of the η^3-π-allyl complex, is favored by a coordination of the hydroxy group with the proton of a protic solvent. In our case, the hydroxy group was coordinated with the proton of the carbamate nitrogen. The energies were calculated for π complex **A**, the palladium being *anti* to the hydroxy group, transition state **B** and η^3-π-allyl complex **C** (Figure 1). Calculations showed an activation energy of 27 kcal/mol, then a loss of 7 kcal/mol between **B** and **C**.

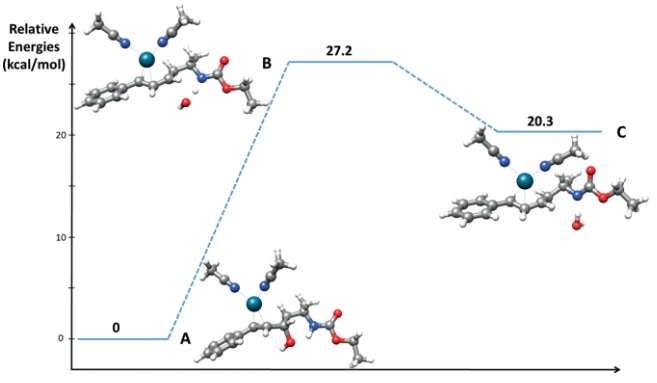


Figure 1. Theoretical calculation for water elimination.

According these theoretical calculations and experimental results, intermediate **C**, precursor of the cyclization, must be formed to initiate the C–N bond formation. Then, after departure of water, the nitrogen atom of intermediate **D**, a conformational isomer of **C**, goes positioned close to the η^3-π-allyl complex to allow the cyclization via transition state **E** in the course of an exergonic reaction (Figure 2). The calculated activation energy was about 10 kcal/mol, followed by a loss of 30 kcal/mol to complex **F**, in a favorable cyclization process. When no reaction occurred, the starting material was recovered without loss of the stereochemistry of the alcohol center, showing that water release and formation of the η^3-π-allyl complex **D** was a key step for this cyclization.

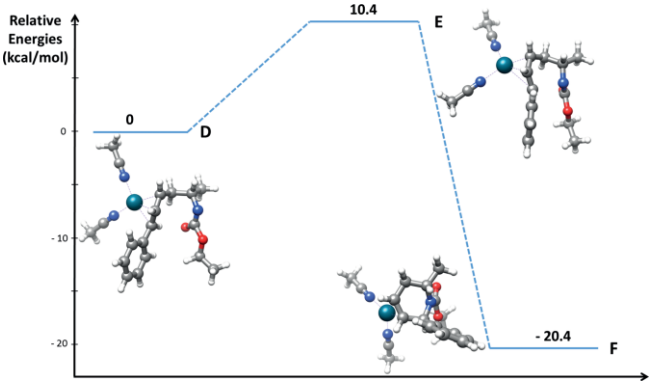
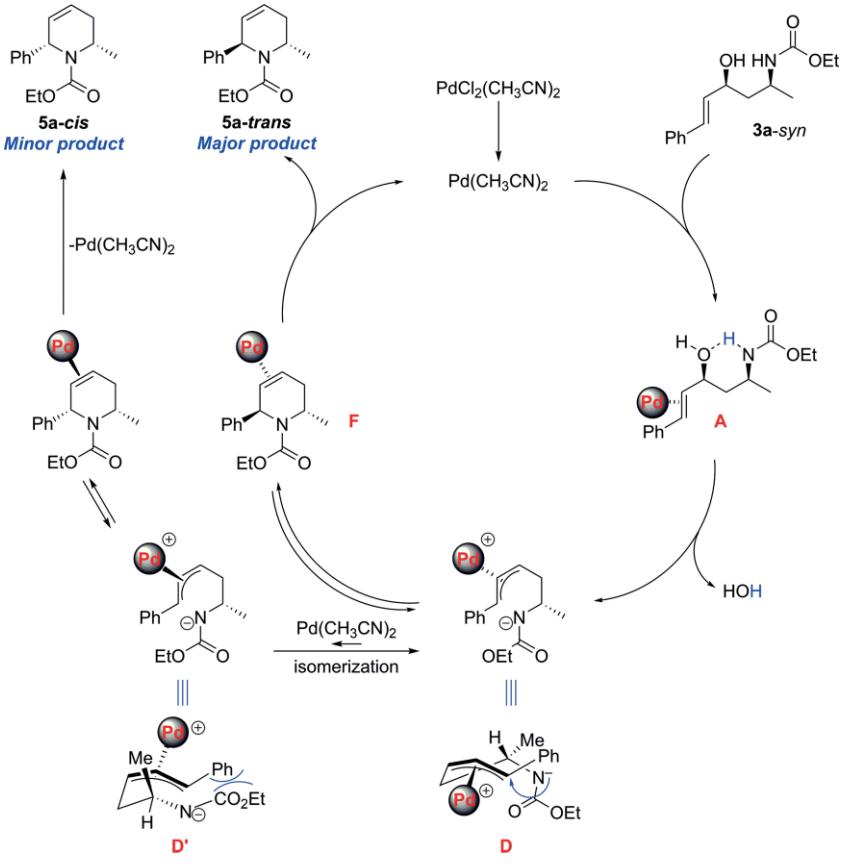
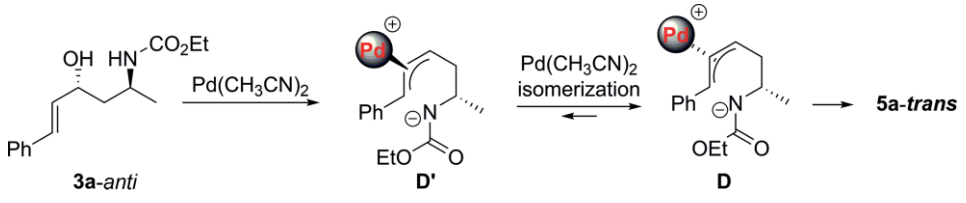


Figure 2. Theoretical calculation for cyclization via C-N bond formation.

A proposed mechanism for this amination reaction is depicted Scheme 3, starting from allylic alcohol **3a-*syn***. After complexation of the palladium, presumably *anti* to the hydroxy group, leading to **A**, and departure of the water molecule with assistance of the carbamate NH, η^3-π-allyl complex intermediate **D** was obtained. As shown in Scheme 3, **D** has a sickle-shaped geometry appropriate for cyclization to **5a-*trans***, with nitrogen attack that occurs *anti* to the palladium. Alternatively, W-shaped complex can also be formed but would need to isomerize to **D** before cyclization via an $\eta^3 \rightarrow \eta^1 \rightarrow \eta^3$ isomerization process. To explain the formation of **5a-*cis***, we could suppose an isomerization of **D**, with a switch of the face coordinated to the metal, via a nucleophilic displacement by palladium(0), to give **D′**.[17d,19] However, due to steric hindrance, **D′** would be disfavored, which could explain the kinetic preference for **5a-**



Scheme 3. Proposed mechanism for the formation of 2,6-*trans*-TP from **3a-*syn***.



Scheme 4. Formation of complexes D and D′ from **3a-*anti***.

trans via intermediate **D**, in the reaction conditions that minor epimerization.

A similar mechanistic pathway could explain why the *syn*/*anti* relative configuration of the starting alcohol did not affect the stereochemical outcome of the reaction. We can reasonably suggest that **D** and **D′** are common intermediates, and that they are also formed from **3a-*anti***. Thus, **3a-*anti*** would first lead to π-allyl complex **D′**, and then a fast isomerization via a nucleophilic displacement by palladium(0) would give **D**, leading preferentially to the kinetic **5a-*trans*** diastereoisomer (Scheme 4).

Conclusions

In conclusion, we described an efficient palladium-catalyzed intramolecular cyclization of N-protected β-amino-allylic alcohols **3** as well as the stereoselectivity of the transformation into 2,6-*trans*-TP **5**. The allylic alcohol precursors could be prepared from the corresponding phosphonate in two steps in good to excellent yields. The configuration of the alcohol stereocenter, generated after reduction of the corresponding ketone, did not influence the stereochemical outcome of the cyclization reaction into 2,6-*trans*-TP. According to calculations, the η^3-π-allyl complex could be formed with the assistance of the carbamate NH, and the stereoselectivity could be explained by steric constraints in the η^3-π-allyl complex.

Experimental Section

General Information: Commercially available reagents were purchased from Sigma-Aldrich, Fisher, TCI, Alfa Aesar or Fluorochem and were used without purification unless stated otherwise. Solvents were purchased from VWR Chemicals or Sigma-Aldrich and used without purification, unless stated otherwise. All ^{1}H and ^{13}C NMR spectra were measured at 295 K in $CDCl_3$ or CD_3OD on a Bruker AVANCE III HD 400 (101 MHz for ^{13}C) spectrometer. NOESY were performed on a Bruker AVANCE III HD 500. Chemical shifts (δ)

are given in ppm and are calibrated to the residual proton and carbon resonance of the solvent: $CDCl_3$ (^1H δ = 7.26; ^{13}C δ = 77.16); CD_3OD (^1H δ = 3.31; ^{13}C δ = 49.00). Coupling constant (J) are quoted in Hertz (Hz). The following abbreviations are used: singlet (s), broad singlet (brs), doublet (d), doublet of triplet (dt), triplet of doublet (td), doublet of triplet of doublet (dtd), doubled doublet (dd), triplet (t), quadruplet (q), quadruplet of doublet (qd), quintuplet (quint), doublet of quintuplet (dquint), doublet of quintuplet of doublet (dquintd), multiplet (m). High resolution mass spectroscopy (HRMS) were carried out in electrospray mode. Monitoring of the reactions was performed using silica gel TLC plates. Spots were visualized by UV light at 254 nm and by dipping the plate into a solution of p-anisaldehyde/H_2SO_4/AcOH in EtOH, followed by heating. Flash chromatography columns were performed using silica gel 60 (70–230 mesh). Melting points were obtained with the Mettler Toledo apparatus MP50 Melting Point System.

Procedure A: Synthesis of Ketones 2 from Phosphonates 1: All phosphonates **1** and ketones **2** were prepared according to the method we reported in our previous work.[12] To a solution of phosphonate **1a**–**g** (1 equiv.) in THF (0.23 M) was added $Ba(OH)_2{\cdot}H_2O$ (1.25 equiv.) at room temperature. After 30 min of stirring, a solution of corresponding aldehyde (1.05 equiv.) in THF/H_2O (40:1) (0.24 M) was added at room temperature. The end of reaction was monitored by TLC, and then the reaction mixture was quenched with a saturated aqueous NH_4Cl solution and extracted 3 times with EtOAc. Then the organic layer was dried with $MgSO_4$, filtered, and concentrated under vacuum. The crude was purified by silica gel column chromatography as described in the corresponding synthetic procedure to give the ketone **2a**–**x**.

Benzyl (*R*,*E*)-(6-Oxo-8-phenyloct-7-en-4-yl)carbamate (2e): was prepared from benzyl (*R*)-(1-(diethoxyphosphoryl)-2-oxoheptan-4-yl)carbamate **1e** (1 g, 2.50 mmol). The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 8:2 cyclohexane/EtOAc) providing **2e** as a white solid in 91 % yield (800 mg, 2.28 mmol). TLC R_f = 0.49 (cyclohexane/EtOAc, 7:3); Mp 93 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.62–7.48 (m, 3H), 7.42–7.37 (m, 3H), 7.36–7.27 (m, 5H), 6.72 (d, J = 16.1 Hz, 1H), 5.27 (d, J = 8.7 Hz, 1H), 5.08 (s, 2H), 4.11–3.99 (m, 1H), 3.02 (dd, J_1 = 16.2 Hz, 4.6 Hz, 1H), 2.85 (dd, J_1 = 16.2 Hz, J_2 = 5.6 Hz, 1H), 1.57–1.49 (m, 2H), 1.47–1.19 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 199.1, 156.1, 143.4, 136.7, 134.4, 130.8, 129.1, 128.6, 128.5, 128.2, 128.1, 126.4, 66.7, 48.5, 44.8, 36.6, 19.7, 14.0; HRMS (ESI^+) calcd. for $C_{22}H_{26}NO_3$ $[M + H]^+$ 352.1907, found 352.1911.

Benzyl (*S*,*E*)-(3-Oxo-1,5-diphenylpent-4-en-1-yl)carbamate 2f: was prepared from benzyl (*S*)-(4-(diethoxyphosphoryl)-3-oxo-1-phenylbutyl)carbamate **1f** (100 mg, 0.231 mmol). The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 8:2 cyclohexane/EtOAc) providing **2f** as a beige solid in 81 % yield (71.6 mg, 0.186 mmol). TLC R_f = 0.47 (cyclohexane/EtOAc, 7:3); Mp 114 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.57–7.44 (m, 3H), 7.43–7.19 (m, 13H), 6.66 (d, J = 16.2 Hz, 1H), 5.86 (brs, 1H), 5.25 (m, 1H), 5.12 (d, J = 12.0 Hz, 1H), 5.07 (d, J = 12.0 Hz, 1H), 3.35 (d, J = 17.0 Hz, 1H), 3.16 (dd, J_1 = 17.0 Hz, J_2 = 6.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.0, 155.8, 143.8, 141.4, 136.5, 134.3, 130.9, 129.1, 128.8, 128.6, 128.5, 128.2, 128.2, 127.6, 126.4, 126.1, 66.9, 52.0, 46.1; HRMS (ESI^+) calcd. for $C_{25}H_{24}NO_3$ $[M + H]^+$ 386.1751, found 386.1747.

Ethyl (*S*,*E*)-(6-(Naphthalen-2-yl)-4-oxohex-5-en-2-yl)carbamate (2g): was prepared from ethyl (*S*)-(5-(diethoxyphosphoryl)-4-oxopentan-2-yl)carbamate **1a** (500 mg, 1.62 mmol) and the corresponding aldehyde (234 mg, 1.50 mmol). The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 7:3 cyclohexane/EtOAc) providing **2g** as a white solid in 71 % yield (356 mg, 1.14 mmol). TLC R_f = 0.17 (cyclohexane/EtOAc, 8:2); Mp 109 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.97 (s, 1H), 7.85 (m, 3H), 7.75 (d, J = 16.2 Hz, 1H), 7.68 (dd, J_1 = 8.7 Hz, J_2 = 1.7 Hz, 1H), 7.58–7.43 (m, 2H), 6.84 (d, J = 16.2 Hz, 1H), 5.23 (s, 1H), 4.18 (dquintd, J_1 = 8.4 Hz, J_2 = 6.7 Hz, J_3 = 4.8 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.07 (dd, J_1 = 16.0 Hz, J_2 = 4.4 Hz, 1H), 2.83 (dd, J_1 = 16.0 Hz, J_2 = 6.5 Hz, 1H), 1.31 (t, J = 6.8 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.9, 156.1, 143.6, 134.6, 133.5, 132.0, 130.8, 129.0, 128.8, 128.0, 127.6, 127.0, 126.6, 123.7, 60.8, 46.5, 44.4, 20.7, 14.8; HRMS (ESI^+) calcd. for $C_{19}H_{22}NO_3$ $[M + H]^+$ 312.1594, found 312.1599.

Ethyl (*S*,*E*)-(5-(4-Bromophenyl)-3-oxo-1-phenylpent-4-en-1-yl)-carbamate (2h): was prepared from ethyl (*S*)-(4-(diethoxyphosphoryl)-3-oxo-1-phenylbutyl)carbamate **1c** (370 mg, 1.00 mmol). The crude product was purified by silica gel column chromatography (SiO_2, 9:1 cyclohexane/EtOAc to 7:3 cyclohexane/EtOAc) providing **2h** as a white solid in 97 % yield (390 mg, 0.969 mmol). TLC R_f = 0.38 (cyclohexane/EtOAc, 7:3); Mp 118 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.51 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 16.1 Hz, 1H), 7.39–7.22 (m, 8H), 5.67 (brs, 1H), 5.22 (m, 1H), 4.10 (q, J = 7.2 Hz, 2H), 3.34 (dd, J_1 = 16.2, J_2 = 5.3 Hz, 1H), 3.13 (dd, J_1 = 16.2 Hz, J_2 = 6.0 Hz, 1H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 197.8, 155.7, 143.3, 142.3, 133.3, 132.4, 129.9, 128.8, 127.7, 126.5, 126.4, 125.2, 61.2, 51.9, 46.5, 14.7; HRMS (ESI^+) calcd. for $C_{20}H_{21}BrNO_3$ $[M + H]^+$ 402.0699, found 402.0699.

Ethyl (*R*,*E*)-(6-(3-Bromophenyl)-4-oxohex-5-en-2-yl)carbamate (2j): was prepared from ethyl (*R*)-(5-(diethoxyphosphoryl)-4-oxopentan-2-yl) **1a** (464 mg, 1.5 mmol). The crude product was purified by silica gel column chromatography (SiO_2, 9:1 to 7:3 cyclohexane/EtOAc) providing **2j** as a white solid in 71 % yield (362 mg, 1.06 mmol). TLC R_f = 0.33 (cyclohexane/EtOAc, 7:3); Mp 67 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.69 (t, J = 1.8 Hz, 1H), 7.52 (dd, J_1 = 7.9 Hz, J_2 = 1.8 Hz, 1H), 7.49 (d, J = 16.1 Hz, 1H), 7.46 (dt, J_1 = 7.9 Hz, J_2 = 1.8 Hz, 1H), 7.27 (t, J = 7.9 Hz, 1H), 6.70 (d, J = 16.1 Hz, 1H), 5.09 (brs, 1H), 4.25–3.99 (m, 3H), 3.00 (dd, J_1 = 16.1 Hz, J_2 = 3.9 Hz, 1H), 2.78 (dd, J_1 = 16.1 Hz, J_2 = 6.5 Hz, 1H), 1.27 (d, J = 6.7 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.6, 156.0, 141.6, 136.6, 133.5, 131.1, 130.6, 127.5, 127.1, 123.2, 60.9, 46.8, 44.2, 20.6, 14.8; HRMS (ESI^+) calcd. for $C_{15}H_{19}BrNO_3$ $[M + H]^+$ 340.0543, found 340.0547.

Ethyl (*S*,*E*)-(6-(4-Fluorophenyl)-4-oxohex-5-en-2-yl)carbamate (2l): was prepared from ethyl (*S*)-(5-(diethoxyphosphoryl)-4-oxopentan-2-yl)carbamate **1a** (500 mg, 1.62 mmol) and the corresponding aldehyde (160 µL, 1.49 mmol). The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 7:3 cyclohexane/EtOAc) providing **2l** as a white solid in 76 % yield (317 mg, 1.13 mmol). Mp 71 °C; TLC R_f = 0.29 (cyclohexane/EtOAc, 8:2); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.55 (d, J = 16.1 Hz, 1H), 7.54 (dd, J = 8.7 Hz, J_{HF} = 5.5 Hz, 2H), 7.08 (t, $J_{HH,HF}$ = 8.7 Hz, 2H), 6.65 (d, J = 16.1 Hz, 1H), 5.11 (brs, 1H), 4.26–4.01 (m, 3H), 3.01 (dd, J_1 = 16.1 Hz, J_2 = 4.3 Hz, 1H), 2.77 (dd, J_1 = 16.1 Hz, J_2 = 6.6 Hz, 1H), 1.29 (d, J = 6.6 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.6, 164.1 (d, J_{CF} = 252 Hz), 155.9, 142.1, 130.6 (d, J_{CF} = 3 Hz), 130.3 (d, J_{CF} = 9 Hz), 126.0 (d, J_{CF} = 2 Hz), 116.2 (d, J_{CF} = 22 Hz), 60.7, 46.5, 44.2, 20.5, 14.6; HRMS (ESI^+) calcd. for $C_{15}H_{19}FNO_3$ $[M + H]^+$ 280.1344, found 280.1344.

Ethyl (*S*,*E*)-(6-(3-Nitrophenyl)-4-oxohex-5-en-2-yl)carbamate (2o): was prepared from ethyl (*S*)-(5-(diethoxyphosphoryl)-4-oxopentan-2-yl)carbamate **1a** (500 mg, 1.62 mmol) and the corresponding aldehyde (227 m mg, 1.50 mmol). The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane

to 7:3 cyclohexane/EtOAc) providing **2o** as a white solid in 73 % yield (335 mg, 1.09 mmol). TLC R_f = 0.15 (cyclohexane/EtOAc, 8:2); Mp > 135 °C (decomposition); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.40 (t, J = 1.9 Hz, 1H), 8.25 (ddd, J_1 = 8.2 Hz, J_2 = 1.9 Hz, J_3 = 0.8 Hz, 1H), 7.83 (dt, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1H), 7.62 (d, J = 16.1 Hz, 1H), 7.60 (t, J = 8 Hz, 1H), 6.83 (d, J = 16.1 Hz, 1H), 5.05 (brs, 1H), 4.17 (dquintd, J_1 = 8.4 Hz, J_2 = 6.7 Hz, J_3 = 4.7 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.04 (dd,, J_1 = 16.1 Hz, J_2 = 4.7 Hz, 1H), 2.81 (dd, J_1 = 16.1 Hz, J_2 = 6.7 Hz, 1H), 1.31 (d, J = 6.7 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.2, 156.0, 148.9, 140.3, 136.3, 134.1, 130.2, 128.7, 124.9, 122.8, 60.9, 47.2, 44.2, 20.7, 14.73; HRMS (ESI$^+$) calcd. for $C_{15}H_{19}N_2O_5$ [M + H]$^+$ 307.1289, found 307.1280.

Ethyl (*S*,*E*)-(6-(4-Methoxy-3-nitrophenyl)-4-oxohex-5-en-2-yl)-carbamate (2q): was prepared from ethyl (*S*)-(5-(diethoxyphosphoryl)-4-oxopentan-2-yl)carbamate **1a** (500 mg, 1.62 mmol). The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 8:2 cyclohexane/EtOAc) providing **2q** as a yellow solid in 70 % yield (380 mg, 1.13 mmol). TLC R_f = 0.61 (cyclohexane/EtOAc, 5:5); Mp 123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.04 (d, J = 2.1 Hz, 1H), 7.72 (dd, J_1 = 8.7 Hz, J_2 = 2.1 Hz, 1H), 7.52 (d, J = 16.3 Hz, 1H), 7.12 (d, J = 8.7 Hz, 1H), 6.67 (d, J = 16.3 Hz, 1H), 5.07 (s, 1H), 4.24–4.03 (m, 3H), 4.00 (s, 3H), 3.00 (dd, J_1 = 16.0 Hz, J_2 = 3.8 Hz, 1H), 2.77 (dd, J_1 = 16.0 Hz, J_2 = 6.6 Hz, 1H), 1.27 (d, J = 6.8 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.2, 156.0, 154.4, 140.3, 140.0, 134.0, 127.2, 126.6, 125.3, 114.1, 60.8, 56.9, 46.9, 44.2, 20.6, 14.7; HRMS (ESI$^+$) calcd. for $C_{16}H_{21}N_2O_6$ [M + H]$^+$ 337.1394, found 337.1383.

Ethyl (*S*,*E*)-(6-(2-Fluoro-5-nitrophenyl)-4-oxohex-5-en-2-yl)carbamate (2r): was prepared from ethyl (*S*)-(5-(diethoxyphosphoryl)-4-oxopentan-2-yl)carbamate **1a** (500 mg, 1.62 mmol). The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 8:2 cyclohexane/EtOAc) providing **2r** as a white solid in 65 % yield (340 mg, 1.05 mmol). TLC R_f = 0.16 (cyclohexane/EtOAc, 8:2); Mp 107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.50 (dd, J_1 = 6.2 Hz, J_2 = 2.8 Hz, 1H), 8.27 (ddd, J_1 = 9.1 Hz, J_2 = 4.4 Hz, J_3 = 2.8 Hz, 1H), 7.69 (d, J = 16.3 Hz, 1H), 7.29 (t, J = 9.1 Hz, 1H), 6.94 (t, J = 16.3 Hz, 1H), 5.04 (brs, 1H), 4.17 (dquintd, J_1 = 8.4 Hz, J_2 = 6.7 Hz, J_3 = 4.8 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.04 (dd, J_1 = 16.3 Hz, J_2 = 4.8 Hz, 1H), 2.84 (dd, J_1 = 16.3 Hz, J_2 = 6.4 Hz, 1H), 1.29 (d, J = 6.7 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.0, 165.5 (d, J_{CF} = 264 Hz), 156.0, 144.7, 132.8, 130.6 (d, J_{CF} = 5.25 Hz), 127.0 (d, J_{CF} = 11 Hz), 124.6 (d, J_{CF} = 5 Hz), 124.0 (d, J_{CF} = 14 Hz), 117.5 (d, J_{CF} = 25 Hz), 60.9, 47.3, 44.1, 20.7, 14.72; HRMS (ESI$^+$) calcd. for $C_{15}H_{18}FN_2O_5$ [M + H]$^+$ 325.1194, found 325.1183.

Ethyl (*S*,*E*)-(4-Oxo-6-(3-phenoxyphenyl)hex-5-en-2-yl)carbamate (2t): was prepared from ethyl (*S*)-(5-(diethoxyphosphoryl)-4-oxopentan-2-yl)carbamate **1a** (500 mg, 1.62 mmol). The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 7:3 cyclohexane/EtOAc) providing **2t** as a yellow oil in 81 % yield (460 mg, 1.30 mmol). TLC R_f = 0.24 (cyclohexane/EtOAc, 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51 (d, J = 16.2, 1H), 7.36 (m, 3H), 7.25 (s, 1H), 7.19–7.08 (m, 2H), 7.07–6.96 (m, 3H), 6.65 (d, J = 16.2 Hz, 1H), 5.12 (brs, 1H), 4.26–3.95 (m, 3H), 2.99 (dd, J_1 = 16.1 Hz, J_2 = 4.5 Hz, 1H), 2.77 (dd, J_1 = 16.1 Hz, J_2 = 6.3 Hz, 1H), 1.26 (d, J = 6.7 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.8, 158.1, 156.7, 156.0, 142.8, 136.3, 130.4, 130.1, 127.1, 123.9, 123.4, 121.0, 119.3, 118.0, 60.8, 46.4, 44.2, 20.6, 14.7; HRMS (ESI$^+$) calcd. for $C_{21}H_{24}NO_4$ [M + H]$^+$ 354.1700, found 354.1689.

Ethyl (*S*,*E*)-(6-(4-Acetamidophenyl)-4-oxohex-5-en-2-yl)carbamate (2u): was prepared from ethyl (*S*)-(5-(diethoxyphosphoryl)-4-oxopentan-2-yl)carbamate **1a** (500 mg, 1.62 mmol) and the corresponding aldehyde (245 mg, 1.50 mmol. The crude product was purified by silica gel column chromatography (SiO_2, 5:5 cyclohexane/EtOAc to 2:8 cyclohexane/EtOAc) providing **2u** as a white solid in 60 % yield (286 mg, 0.898 mmol). TLC R_f = 0.2 (cyclohexane/EtOAc, 5:5); Mp 199 °C; ^{1}H NMR (400 MHz, MeOD) δ = 7.62 (d, J = 8.6 Hz, 2H) 7.60(d, J = 15.8 Hz, 1H), 7.58 (d, J = 8.6 Hz, 2H), 6.74 (d, J = 15.8 Hz, 1H), 4.08 (m, 4H), 2.98 (dd, J = 15.2, 6.0 Hz, 1H), 2.73 (dd, J_1 = 15.2 Hz, J_2 = 6.9 Hz, 1H), 2.14 (s, 3H), 1.20 (d, J = 6.7 Hz, 3H), 1.19 (m, 3H); ^{13}C NMR (101 MHz, MeOD) δ = 200.8, 171.6, 158.1, 144.5, 142.2, 131.2, 130.3, 126.0, 120.8, 61.5, 47.8, 45.2, 24.0, 21.0, 14.9; HRMS (ESI$^+$) calcd. for $C_{17}H_{23}N_2O_4$ [M + H]$^+$ 319.1652, found 319.1644.

Ethyl (*R*,*E*)-(4-Oxoheptadec-5-en-2-yl)carbamate (2v): was prepared from ethyl (*R*)-(5-(diethoxyphosphoryl)-4-oxopentan-2-yl)-carbamate **1a** (1.647 g, 5.33 mmol). The reaction was quenched after 3h and the crude product was purified by silica gel column chromatography (SiO_2, 9:1 to 8:2 cyclohexane/EtOAc) providing **2v** as a white solid in 90 % yield (1.63 g, 4.80 mmol). TLC R_f = 0.50 (cyclohexane/EtOAc, 7:3); Mp 35 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.86 (dt, J_1 = 15.9 Hz, J_2 = 6.9 Hz, 1H), 6.08 (dt, J_1 = 15.9 Hz, J_2 = 1.5 Hz, 1H), 5.13 (brs, 1H), 4.22–3.93 (m, 3H), 2.88 (dd, J_1 = 16.1 Hz, J_2 = 4.7 Hz, 1H), 2.63 (dd, J_1 = 16.1 Hz, J_2 = 6.5 Hz, 1H), 2.21 (qd, J_1 = 6.9 Hz, J_2 = 1.5 Hz, 2H), 1.51–1.38 (m, 2H), 1.38–0.96 (m, 22H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 199.2, 156.0, 148.9, 130.7, 60.8, 45.5, 44.2, 32.7, 32.0, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 28.2, 22.8, 20.6, 14.7, 14.2; HRMS (ESI$^+$) calcd. for $C_{20}H_{38}NO_3$ [M + H]$^+$ 340.2846, found 340.2838.

Ethyl (*R*,*E*)-6-(((Benzyloxy)carbonyl)amino)-4-oxohept-2-enoate (2x) and Ethyl (*R*,*Z*)-6-(((Benzyloxy)carbonyl)amino)-4-oxohept-2-enoate (2x′): These compounds were prepared from benzyl (*R*)-(5-(diethoxyphosphoryl)-4-oxopentan-2-yl)carbamate 1d (600 mg, 1.62 mmol). The crude product was purified by flash chromatography (SiO_2, 8:2 pentane/EtO_2 to 3:7 pentane) providing 2x as a white solid in 28 % yield (145.7 mg, 0.456 mmol) and its isomer Z 2x′ as a white solid in 37 % yield (188.4 mg, 0.590 mmol). 2x: TLC R_f = 0.46 (cyclohexane/EtOAc, 7:3); Mp 81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40–7.28 (m, 5H), 7.02 (d, J = 16.1 Hz, 1H), 6.67 (d, J = 16.1 Hz, 1H), 5.15–4.93 (m, 3H), 4.25 (q, J = 7.1 Hz, 2H), 4.14 (dquintd, J_1 = 7.6 Hz, J_2 = 6.2 Hz, J_3 = 4.2 Hz, 1H), 2.98 (dd, J = 16.9 Hz, J_2 = 4.2 Hz, 1H), 2.79 (dd, J = 16.9 Hz, J_2 = 6.2 Hz, 1H), 1.32 (t, J = 7.1 Hz, 3H), 1.25 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.3, 165.5, 155.7, 139.4, 136.5, 131.6, 128.7, 128.3, 128.2, 66.8, 61.6, 47.0, 43.9, 20.5, 14.2; HRMS (ESI$^+$) calcd. for $C_{17}H_{22}NO_5$ [M + H]$^+$ 320.1493, found 320.1483. 2x′: TLC R_f = 0.35 (cyclohexane/EtOAc, 7:3); Mp 30 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41–7.27 (m, 5H), 6.44 (d, J = 12.0 Hz, 1H), 6.01 (d, J = 12.0 Hz, 1H), 5.21 (brs, 1H), 5.14–4.98 (m, 2H), 4.20 (q, J = 7.1 Hz, 2H), 4.20–4.09 (m, 1H), 2.89 (dd, J_1 = 17.2 Hz, J_2 = 5.8 Hz, 1H), 2.81 (dd, J_1 = 17.2 Hz, J_2 = 5.5 Hz, 1H), 1.30 (d, J = 6.8 Hz, 3H), 1.28 (t, J = 7.1Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 202.2, 165.3, 155.8, 141.7, 136.7, 128.6, 128.1, 128.1, 125.1, 66.6, 61.4, 48.3, 43.7, 20.6, 14.1; HRMS (ESI$^+$) calcd. for $C_{17}H_{22}NO_5$ [M + H]$^+$ 320.1493, found 320.1483.

Procedure B: Synthesis of Alcohols 3 from Ketones 2: To a solution of the corresponding ketone **2a**–**x** (1.0 equiv.) in MeOH (0.08 M) was added $CeCl_3$ (1.0 equiv.). Then the reaction mixture was cooled to –78 °C and then $NaBH_4$ (1.0 equiv.) was added slowly portionwise. The reaction mixture was stirred for 1 h, at –78 °C and overnight at room temperature. After concentration, the crude mixture was diluted in EtOAc and washed with a saturated aqueous NH_4Cl solution and H_2O. The organic layer was dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography as described in the corresponding synthetic procedure to give the alcohols **3a**–**x**.

Ethyl ((2*R*,4*S*,*E*)-4-Hydroxy-6-phenylhex-5-en-2-yl)carbamate (3a-*anti*) and Ethyl ((2*R*,4*R*,*E*)-4-Hydroxy-6-phenylhex-5-en-2-yl)carbamate (3a-*syn*): Ketone **2a** (600 mg, 2.30 mmol) was used in general procedure B. The crude product was purified by flash chromatography (SiO_2, 9:1 cyclohexane/EtOAc to 6:4 cyclohexane/EtOAc) providing **3a-*anti*** as a white oil (50 mg, 0.190 mmol) and 3a-***syn*** as a white oil (463 mg, 1.758 mmol). The alcohols **3a** were globally obtained in 85 % yield in a ratio of 90:10 in favor of the *syn* product. **3a-*anti***: TLC R_f = 0.33 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) 7.38 (d, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 6.63 (d, *J* = 15.9 Hz, 1H), 6.23 (dd, J_1 = 15.9 Hz, J_2 = 5.9 Hz, 1H), 4.68 (d, *J* = 8.3 Hz, 1H), 4.42–4.32 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 4.09–3.95 (m, 1H), 3.86 (s, 1H), 1.74 (ddd, J_1 = 13.9 Hz, J_2 = 10.6 Hz, J_3 = 3.2 Hz, 1H), 1.54 (ddd, J_1 = 13.9 Hz, J_2 = 10.6 Hz, J_3 = 3Hz, 1H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.24 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.5, 137.0, 131.7, 129.5, 128.6, 127.5, 126.5, 68.8, 61.3, 45.8, 44.0, 21.5, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{21}NO_3Na$ [M + Na]$^+$ 286.1414, found 286.1413. **3a-*syn***: TLC R_f = 0.19 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) 7.38 (d, *J* = 7.3 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 6.60 (d, *J* = 16.0 Hz, 1H), 6.24 (dd, J_1 = 16.0 Hz, J_2 = 6.1 Hz, 1H), 4.71 (s, 1H), 4.43 (q, *J* = 6.8 Hz, 1H), 4.16–3.97 (m, 2H), 3.91 (m, 1H), 2.46 (s, 1H), 1.78 (t, *J* = 6.5 Hz, 2H), 1.22 (d, *J* = 6.6 Hz, 3H), 1.17 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.5, 136.8, 132.3, 128.6, 128.5, 127.7, 126.5, 70.7, 60.9, 44.9, 44.6, 21.8, 14.6; HRMS (ESI$^+$) calcd. for $C_{15}H_{21}NO_3Na$ [M + Na]$^+$ 286.1414, found 286.1413.

Benzyl ((2*R*,4*S*,*E*)-4-Hydroxy-6-phenylhex-5-en-2-yl)carbamate (3b-*anti*) and Benzyl ((2*R*,4*R*,*E*)-4-Hydroxy-6-phenylhex-5-en-2-yl)carbamate (3b-*syn*): Ketone **2b** (685 mg, 2.12 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, cyclohexane to 7:3 cyclohexane/EtOAc) providing **3b-*anti*** as a colorless oil (110 mg, 0.338 mmol) and **3b-*syn*** as a white solid (539.9 mg, 1.659 mmol). The alcohols **3b** were globally obtained in 94 % yield in a ratio of 83:17 in favor of the *syn* product. **3b-*anti*:** TLC R_f = 0.39 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40–7.27 (m, 9H), 7.22 (t, *J* = 7.1 Hz, 1H), 6.61 (d, *J* = 15.9 Hz, 1H), 6.22 (dd, J_1 = 15.9 Hz, J_2 = 5.9 Hz, 1H), 5.12 (s, 2H), 4.80 (d, *J* = 8.7 Hz, 1H), 4.35 (m, 1H), 4.04 (m, 1H), 1.74 (ddd, J_1 = 14.0 Hz, J_2 = 10.6 Hz, J_3 = 3.2 Hz, 1H), 1.64–1.49 (m, H_2O +1H), 1.24 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.2, 137.0, 136.4, 131.7, 129.7, 128.7, 128.7, 128.4, 128.3, 127.6, 126.6, 68.9, 67.2, 45.8, 44.3, 21.6; HRMS (ESI+) calcd. for $C_{20}H_{23}NaNO_3$ [M + Na]$^+$ 348.1570, found 348.1574. **3b-*syn***: TLC R_f = 0.30 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41–7.19 (m, 10H), 6.60 (d, *J* = 15.9 Hz, 1H), 6.23 (dd, J_1 = 15.9 Hz, J_2 = 5.9 Hz, 1H), 5.08 (d, *J* = 12.1 Hz, 1H), 4.97 (d, *J* = 12.1 Hz, 1H), 4.83 (brs, 1H), 4.43 (m, 1H), 3.93 (m, 1H), 1.79 (t, *J* = 6.5 Hz, 2H), 1.24 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.2, 136.8, 136.5, 132.2, 130.0, 128.7, 128.6, 128.3, 128.2, 127.8, 126.6, 70.8, 66.9, 45.1, 44.6, 21.9; HRMS (ESI$^+$) calcd. for $C_{20}H_{23}NaNO_3$ [M + Na]$^+$ 348.1570, found 348.1574.

tert*-Butyl ((2*R*,4*S*,*E*)-4-Hydroxy-6-phenylhex-5-en-2-yl)carbamate (3c-*anti*) and *tert*-Butyl ((2*R*,4*R*,*E*)-4-Hydroxy-6-phenylhex-5-en-2-yl)carbamate (3c-*syn*).** Ketone **2c** (770 mg, 2.66 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 8:2 cyclohexane/EtOAc) providing **3c-*anti as a yellow oil (133 mg, 0.456 mmol) and **3c-*syn*** as a white solid (396 mg, 1.36 mmol). The alcohols **3c** were globally obtained in 68 % yield in a ratio of 75:25 in favor of the *syn* product. **3c-*anti***: TLC R_f = 0.29 (cyclohexane/EtOAc, 8:2); ^{1}H NMR (400 MHz, CDCl3) δ = 7.37 (d, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.21 (t, *J* = 7.7 Hz, 1H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.24 (dd, J_1 = 16.0 Hz, J_2 = 5.6 Hz, 1H), 4.52 (brs, 1H), 4.34 (m, 1H), 3.98 (m, 1H), 1.71 (ddd, J_1 = 14.0 Hz, J_2 = 10.5 Hz, J_3 = 3.1 Hz, 1H), 1.49 (m, 1H), 1.46 (s, 9H), 1.21 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, CDCl3) δ = 157.1, 137.2, 131.8, 129.3, 128.6, 127.5, 126.5, 80.2, 68.6, 46.5, 43.5, 28.5, 21.7; HRMS (ESI$^+$) calcd. for $C_{17}H_{25}NaNO_3$ [M + Na]$^+$ 314.1727, found 314.1727. **3c-*syn***: TLC R_f = 0.14 (cyclohexane/EtOAc, 8:2); Mp 103 °C; ^{1}H NMR (400 MHz, CDCl3) δ = 7.36 (d, *J* = 7.4 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 16.0 Hz, 1H), 6.23 (dd, J_1 = 16.0 Hz, J_2 = 6.2 Hz, 1H), 4.57 (brs, 1H), 4.40 (td, J_1 = 6.2 Hz, J_2 = 6.6 Hz, 1H), 3.88 (m, 1H), 2.80 (brs, 1H), 1.76 (ddd, J_1 = 14.0 Hz, J_2 = 7.3 Hz, J_3 = 6.6 Hz, 1H), 1.72 (m, 1H), 1.41 (s, 9H), 1.19 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, CDCl3) δ = 155.8, 136.9, 132.5, 129.9, 128.6, 127.6, 126.6, 79.6, 70.8, 45.0, 44.6, 28.5, 21.9; HRMS (ESI$^+$) calcd. for $C_{17}H_{25}NaNO_3$ [M + Na]$^+$ 314.1727, found 314.1727.

Ethyl ((4*R*,6*S*,*E*)-6-Hydroxy-8-phenyloct-7-en-4-yl)carbamate (3d-*anti*) and Ethyl ((4*R*,6*R*,*E*)-6-Hydroxy-8-phenyloct-7-en-4-yl)-carbamate (3d-*syn*). Ketone **2d** (189.6 mg, 0.655 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, cyclohexane to 8:2 cyclohexane/EtOAc) providing **3d-*anti*** as a colorless oil (17.6 mg, 0.0604 mmol) and **3d-*syn*** as a colorless oil (133.4 mg, 0.458 mmol). The alcohols **3d** were globally obtained in 79 % yield in a ratio of 88:12 in favor of the *syn* product. **3d-*anti***: TLC R_f = 0.20 (cyclohexane/EtOAc, 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37 (d, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.22 (dd, J_1 = 16.0 Hz, J_2 = 5.6 Hz, 1H), 4.59 (d, *J* = 9.0 Hz, 1H), 4.37 (m, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.90 (m, 1H), 1.74 (ddd, J_1 = 13.9 Hz, J_2 = 10.8 Hz, J_3 = 3.0 Hz, 1H), 1.57–1.29 (m, 5H), 1.23 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 158.0, 137.1, 131.8, 129.4, 128.6, 127.5, 126.5, 68.6, 61.4, 48.0, 44.5, 37.9, 19.5, 14.7, 14.0; HRMS (ESI$^+$) calcd. for $C_{17}H_{25}NaNO_3$ [M + Na]$^+$ 314.1727, found 314.1720. **3d-*syn***: TLC R_f = 0.09 (cyclohexane/EtOAc, 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38 (d, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 6.61 (d, *J* = 15.5 Hz, 1H), 6.24 (dd, J_1 = 15.5 Hz, J_2 = 5.8 Hz, 1H), 4.58 (d, *J* = 8.6 Hz, 1H), 4.45 (m, 1H), 4.19–3.92 (m, 2H), 3.79 (m, 1H), 2.66 (brs, 1H), 1.93–1.29 (m, 6H), 1.15 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.2, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.9, 136.9, 132.4, 129.6, 128.7, 127.7, 126.6, 70.7, 61.0, 48.7, 43.5, 38.3, 19.2, 14.6, 14.1; HRMS (ESI$^+$) calcd. for $C_{17}H_{25}NaNO_3$ [M + Na]$^+$ 314.1727, found 314.1720.

Benzyl ((4*R*,6*S*,*E*)-6-Hydroxy-8-phenyloct-7-en-4-yl)carbamate (3e-*anti*) and Benzyl ((4*R*,6*R*,E)-6-Hydroxy-8-phenyloct-7-en-4-yl)carbamate (3e-*syn*). Ketone **2e** (200.8 mg, 0.571 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, cyclohexane to 7:3 cyclohexane/EtOAc) providing **3e-*anti*** as a white solid (23.2 mg, 0.0656 mmol) and **3e-*syn*** as a white solid (152.2 mg, 0.430 mmol). The alcohols **3e** were globally obtained in 87 % yield in a ratio of 87:13 in favor of the *syn* product. **3e-*anti***: TLC R_f = 0.42 (cyclohexane/EtOAc, 7:3); Mp 109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42–7.33 (m, 7H), 7.29 (t, *J* = 7.3 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 6.61 (d, *J* = 15.8 Hz, 1H), 6.22 (dd, J_1 = 15.8 Hz, J_2 = 5.8 Hz, 1H), 5.14 (d, *J* = 12.2 Hz, 1H), 5.10 (d, *J* = 12.2 Hz, 1H), 4.70 (d, *J* = 9.1 Hz, 1H), 4.35 (m, 1H), 3.94 (m, 1H), 3.79 (d, *J* = 2.8 Hz, 1H), 1.75 (ddd, J_1 = 13.9, J_2 = 10.8, J_3 = 3.0 Hz, 1H), 1.54–1.30 (m, 5H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.6, 137.1, 136.4, 131.7, 129.5, 128.7, 128.6, 128.4, 128.3, 127.6, 126.5, 68.6, 67.2, 48.2, 44.2, 37.8, 19.4, 14.0; HRMS (ESI$^+$) calcd. for $C_{22}H_{27}NaNO_3$ [M + Na]$^+$ 376.1883, found 376.1901. **3e-*syn***: TLC R_f = 0.26 (cyclohexane/EtOAc, 7:3); Mp 69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46–7.13 (m, 10H), 6.61 (d, *J* = 15.9Hz, 1H), 6.24 (dd, J_1 = 15.9 Hz, J_2 = 5.8 Hz, 1H), 5.08 (d, *J* = 11.9 Hz, 1H), 4.95 (d, *J* = 11.9 Hz, 1H), 4.71 (d, *J* = 8.6 Hz, 1H), 4.45 (td, J_1 = 6.3 Hz, J_2 = 5.8 Hz, 1H), 3.82 (m, 1H), 1.86 (dt, J_1 = 14.4 Hz,

J_2 = 6.3 Hz, 1H), 1.72 (ddd, J_1 = 14.4 Hz, J_2 = 8.9 Hz, J_3 = 6.3 Hz, 1H), 1.60–1.17 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.6, 136.9, 136.5, 132.3, 129.8, 128.7, 128.6, 128.3, 128.3, 127.7, 126.6, 70.7, 67.0, 48.8, 43.3, 38.2, 19.1, 14.0; HRMS (ESI$^+$) calcd. for $C_{22}H_{27}NaNO_3$ $[M + Na]^+$ 376.1883, found 376.1901.

Benzyl (1*S*,3*S*,*E*)-(3-Hydroxy-1,5-diphenylpent-4-en-1-yl)carbamate (3f-*anti*) and Benzyl (1*S*,3*R*,*E*)-(3-Hydroxy-1,5-diphenylpent-4-en-1-yl)carbamate (3f-*syn*): Ketone **2f** (50.9 mg, 0.132 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 9:1 cyclohexane/EtOAc to 8:2 cyclohexane/EtOAc) providing **3f-*anti*** as a colorless oil (9 mg, 0.0232 mmol) and **3f-*syn*** as a white oil (38.5 mg, 0.993 mmol). The alcohols **3f** were globally obtained in 93 % yield in a ratio of 81:19 in favor of the *syn* product. **3f-*anti*:** TLC R_f = 0.42 (cyclohexane/EtOAc, 7:3); The product was not stable and deteriorated. **3f-*syn***: TLC R_f = 0.33 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40–7.17 (m, 15H), 6.55 (d, J = 16.0 Hz, 1H), 6.21 (dd, J_1 = 16.0 Hz, J_2 = 6.3 Hz, 1H), 5.44 (d, J = 7.3 Hz, 1H), 5.05 (d, J = 12.4 Hz, 1H), 5.01 (d, J = 12.4 Hz, 1H), 4.92 (m, 1H), 4.30 (m, 1H), 2.30–1.85 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.0, 142.3, 136.6, 136.5, 131.8, 130.4, 128.9, 128.7, 128.6, 128.4, 128.3, 127.9, 127.7, 126.6, 126.6, 70.8, 67.0, 53.6, 44.2; HRMS (ESI$^+$) calcd. for $C_{25}H_{25}NaNO_3$ $[M + Na]^+$ 410.1727, found 410.1715.

Ethyl ((2*S*,4R,E)-4-Hydroxy-6-(naphthalen-2-yl)hex-5-en-2-yl)carbamate (3g-anti) and Ethyl ((2*S*,4*S*,E)-4-Hydroxy-6-(naphthalen-2-yl)hex-5-en-2-yl)carbamate (3g-syn): Ketone **2g** (297 mg, 0.954 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 9:1 cyclohexane/EtOAc to 6:4 cyclohexane/EtOAc) providing **3g-*anti*** as a white solid (31.2 mg, 0.10 mmol) and **3g-*syn*** as a white solid (265 mg, 0.846 mmol). The alcohols **3g** were globally obtained in 99 % yield in a ratio of 89:11 in favor of the *syn* product. **3g-*anti***: TLC R_f = 0.33 (cyclohexane/EtOAc, 7:3); Mp 70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.79–7.75 (m, 3H), 7.76 (d, J = 1.2 Hz, 1H), 7.59 (dd, J_1 = 8.6 Hz, J_2 = 1.8 Hz, 1H), 7.48–7.39 (m, 2H), 6.81 (d, J = 15.9 Hz, 1H), 6.35 (dd, J_1 = 15.9 Hz, J_2 = 5.8 Hz, 1H), 4.75 (d, J = 8.5 Hz, 1H), 4.42 (m, 1H), 4.13 (q, J = 7.2 Hz, 2H), 4.04 (m, 2H), 1.79 (ddd, J_1 = 3.2 Hz, J_2 = 10.6 Hz, J_3 = 14.0 Hz, 1H), 1.56 (ddd, J_1 = 2.7 Hz, J_2 = 10.5 Hz, J_3 = 14.0 Hz, 1H), 1.26 (t, J = 7.2 Hz, 3H), 1.24 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.6, 134.5, 133.7, 133.0, 132.1, 129.6, 128.2, 128.1, 127.7, 126.4, 126.3, 125.9, 123.7, 68.8, 61.4, 45.9, 44.1, 21.6, 14.7; HRMS (ESI$^+$) calcd. for $C_{19}H_{23}NNaO_3$ $[M + Na]^+$ 336.1570, found 336.1573. **3g-*syn***: TLC R_f = 0.21 (cyclohexane/EtOAc, 7:3); Mp 60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.83–7.73 (m, 3H), 7.71 (d, J = 1.1 Hz, 1H), 7.57 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.48–7.39 (m, 2H), 6.77 (d, J = 15.8 Hz, 1H), 6.35 (dd, J_1 = 15.8 Hz, J_2 = 6.1 Hz, 1H), 4.73 (brs, 1H), 4.49 (brs, 1H), 4.15–4.04 (m, 1H), 3.93 (m, 1H), 2.51 (brs, 1H), 1.81 (dd, J_1 = 7.0 Hz, J_2 = 7.8 Hz, 1H), 1.63–1.52 (m, 1H), 1.23 (d, J = 6.6 Hz, 3H), 1.16 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.5, 134.3, 133.7, 133.1, 132.7, 129.9, 128.3, 128.1, 127.8, 126.5, 126.4, 126.0, 123.7, 70.8, 60.9, 44.9, 44.8, 28.5, 21.9, 14.7; HRMS (ESI$^+$) calcd. for $C_{19}H_{23}NNaO_3$ $[M + Na]^+$ 336.1570, found 336.1573.

Ethyl ((1S,3S,E)-5-(4-Bromophenyl)-3-hydroxy-1-phenylpent-4-en-1-yl)carbamate (3h-anti) and Ethyl ((1S,3R,E)-5-(4-Bromophenyl)-3-hydroxy-1-phenylpent-4-en-1-yl)carbamate (3h-syn): Ketone **2h** (90 mg, 0.224 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 9:1 cyclohexane/EtOAc to 7:3 cyclohexane/EtOAc) providing **3h-*anti*** as a colorless oil (12.7 mg, 0.0314 mmol) and **3h-*syn*** as a colorless oil (72.5 mg, 0.179 mmol). The alcohols **3h** were globally obtained in 94 % yield in a ratio of 85:15 in favor of the *syn* product. **3h-*anti***: TLC R_f = 0.27 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42 (d, J = 8.4 Hz, 2H), 7.39–7.27 (m, 5H), 7.21 (d, J = 8.4 Hz, 2H), 6.55 (d, J = 15.8 Hz, 1H), 6.21 (dd, J_1 = 15.8 Hz, J_2 = 6.0 Hz, 1H), 5.36 (d, J = 8.1, 1H), 5.03 (m, 1H), 4.36 (m, 1H), 4.10 (q, J = 7.0 Hz, 2H), 3.51 (brs, 1H), 2.07–1.95 (m, 2H), 1.25 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.3, 141.6, 135.9, 132.3, 131.8, 129.0, 128.9, 128.1, 127.8, 126.5, 121.5, 69.0, 61.5, 52.4, 44.3, 14.7; HRMS (ESI$^+$) calcd. for $C_{20}H_{22}BrNaNO_3$ $[M + Na]^+$ 426.0675, found 426.0671. **3h-*syn***: TLC R_f = 0.17 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42 (d, J = 8.5 Hz, 2H), 7.39–7.25 (m, 5H), 7.20 (d, J = 8.5 Hz, 2H), 6.50 (d, J = 15.9 Hz, 1H), 6.21 (dd, J_1 = 15.9 Hz, J_2 = 6.1 Hz, 1H), 5.27 (d, J = 6.7 Hz, 1H), 4.89 (m, 1H), 4.31 (m, 1H), 4.05 (q, J = 7.0 Hz, 2H), 2.25–1.96 (m, 2H), 1.18 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.3, 142.4, 135.6, 132.8, 131.8, 129.0, 128.9, 128.1, 127.8, 126.6, 121.6, 70.7, 61.2, 53.3, 44.2, 14.7; HRMS (ESI$^+$) calcd. for $C_{20}H_{22}BrNaNO_3$ $[M + Na]^+$ 426.0675, found 426.0671.

Ethyl ((2*R*,4*S*,*E*)-6-(2-Bromophenyl)-4-hydroxyhex-5-en-2-yl)carbamate (3i-*anti*) and Ethyl ((2*R*,4*R*,*E*)-6-(2-Bromophenyl)-4-hydroxyhex-5-en-2-yl)carbamate (3i-*syn*): Ketone **2i** (77 mg, 0.226 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 85:15 cyclohexane/EtOAc to 7:3 cyclohexane/EtOAc) providing **3i-*anti*** as a yellow oil (10.9 mg, 0.0319 mmol) and **3i-*syn*** as a colorless oil (44.5 mg, 0.130 mmol). The alcohols **3i** were globally obtained in 72 % yield in a ratio of 80:20 in favor of the *syn* product. **3i-*anti***: TLC R_f = 0.16 (cyclohexane/EtOAc, 8:2); The product was not stable and deteriorated. **3i-*syn***: TLC R_f = 0.09 (cyclohexane/EtOAc, 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.49 (dd, J_1 = 7.8 Hz, J_2 = 1.7 Hz, 1H), 7.28–7.22 (m, 1H), 7.10 (td, J_1 = 7.8 Hz, J_2 = 1.7 Hz, 1H), 6.94 (dd, J_1 = 15.9 Hz, J_2 = 1.1 Hz, 1H), 6.20 (dd, J_1 = 15.9 Hz, J_2 = 6.0 Hz, 1H), 4.71 (brs, 1H), 4.48 (qd, J_1 = 6.1 Hz, J_2 = 1.4 Hz, 1H), 4.14–3.98 (m, 2H), 3.92 (m, 1H), 1.80 (t, J = 7.1 Hz, 2H), 1.25 (d, J = 6.6 Hz, 3H), 1.17 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.5, 136.7, 135.5, 133.0, 128.9, 128.5, 127.5, 127.2, 123.8, 70.6, 61.0, 44.9, 44.5, 21.8, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}BrNaNO_3$ $[M + Na]^+$ 364.0519, found 364.0518.

Ethyl ((2*R*,4*S*,*E*)-6-(3-Bromophenyl)-4-hydroxyhex-5-en-2-yl)carbamate (3j-*anti*) and Ethyl ((2*R*,4*R*,*E*)-6-(3-Bromophenyl)-4-hydroxyhex-5-en-2-yl)carbamate (3j-*syn*): Ketone **2j** (230 mg, 0.676 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 8:2 cyclohexane/EtOAc to 7:3 cyclohexane/EtOAc) providing **3j-*anti*** as a colorless oil (31.1 mg, 0.0909 mmol) and **3j-*syn*** as a colorless oil (177.2 mg, 0.518 mmol). The alcohols **3j** were globally obtained in 90 % yield in a ratio of 85:15 in favor of the *syn* product. **3j-*anti***: TLC R_f = 0.27 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.50 (t, J = 1.8 Hz, 1H), 7.33 (ddd, J_1 = 7.9 Hz, J_2 = 1.8 Hz, J_3 = 1.1 Hz, 1H), 7.26 (ddd, J_1 = 7.9 Hz, J_2 = 1.8 Hz, J_3 = 1.5 Hz, 1H), 7.15 (t, J = 7.9 Hz, 1H), 6.56 (dd, J_1 = 16.0 Hz, J_2 = 1.3 Hz, 1H), 6.21 (dd, J_1 = 16 Hz, J_2 = 5.5 Hz, 1H), 4.74 (d, J = 8.6 Hz, 1H), 4.35 (m, 1H), 4.12 (q, J = 7.1 Hz, 2H), 4.09–3.90 (m, 2H), 1.72 (ddd, J_1 = 14.0 Hz, J_2 = 10.8 Hz, J_3 = 3.2 Hz, 1H), 1.51 (ddd, J_1 = 14.0 Hz, J_2 = 10.7 Hz, J_3 = 2.9 Hz, 1H), 1.25 (t, J = 7.1 Hz, 3H), 1.23 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.7, 139.3, 133.3, 130.3, 130.2, 129.3, 127.9, 125.2, 122.8, 68.4, 61.4, 46.0, 44.0, 21.6, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}BrNaNO_3$ $[M + Na]^+$ 364.0519, found 364.0518. **3j-*syn***: TLC R_f = 0.16 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51 (t, J = 1.8 Hz, 1H), 7.35 (ddd, J_1 = 7.9 Hz J_2 = 1.8 Hz, J_3 = 1.5 Hz, 1H), 7.27 (ddd, J_1 = 7.9 Hz, J_2 = 1.8 Hz, J_3 = 1.5 Hz, 1H), 7.17 (t, J = 7.9 Hz, 1H), 6.54 (dd, J_1 = 15.9 Hz J_2 = 1.6 Hz, 1H), 6.24 (dd, J_1 = 15.9, J_2 = 5.8 Hz, 1H), 4.67 (brs, 1H), 4.43 (q, J = 5.8 Hz, 1H), 4.15–3.95 (m, 2H), 3.90 (m, 1H), 1.88–1.69 (m, 2H), 1.23 (d, J =

6.7Hz, 3H), 1.16 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.5, 139.1, 134.0, 130.4, 130.1, 129.3, 128.1, 125.3, 122.8, 70.3, 61.0, 44.7, 44.6, 21.8, 14.6; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}BrNaNO_3$ [M + Na]$^+$ 364.0519, found 364.0518.

Ethyl ((2*R*,4*S*,*E*)-6-(4-Bromophenyl)-4-hydroxyhex-5-en-2-yl)-carbamate (3k-anti) and Ethyl ((2*R*,4*R*,*E*)-6-(4-Bromophenyl)-4-hydroxyhex-5-en-2-yl)carbamate (3k-syn): Ketone **2k** (224 mg, 0.658 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 8:2 cyclohexane/EtOAc to 7:3 cyclohexane/EtOAc) providing **3k-*anti*** as a white solid (31.5 mg, 0.0920 mmol) and **3k-*syn*** as a white solid (177.6 mg, 0.519 mmol). The alcohols **3k** were globally obtained in 93 % yield in a ratio of 85:15 in favor of the *syn* product. **3k-*anti***: TLC R_f = 0.43 (cyclohexane/EtOAc, 6:4); Mp 65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H), 6.58 (d, J = 15.8 Hz, 1H), 6.22 (dd, J_1 = 15.8 Hz, J_2 = 5.6 Hz, 1H), 4.64 (d, J = 8.7 Hz, 1H), 4.35 (m, 1H), 4.14 (q, J = 7.0 Hz, 2H), 4.01 (m, 1H), 1.72 (ddd, J_1 = 13.9 Hz, J_2 = 10.7 Hz, J_3 = 3.2 Hz, 1H), 1.62–1.46 (m, 1H), 1.26 (t, J = 7.0 Hz, 3H), 1.24 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.7, 136.1, 132.5, 131.8, 128.3, 128.1, 121.3, 68.5, 61.4, 46.0, 44.0, 21.7, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}BrNaNO_3$ [M + Na]$^+$ 364.0519, found 364.0518. **3k-*syn***: TLC R_f = 0.29 (cyclohexane/EtOAc, 6:4); Mp 76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 6.53 (d, J = 15.9 Hz, 1H), 6.23 (dd, J_1 = 15.9 Hz, J_2 = 5.9 Hz, 1H), 4.67 (brs, 1H), 4.42 (m, 1H), 4.14–3.96 (m, 2H), 3.90 (m, 1H), 2.57 (s, 1H, OH), 1.77 (m, 2H), 1.22 (d, J = 6.6 Hz, 3H), 1.17 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.5, 135.8, 133.2, 131.8, 128.5, 128.1, 121.4, 70.6, 61.0, 44.8, 44.8, 22.0, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}BrNaNO_3$ [M + Na]$^+$ 364.0519, found 364.0518.

Ethyl ((2*S*,4*R*,*E*)-6-(4-Fluorophenyl)-4-hydroxyhex-5-en-2-yl)-carbamate 3l-*anti* and Ethyl ((2*S*,4*S*,*E*)-6-(4-Fluorophenyl)-4-hydroxyhex-5-en-2-yl)carbamate (3l-*syn*): Ketone **2l** (260 mg, 0.931 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 9:1 cyclohexane/EtOAc to 6:4 cyclohexane/EtOAc) providing **3l-*anti*** as a white solid (30.7 mg, 0.109 mmol) and **3l-*syn*** as a colorless oil (209.5 mg, 0.745 mmol). The alcohols **3l** were globally obtained in 92 % yield in a ratio of 87:13 in favor of the *syn* product. **3l-*anti***: TLC R_f = 0.33 (cyclohexane/EtOAc, 7:3); Mp 64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.32 (dd, J_{HH} = 8.7 Hz, J_{HF} = 5.4 Hz, 2H), 6.98 (t, J = 8.7 Hz, 2H), 6.61 (d, J = 15.7 Hz, 1H), 6.13 (dd, J_1 = 15.7 Hz, J_2 = 5.8 Hz, 1H), 4.72 (d, J = 8.6 Hz, 1H), 4.40–4.34 (m, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.98 (m, 1H), 1.74 (ddd, J_1 = 14.0 Hz, J_2 = 10.6 Hz, J_3 = 3.2 Hz, 1H), 1.52 (ddd, J_1 = 14.0 Hz, J_2 = 10.5 Hz, J_3 = 2.9 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H), 1.22 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.3 (d, J_{CF} = 246 Hz), 157.6, 133.2, 131.4 (d, J_{CF} = 2 Hz), 128.4, 127.9 (d, J_{CF} = 8 Hz), 115.5 (d, J_{CF} = 22 Hz), 68.6, 61.4, 46.0, 44.0, 21.6, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}FNNaO_3$ [M + Na]$^+$ 304.1319, found 304.1313. **3l-*syn***: TLC R_f = 0.23 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33 (dd, J_{HH} = 8.7 Hz, J_{HF} = 5.5 Hz, 2H), 6.99 (t, $J_{HH,HF}$ = 8.7 Hz, 2H), 6.57 (d, J = 16.0 Hz, 1H), 6.15 (dd, J_1 = 16.0 Hz, J_2 = 6.1 Hz, 1H), 4.69 (brs, 1H), 4.41 (m, 1H), 4.16–3.96 (m, 2H), 3.90 (m, 1H), 2.51 (brs, 1H), 1.77 (t, J = 6.3 Hz, 2H), 1.22 (d, J = 6.6 Hz, 3H), 1.17 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.4 (d, J_{CF} = 247 Hz), 156.6, 133.0 (d, J_{CF} = 2 Hz), 132.0, 128.7, 128.1 (d, J_{CF} = 8 Hz), 115.6 (d, J_{CF} = 21 Hz), 70.7, 61.0, 44.8, 44.8, 21.9, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}FNNaO_3$ [M + Na]$^+$ 304.1319, found 304.1313.

Ethyl ((2*R*,4*S*,*E*)-4-Hydroxy-6-(pyridin-3-yl)hex-5-en-2-yl)carbamate 3m-*anti* and Ethyl ((2*R*,4*R*,*E*)-4-Hydroxy-6-(pyridin-3-yl)hex-5-en-2-yl)carbamate (3m-*syn*): Ketone **2m** (186.5 mg, 0.711 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 4:6 cyclohexane/EtOAc to 2:8 cyclohexane/EtOAc) providing **3m-*anti*** as a white solid (29.1 mg, 0.110 mmol) and **3m-*syn*** as a white solid (117.1 mg, 0.443 mmol). The alcohols **3m** were globally obtained in 78 % yield in a ratio of 80:20 in favor of the *syn* product. **3m-*anti***: TLC R_f = 0.13 (cyclohexane/EtOAc, 4:6); Mp 151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.58 (m, 1H), 8.45 (m, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.19 (m, 1H), 6.59 (d, J = 16.0 Hz, 1H), 6.29 (dd, J_1 = 16.0 Hz, J_2 = 5.4 Hz, 1H), 4.84 (m, 1H), 4.37 (m, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.98 (m, 1H), 1.72 (ddd, J_1 = 13.9, J_2 = 10.9 Hz, J_3 = 3.2 Hz, 1H), 1.53 (ddd, J_1 = 13.9, J_2 = 10.6 Hz, J_3 = 2.7 Hz, 1H), 1.34–1.02 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.7, 148.4, 148.2, 137.1, 136.3, 134.3, 133.0, 125.7, 68.4, 61.4, 46.0, 44.0, 21.7, 14.7; HRMS (ESI$^+$) calcd. for $C_{14}H_{21}N_2O_3$ [M + H]$^+$ 265.1547, found 265.1545; **3m-*syn***: TLC R_f = 0.06 (cyclohexane/EtOAc, 4:6); Mp 115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.63 (m, 1H), 8.50 (m, 1H), 7.72 (d, J = 7.6 Hz, 1H), 7.27 (m, 1H), 6.62 (d, J = 15.9 Hz, 1H), 6.34 (dd, J_1 = 15.9 Hz, J_2 = 5.5 Hz, 1H), 4.68 (brs, 1H), 4.47 (q, J = 5.5 Hz, 1H), 4.12–3.86 (m, 3H), 2.77 (brs, 1H), 1.88–1.67 (m, 2H), 1.24 (d, J = 6.7 Hz, 3H), 1.16 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.5, 148.4, 148.2, 136.9, 135.1, 133.1, 125.9, 123.7, 70.3, 61.0, 44.8, 44.8, 22.0, 14.7; HRMS (ESI$^+$) calcd. for $C_{14}H_{21}N_2O_3$ [M + H]$^+$ 265.1547, found 265.1545.

Ethyl ((2*R*,4*S*,*E*)-4-Hydroxy-6-(2-nitrophenyl)hex-5-en-2-yl)carbamate 3n-*anti* and Ethyl ((2*R*,4*R*,*E*)-4-Hydroxy-6-(2-nitrophenyl)hex-5-en-2-yl)carbamate (3n-*syn*): Ketone **2n** (167 mg, 0.545 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 7:3 cyclohexane to 6:4 cyclohexane/EtOAc) providing **3n-*anti*** as a yellow oil (33.5 mg, 0.109 mmol) and **3n-*syn*** as a yellow oil (132.4 mg, 0.429 mmol). The alcohols **3n** were globally obtained in 99 % yield in a ratio of 80:20 in favor of the *syn* product. **3n-*anti***: TLC R_f = 0.36 (cyclohexane/EtOAc, 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.85 (dd, J_1 = 8.2 Hz, J_2 = 1.1 Hz, 1H), 7.52 (dd, J_1 = 7.9 Hz, J_2 = 1.7 Hz, 1H), 7.47 (ddd, J_1 = 7.9 Hz, J_2 = 7.4 Hz, J_3 = 1.7 Hz, 1H), 7.31 (ddd, J_1 = 8.1 Hz, J_2 = 7.4 Hz, J_3 = 1.1 Hz, 1H), 6.99 (dd, J_1 = 15.8 Hz, J_2 = 1.5 Hz, 1H), 6.16 (dd, J_1 = 15.8 Hz, J_2 = 5.8 Hz, 1H), 4.70 (d, J = 8.5 Hz, 1H), 4.33 (m, 1H), 4.07 (q, J = 7.1 Hz, 2H), 3.94 (m, 1H), 1.67 (ddd, J_1 = 13.8 Hz, J_2 = 10.8 Hz, J_3 = 3.2 Hz, 1H), 1.49 (ddd, J_1 = 13.8 Hz, J_2 = 10.6 Hz, J_3 = 2.8 Hz, 1H), 1.19 (t, J = 7.1 Hz, 3H), 1.17 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.7, 148.0, 137.4, 133.1, 132.8, 128.8, 128.1, 124.9, 124.6, 68.6, 61.4, 45.7, 43.9, 21.6, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{21}N_2O_5$ [M + H]$^+$ 309.1445, found 309.1454. **3n-*syn***: TLC R_f = 0.26 (cyclohexane/EtOAc, 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 (d, J = 7.9 Hz, 1H), 7.52–7.59 (m, 2H), 7.42 (ddd, J_1 = 8.4 Hz, J_2 = 6.6 Hz, J_3 = 2.1 Hz, 1H), 7.07 (dd, J_1 = 15.8 Hz, J_2 = 1.2 Hz, 1H), 6.24 (dd, J_1 = 15.8 Hz, J_2 = 5.8 Hz, 1H), 4.71 (brs, 1H), 4.49 (q, J = 7.1 Hz, 1H), 4.00–4.12 (m, 2H), 3.92 (m, 1H), 2.60 (s, 1H), 1.75–1.87 (m, 2H), 1.26 (d, J = 6.7 Hz, 3H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.5, 148.0, 137.9, 133.2, 132.7, 128.9, 128.2, 125.2, 124.7, 70.5, 61.0, 45.0, 44.5, 21.9, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{21}N_2O_5$ [M + H]$^+$ 309.1445, found 309.1450.

Ethyl ((2S,4R,E)-4-Hydroxy-6-(3-nitrophenyl)hex-5-en-2-yl)carbamate 3o-*anti* and Ethyl ((2S,4S,E)-4-Hydroxy-6-(3-nitrophenyl)hex-5-en-2-yl)carbamate (3o-*syn*): Ketone **2o** (296 mg, 0.966 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 85:15 cyclohexane/EtOAc to 6:4 cyclohexane/EtOAc) providing **3o-*anti*** as a yellow oil (30.0 mg, 0.0973 mmol) and **3o-*syn*** as a yellow oil (267.9 mg, 0.869 mmol). The alcohols **3o** were globally obtained in 100 % yield in a ratio of 90:10 in favor of the *syn* product. **3o-*anti***: TLC R_f = 0.23 (cyclohexane/EtOAc, 7:3); The product was not stable

and deteriorated. **3o-*syn***: TLC R_f = 0.14 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.20 (d, J = 1.7 Hz, 1H), 8.07 (d, J = 8.2 Hz, 1H), 7.66 (d, J = 7.8 Hz, 1H), 7.47 (dd, J_1 = 8.2 Hz, J_2 = 7.8 Hz, 1H), 6.69 (dd, J_1 = 15.9 Hz, J_2 = 1.5 Hz, 1H), 6.39 (dd, J_1 = 15.9, J_2 = 5.4 Hz, 1H), 4.64 (m, 1H), 4.48 (m, 1H), 4.19–3.77 (m, 3H), 2.86 (brs, 1H), 1.92–1.69 (m, 2H), 1.24 (d, J = 6.6 Hz, 3H), 1.15 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.6, 148.7, 138.8, 135.8, 132.5, 129.6, 127.2, 122.2, 121.0, 70.2, 61.1, 44.9, 44.7, 22.0, 14.6; HRMS (ESI$^+$) calcd. for $C_{15}H_{21}N_2O_5$ [M + H]$^+$ 309.1445, found 309.1444.

Ethyl ((2*R*,4*S*,*E*)-4-Hydroxy-6-(4-nitrophenyl)hex-5-en-2-yl)carbamate 3p-*anti* and Ethyl ((2*R*,4*R*,*E*)-4-Hydroxy-6-(4-nitrophenyl)hex-5-en-2-yl)carbamate (3p-*syn*): Ketone **2p** (169.0 mg, 0.552 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 7:3 cyclohexane/EtOAc to 6:4 cylohexane/EtOAc) providing **3p-*anti*** as a yellow solid (29.2 mg, 0.0947 mmol) and **3p-*syn*** as a yellow oil (129.2 mg, 0.419 mmol). The alcohols **3p** were globally obtained in 93 % yield in a ratio of 82:18 in favor of the *syn* product. **3p-*anti***: TLC R_f = 0.36 (cyclohexane/EtOAc, 6:4); Mp 115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.15 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 8.8 Hz, 2H), 6.73 (d, J = 15.9 Hz, 1H), 6.40 (dd, J_1 = 15.9 Hz, J_2 = 5.0 Hz, 1H), 4.67 (d, J = 8.3 Hz, 1H), 4.32 (m, 1H), 4.12 (q, J = 7.1 Hz, 2H), 4.01 (m, 1H), 1.74 (ddd, J_1 = 14.0 Hz, J_2 = 11.0 Hz, J_3 = 3.3 Hz, 1H), 1.54 (ddd, J_1 = 14.1 Hz, J_2 = 10.9 Hz, J_3 = 2.8 Hz, 1H), 1.25 (t, J = 7.1 Hz, 3H), 1.24 (d, J = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.8, 146.9, 143.8, 136.7, 127.2, 127.0, 124.1, 68.1, 61.5, 46.0, 44.0, 21.7, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}NaN_2O_5$ [M + Na]$^+$ 331.1264, found 331.1262. **3p-*syn***: TLC R_f = 0.23 (cyclohexane/EtOAc, 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) 8.19 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 8.8 Hz, 2H), 6.71 (dd, J_1 = 15.9 Hz, J_2 = 1.0 Hz, 1H), 6.44 (dd, J_1 = 15.9 Hz, J_2 = 5.2 Hz, 1H), 4.64 (brs, 1H), 4.49 (m, 1H), 3.86–4.14 (m, 3H), 2.86 (s, 1H), 1.88–1.73 (m, 2H), 1.26 (d, J = 6.7 Hz, 3H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.6, 147.0, 143.5, 137.4, 127.4, 127.1, 124.1, 70.3, 61.2, 45.0, 44.7, 22.1, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}NaN_2O_5$ [M + Na]$^+$ 331.1264, found 331.1262.

Ethyl ((2S,4R,E)-4-Hydroxy-6-(4-methoxy-3-nitrophenyl)hex-5-en-2-yl)carbamate 3q-*anti* and Ethyl ((2S,4S,E)-4-Hydroxy-6-(4-methoxy-3-nitrophenyl)hex-5-en-2-yl)carbamate (3q-*syn*): Ketone **2q** (320 mg, 0.951 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 8:2 cyclohexane/EtOAc to 55:45 cyclohexane/EtOAc) providing **3q-*anti*** as a yellow oil (33.3 mg, 0.0984 mmol) and **3q-*syn*** as a yellow oil (280.6 mmol 0.829 mmol). The alcohols **3q** were globally obtained in 98 % yield in a ratio of 90:10 in favor of the *syn* product. **3q-*anti***: TLC R_f = 0.15 (cyclohexane/EtOAc, 6:4). The product was not stable and deteriorated. **3q-*syn***: TLC R_f = 0.08 (cyclohexane/EtOAc, 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.86 (d, J = 2.3 Hz, 1H), 7.51 (dd, J_1 = 8.6 Hz, J_2 = 2.3Hz, 1H), 7.04 (d, J = 8.6 Hz, 1H), 6.57 (dd, J_1 = 16.0 Hz, J_2 = 1.4 Hz, 1H), 6.20 (dd, J_1 = 16.0 Hz, J_2 = 5.7 Hz, 1H), 4.67 (brs, 1H), 4.43 (quint, J = 5.7 Hz, 1H), 4.22–3.98 (m, 2H), 3.96 (s, 3H), 3.89 (m, 1H), 2.70 (brs, 1H), 1.81–1.73 (m, 2H), 1.23 (d, J = 6.9 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.6, 152.3, 139.8, 133.4, 132.1, 129.9, 126.9, 123.3, 113.7, 70.4, 61.0, 56.8, 44.9, 44.8, 22.0, 14.7; HRMS (ESI$^+$) calcd. for $C_{16}H_{22}N_2NaO_6$ [M + Na]$^+$ 361.1370, found 361.1364.

Ethyl ((2S,4R,E)-6-(2-Fluoro-5-nitrophenyl)-4-hydroxyhex-5-en-2-yl)carbamate 3r-*anti* and Ethyl ((2S,4S,E)-6-(2-Fluoro-5-nitrophenyl)-4-hydroxyhex-5-en-2-yl)carbamate (3r-*syn*): Ketone **2r** (280 mg, 0.863 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 9:1 cyclohexane/EtOAc, 6:4 cyclohexane/EtOAc) providing **3r-*anti*** as a colorless oil (42.3 mg, 0.130 mmol) and **3r-*syn*** as a yellow oil (234.3 mg, 0.718 mmol). The alcohols **3r** were globally obtained in 98 % yield in a ratio of 85:15 in favor of the *syn* product. **3r-*anti***: TLC R_f = 0.42 (cyclohexane/EtOAc, 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.34 (dd, J_{HF} = 6.4 Hz, J_{HH} = 2.8 Hz, 1H), 8.07 (ddd, J_{HH} = 9.2 Hz, J_{HF} = 4.2 Hz, J_{HH} = 2.8 Hz, 1H), 7.17 (t, $J_{HF,HH}$ = 9.2 Hz, 1H), 6.81 (d, J_1 = 16.2 Hz, 1H), 6.46 (dd, J_1 = 16.2 Hz, J_2 = 5.0 Hz, 1H), 4.76 (d, J = 8.2 Hz, 1H), 4.40 (m,1H), 4.13 (q, J = 7.1 Hz, 2H), 4.01 (m, 1H), 1.71 (ddd, J_1 = 13.8 Hz, J_2 = 10.9 Hz, J_3 = 2.7 Hz, 1H), 1.54 (ddd, J_1 = 13.8 Hz, J_2 = 10.9 Hz, J_3 = 2.7 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H), 1.24 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.4 (d, J_{CF} = 260.2 Hz), 157.8, 144.5 (d, J_{CF} = 2.9 Hz), 137.7 (d, J_{CF} = 4.5 Hz), 126.5 (d, J_{CF} = 14.4 Hz), 124.0 (d, J_{CF} = 10.2 Hz), 123.3 (d, J_{CF} = 6.0 Hz), 119.6 (d, J_{CF} = 3.0 Hz), 116.8 (d, J_{CF} = 16.8 Hz), 68.2, 61.5, 45.9, 43.9, 21.6, 14.7; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}FN_2O_5$ [M + H]$^+$ 327.1351, found 327.1352. **3r-*syn***: TLC R_f = 0.28 (cyclohexane/EtOAc, 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.31 (dd, J_{HF} = 6.4 Hz, J_{HH} = 2.8 Hz, 1H), 8.06 (ddd, J_{HH} = 9.1 Hz, J_{HF} = 4.4 Hz, J_{HH} = 2.8 Hz, 1H), 7.14 (t, $J_{HF,HH}$ = 9.2 Hz, 1H), 6.72 (d, J_1 = 16.0 Hz, 1H), 6.46 (dd, J_1 = 16.0 Hz, J_2 = 5.3 Hz, 1H), 4.84 (d, J = 8.0 Hz, 1H), 4.45 (m, 1H), 4.12–3.82 (m, 3H), 3.14 (brs, 1H), 1.82–1.75 (m, 2H), 1.22 (d, J = 6.7 Hz, 3H), 1.16 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.4 (d, J_{CF} = 260.4 Hz), 156.6, 144.5 (d, J_{CF} = 2.6 Hz), 138.5, 126.3 (d, J_{CF} = 14.7 Hz), 124.1 (d, J_{CF} = 10.3 Hz), 123.3 (d, J_{CF} = 6.1 Hz), 119.7, 116.8 (d, J_{CF} = 24.9 Hz), 70.2, 61.0, 44.7, 44.6, 21.7, 14.6; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}FN_2O_5$ [M + H]$^+$ 327.1351, found 327.1352.

Ethyl ((2*R*,4*S*,*E*)-4-Hydroxy-6-(4-methoxyphenyl)hex-5-en-2-yl)-carbamate (3s-anti) and Ethyl ((2*R*,4*R*,*E*)-4-Hydroxy-6-(4-methoxyphenyl)hex-5-en-2-yl)carbamate (3s-syn). Ketone **2s** (159.0 mg, 0.546 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 8:2 cyclohexane/EtOAc to 6:4cyclohexane/EtOAc) providing **3s-*anti*** as a colorless oil (19.1 mg, 0.0651 mmol) and **3s-*syn*** as a colorlessoil (124.2 mg, 0.423 mmol). The alcohols **3s** were globally obtained in 90 % yield in a ratio of 87:13 in favor of the *syn* product. **3s-*anti***: TLC R_f = 0.39 (cyclohexane/EtOAc, 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 6.56 (d, J = 15.8 Hz, 1H), 6.08 (dd, J_1 = 15.8 Hz, J_2 = 6.1 Hz, 1H), 4.75 (d, J = 8.5 Hz, 1H), 4.35 (m, 1H), 4.13 (q, J = 7.1 Hz, 2H), 4.07–3.93 (m, 1H), 3.79 (s, 3H), 1.73 (ddd, J_1 = 13.9 Hz, J_2 = 10.6 Hz, J_3 = 3.3 Hz, 1H), 1.59–1.47 (ddd, J_1 = 13.9 Hz, J_2 = 10.5 Hz, J_3 = 3.0 Hz, 1H), 1.31–1.14 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 159.3, 157.5, 129.8, 129.6, 129.2, 127.7, 114.1, 69.0, 61.3, 55.4, 45.9, 44.1, 21.6, 14.7; HRMS (ESI$^+$) calcd. for $C_{16}H_{23}NaNO_4$ [M + Na]$^+$ 316.1519, found 316.1516. **3s-*syn***: TLC R_f = 0.27 (cyclohexane/EtOAc, 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 6.54 (d, J = 15.8 Hz, 1H), 6.09 (dd, J_1 = 15.8 Hz, J_2 = 6.3 Hz, 1H), 4.72 (brs, 1H), 4.40 (q, J = 6.3 Hz, 1H), 4.17–3.96 (m, 2H), 3.86 (m, 1H), 3.79 (s, 3H), 1.82–1.69 (m, 2H), 1.22 (d, J = 6.6 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) 159.4, 156.5, 130.1, 129.6, 129.4, 127.8, 114.1, 71.0, 61.1, 55.4, 45.0, 44.8, 21.9, 14.7; HRMS (ESI$^+$) calcd. for $C_{16}H_{23}NaNO_4$ [M + Na]$^+$ 316.1519, found 316.1516.

Ethyl ((2S,4R,E)-4-Hydroxy-6-(3-phenoxyphenyl)hex-5-en-2-yl)-carbamate (3t-*anti*) and Ethyl ((2S,4S,E)-4-Hydroxy-6-(3-phenoxyphenyl)hex-5-en-2-yl)carbamate (3t-*syn*): Ketone **2t** (400 mg, 1.13 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 9:1 cyclohexane/EtOAc to 5:5 cyclohexane/EtOAc) providing **3t-*anti*** as a colorless oil (54.1 mg, 0.152 mmol) and **3t-*syn*** as a colorless oil (280 mg,0.788 mmol). The alcohols **3t** were globally obtained in 83 % yield in a ratio of 84:16 in favor of the *syn* product. **3t-*anti***: TLC R_f = 0.40 (cyclohexane/EtOAc, 7:3); The product was not stable and deteriorated. **3t-*syn***: TLC R_f = 0.28 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34 (dd, J_1 = 8.5 Hz, J_2 = 7.4 Hz, 2H),

7.26 (t, *J* = 7.9 Hz, 1H), 7.13–7.07 (m, 2H), 7.02–6.99 (m, 3H), 6.88 (ddd, J_1 = 7.9 Hz, J_2 = 2.5 Hz, J_3 = 0.8 Hz, 1H), 6.55 (dd, J_1 = 15.9 Hz, J_2 = 1.1 Hz, 1H), 6.20 (dd, J_1 = 15.9 Hz, J_2 = 6.0 Hz, 1H), 4.69 (brs, 1H), 4.41 (q, *J* = 6.2 Hz, 1H), 4.19–3.97 (m, 2H), 3.89 (m, 1H), 2.57 (brs, 1H), 1.75 (t, *J* = 6.2 Hz, 2H), 1.21 (d, *J* = 6.7 Hz, 3H), 1.17 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.5, 157.2, 156.4, 138.7, 133.0, 129.8, 129.7, 129.0, 123.3, 121.6, 118.8, 118.1, 116.7, 70.5, 60.9, 44.8, 44.6, 21.8, 14.6; HRMS (ESI$^+$) calcd. for $C_{21}H_{25}NNaO_4$ [M + Na]$^+$ 378.1676, found 378.1673.

Ethyl ((2S,4R,E)-6-(4-Acetamidophenyl)-4-hydroxyhex-5-en-2-yl)carbamate (3u-*anti*) and Ethyl ((2S,4S,E)-6-(4-Acetamidophenyl)-4-hydroxyhex-5-en-2-yl)carbamate (3u-*syn*): Ketone **2u** (232 mg, 0.729 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 4:6 cyclohexane/EtOAc to 2:8 cyclohexane/EtOAc) providing **3u-*anti*** as a white solid (24.8 mg, 0.0774 mmol) and **3u-*syn*** as a white solid (182 mg, 0.568 mmol). The alcohols **3u** were globally obtained in 89 % yield in a ratio of 88:12 in favor of the *syn* product. **3u-*anti***: TLC R_f = 0.21 (cyclohexane/EtOAc, 7:3); Mp 122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.78 (brs, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.52 (d, *J* = 16.0 Hz, 1H), 6.13 (dd, J_1 = 16.0 Hz, J_2 = 6.0 Hz, 1H), 4.91 (d, *J* = 8.5 Hz, 1H), 4.34 (m, 1H), 4.11 (q, *J* = 7.0 Hz, 2H), 4.01 (m, 1H), 2.14 (s, 3H), 1.71 (ddd, J_1 = 13.8 Hz, J_2 = 10.6 Hz, J_3 = 3.2 Hz, 1H), 1.53 (ddd, J_1 = 13.8 Hz, J_2 = 10.6 Hz, J_3 = 3.2 Hz, 1H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.22 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.7, 157.6, 137.4, 133.0, 130.8, 129.1, 127.0, 120.1, 68.9, 61.3, 45.7, 44.1, 24.6, 21.6, 14.7; HRMS (ESI$^+$) calcd. for $C_{17}H_{24}N_2NaO_4$ [M + Na]$^+$ 343.1628, found 343.1626. **3u-*syn***: TLC R_f = 0.14 (cyclohexane/EtOAc); Mp 128 °C; ^{1}H NMR (400 MHz, MeOD) δ = 7.50 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 6.48 (d, *J* = 15.7 Hz, 1H), 6.17 (dd, J_1 = 15.7 Hz, J_2 = 6.6 Hz, 1H), 4.25 (q, *J* = 6.6 Hz, 1 H), 4.03 (q, *J* = 7.0 Hz, 2H), 3.78 (dquint, J_1 = 8.3 Hz, J_2 = 6.6 Hz, 1H), 2.14 (s, 3H), 1.82 (ddd, J_1 = 13.7 Hz, J_2 = 8.3 Hz, J_3 = 6.6 Hz, 1H), 1.62 (ddd, J_1 = 13.7 Hz, J_2 = 8.3 Hz, J_3 = 6.7 Hz, 1H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, MeOD) δ = 171.5, 158.4, 139.2, 134.3, 132.4, 130.7, 127.9, 121.1, 71.2, 61.5, 45.2, 45.2, 23.8, 21.6, 15.0; HRMS (ESI$^+$) calcd. for $C_{17}H_{24}N_2NaO_4$ [M + Na]$^+$ 343.1628, found 343.1626.

Ethyl ((2*R*,4*S*,*E*)-4-Hydroxyheptadec-5-en-2-yl)carbamate (3v-*anti*) and Ethyl ((2*R*,4*R*,*E*)-4-Hydroxyheptadec-5-en-2-yl)carbamate (3v-*syn*): Ketone **2v** (1.00 g, 2.95 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 9:1 cyclohexane/EtOAc to 6:4 cyclohexane/EtOAc) providing **3v-*anti*** as a colorless oil (150 mg, 0.439 mmol) and **3v-*syn*** as a colorless oil (785 mg, 2.30 mmol). The alcohols **3v** were globally obtained in 93 % yield in a ratio of 84:16 in favor of the *syn* product. **3v-*anti***: TLC R_f = 0.34 (cyclohexane/EtOAc, 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.66 (dtd, J_1 = 15.3 Hz, J_2 = 6.8 Hz, J_3 = 1.1 Hz, 1H), 5.44 (dd, J_1 = 15.4 Hz, J_2 = 6.3 Hz, 1H), 4.76 (d, *J* = 8.6 Hz, 1H), 4.17 (m, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.95 (m, 1H), 2.32 (t, *J* = 7.5 Hz, 1H), 2.00 (q, *J* = 6.8 Hz, 2H), 1.62 (ddd, J_1 = 14.0 Hz, J_2 = 10.4 Hz, J_3 = 3.5 Hz, 1H), 1.42 (ddd, J_1 = 14.0 Hz, J_2 = 10.1 Hz, J_3 = 3.0 Hz, 1H), 1.47–1.11 (m, 21H), 1.19 (d, *J* = 6.7 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.3, 131.8, 131.5, 68.8, 61.1, 45.6, 44.0, 32.3, 31.9, 29.7, 29.6, 29.6, 29.5, 29.4, 29.2, 29.2, 22.7, 21.4, 14.6, 14.1; HRMS (ESI$^+$) calcd. for $C_{20}H_{39}NaNO_3$ [M + Na]$^+$ 364.2822, found 364.2821. **3v-*syn***: TLC R_f = 0.24 (cyclohexane/EtOAc, 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.66 (dt, J_1 = 15.4 Hz, J_2 = 6.7 Hz, 1H), 5.46 (ddt, J_1 = 15.4 Hz, J_2 = 6.8 Hz, J_3 = 1.4 Hz, 1H), 4.72 (brs, 1H), 4.17 (q, *J* = 6.8 Hz, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 3.80 (m, 1H), 2.01 (q, *J* = 6.7 Hz, 2H), 1.93 (brs, 1H), 1.71–1.56 (m, 3H), 1.40–1.15 (m, 20H), 1.19 (d, *J* = 6.6 Hz, 3H), 0.88 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.8, 132.6, 132.4, 71.2, 60.8, 45.3, 44.7, 32.3, 32.1, 29.8, 29.6, 29.5, 29.4, 29.3, 22.8, 22.0, 14.8, 14.3; HRMS (ESI$^+$) calcd. for $C_{20}H_{39}NaNO_3$ [M + Na]$^+$ 364.2822, found 364.2823.

Benzyl (1*S*,3*S*,*E*)-(3-Hydroxy-1-phenylhex-4-en-1-yl)carbamate (3w-*anti*) and Benzyl (1*S*,3*R*,*E*)-(3-Hydroxy-1-phenylhex-4-en-1-yl)carbamate (3w-*syn*): Ketone **2w** (250 mg, 0.773 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, 8:2 cyclohexane/EtOAc to 7:3 cylohexane/EtOAc) providing **3w-*anti*** as a colorless oil (62.9 mg, 0.193 mmol) and **3w-*syn*** as a brown solid (138.2 mg, 0.425 mg). The alcohols **3w** were globally obtained in 80 % yield in a ratio of 69:31 in favor of the *syn* product. **3w-*anti***: TLC R_f = 0.25 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.45–7.18 (m, 10H), 5.63 (m, 1H), 5.51 (dd, *J* = 14.4 Hz, J_2 = 6.6 Hz, 1H), 5.13 (d, *J* = 12.2 Hz, 1H), 5.07 (d, *J* = 12.2 Hz, 1H), 4.96 (m, 1H), 4.08 (m, 1H), 2.79 (brs, 1H), 1.97 (ddd, J_1 = 14.0 Hz, J_2 = 4.3 Hz, J_3 = 9.0 Hz, 1H), 1.89 (ddd, J_1 = 14.0 Hz, J_2 = 3.7 Hz, J_3 = 8.7 Hz, 1H), 1.67 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.6, 141.8, 136.5, 133.3, 132.6, 128.8, 128.7, 128.3, 127.6, 127.0, 126.5, 69.4, 67.1, 52.7, 43.9, 17.8; HRMS (ESI$^+$) calcd. for $C_{20}H_{23}NaNO_3$ [M + Na]$^+$ 348.1570, found 348.1565. **3w-*syn***: TLC R_f = 0.18 (cyclohexane/EtOAc, 7:3); Mp 57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41–7.23 (m, 10H), 5.62 (m, 1H), 5.55–5.34 (m, 2H), 5.09 (d, *J* = 12.3 Hz, 1H), 5.03 (d, *J* = 12.3 Hz, 1H), 4.82 (m, 1H), 4.05 (m, 1H), 2.06–1.83 (m, 2H), 1.66 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 155.9, 142.6, 136.6, 133.7, 128.8, 128.6, 128.3, 128.2, 127.5, 127.5, 126.5, 71.0, 66.9, 53.7, 44.1, 17.8; HRMS (ESI$^+$) calcd. for $C_{20}H_{23}NaNO_3$ [M + Na]$^+$ 348.1570, found 348.1565.

Ethyl (4*R*,6*R*,*E*)-6-(((Benzyloxy)carbonyl)amino)-4-hydroxyhept-2-enoate (3x-*syn*): Ketone **2x** (124 mg, 0.388 mmol) was used in general procedure B. The crude product was purified by silica gel column chromatography (SiO_2, cyclohexane to 6:4 cyclohexane/EtOAc) providing **3x-*syn*** as a colorless oil (86 mg, 0.268 mmol) in 69 % yield. TLC R_f = 0.23 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40–7.28 (m, 5H), 6.96 (dd, J_1 = 15.7 Hz, J_2 = 4.2 Hz, 1H), 6.07 (dd, J_1 = 15.5 Hz, J_2 = 1.3 Hz, 1H), 5.12 (d, *J* = 12.2 Hz, 1H), 5.00 (d, *J* = 12.2 Hz, 1H), 4.76 (brs, 1H), 4.44 (m, 1H), 4.17 (d, *J* = 7.2 Hz, 2H), 3.92 (m, 1H), 2.98 (s, 1H), 1.89–1.66 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.22 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.7, 156.3, 150.4, 136.4, 128.6, 128.2, 128.1, 119.8, 69.0, 66.9, 60.6, 44.7, 43.8, 21.5, 14.3; HRMS (ESI$^+$) calcd. for $C_{17}H_{24}NO_5$ [M + H]$^+$ 322.1649, found 322.1639.

Synthesis of Carbonates 4 from Alcohols 3

Ethyl ((2*R*,4*R*,*E*)-4-((Methoxycarbonyl)oxy)-6-phenylhex-5-en-2-yl)carbamate (4a-*syn*): To a solution of alcohol **3a-*syn*** (110 mg, 0.418 mmol, 1 equiv.) in dry DCM (5 mL) at 0 °C was added anhydrous pyridine (135 μL, 1.67 mmol, 4.8 equiv.). The solution was stirred for 10 min then methyl chloroformate (195 μL, 2.52 mmol, 6 equiv.) was added dropwise at 0 °C. The reaction mixture was stirred for 30 min at 0 °C and overnight at room temperature. A 0.1 M HCl aqueous solution was added until pH 2. The aqueous layer was then extracted with DCM. The organic layer was washed with a saturated aqueous $NaHCO_3$, dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 8:2 cyclohexane/EtOAc) providing the carbonate **4a-*syn*** as a yellow solid in 80 % yield (107 mg, 0.333 mmol). TLC R_f = 0.43 (cyclohexane/EtOAc, 7:3); Mp 106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38 (d, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 6.70 (t, *J* = 15.9 Hz, 1H), 6.15 (dd, J_1= 15.9 Hz, J_2 = 7.1 Hz, 1H), 5.31 (td, J_1 = 7.1 Hz, J_2 = 6.7 Hz, 1H), 4.64 (brs, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 3.83 (m, 1H), 3.77 (s, 3H), 2.00 (ddd, J_1 = 14.8 Hz, J_2 =

7.1 Hz, J_3 = 6.7 Hz, 1H), 1.79 (m, 1H), 1.26–1.15 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.0, 155.2, 136.1, 133.6, 128.7, 128.3, 126.8, 126.3, 76.9, 60.8, 54.8, 44.2, 41.9, 21.8, 14.7; HRMS (ESI$^+$) calcd. for $C_{17}H_{23}NaNO_5$ [M + Na]$^+$ 344.1468, found 344.1465.

Ethyl ((2*R*,4*S*,*E*)-4-((Methoxycarbonyl)oxy)-6-phenylhex-5-en-2-yl)carbamate (4a-*anti*): To a solution of alcohol **3a-*anti*** (44 mg, 0.167 mmol, 1 equiv.) in dry DCM (2 mL) at 0 °C was added anhydrous pyridine (40 μL, 0.495 mmol, 3 equiv.). The solution was stirred for 10 min then methyl chloroformate (80 μL, 1.04 mmol, 6.2 equiv.) was added dropwise at 0 °C. These additions were repeated 2 times (cooling to 0 °C, addition of 3 equiv. of anhydrous pyridine, stirring for 10 min at 0 °C, slowly addition of 6 equiv. of methyl chloroformate, stirring at 0 °C for 30 min and overnight at room temperature) in order to complete reaction. A 0.1 M HCl aqueous solution was added until pH 2. The aqueous layer was then extracted with DCM. The organic layer was washed with a saturated aqueous $NaHCO_3$, dried with anhydrous MgSO4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 8:2 cyclohexane/EtOAc) providing the carbonate **4a-*anti*** as a yellow oil in 67 % yield (35.8 mg, 0.111 mmol). TLC R_f = 0.40 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37 (d, J = 7.1 Hz, 2H), 7.31 (t, J = 7.1 Hz, 2H), 7.24 (t, J = 7.1 Hz, 1H), 6.66 (d, J = 15.9 Hz, 1H), 6.13 (dd, J_1 = 15.9 Hz, J_2 = 7.6 Hz, 1H), 5.30 (dt, J_1 = 7.6 Hz, J_2 = 4.7 Hz, 1H), 4.59 (d, J = 6.5 Hz, 1H), 4.06 (q, J = 7.0 Hz, 2H), 3.88 (m, 1H), 3.76 (s, 3H), 1.94 (ddd, J_1 = 14.2 Hz, J_2 = 8.4 Hz, J_3 = 4.7 Hz, 1H), 1.80 (m, 1H), 1.24–1.16 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.0, 155.1, 136.1, 133.7, 128.7, 128.3, 126.8, 126.5, 76.4, 60.8, 54.8, 43.9, 41.8, 21.6, 14.7; HRMS (ESI$^+$) calcd. for $C_{17}H_{23}NaNO_5$ [M + Na]$^+$ 344.1468, found 344.1465.

tert*-Butyl ((2*R*,4*R*,*E*)-4-((Methoxycarbonyl)oxy)-6-phenylhex-5-en-2-yl)carbamate (4c-*syn*):** To a solution of alcohol **3c-*syn (201 mg, 0.690 mmol, 1 equiv.) in dry DCM (5 mL) at 0 °C was added anhydrous pyridine (223 μL, 2.76 mmol, 4 equiv.). The solution was stirred for 10 min then methyl chloroformate (267 μL, 3.46 mmol, 5 equiv.) was added dropwise at 0 °C. The reaction mixture was stirred for 30 min at 0 °C and overnight at room temperature. Methyl chloroformate (54 μL, 0.690 mmol, 1 equiv.) was again added dropwise at room temperature and the reaction mixture was stirred for 2 h. A 0.1 M HCl aqueous solution was added until pH 2. The aqueous layer was then extracted with DCM. The organic layer was washed with a saturated aqueous $NaHCO_3$, dried with anhydrous MgSO4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 8:2 cyclohexane/EtOAc) providing the carbonate **4c-*syn*** as a white solid in 91 % yield (219 mg, 0.627 mmol). TLC R_f = 0.70 (cyclohexane/EtOAc, 7:3); Mp 104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.39 (d, J = 7.4 Hz, 2H), 7.31 (t, J = 7.4 Hz, 2H), 7.25 (m, 1H), 6.68 (d, J = 15.9 Hz, 1H), 6.15 (dd, J_1 = 15.9 Hz, J_2 = 7.4 Hz, 1H), 5.31 (q, J = 7.4 Hz, 1H), 4.45 (brs, 1H), 3.80 (m, 1H), 3.78 (s, 3H), 1.99 (dd, J_1 = 14 Hz, J_2 = 7.4 Hz, J_3 = 6.8 Hz 1H), 1.77 (m, 1H), 1.44 (s, 9H), 1.18 (d, J = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 155.3, 155.2, 136.2, 133.7, 128.7, 128.3, 126.9, 126.4, 79.3, 77.0, 54.8, 43.8, 41.9, 28.5, 21.8; HRMS (ESI$^+$) calcd. for $C_{19}H_{27}NaNO_5$ [M + Na]$^+$ 372.1781, found 372.1788.

Procedure C: Synthesis of 1,2,3,6-Tetrahydropyridines 5 from Alcohols 3 or Carbonates 4: To a solution of alcohol **3a–x** or carbonate **4a/4c-*syn*** (1 equiv.) in DCE (0.03 M) was added the catalyst $PdCl_2(MeCN)_2$ (5 to 30 mol-%). The reaction mixture was then stirred at the temperature specified in the corresponding synthetic procedure (room temperature, 40 °C or reflux). The reaction was monitored by TLC and stopped by filtration through a pad of Celite. The solide was washed with DCM and the filtrate was concentrated. Conversions and *trans*/*cis* ratios were determined by ^{1}H-NMR integration analysis on crude mixtures. The crude was then purified by silica gel column chromatography as described in the corresponding synthetic procedure to give the tetrahydropyridines 5**a–x**. When separable, the two *trans* and *cis* stereoisomers were purified by column chromatography. Characterization were performed for the major and/or stable diastereoisomer.

Ethyl (2*R*,6*S*)-2-Methyl-6-phenyl-3,6-dihydropyridine-1(2H)-carboxylate (5a-*trans*): Alcohol **3a-*syn*** (100 mg, 0.380 mmol) was used in general procedure C. The reaction mixture was stirred at 40 °C for 3 h 20 min. The conversion, compared to the starting material, was 100 % and the ratio between the products **5a-*cis*** and **5a-*trans*** was 5:95 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (SiO_2, cyclohexane to 95:5 cyclohexane/EtOAc) providing a mixture of **5a-*cis*** and **5a-*trans*** (4:96) as a colorless oil in 61 % yield (56.7 mg, 0.231 mmol). **5a-*trans***: TLC R_f = 0.75 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31–7.22 (m, 4H), 7.20 (m, 1H), 5.76 (d, J = 10.4, 1H), 5.72 (d, J = 10.4 Hz, 1H), 5.07 (m, 1H), 4.55 (m, 1H), 4.21–3.77 (m, 2H), 2.62 (dd, J_1 = 14.8 Hz, J_2 = 5.8 Hz, 1H), 2.08 (dd, J_1 = 14.8 Hz, J_2 = 2.0 Hz, 1H), 1.25 (d, J = 6.5 Hz, 3H), 1.13–0.64 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.6, 144.6, 129.1, 128.4, 126.7, 126.2, 121.2, 61.1, 56.9, 47.0, 30.6, 19.4, 14.4; HRMS (ESI$^+$) calcd. for $C_{15}H_{20}NO_2$ [M + H]$^+$ 246.14886, found 246.1491.

Benzyl (2*R*,6*S*)-2-Methyl-6-phenyl-3,6-dihydropyridine-1(2H)-carboxylate (5b-*trans*): Alcohol **3b-*syn*** (102.0 mg, 0.313 mmol) was used in general procedure C. The reaction mixture was stirred at 40 °C for 6 h. The conversion, compared to the starting material, was 100 % and the ratio between the products **5b-*cis*** and **5b-*trans*** was 4:96 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane + 0.5 % NEt_3 to 95:5 cyclohexane/EtOAc + 0.5 % NEt_3) providing a mixture of **5b-*cis*** and **5b-*trans*** (5:95) as a yellow oil in 56 % yield (53.7 mg, 0.175 mmol). **5b-*trans*:** TLC R_f = 0.62 (cyclohexane/EtOAc, 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43–7.10 (m, 10H), 5.85–5.66 (m, 2H), 5.19 (m, 1H), 5.05 (d, J = 11.4 Hz, 1H), 4.94 (d, J = 11.4 Hz, 1H), 4.60 (m, 1H), 2.64 (dd, J_1 = 15.9 Hz, J_2 = 5.4 Hz 1H), 2.08 (m, 1H), 1.28 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.3, 144.5, 136.6, 129.1, 128.6, 128.4, 127.9, 127.8, 126.7, 126.1, 121.2, 67.1, 57.0, 47.3, 30.5, 19.5; HRMS (ESI$^+$) calcd. for $C_{20}H_{22}NO_2$ (M + H)$^+$ 308.1645, found 308.1649.

tert*-Butyl (2*R*,6*S*)-2-Methyl-6-phenyl-3,6-dihydropyridine-1(2H)-carboxylate (5c-*trans*):** To a solution of carbonate **4c-*syn (100 mg, 0.286 mmol) under argon in dry DCE (0.03 M) was added the catalyst $PdCl_2(MeCN)_2$ (22.3 mg, 0.0860 mmol, 0.3 equiv.). After 56 h at room temperature, the reaction mixture was refluxed because no significant conversion was observed by TLC. After 46 h of reflux, catalyst was added (15 mg, 0.0578 mmol, 0.2 equiv.). The reaction mixture was refluxed another 44 h. The reaction mixture was filtered through a pad of Celite which was then washed with DCM. The filtrate was concentrated. The conversion, compared to the starting material, was 46 % and the ratio between the products **5c-*cis*** and **5c-*trans*** was 2:98 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane + 0.5 % NEt_3 to 95:5 cyclohexane/EtOAc + 0.5 % NEt_3) providing **5c-*trans*** (3:97) as a colorless oil in 20 % yield (16 mg, 58.5 μmol). TLC R_f = 0.70 (cyclohexane/EtOAc, 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37–7.00 (m, 5H), 5.73–5.55 (m, 2H), 4.93 (m, 1H), 4.59 (m, 1H), 2.57 (dd, J_1 = 15.5 Hz, J_2 = 4.5 Hz, 1H), 2.06 (dd, J_1 = 15.5 Hz, J_2 = 5.0 Hz, 1H), 1.23 (d, J = 6.8 Hz, 3H), 1.22–1.08 (brs, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 155.7, 138.9, 129.2,

128.4, 126.5, 125.8, 120.8, 79.8, 56.9, 46.5, 30.6, 29.8, 28.2; HRMS (ESI$^+$) calcd. for $C_{17}H_{23}NO_2$ [M + Na]$^+$ 296.1621, found 296.1624.

Ethyl (2*R*,6*S*)-6-Phenyl-2-propyl-3,6-dihydropyridine-1(2H)-carboxylate (5d-*trans*): Alcohol **3d-*syn*** (24.8 mg, 0.0851 mmol) was used in general procedure C. The reaction mixture was stirred at 40 °C for 21 h. Because of the low conversion, the reaction mixture was then refluxed 2 h 30 min in order to complete reaction. The conversion, compared to the starting material, was 100 % and the ratio between the products **5d-*cis*** and **5d-*trans*** was 4:96 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane to 85:15 cyclohexane/EtOAc) providing a mixture of **5d-*cis*** and **5d-*trans*** (3:97) as a colorless oil in 81 % yield (18.9 mg, 0.0691 mmol). **5d-*trans***: TLC R_f = 0.70 (cyclohexane/EtOAc, 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40–7.22 (m, 4H), 7.22–7.11 (m, 1H), 5.73 (d, J = 10.5 Hz, 1H), 5.72 (d, J = 10.5 Hz, 1H), 5.05 (m,1H), 4.29 (m, 1H), 4.12–3.74 (m, 2H), 2.52 (ddd, J_1 = 17.0 Hz, J_2 = 5.3 Hz, J_3 = 2.7 Hz, 1H), 2.21 (d, J_1 = 17.0 Hz, J_2 = 3.9 Hz, 1H), 1.71–1.52 (m, 2H), 1.42–1.17 (m, 2H), 1.17–0.62 (m, 3H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.8, 144.5, 129.4, 128.4, 126.7, 126.3, 121.6, 61.0, 57.4, 51.2, 35.6, 28.0, 20.2, 14.3, 14.1; HRMS (ESI$^+$) calcd. for $C_{17}H_{24}NO_2$ [M + H]$^+$ 274.1802, found 274.1809.

Benzyl (2*R*,6*S*)-6-Phenyl-2-propyl-3,6-dihydropyridine-1(2H)-carboxylate (5e-*trans*): Alcohol **3e-*syn*** (24.6 mg, 69.6 μmol) was used in general procedure C. The reaction mixture was stirred at 40 °C for 24 h. Because of the low conversion, the reaction mixture was then refluxed 8 h. The conversion, compared to the starting material, by proton NMR, was 15 % and the ratio between the products **5e-*cis*** and **5e-*trans*** was up to 4:96 in favor of the *trans* product. Due to the low conversion and quantity of engaged product, **5e-*trans*** was not isolated as pur product. TLC R_f = 0.82 (cyclohexane/EtOAc, 7:3).

Benzyl (2*S*,6*R*)-2,6-Diphenyl-3,6-dihydropyridine-1(2H)-carboxylate 5f-*cis* and Benzyl (2*S*,6*S*)-2,6-Diphenyl-3,6-dihydropyridine-1(2H)-carboxylate (5f-*trans*): Alcohol **3f-*syn*** (23.4 mg, 0.0604 mmol) was used in general procedure C. The reaction mixture was stirred at 40 °C for 21 h. To complete the reaction, the reaction mixture was then refluxed for 2 h 30 min. The conversion, compared to the starting material, was 100 % and the ratio between the products **5f-*cis*** and **5f-*trans*** was 10:90 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane + 0.5 % NEt_3 to 95:5 cyclohexane/EtOAc + 0.5 % NEt_3) providing **5f-*cis*** (2 mg, 5.41 μmol) as a colorless oil and **5f–*trans*** (11.8 mg, 0.0319 mmol) as a white solid. The tetrahydropyridines **5f–*cis*** and **5f–*trans*** were obtained with a global yield of 62 %. **5f–*trans***: TLC R_f = 0.66 (cyclohexane/EtOAc, 8:2); Mp 132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.48–7.10 (m, 13H), 6.80 (m, 2H), 5.97 (m, 1H), 5.68 (m, 1H), 5.74–5.41 (m, 2H), 4.99 (d, J = 12.5 Hz, 1H), 4.86 (d, J = 12.5 Hz, 1H), 2.98 (ddt, J_1 = 16.7 Hz, J_2 = 3.0 Hz, J_3 = 6.0 Hz, 1H), 2.52 (dd, J_1 = 16.7 Hz, J_2 = 6.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.3, 140.0 136.4, 130.1, 128.7, 128.4, 128.3, 127.7, 127.6, 127.0, 126.8, 126.2 (2C), 121.3, 120.8, 67.2, 58.2, 54.9, 31.0; HRMS (ESI$^+$) calcd. for $C_{25}H_{24}NO_2$ [M + H]$^+$ 370.1802, found 370.1796.

Ethyl (2*S*,6*R*)-2-Methyl-6-(naphthalen-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate (5g-*trans*): Alcohol **3g-*syn*** (49.5 mg, 0.158 mmol) was used in general procedure C. The reaction mixture was stirred at room temperature for 3 h. The conversion, compared to the starting material, was 100 % and the ratio between the products **5g-*cis*** and **5g-*trans*** was 6:94 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (neutralized SiO_2, 100 % cyclohexane to 95:5 cyclohexane/EtOAc) providing a mixture of **5g-*cis*** and **5g-*trans*** (3:97) as a yellow oil in 58 % yield (26.9 mg, 0.0910 mmol). **5g-*trans***: TLC R_f = 0.20 (cyclohexane/EtOAc, 95:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.82–7.74 (m, 3H), 7.68 (s, 1H), 7.48–7.36 (m, 3H), 5.84–5.74 (m, 2H), 5.25 (m, 1H), 4.60 (m, 1H), 4.06–3.84 (m, 2H), 2.72 (dd, J = 16.4 Hz, J = 5.4 Hz, 1H), 2.13 (dd, J = 16.4 Hz, J = 5.3 Hz, 1H), 1.27 (d, J = 6.5 Hz, 3H), 1.07–0.78 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.6, 141.8, 133.5, 132.6, 128.9, 128.1, 127.7, 127.6, 125.9, 125.4, 124.6 (2C), 121.5, 61.1, 57.0, 47.0, 30.6, 19.3, 14.3; HRMS (ESI$^+$) calcd. for $C_{19}H_{22}NO_2$ [M + H]$^+$ 296.1645, found 296.1648.

Ethyl (2*S*,6*S*)-6-(4-Bromophenyl)-2-phenyl-3,6-dihydropyridine-1(2H)-carboxylate (5h-*trans*): Alcohol **3h-*syn*** (46.7 mg, 0.116 mmol) was used in general procedure C. The reaction mixture was stirred at 40 °C for 24 h. The conversion, compared to the starting material, was 100 % and the ratio between the products **5h-*cis*** and **5h-*trans*** was 5:95 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane +0.5 % NEt_3 to 95:5 cyclohexane/EtOAc +0.5 %NEt_3) providing a mixture of **5h-*cis*** and **5h-*trans*** (4:96) as a yellow oil in 71 % yield (31.7 mg, 0.0821 mmol). TLC R_f = 0.68 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44 (d, J = 8.4 Hz, 2H), 7.36–7.13 (m, 7H), 5.88 (m, 1H), 5.70 (m, 1H), 5.52 (m, 1H), 5.40 (m, 1H), 4.00–3.83 (m, 2H), 2.94 (ddt, J_1 = 16.8 Hz, J_2 = 6.0 Hz, J_3 = 2.6 Hz, 1H), 2.55 (dd, J_1 = 16.8 Hz, J_2 = 6.0 Hz, 1H), 0.90 (t, J = 7.1 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ = 156.6, 139.3, 136.9, 131.7, 129.6, 128.4, 128.1, 126.9, 126.1, 121.8, 61.5, 57.6, 54.5, 30.8, 14.3; HRMS (ESI$^+$) calcd. for $C_{20}H_{21}BrNO_2$ [M + H]$^+$ 386.0750, found 386.0752.

Ethyl (2*R*,6*S*)-6-(2-Bromophenyl)-2-methyl-3,6-dihydropyridine-1(2H)-carboxylate (5i-*trans*): Alcohol **3i-*syn*** (31.2 mg, 91.2 μmol) was used in general procedure C. After 24 h at 40 °C, the conversion, compared to the starting material, was 25 %. Because of the low conversion, the reaction mixture was then refluxed 30 h in order to complete reaction. The conversion, compared to the starting material, was then 66 % and the ratio between the products **5i-*cis*** and **5i-*trans*** was 2:98 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane + 0.5 % NEt_3 to 95:5 cyclohexane/EtOAc + 0.5 % NEt_3) providing **5i-*trans*** as a colorless oil in 38 % yield (11.1 mg, 34.2 μmol). TLC R_f = 0.35 (cyclohexane/EtOAc, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.49 (d, J_1 = 8.6 Hz, 1H), 7.28 (dd, J_1 = 7.3 Hz, J_2 = 1.8 Hz, 1H), 7.21 (td, J_1 = 7.3 Hz, J_2 = 1.4 Hz, 1H), 7.03 (ddd, J_1 = 8.0 Hz, J_2 = 7.3 Hz, J_3 = 1.8 Hz, 1H), 5.93–5.70 (m, 2H), 5.50 (m, 1H), 4.69 (m, 1H), 4.18–3.80 (m, 2H), 2.68 (dd, J_1 = 16.6 Hz, J_2 = 3.1 Hz, 1H), 2.07 (dd, J_1 = 16.6 Hz, J_2 = 6.2 Hz, 1H), 1.36–1.13 (m, 3H), 1.25 (d, J = 6.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.4, 144.2, 132.7, 128.0 (2CH), 126.6, 126.5, 126.4, 122.1, 121.5, 61.2, 55.7, 47.0, 30.3, 19.4, 14.3; HRMS (ESI$^+$) calcd. for $C_{15}H_{18}BrNaNO_2$ [M + Na]$^+$ 346.0413, found 346.0409.

Ethyl (2*R*,6*S*)-6-(3-Bromophenyl)-2-methyl-3,6-dihydropyridine-1(2H)-carboxylate (5j-*trans*): Alcohol **3j-*syn*** (50.7 mg, 0.148 mmol) was used in general procedure C. After 27 h at 40 °C, the conversion, compared to the starting material, was 40 %. Because of the low conversion, the reaction mixture was then refluxed 6 h in order to complete reaction. The conversion, compared to the starting material, was then 86 % and the ratio between the products **5j-*cis*** and **5j-*trans*** was 5:95 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane + 0.5 % NEt_3 to 95:5 cyclohexane/EtOAc + 0.5 % NEt_3) providing a mixture of **5j-*cis*** and **5j-*trans*** (3:97) as a colorless oil in 36 % yield (17.4 mg, 0.0537 mmol). TLC R_f = 0.68 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38 (t, J = 1.6 Hz, 1H),

7.31 (dt, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 7.19 (dt, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 5.76 (m, 1H), 5.69 (ddd, J_1 = 10.0 Hz, J_2 = 4.0 Hz, J_3 = 2.9 Hz, 1H), 5.05 (m, 1H), 4.54 (m, 1H), 4.16–3.78 (m, 2H), 2.63 (m, 1H), 2.07 (ddt, J_1 = 16.8 Hz, J_2 = 6.5 Hz, J_3 = 1.8 Hz, 1H), 1.27 (d, J = 6.5 Hz, 3H), 1.18–0.80 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.5, 147.1, 130.0, 129.8, 129.2, 128.4, 125.0, 122.5, 121.8, 61.3, 56.5, 47.0, 30.5, 19.3, 14.4; HRMS (ESI$^+$) calcd. for $C_{15}H_{19}BrNO_2$ [M + H]$^+$ 324.0594, found 324.0600.

Ethyl (2*R*,6*S*)-6-(4-Bromophenyl)-2-methyl-3,6-dihydropyridine-1(2H)-carboxylate (5k-*trans*): Alcohol **3k-*syn*** (74.6 mg, 0.218 mmol) was used in general procedure C. The reaction mixture was stirred at 40 °C for 1 h 45 min. The conversion, compared to the starting material, was 100 % and the ratio between the products **5k-*cis*** and **5k-*trans*** was 3:97 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane + 0.5 % NEt_3 to 95:5 cyclohexane/EtOAc 0.5 % NEt_3) providing a mixture of **5k-*cis*** and **5k-*trans*** (3:97) as a colorless oil in 84 % yield (59.2 mg, 0.183 mmol). TLC R_f = 0.61 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.39 (d, J = 8.5 Hz, 2H), 7.15 (d, J = 8.5 Hz, 2H), 5.74 (m, 1H), 5.68 (ddd, J_1 = 10.0 Hz, J_2 = 5.0 Hz, J_3 = 6.5 Hz, 1H), 5.06 (m, 1H), 4.53 (m, 1H), 4.10–3.88 (m, 2H), 2.62 (ddt, J_1 = 16.9 Hz, J_2 = 5.0 Hz, J_3 = 2.5 Hz, 1H), 2.08 (dddd, J_1 = 16.9 Hz, J_2 = 6.3 Hz, J_3 = 2.1 Hz, J_4 = 1.6 Hz, 1H), 1.24 (d, J = 6.5 Hz, 3H), 1.17–0.79 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.6, 143.8, 131.6, 128.6, 128.0, 121.6, 120.3, 61.3, 56.4, 47.0, 30.5, 19.3, 14.5; HRMS (ESI$^+$) calcd. for $C_{15}H_{19}BrNO_2$ [M + H]$^+$ 324.0594, found 324.0580.

Ethyl (2*S*,6*R*)-6-(4-Fluorophenyl)-2-methyl-3,6-dihydropyridine-1(2H)-carboxylate (5l-*trans*): Alcohol **3l-*syn*** (49.4 mg, 0.176 mmol) was used in general procedure C. The reaction mixture was stirred at room temperature for 1 h 30 min. The conversion, compared to the starting material, was 100 % and the ratio between the products **5l-*cis*** and **5l-*trans*** was 3:97 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (neutralized SiO_2, cyclohexane to 95:5 cyclohexane/EtOAc) providing a mixture of **5l-*cis*** and **5l-*trans*** (2:98) as a colorless oil in 67 % yield (31 mg, 0.118 mmol). TLC R_f = 0.37 (*cis*), 0.33 (*trans*) (cyclohexane/EtOAc, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.22 (dd, J_1 = 8.4 Hz, J_2 = 5.6 Hz, 2H), 6.96 (t, $J_{HH,HF}$ = 8.4 Hz, 2H), 5.74 (m, 1H), 5.69 (ddd, J_1 = 10.0 Hz, J_2 = 4.4 Hz, J_3 = 6.4 Hz, 1H), 5.06 (s, 1H), 4.52 (m, 1H), 4.13–3.86 (m, 2H), 2.62 (ddd, J_1 = 16.7 Hz, J_2 = 4.4 Hz, J_3 = 2.4 Hz, 1H), 2.07 (dddd, J_1 = 16.8 Hz, J_2 = 6.4 Hz, J_3 = 1.8 Hz, J_4 = 1.4 Hz, 1H), 1.25 (d, J = 6.5 Hz, 3H), 1.16–0.92 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 161.8 (d, J_{CF} = 244 Hz), 156.7, 140.4, 129.1, 127.9 (d, J_{CF} = 8 Hz), 121.4, 115.3 (d, J_{CF} = 21 Hz), 61.3, 56.3, 47.1, 30.6, 19.4, 14.6; HRMS (ESI$^+$) calcd. for $C_{15}H_{19}NO_2$ [M + H]$^+$ 264.1394, found 264.1394.

Ethyl (2*S*,6*R*)-2-Methyl-6-(3-nitrophenyl)-3,6-dihydropyridine-1(2H)-carboxylate (5o-*trans*): Alcohol **3o-*syn*** (43.2 mg, 0.140 mmol) was used in general procedure C with 30 mol-% of $PdCl_2(MeCN)_2$. The reaction mixture was stirred at room temperature for 24 h. The conversion, compared to the starting material, was 100 % and no *cis* product was observed. The crude mixture was purified by silica gel column chromatography (neutralized SiO_2, 100 % cyclohexane to 9:1 cyclohexane/EtOAc) providing **5o-*trans*** as a yellow oil in 27 % yield (10.9 mg, 0.0375 mmol). No cyclization was observed when the reaction was performed at 40 °C or reflux with 5 mol-% of catalyst. TLC R_f = 0.23 (cyclohexane/EtOAc, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.10 (t, J = 2.0 Hz, 1H), 8.06 (ddd, J_1 = 7.8 Hz, J_2 = 2.0 Hz, J_3 = 1.1 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 7.8 Hz, 1H), 5.82 (m, 1H), 5.70 (ddd, J_1 = 10.0 Hz, J_2 = 4 Hz, J_3 = 3.0 Hz, 1H), 5.12 (m, 1H), 4.59 (m, 1H), 4.15–3.88 (m, 2H), 2.70 (m, 1H), 2.12 (ddt, J_1 = 17.1 Hz, J_2 = 6.4 Hz, J_3 = 1.8 Hz, 1H), 1.36–0.76 (m, 3H), 1.26 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.5, 148.6, 147.0, 132.6, 129.4, 127.9, 122.4, 121.9, 121.3, 61.5, 56.4, 47.0, 30.5, 19.2, 14.5; HRMS (ESI$^+$) calcd. for $C_{15}H_{19}N_2O_4$ [M + H]$^+$ 291.1339, found 291.1339.

Ethyl (2*S*,6*R*)-6-(4-Methoxy-3-nitrophenyl)-2-methyl-3,6-dihydropyridine-1(2H)-carboxylate (5q-*trans*): Alcohol **3q-*syn*** (51 mg, 0.151 mmol) was used in general procedure C. The reaction mixture was stirred at room temperature for 22 h. The conversion, compared to the starting material, was 100 % and the ratio between the products **5q-*cis*** and **5q-*trans*** was 4:96 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (neutralized SiO_2, 9:1 cyclohexane/EtOAc to 8:2 cyclohexane/EtOAc) providing **5q-*cis*** (2 mg, 6.24 μmol), **5q-*trans*** (36.1 mg, 0.113 mmol) and a mixture of **5q-*cis*** and **5q-*trans*** (15:85) (5 mg, 0.0156 mmol) as colorless oils. The tetrahydropyridines were obtained with a global yield of 89 %. Due to low quantity obtained for **5q-*cis*,** only **5q-*trans*** the major product was described. TLC R_f = 0.85 (cyclohexane/EtOAc, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.73 (d, J = 2.2 Hz, 1H), 7.46 (dd, J_1 = 8.6 Hz, J_2 = 2.2 Hz, 1H), 7.02 (d, J = 8.6 Hz, 1H), 5.80 (m, 1H), 5.67 (dt, J_1 = 9.9 Hz, J_2 = 3.7 Hz, 1H), 5.56 (m, 1H), 4.52 (m, 1H), 4.12–3.93 (m, 2H), 3.91 (s, 3H), 2.64 (m, 1H), 2.09 (ddt, J_1 = 16.9 Hz, J_2 = 6.5 Hz, J_3 = 1.7 Hz, 1H), 1.23 (d, J = 6.8 Hz, 3H), 1.20–0.96 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.6, 151.9, 139.5, 137.0, 132.6, 128.2, 123.8, 122.2, 113.5, 61.4, 56.7, 55.7, 47.0, 30.5, 19.2, 14.5; HRMS (ESI$^+$) calcd. for $C_{16}H_{21}N_2O_5$ [M + H]$^+$ 321.1445, found 321.1447.

Ethyl (2*R*,6*R*)-6-(4-Methoxyphenyl)-2-methyl-3,6-dihydropyridine-1(2H)-carboxylate 5s-*cis* and Ethyl (2*R*,6*S*)-6-(4-Methoxyphenyl)-2-methyl-3,6-dihydropyridine-1(2H)-carboxylate (5s-*trans*): Alcohol **3s-*syn*** (48.0 mg, 0.164 mmol) was used in general procedure C. The reaction mixture was stirred at 40 °C for 1 min. The conversion, compared to the starting material, was 100 % and the ratio between the products **5s-*cis*** and **5s-*trans*** was 79:21 in favor of the *cis* product. The crude mixture was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane + 0.5 % NEt_3 to 95:5 cyclohexane/EtOAc + 0.5 NEt_3) providing **5s–*cis*** (19 mg. 69.0 μmol) and two mixtures of **5s–*cis*** and **5s–*trans*** (44:56 and 10:90) (10.7 mg, 38.9 μmol and 4.3 mg, 15.6 μmol) as a colorless oils. The tetrahydropyridines **5s–*cis*** and **5s–*trans*** were obtained with a global yield of 75 %.

Alcohol **3s-*syn*** (26.0 mg, 88.6 μmol mmol) was used in general procedure C. The reaction mixture was stirred at room temperature for 25 min. The conversion, compared to the starting material, was 100 % and the ratio between the products **5s-*cis*** and **5s-*trans*** was 79:21 in favor of the *cis* product. The crude mixture was purified by silica gel column chromatography (SiO_2, 100 % cyclohexane + 0.5 % NEt_3 to 95:5 cyclohexane/EtOAc + 0.5 NEt_3) providing two mixtures of **5s-*cis*** and **5s-*trans*** (96:4 and 53:47) (4.3 mg, 15.6 μmol and 7.4 mg, 26.9 μmol) as a colorless oils. The tetrahydropyridines **5s-*cis*** and **5s-*trans*** were obtained with a global yield of 48 %. **5s-*cis***: TLC R_f = 0.55 (cyclohexane/EtOAc, 7:3); The product was not stable and quickly deteriorated. **5s-*trans***: TLC R_f = 0.50 (cyclohexane/EtOAc, 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.18 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 5.80–5.65 (m, 2H), 5.04 (m, 1H), 4.54–4.42 (m, 1H), 4.11–3.90 (m, 2H), 3.78 (s, 3H), 2.61 (ddd, J_1 = 16.7 Hz, J_2 = 5.7 Hz, J_3 = 2.6 Hz, 1H), 2.07 (ddd, J_1 = 16.7 Hz, J_2 = 6.2 Hz, J_3 = 2.4 Hz, 1H), 1.6 (d, J = 6.5 Hz, 3H), 1.17–0.92 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 158.4, 156.6, 136.5, 129.4, 127.5, 121.0, 113.8, 61.0, 56.3, 55.3, 47.1, 30.6, 19.4, 14.5; HRMS (ESI$^+$) calcd. for $C_{16}H_{22}NO_3$ [M + H]$^+$ 276.1594, found 276.1599.

Ethyl (2*S*,6*R*)-2-Methyl-6-(3-phenoxyphenyl)-3,6-dihydropyridine-1(2H)-carboxylate (5t-*trans*): Alcohol **3t-*syn*** (49.4 mg, 0.139 mmol) was used in general procedure C. The reaction mixture was stirred at room temperature for 23 h. The conversion, compared to the starting material, was 100 % and the ratio between the products **5t-*cis*** and **5t-*trans*** was 2:98 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (neutralized SiO_2, 100 % cyclohexane to 95:5 cyclohexane/EtOAc) providing a mixture of **5t-*cis*** and **5t-*trans*** (3:97) as a yellow oil in 78 % yield (36.5 mg, 0.108 mmol). TLC R_f = 0.40 (cyclohexane/EtOAc, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.32 (dd, J_1 = 7.7 Hz, J_2 = 7.4 Hz, 2H), 7.23 (t, J = 7.9 Hz, 1H), 7.07 (t, J = 7.4 Hz, 1H), 7.01 (d, J = 7.9 Hz, 1H), 6.98 (d, J = 7.7 Hz, 2H), 6.94 (t, J = 1.8 Hz, 1H), 6.80 (dd, J_1 = 7.9 Hz, J_2 = 1.8 Hz, 1H), 5.75 (d, J = 10.0 Hz, 1H), 5.72 (d, J = 10.0 Hz, 1H), 5.03 (m, 1H), 4.52 (m, 1H), 4.15–3.86 (m, 2H), 2.58 (dd, J_1 = 15.0 Hz, J_2 = 5.8 Hz, 1H), 2.05 (dd, J_1 = 15.0 Hz, J_2 = 2.5 Hz, 1H), 1.24 (d, J = 6.5 Hz, 3H), 1.16–0.94 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 157.4, 157.2, 156.5, 146.9, 129.8, 129.7, 128.7, 123.2, 121.5, 121.0, 118.8, 116.9, 116.7, 61.1, 56.6, 46.9, 30.5, 19.4, 14.5; HRMS (ESI$^+$) calcd. for $C_{21}H_{24}NO_3$ [M + H]$^+$ 338.1751, found 338.1737.

Ethyl (2*S*,6*R*)-6-(4-Acetamidophenyl)-2-methyl-3,6-dihydropyridine-1(2H)-carboxylate (5u-*trans*): Alcohol **3u-*syn*** (50.7 mg, 0.158 mmol) was used in general procedure C. Due to a poor solubility of the product in DCE, the solution of **3u-*syn*** in DCE was 0.015 M instead of 0.03 M. The reaction mixture was stirred at room temperature for 1 h. The conversion, compared to the starting material, was 100 % and the ratio between the products **5u-*cis*** and **5u-*trans*** was 26:74 in favor of the *trans* product. The crude mixture was purified by silica gel column chromatography (neutralized SiO_2, 8:2 cyclohexane/EtOAc to 5:5 cyclohexane/EtOAc) providing a mixture of **5u-*cis*** (4.8 mg, 0.0159 mmol), **5u-*trans*** (28.1 mg, 0.0929 mmol) and a mixture of **5u-*cis*** and **5u-*trans*** (38:62) (1.3 mg, 4.3 μmol) as a colorless oils. The tetrahydropyridines **5u-*cis*** and **5u-*trans*** were obtained with a global yield of 71 %. **5u-*cis***: TLC R_f = 0.20 (cyclohexane/EtOAc, 6:4); The product was not stable and deteriorated. **5u-*trans***: TLC R_f = 0.15 (cyclohexane/EtOAc, 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.76 (brs, 1H), 7.37 (d, J = 8.1 Hz, 2H), 7.16 (d, J = 8.1 Hz, 2H), 5.76–5.63 (m, 2H), 5.02 (m, 1H), 4.50 (m, 1H), 4.23–3.83 (m, 2H), 2.60 (dd, J_1 = 16.4 Hz, J_2 = 5.4 Hz, 1H), 2.16–1.97 (m, 1H), 2.11 (s, 3H), 1.27 (d, J = 6.7 Hz, 3H), 1.26–0.94 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.6, 156.6, 140.2, 136.7, 129.0, 126.7, 121.1, 120.1, 61.2, 56.4, 47.0, 30.5, 24.5, 19.4, 14.5; HRMS (ESI$^+$) calcd. for $C_{17}H_{23}N_2O_3$ [M + H]$^+$ 303.1703, found 303.1701.

Acknowledgments

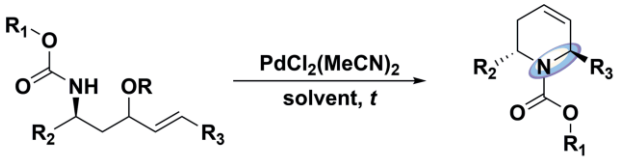
Computations have been performed on the supercomputer facilities of the Mésocentre Clermont Auvergne. We acknowledge the CNRS and the Ministère de l'Enseignement Supérieur et de la Recherche for providing research facilities and financial support.

Keywords: Tetrahydropyridines · Intramolecular allylic amination · Diastereoselective cyclization · Palladium catalysis

[1] a) N. N. Mateeva, L. L. Winfield, K. K. Redda, *Curr. Med. Chem.* **2005**, *12*, 551–571; b) F.-X. Felpin, J. Lebreton, *Eur. J. Org. Chem.* **2003**, *2003*, 3693–3712; c) C. Allais, W. R. Roush, *Org. Lett.* **2017**, *19*, 2646–2649.
[2] a) S. Chen, B. Q. Mercado, R. G. Bergman, J. A. Ellman, *J. Org. Chem.* **2015**, *80*, 6660–6668; b) M. G. P. Buffat, E. J. Thomas, *Tetrahedron* **2016**, *72*, 451–463; c) X. E. Hu, N. K. Kim, B. Ledoussal, A.-O. Colson, *Tetrahedron Lett.* **2002**, *43*, 4289–4293; d) R. Kumar, R. Chandra, *Adv. Heterocycl. Chem.* **2001**, *78*, 269–313.
[3] a) Y. Dudognon, J. Rodriguez, T. Constantieux, X. Bugaut, *Eur. J. Org. Chem.* **2018**, *2018*, 2432–2442; b) F. A. Davis, H. Xu, J. Zhang, *J. Org. Chem.* **2007**, *72*, 2046–2052; c) S. M. Hande, N. Kawai, J. Uenishi, *J. Org. Chem.* **2009**, *74*, 244–253; d) S. Mix, S. Blechert, *Adv. Synth. Catal.* **2007**, *349*, 157–160; e) P. Das, J. T. Njardarson, *Org. Lett.* **2015**, *17*, 4030–4033; f) M. Ferles, J. Pliml, *Adv. Heterocycl. Chem.* **1970**, *12*, 43–101.
[4] F.-X. Felpin, J. Lebreton, *Curr. Org. Synth.* **2004**, *1*, 83–109.
[5] a) T. Xin, S. Okamoto, F. Sato, *Tetrahedron Lett.* **1998**, *39*, 6927–6930; b) X. Dong, Y. Han, F. Yan, Q. Liu, P. Wang, K. Chen, Y. Li, Z. Zhao, Y. Dong, H. Liu, *Org. Lett.* **2016**, *18*, 3774–3777.
[6] F.-X. Felpin, K. Boubekeur, J. Lebreton, *Eur. J. Org. Chem.* **2003**, *2003*, 4518–4527.
[7] P. G. M. Wuts, Y. W. Jung, *J. Org. Chem.* **1988**, *53*, 1957–1965.
[8] J. Åhman, T. Jarevång, P. Somfai, *J. Org. Chem.* **1996**, *61*, 8148–8159.
[9] a) G. Wang, Y. Mao, L. Liu, *Org. Lett.* **2016**, *18*, 6476; b) M. B. Tait, S. Butterworth, J. Clayden, *Org. Lett.* **2015**, *17*, 1236–1239.
[10] Y. N. Bubnov, E. V. Klimkina, A. V. Ignatenko, I. D. Gridnev, *Tetrahedron Lett.* **1997**, *38*, 4631–4634.
[11] I. Abrunhosa-Thomas, A. Plas, A. Vogrig, N. Kandepedu, P. Chalard, Y. Troin, *J. Org. Chem.* **2013**, *78*, 2511–2526.
[12] I. Abrunhosa-Thomas, A. Plas, N. Kandepedu, P. Chalard, Y. Troin, *Beilstein J. Org. Chem.* **2013**, *9*, 486–495.
[13] a) E. Schweizer, T. Gaich, L. Brecker, J. Mulzer, *Synthesis* **2007**, 3807–3814; b) J. W. Bae, S. H. Lee, Y. J. Jung, C.-O. M. Yoon, C. M. Yoon, *Tetrahedron Lett.* **2001**, *42*, 2137–2139; c) A. C. Rodriguez, A. P. Ramos, G. E. Hawkes, F. Berti, M. Resmini, *Tetrahedron: Asymmetry* **2004**, *15*, 1847–1855.
[14] a) H. Yokoyama, Y. Hayashi, Y. Nagasawa, H. Ejiri, M. Miyazawa, Y. Hirai, *Tetrahedron* **2010**, *66*, 8458–8463; b) H. Makabe, L. K. Kong, M. Hirota, *Org. Lett.* **2003**, *5*, 27–29; c) C. Welter, A. Dahnz, B. Brunner, S. Streiff, P. Dübon, G. Helmchen, *Org. Lett.* **2005**, *7*, 1239–1242; d) C. Gnamm, C. M. Krauter, K. Brödner, G. Helmchen, *Chem. Eur. J.* **2009**, *15*, 2050–2054.
[15] Z. Wang, S. Li, B. Yu, H. Wu, Y. Wang, X. Sun, *J. Org. Chem.* **2012**, *77*, 8615–8620.
[16] a) P. Kothandaraman, S. J. Foo, P. W. H. Chan, *J. Org. Chem.* **2009**, *74*, 5947–5952; b) J. Jing, X. Huo, J. Shen, J. Fu, Q. Meng, W. Zhang, *Chem. Commun.* **2017**, *53*, 5151–5154.
[17] a) S. Sawadjoon, P. J. R. Sjöberg, A. Orthaber, O. Matsson, J. S. M. Samec, *Chem. Eur. J.* **2014**, *20*, 1520–1524; b) H. Kinoshita, H. Shinokubo, K. Oshima, *Org. Lett.* **2004**, *6*, 4085–4088; c) N. A. Butt, W. Zhang, *Chem. Soc. Rev.* **2015**, *44*, 7929–7967; d) S. Akkarasamiyo, S. Sawadjoon, A. Orthaber, J. S. M. Samec, *Chem. Eur. J.* **2018**, *24*, 3488–3498.
[18] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, *Gaussian 09, Revision ABCD.0123*, Gaussian, Inc., Wallingford CT, **2016.**
[19] K. L. Granberg, J.-E. Bäckvall, *J. Am. Chem. Soc.* **1992**, *114*, 6858–6863.

Received: October 16, 2019

Tetrahydropyridine Synthesis



R_1 = Et, Bn, *t*-Bu
R_2 = Alkyl, Aryl
R_3 = Aryl, Alkyl, CO_2Et
R = H, CO_2Me

17 examples, *de* up to 100%
Pd-catalyzed intramolecular allylic amination
Mild reaction conditions
High selectivity to 2,6-*trans*-TP

A highly diastereoselective palladium-catalyzed intramolecular allylic amination from non-activated allylic alcohols is reported, leading to 2,6-disubstituted-1,2,3,6-tetrahydropyridines under mild conditions in moderate to good yields.

DOI: 10.1002/ejoc.201901520