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A Configurational Switch Based on Iridium-Catalyzed Allylic Cyclization: Application in Asymmetric Total Syntheses of Prosopis, Dendrobate, and Spruce Alkaloids

Christian Gnamm, Kerstin Brödner, Caroline M. Krauter, and Günter Helmchen*[a]

Dedicated to Professor Werner Tochtermann on the occasion of his 75th birthday

Abstract: A method for the stereoselective synthesis of 2,6-disubstituted piperidines has been developed that is based on the use of an intramolecular iridium-catalyzed allylic substitution as a configurational switch. The procedure allows the preparation of 2-vinylpiperidines with enantiomeric excesses (*ee*) of greater than 99%. As applications, total syntheses of piperidine alkaloids have been elaborated, most often by using Ru-catalyzed cross-metatheses as a key step for introduction of a side chain. Asymmetric total syntheses of the prosopis alkaloids (+)-prosopinine, (+)-prosophylline, (+)-prosopine, and of the dendrobate alkaloid (+)-241D and its C6 epimer are described.

Keywords: alkaloids · allylic amination · heterocycles · iridium · natural products · total synthesis

Introduction

Piperidine alkaloids[1] often possess potent biological activity and are therefore of interest for organic and medicinal chemists.[2] Structural types that were addressed in our work are described in Figure 1.[3] Commonly, construction of the piperidine involves ring closure by C–N bond formation. As most alkaloids possess chirality centers at C2 and C6, stereoselectivity is essential for this step. High levels of diastereoselectivity have been achieved in substrate-controlled cyclizations, for example, by allylic substitution.[4] However, there is a drawback of this approach in that the selectivity of the cyclization process is predetermined by the substrate configuration and only one of a pair of diastereomers can usually be provided.

Recently we have communicated a method using the Ir-catalyzed allylic substitution[5] as a configurational switch that allows either of a pair of diastereomeric cyclization products to be generated selectively by external (reagent) control (Scheme 1).[6] To the best of our knowledge, such a configurational switch has not been achieved for an allylic substitution,[7,8] whereas it has been developed for other reagent-controlled reactions such as the Brown allylation,[9] and most prominently, the Katsuki–Sharpless epoxidation.[10] In our previous communication,[6] we have presented one example of the configurational switch, which was used in a synthesis of the 4-hydroxypiperidine (+)-241D. In the meantime this work was considerably extended to include a variety of 3-hydroxypiperidines such as the prosopis alkaloids listed in Figure 1. Here we present a full account of our investigations.

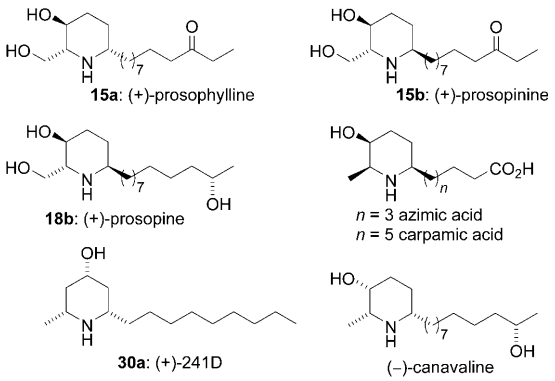

Figure 1. Examples of naturally occuring 2,6-dialkylpiperidine alkaloids.

[a] Dipl.-Chem. C. Gnamm, K. Brödner, C. M. Krauter, Prof. Dr. G. Helmchen
Organisch-Chemisches Institut der Universität Heidelberg
Im Neuenheimer Feld 270, 69120 Heidelberg (Germany)
Fax: (+49) 6221-544205
E-mail: g.helmchen@oci.uni-heidelberg.de

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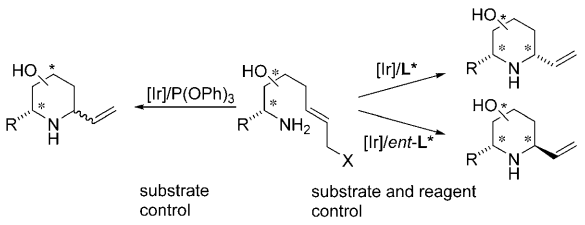
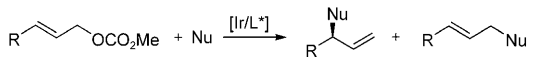


Scheme 1. Double stereodifferentiation: interplay between substrate- and reagent-induced selectivity ([Ir] = Ir catalyst; **L*** = **L1** or **L2**).

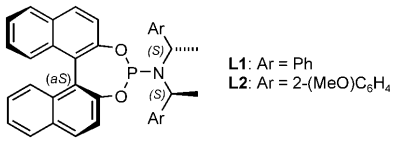
Results and Discussion

Synthesis of prosopis alkaloids: The alkaloids (+)-prosopinine (**15b**) and (+)-prosopine (**18b**) were isolated by Ratle et al. from leaves of a *Prosopis africana* species in 1966.[11] They possess antihypertensive and local anesthetic properties as well as antibiotic activity against *Staphyllococcus aureus* and are being used by African natives against toothache and for the treatment of wounds.[12] Their relative and absolute configuration was disclosed in 1972 by the same group,[13] which also reported the isolation of racemic (±)-prosophylline in the same year.[14] Since then, various syntheses have been reported for prosopinine,[15,16] prosophylline,[17,18] and their desoxo derivatives.[19,20]

Ir-catalyzed allylic amination: The Ir-catalyzed allylic substitution, introduced in 1997,[21] has emerged as a versatile tool for the enantioselective construction of allylic stereocenters.[5] High degrees of enantio- and regioselectivity in favor of the branched substitution products can routinely be obtained (Scheme 2). Of particular value are aminations[22]

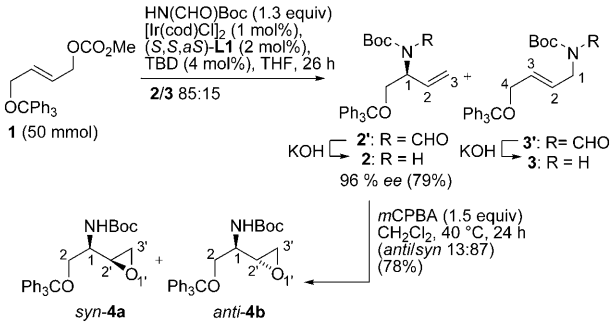


Scheme 2. General scheme for iridium-catalyzed allylic substitution.



with diacylimines, which react with carbonates to give allylamines with a broad range of N-protecting groups suitable in alkaloid synthesis, such as *tert*-butoxycarbonyl (Boc) and carbobenzyloxy (Cbz).[23] Furthermore, salt-free reaction conditions can be applied with diacylimines.[24]

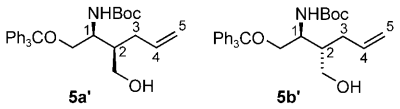
The catalyst was prepared from [{IrCl(cod)}$_2$] (cod = 1,5-cyclooctadiene) and a chiral phosphoramidite **L*** by activation with a strong base. The commercially available ligand **L1**, introduced by Feringa,[25] and the usually superior ligand **L2**, developed by Alexakis, were used.[26] The Ir-catalyzed amination of the carbonate **1** with HN(CHO)Boc as ammonia equivalent has already been described by us (Scheme 3).[23a] The present project was used to test the scale-up capability. The reaction was run on a scale of 50 mmol with a reduced catalyst loading of 1 mol% of Ir. After cleavage of the formyl group, the allylic amide **2** was obtained with 96% *ee* in 79% yield.



Scheme 3. Synthesis of the epoxides *anti*-**4** and *syn*-**4** (TBD = 1,5-triazabicyclo[4.4.0]-dec-5-ene).

Synthesis of the cyclization precursor 9: For the introduction of the OH group of the piperidine ring, epoxidation or dihydroxylation of the amination product **2** was planned. Thus, treatment of **2** with *meta*-chloroperbenzoic acid (*m*CPBA) gave the epoxides **4a** and **4b** as an 87:13 mixture of diastereoisomers in 78% yield, in favor of *syn*-**4a** as expected (Scheme 3).[27] The epoxides were separated by preparative HPLC and crystallization, and the relative configuration of *syn*-**4a** was confirmed by single-crystal X-ray structural analysis.[28] Several other reagents and methods for the epoxidation of **2** as well as various dihydroxylation methods were tested, but none of them provided a useful access to the requisite *anti*-**4b** or gave otherwise improved results. Similar results were obtained with the corresponding *N*-phthaloyl derivative (formula not shown).

The epoxides *syn*-**4a** and *anti*-**4b** were each subjected to the copper-mediated addition of allylmagnesium chloride,[29] which generated the alcohols *syn*-**5a** and *anti*-**5b** in 78 and 83% yield, respectively (Scheme 4). In both cases < 10% of the byproduct, **5a′** and **5b′**, respectively, resulting from reaction of the cuprate at C2′ of the epoxide was formed.



The *syn*-alcohol **5a** was transformed into the *anti*-alcohol **5b** by inversion of configuration using the Mitsunobu reaction followed by saponification of the resultant acetate. Initially, this seemingly simple task met with difficulties. It turned out to be crucial, concerning yield and reproducibility, to add diisopropyl azodicarboxylate *after* having stirred a solution of the alcohol, PPh_3, and AcOH for a period of

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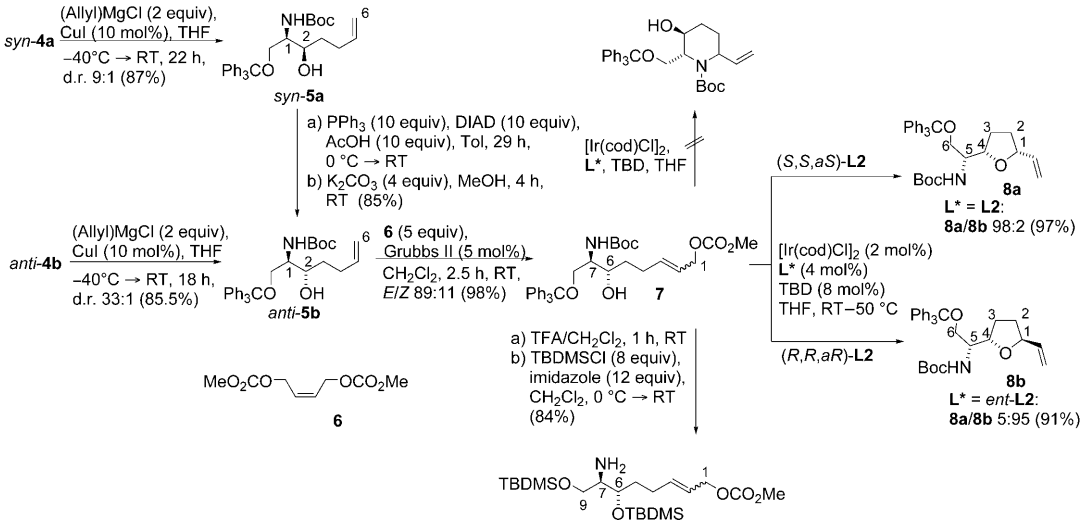


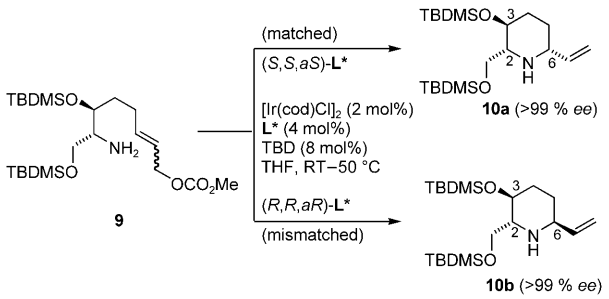
Scheme 4. Synthesis of the cyclization precursor **9**.

15 min (yield: 85%). Next, **5b** was reacted with the bis-carbonate **6** (5 equiv) in the presence of Grubbs II catalyst (5 mol%). The metathesis product **7** was obtained in almost quantitative yield as an 89:11 mixture of the *E* and the *Z* isomers, which were separated by preparative HPLC.

The Ir-catalyzed substitution reaction of the Boc-protected amide **7** exclusively gave the tetrahydrofuran derivatives **8a** and **8b** (91–97%). Thus, an intramolecular Ir-catalyzed etherification[30] rather than an amination had occurred. The diastereoselectivity of the reaction was very high, both upon use of ligand **L2** (98:2) as well as ligand *ent*-**L2** (5:95).

Hence, a change in the protecting-group strategy was required for the preparation of the desired piperidines. Using standard procedures, the amines (*E*)-**9** and (*Z*)-**9** with two *tert*-butyldimethylsilyl (TBDMS)-protected OH groups were prepared from the isomerically pure precursors (*E*)-**7** and (*Z*)-**7**, respectively. It was of interest to investigate the influence of the double-bond geometry on the cyclization.

Ir-catalyzed cyclizations of (*E*)- and (*Z*)-9: Intramolecular allylic aminations usually give excellent results.[7] This was also true for the cyclization of (*E*)-**9**, which proceeded smoothly under standard conditions to give the vinylpiperidines in good yield and with high selectivity (Scheme 5, Table 1).[31] Control experiments using $P(OPh)_3$ as ligand indicated that substrate control is weak in this system (**10a**/**10b** = 60:40). The use of isomerically pure (*E*)-**9** in conjunction with ligand **L1** (matched case) furnished the cyclization product **10a** with a diastereoselectivity of 97.5:2.5 in 85% yield (entry 1). The ligand **L2** induced even higher reactivity and diastereoselectivity (98.5:1.5, entry 2); the latter was slightly reduced upon heating (entries 3–4). With a 9:1-mixture of (*E*)- and (*Z*)-**9**, the diastereoselectivity was slightly reduced (entries 4–5). The configuration of the cyclization products was as expected according to a general rule for the steric course of the Ir-catalyzed substitutions.[5a]



Scheme 5. Ir-catalyzed cyclizations of the allylic carbonate **9**.

Table 1. Iridium-catalyzed allylic cyclizations of carbonate **9** according to Scheme 5.

Entry[a]	Substrate	L*	Ir [mol%]	*T* [°C]	*t* [h]	Yield[b] [%]	**10a**/**10b**[c]
1	(*E*)-**9**	**L1**	4	RT	22	85	97.5:2.5
2	(*E*)-**9**	**L2**	4	RT	6.5	89	98.5:1.5
3	(*E*)-**9**	**L2**	4	50	2	78	97:3
4	(*E*)-**9**/(*Z*)-**9** 9:1	**L2**	4	50	1	88	95.5:4.5
5	(*E*)-**9**/(*Z*)-**9** 9:1	**L2**	2	50	3	76	94:6
6	(*E*)-**9**	*ent*-**L1**	4	RT	24	76 (86)	6:94
7	(*E*)-**9**	*ent*-**L2**	4	RT	5.5	87	2.5:97.5
8	(*E*)-**9**	*ent*-**L1**	4	50	3	88	4.5:95.5
9	(*E*)-**9**	*ent*-**L2**	4	50	1.3	92	3:97
10	(*E*)-**9**/(*Z*)-**9** 9:1	*ent*-**L1**	4	RT	22	82	5.5:94.5
11	(*E*)-**9**/(*Z*)-**9** 9:1	*ent*-**L2**	4	50	1	87	4.5:95.5
12	(*E*)-**9**/(*Z*)-**9** 9:1	*ent*-**L2**	2	50	3	77	5:95
13	(*Z*)-**9**	**L2**	4	RT	6	60 (90)	51:49

[a] All reactions were carried out according to GP2 (see Experimental Section). [b] Isolated yield of the major diastereoisomer; in parentheses: yield corrected for recovered starting material. [c] Determined by GC.

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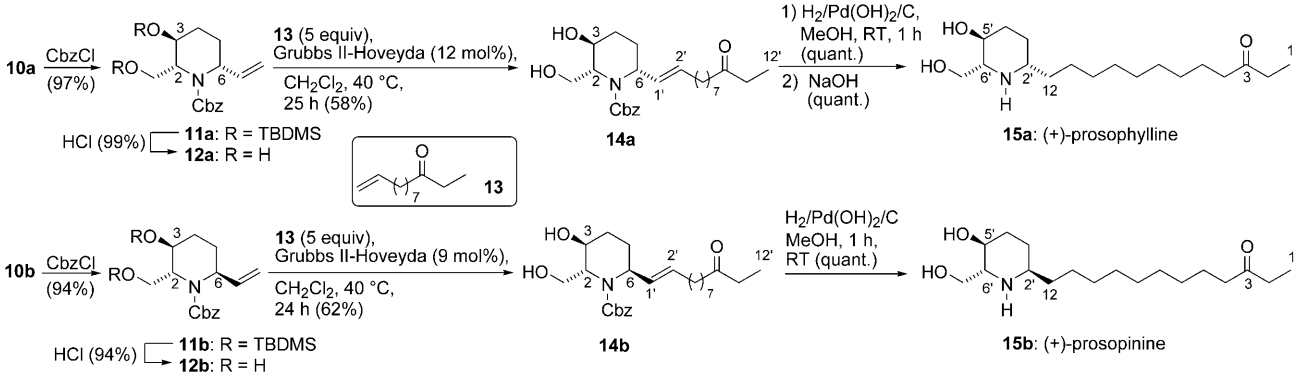


Scheme 6. Synthesis of (+)-prosopinine and (+)-prosophylline.

In the mismatched case (entries 6–9, *ent*-**L***) yields and selectivities were only marginally lower than in the matched case (**L***). Again, yields and selectivities were little affected by an increase of the reaction temperature, reduced catalyst loading, and use of the 9:1 mixture of (*E*)- and (*Z*)-**9** as substrate (entries 10–12).

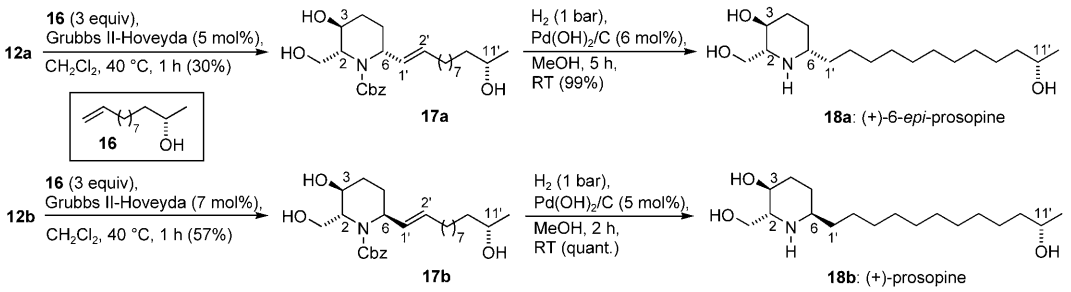
When isomerically pure (*Z*)-**9** was used as substrate, the reaction was nonselective (**10a**/**10b** = 51:49) and slow (entry 13). This result reflects observations that intermolecular Ir-catalyzed allylic substitutions of (*Z*)-allylic substrates yield linear substitution products[32] and the formation of vinylcyclopropanes by Ir-catalyzed cyclizations of (*Z*)-allylic substrates proceed with very poor yield.[24]

Synthesis of (+)-prosophylline (15a) and (+)-prosopinine (15b): The cyclization products **10a** and **10b** were transformed into benzyl carbamates **11a** or **11b** under standard conditions (Scheme 6). Unexpectedly, the carbamates did not undergo cross-metathesis with the ketone **13** (10 mol% Grubbs II or Grubbs II–Hoveyda, CH_2Cl_2 or $ClCH_2CH_2Cl$, reflux). The same observation was made when the bulky TBDMS groups of **11b** were replaced by acetyl groups (not shown). Initial attempts with the free diols **12** as substrates gave only little conversion under standard conditions (catalyst: 5 mol% Grubbs II or Grubbs II–Hoveyda, CH_2Cl_2, reflux). The reaction never went to completion, and the products were isolated in low yields (15–20%). Changing the solvent and increasing the reaction temperature (1,2-dichloroethane or toluene, reflux) led to predominant formation of an unidentified side product. Using the dioxolane derived from ketone **13** or adding Lewis acids such as $Ti(OiPr)_4$ or Cy_2BCl (Cy = cyclohexyl) did not give improved results either.[33] Finally, moderate yields of **14a** (58%) and **14b** (62%) were obtained, when Grubbs II–Hoveyda catalyst (9–12 mol%) was used and added in 3–6 portions to a solution of the reactants in CH_2Cl_2 at reflux.

The synthesis of (+)-prosopinine was completed by catalytic hydrogenation of the metathesis product **14b** using Pearlman's catalyst ($Pd(OH)_2/C$).[34] Other than anticipated, no epimerization occurred within the limits of detection (^1H NMR spectroscopy). After recrystallization from acetone (+)-prosopinine (**15b**) was obtained as colorless needles suitable for X-ray structural analysis.[28] The synthesis of (+)-prosophylline was carried out similarly, except for workup of the hydrogenation reaction; in this case, a solution of the crude product had to be washed with aqueous 1 N NaOH before the desired compound could be extracted. Recrystallization from acetone gave analytically pure (+)-prosophylline (**15a**) as colorless needles.

Synthesis of (+)-prosopine (18b) and its C6 epimer (18a): Various syntheses of prosopinine and prosophylline have been carried out,[15–20] however, no synthesis of (+)-prosopine has been reported. With the piperidine **12b** in hand, introduction of an appropriate side chain by means of cross-metathesis appeared of interest (Scheme 7). Thus, the chiral alcohol **16**[35] was prepared from (−)-(*S*)-propylene oxide in analogy to a known procedure.[29,36]

Other than the cross-metatheses with **13**, the reaction between **12b** and the unsaturated alcohol **16** (3 equiv) using



Scheme 7. Synthesis of (+)-prosopine and (+)-6-*epi*-prosopine.

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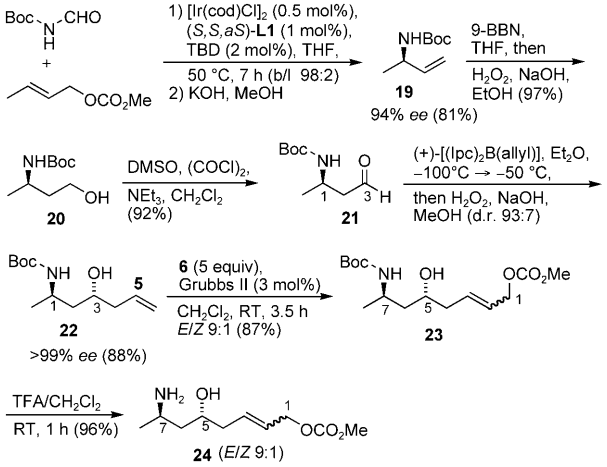
Grubbs–Hoveyda catalyst (7 mol%) was fast (1 h, CH_2Cl_2, reflux). However, selectivity was low and only a modest yield of 57% of **17b** was obtained. Subsequent hydrogenation with $Pd(OH)_2$ as catalyst quantitatively gave (+)-prosopine, which crystallized from acetone in the form of colorless needles. To the best of our knowledge, this constitutes the first synthesis of prosopine (**18b**).

Furthermore, the heretofore unknown C6 epimer of (+)-prosopine was synthesized, using *cis*-piperidine **12a** as substrate for the cross-metathesis with **16**. Subsequent hydrogenation furnished (+)-6-*epi*-prosopine (**18a**) as colorless oil ($[\alpha]_D^{20} = +29.9$, $c = 0.84$ in MeOH, >99% *ee*).

Synthesis of dendrobate and spruce alkaloids: *Dendrobatidae* (belonging to the poison or dart frogs) are a family of small frogs living in the rain forests of Central and South America. They are usually brightly colored and often show high toxicity against the central nervous system. From their skins, numerous alkaloids have been isolated, for example, batrachotoxines, histrionicotoxines, indolizidines, pumilotoxines, decahydrochinolines, and various 2,6-disubstituted pyrrolidines and piperidines.[37]

The alkaloid (+)-241D (**30a**) was isolated by Daly et al. from the skin of *Dendrobates speciosus*,[37b,38] and was found to be a potent inhibitor of binding of [^{3}H]perhydrohistrionicotoxin to nicotinic acetylcholine receptor channels.[39] Subsequent to a synthesis of the racemate,[39] asymmetric syntheses of (+)-241D and (−)-241D and their C4 epimers have been reported.[40]

Synthesis of the cyclization precursor 24: The Ir-catalyzed amination of *trans*-crotyl methyl carbonate with HN(CHO)Boc as nucleophile (Scheme 7) has previously been carried out on a submillimol scale.[41] In the present project, the catalyzed reaction was conducted on a preparatively significant scale of 77 mmol with a reduced catalyst loading of 1 mol% of **L1**. After cleavage of the formyl group, the Boc-protected amine **19** was obtained in 81% yield with 94% *ee*.[42] Hydroboration/oxidation[43] and Swern reaction of the resultant primary alcohol **20**[44] furnished the sensitive aldehyde **21** in 89% yield over two steps.[45] Treatment of **21** with (+)-*B*-allyldiisopinocampheylborane[46] ((+)-Ipc$_2$B(allyl)) at low temperature gave a 93:7 mixture (GC) of the homoallylic alcohols **22** and 3-*epi*-**22**, which were separated by flash chromatography. Pure **22**[28] was obtained in 88% yield with >99% *ee*.[31] As before, the allylic unit was introduced by cross-metathesis (Grubbs II catalyst) of **22** and the bis-carbonate **6** (5 equiv), which gave allylic carbonate **23** in 87% yield as a 9:1 mixture (^{1}H NMR spectroscopy) of *E* and *Z* isomers. Cleavage of the Boc group under standard conditions gave the cyclization precursor **24** in 96% yield (Scheme 8).

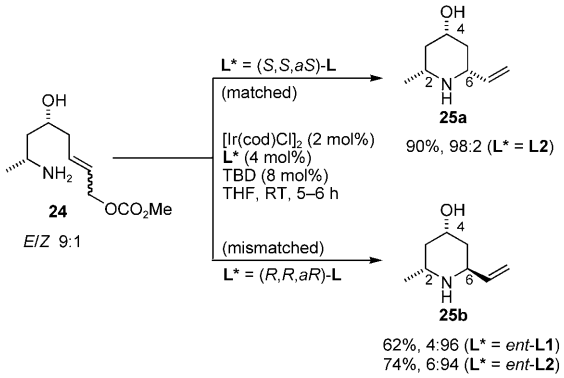


Scheme 8. Synthesis of the cyclization precursor **24** (9-BBN = 9-borabicyclo[3.3.1]nonane).

Ir-catalyzed cyclizations of 24: Under standard conditions, the Ir-catalyzed cyclization of amine **24** ($E/Z = 9:1$) gave very satisfactory results (Scheme 9). Using **L2** as ligand, the piperidine **25a** was isolated in 90% yield with almost perfect diastereoselectivity of **25a**/**25b** = 98:2 (GC). In the mismatched case, upon use of ligand *ent*-**L2**, piperidine **25b** was produced in 74% yield with only slightly reduced selectivity (**25a**/**25b** = 6:94). The yield was marginally lower with *ent*-**L1**, whereas the diastereoselectivity of 4:96 was even higher than that achieved with *ent*-**L2**.

In contrast to the results in the cyclization of **7**, the (*Z*)-allylic carbonate did not markedly contribute to product formation in this case. In contrast, when isomerically enriched (*Z*)-**24** (Z/E >90:10) was reacted according to Scheme 9, using **L2** as ligand, the cyclization was slow and nonselective (**25a**/**25b** 63:37) and gave **25a** in only approximately 20% yield. In a control experiment using P(OPh$_3$) as achiral ligand, the diastereoselectivity was 65:35 in favor of **25a**, thus showing that substrate control is weak in this system.

The configuration of the cyclization product **25a** was verified by an X-ray crystal structural analysis,[28] which confirmed the predicted configuration according to the general rule.[5a]



Scheme 9. Ir-catalyzed cyclizations of amine **24**.

Synthesis of the dendrobate alkaloid (+)-241D (30a) and its C6 epimer 30b: A cross-metathesis was considered as a key

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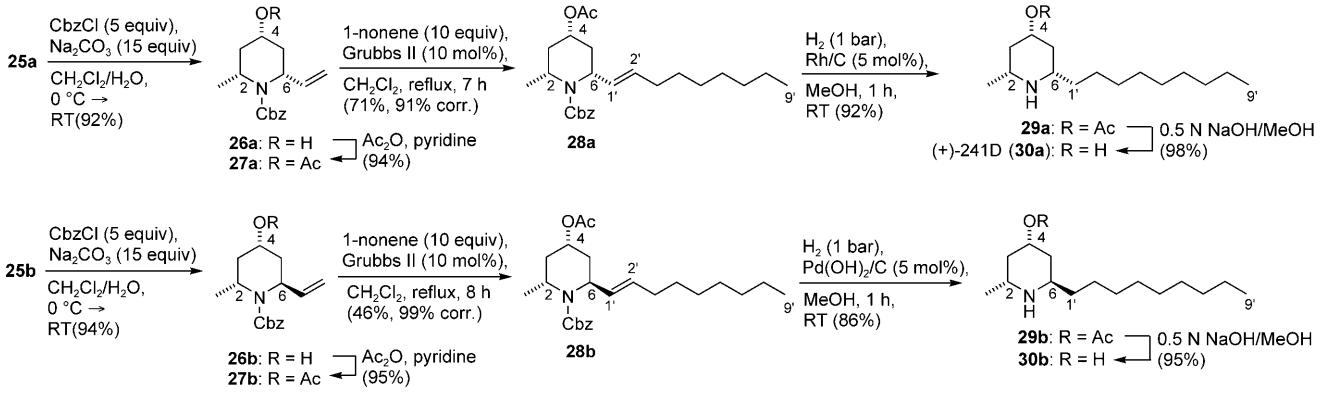


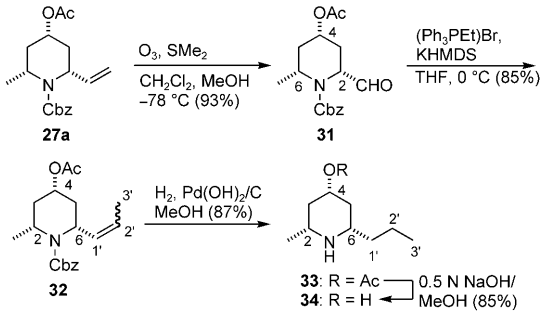
Scheme 10. Synthesis of (+)-241D (**30a**) and its C6 epimer **30b**.

step for the synthesis of (+)-241D from **25a** (Scheme 10). Attempts to use an ammonium salt of **25a** as substrate were not successful, mainly because of low solubility of the salts tried in dichloromethane. Hence, the OH and the NH group were protected by formation of **27a** using standard procedures. The reaction of **27a** with 1-nonene in the presence of Grubbs II catalyst (10 mol%) furnished the cross-metathesis product **28a** in 71% yield, together with some starting material (20%). Catalytic hydrogenation (Rh/C) gave the amine **29a** in 92% yield without epimerization according to ^{1}H NMR spectroscopy. Hydrolysis of the acetate gave the natural product (+)-241D (**30a**) in an overall yield of 27%. The spectroscopic data were in full agreement with those reported.

For the synthesis of the C6 epimer of (+)-241D by means of an analogous route, piperidine **25b** was transformed into **27b**, which was significantly less reactive than **27a** in the cross-metathesis reaction. After testing several reaction conditions, we had to settle with incomplete conversion and a moderate yield of **28b** of 46%; fortunately, the starting material was fully recovered (53%). Similarly, hydrogenation of **28b** using Rh/C as catalyst was not possible; $Pd(OH)_2$ on charcoal was used instead, and amine **29b** was obtained in 86% yield. Other than anticipated, no epimerization occurred (^{1}H NMR spectroscopy). Hydrolysis gave the amino alcohol **30b** in 95% yield, the relative configuration of which was verified by X-ray crystal structural analysis.[28] This concluded the first synthesis of the C6 epimer of the alkaloid (+)-241D. The overall yield was 15%.

Synthesis of the spruce alkaloid 34: This compound has been identified as a trace alkaloid in extracts from Colorado blue spruce (*Picea pungens*) by Stermitz et al. (Scheme 11).[47] They deduced the structure and the relative configuration of **34** from GC–MS data and on the basis of analogy to similar alkaloids and verified it by a synthesis of the racemic compound. The absolute configuration and optical rotation were unknown. The assignment shown in Scheme 11 was based on the observation that, with one exception (euphococcinine), 2,6-disubstituted piperidines occurring in conifers possess the same absolute configuration at the methylated center C2.[47]

In our synthesis of **34**, aldehyde **31** was prepared from carbamate **27a** by oxidative cleavage of the double bond (O_3/SMe_2). This was subjected to a Wittig olefination, which gave the olefin **32** in 81% yield as a mixture of isomers (Z/E = 87:13, ^{1}H NMR spectroscopy). After catalytic hydrogenation using $Pd(OH)_2$/C as catalyst and subsequent hydrolysis of the acetate **33**, compound **34** was obtained in form of colorless polyhedra ($[\alpha]_D^{20} = +8.8$, $c = 0.43$ in MeOH, >99% *ee*), suitable for X-ray crystal structural analysis,[28] in an overall yield of 24%.[48]



Scheme 11. Synthesis of the spruce alkaloid **34**.

Conclusion

In conclusion, we are reporting the first examples of a configurational switch for Ir-catalyzed allylic cyclizations, which allows each of two possible diastereomeric cyclization products to be prepared with a very high degree of diastereoselectivtiy. The concept has been applied in syntheses of 2,6-disubstituted hydroxypiperidine alkaloids. Examples are (+)-prosopinine (**15b**), (+)-prosophylline (**15a**), and (+)-241D (**30a**), which have been synthesized before. The first asymmetric syntheses are reported here for (+)-prosopine (**18b**), (+)-6-*epi*-prosopine (**18a**), (+)-6-*epi*-241D (**30b**), and the spruce alkaloid (+)-**34**.

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Experimental Section

General remarks: ^{1}H NMR spectra were recorded at room temperature using Bruker DRX-200 (199.92 MHz), Bruker Avance DRX-300 (300.13 MHz), Bruker Avance DRX-500 (500.13 MHz), or Bruker Avance III 600 (600.13 MHz) spectrometers. Chemical shifts are reported in δ relative to the solvent residual peak ($CHCl_3$ in $CDCl_3$ at $\delta_H=7.26$ ppm; CD_2HOD in CD_3OD at $\delta_H=3.31$ ppm).[49] The following abbreviations are used for description of the signal multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), dt (doublet of triplet), ddd (doublet of doublet of doublet), and so forth, brs (broad signal), m (multiplet). Diastereotopic hydrogen atoms are described with indices a and b (CH_aH_b) or, if applicable, with the indices ax (axial) and eq (equatorial). Chemical shifts are not reported for acidic protons (NH, OH) when CD_3OD was used as solvent. ^{13}C NMR spectra were recorded at room temperature using Bruker DRX-200 (50.27 MHz), Bruker Avance DRX-300 (75.47 MHz), Bruker Avance DRX-500 (125.76 MHz), and Bruker Avance III 600 (150.90 MHz) spectrometers. Chemical shifts are reported in δ relative to the solvent signal: $CDCl_3$ ($\delta_C=77.16$ ppm (central line of the triplet)), CD_3OD ($\delta_C=49.00$ ppm (central line of the septet)).[49] The following abbreviations were used: s (singlet, quaternary C atom), d (doublet, CH group), t (triplet, CH_2 group), q (quartet, CH_3 group). The multiplicity stated refers to {^{1}H}-decoupled spectra. In every case, the assignments of signals were confirmed by ^{1}H,^{1}H-COSY, ^{1}H,^{13}C-COSY, and DEPT spectra.

Melting points are uncorrected. Optical rotations were measured using a Perkin–Elmer 341 polarimeter using a mercury lamp. High-resolution mass spectra were recorded using a JEOL JMS-700 (EI+, FAB+) or using a Bruker ApexQe FT-ICR (ESI+) mass spectrometer. Elemental analyses were carried out at the Organisch-Chemisches Institut, Universität Heidelberg. Kugelrohr distillations were carried out using a Büchi B-580 instrument; boiling points correspond to air-bath temperatures.

Determination of enantiomeric excess by HPLC was accomplished using an HP 1100 instrument equipped with a Daicel, Chiralpak AD-H column (250×4.6 mm, 5 μm) with guard cartridge AD-H (10×4 mm, 5 μm). GC was carried out on a HP 5890 Series II instrument using helium as carrier gas. As achiral column an HP-1 cross-linked methylsilicon gum (HP-1) (25 m×0.2 mm, 0.33 μm film thickness) was used (injector temperature 250 °C, detector temperature 280 °C). For determination of enantiomeric excess the following column was used: Varian Chrompack-Chirasil-Dex permethyl-β-cyclodextrin (β-CD) (25 m×0.25 mm, 25 μm film thickness) (injector temperature 200 °C, detector temperature 250 °C). Preparative HPLC was carried out using a ProntoSIL (250×20 mm, 5 μ silica gel) or a LATEK (250×21 mm, 5 μ silica gel) column using a Gilson-305 pump coupled with a Knauer Smartline UV detector 2600. Analytical thin-layer chromatography was performed on precoated TLC plates (Polygram SIL G/UV$_{254}$, from Machery & Nagel) using the solvents stated.

Visualization of spots was carried out using UV light ($\lambda=254$ nm) or dipping into the following solutions and heating: aqueous $KMnO_4$ (1.5 g $KMnO_4$, 2.5 g K_2CO_3 in 250 mL of H_2O; referred to as $KMnO_4$), molybdatophosphoric acid (5 g $H_3[P(Mo_3O_{10})_4]\cdot x\,H_2O$ in 250 mL of EtOH; referred to as MPA), *p*-anisaldehyde (45 mL *p*-anisaldehyde, 810 mL of EtOH, 45 mL H_2SO_4, 9 mL HOAc; referred to as PAA). Flash-column chromatography was carried out with silica gel (0.032–0.062) of Macherey, Nagel, and Co. Allylamines are prone to decomposition on column; this can be minimized by the addition of triethylamine (ca. 1%) to the solvent, use of a small column, and fast elution. Tetrahydrofuran was dried over benzophenone ketyl, and the water content was determined by Karl Fischer titration. 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD) was stored in an desiccator over KOH (alternatively, small amounts were stored under argon in a Schlenk tube) and weighed under air. IUPAC names were generated by the ACD/Labs 6.0 program from Advanced Chemistry Development Inc.

The following compounds were prepared according to published procedures: methyl (*E*)-4-(trityloxy)but-2-en-1-yl carbonate (**1**),[23a] *tert*-butyl formyl carbamate (HN(CHO)Boc),[50] (*Z*)-but-2-ene-1,4-diyl dimethyl bis-carbonate (**6**),[51] 11-dodecen-3-one (**13**),[52] 9-bromonon-1-ene,[53] (+)-(*S*)-dodec-11-en-2-ol ((+)-(*S*)-**16**),[35,36] *trans*-crotyl methyl carbonate,[54] (+)-*tert*-butyl formyl[(*R*)-1-methylprop-2-en-1-yl] carbamate,[41,55] (+)-*tert*-butyl [(*R*)-1-methylprop-2-en-1-yl] carbamate ((+)-(*R*)-**19**),[55,56,57] and (−)-*tert*-butyl [(*R*)-3-hydroxy-1-methylpropyl]carbamate ((−)-(*R*)-**20**).[43,44]

(−)-*tert*-Butyl {(*S*)-1-[(trityloxy)methyl]prop-2-en-1-yl}carbamate ((−)-(*S*)-2): A flame-dried Schlenk tube was charged with a solution of [{IrCl-(cod)}$_2$] (336 mg, 0.50 mmol) and (*S*,*S*,*aS*)-**L1** (540 mg, 1.00 mmol) in dry THF (50 mL). Anhydrous TBD (278 mg, 2.00 mmol) was added, and the mixture was stirred for 1 h at room temperature. The carbonate **1** (19.4 g, 50.0 mmol) and the pronucleophile NH(CHO)Boc (9.44 g, 65.0 mmol) were then added, and the reaction mixture was stirred at 50 °C for 26 h until TLC control (petroleum ether/ethyl acetate 3:1, R_f(**1**)=0.44, R_f(**2′**)=0.50, R_f(**3′**)=0.44, $KMnO_4$) showed complete conversion. The mixture was concentrated in vacuo, and the residue was dissolved in dry MeOH (150 mL). KOH (2.81 g, 50.0 mmol) was added, and the mixture was stirred at room temperature for 1.5 h when TLC control showed complete conversion (petroleum ether/diethyl ether 4:1, R_f(**2′**)=0.19, R_f(**2**)=0.15)). An acidic ion exchange resin (Amberlite IR-120, Merck) was added in portions until pH 7 was reached. The mixture was filtered, and the filtrate was concentrated in vacuo. The residue was subjected to flash chromatography (100 g of silica gel, petroleum ether/ethyl acetate 9:1) to give (−)-(*S*)-**2** (17.1 g, 79%, 96% *ee*) and **3** (2.9 g, 13%). (−)-(*S*)-**2**: Colorless solid; m.p. 93–95 °C; $[\alpha]_D^{20}=-19.3$ ($c=0.99$ in $CHCl_3$, 95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.53$–7.49 (m, 6H; Ph), 7.38–7.25 (m, 9H; Ph), 5.95 (ddd, $J=17.2$, 10.5, 5.3 Hz, 1H; C*H*=CH$_2$), 5.30 (ddd, $J=17.3$, 1.4, 1.4 Hz, 1H; CH=CH$_E$H$_Z$), 5.23 (ddd, $J=10.5$, 1.3, 1.3 Hz, 1H; CH=CH$_E$H$_Z$), 4.91 (brs, 1H; NH), 4.44 (brs, 1H; CHN), 3.28 (dd, $J=9.1$, 4.2 Hz, 1H; CH$_a$H$_b$O), 3.23 (dd, $J=9.0$, 4.9 Hz, 1H; CH$_a$H$_b$O), 1.53 ppm (s, 9H; C(CH$_3$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 155.43 (s, CO_2), 143.83 (s, Ph), 136.68 (d, =CH), 128.72, 127.88, 127.12 (3d, Ph), 115.52 (t, =CH$_2$), 86.53 (s, CPh$_3$), 79.41 (s, *C*(CH$_3$)$_3$), 65.71 (t, CH$_2$O), 52.90 (d, CHN), 28.50 ppm (q, C(*C*H$_3$)$_3$); elemental analysis calcd (%) for $C_{28}H_{31}NO_3$: C 78.29, H 7.27, N 3.26; found C 78.15, H 7.27, N 3.24; HRMS (FAB+): *m*/*z*: calcd for $C_{28}H_{32}NO_3^+$: 430.2377; found: 430.2378 $[M+H]^+$; HPLC (Chiralpak AD-H, *n*-hexane/*i*PrOH 99:1, flow 0.5 mL min^{-1}, RT, $\lambda=210$ nm): t_R((+)-(*R*)-**2**)=34.1 min, t_R((−)-(*S*)-**2**)= 47.0 min.

(−)-*tert*-Butyl [(1*R*)-1-[(2′*S*)-oxiran-2′-yl]-2-(trityloxy)ethyl]carbamate ((−)-(1*R*,2′*S*)-4a) and (−)-*tert*-butyl [(1*R*)-1-[(2′*R*)-oxiran-2′-yl]-2-(trityloxy)ethyl]carbamate ((−)-(1*R*,2′*R*)-4b): A flame-dried Schlenk tube under argon was charged with a solution of (−)-(*S*)-**2** (50 mg, 117 μmol) in dry CH_2Cl_2 (1 mL). Then 3-chloroperoxybenzoic acid (ca. 70 wt%) (43 mg, 175 mmol) was added, and the mixture was heated at reflux for 24 h when TLC control (petroleum ether/ethyl acetate 3:1, R_f(**2**)=0.68, R_f(**4**)=0.56, MPA) showed complete conversion. The reaction mixture was allowed to cool to room temperature and a saturated aqueous solution of Na_2SO_3/$NaHCO_3$ (prepared by mixing saturated aqueous Na_2SO_3 with saturated aqueous $NaHCO_3$ in a 1:1 ratio) was added slowly until gas evolution ceased (ca. 1 mL). The mixture was extracted with CH_2Cl_2 (4×3 mL), and the combined organic layers were dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (1 g, petroleum ether/ethyl acetate 6:1) to yield an 87:13 mixture (^{1}H NMR spectroscopy) of (−)-(1*R*,2′*S*)-**4a** and (−)-(1*R*,2′*R*)-**4b** (40 mg, 78%).

Analytically pure samples of (−)-(1*R*,2′*S*)-**4a** and (−)-(1*R*,2′*R*)-**4b** were obtained by repeated crystallization from diethyl ether/petroleum ether and repeated preparative HPLC (petroleum ether/ethyl acetate 9:1, column: ProntoSIL, 250×20 mm, 5 μ silica gel, 18 mL min^{-1}, 50 bar). The relative configuration of (−)-(1*R*,2′*S*)-**4a** was verified by X-ray crystal structural analysis.

*Analytical data for (−)-(1*R*,2′*S*)-**4a***: Colorless columns; m.p. 141–142 °C; $[\alpha]_D^{20}=-37.0$ ($c=0.87$ in $CHCl_3$, 95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.48$–7.44 (m, 6H; Ph), 7.34–7.22 (m, 9H; Ph), 4.65 (d, $J=9.0$ Hz, 1H; NH), 4.13 (brs, 1H; CHN), 3.29–3.22 (m, 2H; CH_2OCPh_3), 3.20 (brs, 1H; 2′-H), 2.74 (dd, $J=4.4$, 4.4 Hz, 1H; 3′-H$_a$), 2.65–2.60 (m, 1H; 3′-H$_b$), 1.44 ppm (s, 9H; C(CH$_3$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 155.71 (s, CO_2), 143.83 (s, Ph), 128.81, 128.01, 127.24 (3d, Ph), 86.88 (s, CPh_3), 79.76 (s, *C*(CH$_3$)$_3$), 64.72 (t, *C*H$_2$OCPh$_3$), 51.84 (d, C-2′), 49.41 (d,

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CHN), 43.71 (t, C-3′), 28.49 ppm (q, C(CH_3)$_3$); elemental analysis calcd (%) for $C_{28}H_{31}NO_4$: C 75.48, H 7.01, N 3.14; found C 75.21, H 7.07, N 3.09; HRMS (FAB+): *m/z*: calcd for $C_{28}H_{32}NO_4^+$: 446.2326; found: 446.2334 $[M+H]^+$.

*Analytical data for (−)-(1*R*,2′*R*)-**4b***: Colorless crystals; m.p. 122–124 °C; $[\alpha]_D^{20}=-3.7$ ($c=1.01$ in $CHCl_3$, 95% *ee*); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.46$ (d, $J=7.5$ Hz, 6H; Ph), 7.33 (t, $J=7.8$ Hz, 6H; Ph), 7.26 (t, $J=7.3$ Hz, 3H; Ph), 4.91 (br s, 1H; NH), 3.51 (br s, 1H; CHN), 3.48 (dd, $J=9.3$, 3.6 Hz, 1H; CH_aH$_b$OCPh$_3$), 3.25–3.19 (m, 2H; CH$_a$H$_b$OCPh$_3$, 2′-H), 2.86 (dd, $J=4.2$, 4.2 Hz, 1H; 3′-H$_a$), 2.79 (br s, 1H; 3′-H$_b$), 1.46 ppm (s, 9H; C(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=155.44$ (s, CO_2), 143.71 (s, Ph), 128.74, 128.06, 127.32 (3d, Ph), 86.96 (s, CPh$_3$), 79.76 (s, *C*(CH_3)$_3$), 63.31 (t, *C*H$_2$OCPh$_3$), 52.68 (d, CHN), 51.78 (d, C-2′), 47.17 (t, C-3′), 28.49 ppm (q, C(CH_3)$_3$); elemental analysis calcd (%) for $C_{28}H_{31}NO_4$: C 75.48, H 7.01, N 3.14; found C 75.20, H 6.98, N 3.10; HRMS (FAB+): *m/z*: calcd for $C_{28}H_{31}KNO_4^+$: 484.1885; found: 484.1901 $[M+K]^+$.

(+)-*tert*-Butyl {(1*R*,2*R*)-2-hydroxy-1-[(trityloxy)methyl]hex-5-en-1-yl}carbamate ((+)-(1*R*,2*R*)-5a) and (−)-*tert*-butyl {(1*S*,2*R*)-2-(hydroxymethyl)-1-[(trityloxy)methyl]pent-4-en-1-yl}-carbamate ((−)-(1*S*,2*R*)-5a′): In a flame-dried Schlenk tube under an argon atmosphere, a solution of allylmagnesium chloride (ca. 0.65 M in THF, 19.8 mL, ca. 12.9 mmol) was diluted with dry THF (58 mL) and cooled to −40 °C. Then CuI (123 mg, 644 μmol) was added. The resultant yellow suspension was stirred for 30 min and was then treated with the epoxide (−)-(1*R*,2′*S*)-**4a** (2.87 g, 6.44 mmol). The mixture was stirred for 6.5 h at −40 °C and was then allowed to warm slowly to room temperature overnight. After 24 h, TLC control (petroleum ether/diethyl ether 3:1, R_f(**4a**)=0.23, R_f(**5a**)=0.18, R_f(**5a′**)=0.15, UV, $KMnO_4$, MPA) showed complete consumption of the substrate. Saturated aqueous NH_4Cl (50 mL) was added, and the mixture was extracted with ethyl acetate (4×50 mL). The organic phases were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was subjected to flash chromatography on silica gel (47 g, petroleum ether/ethyl acetate 4:1) to give (+)-(1*R*,2*R*)-**5a** (2.44 g, 78%) and the regioisomer (−)-(1*S*,2*R*)-**5a′** (286 mg, 9%).

*Analytical data for (+)-(1*R*,2*R*)-**5a***: Colorless oil; $[\alpha]_D^{20}=+2.5$ ($c=1.13$ in $CHCl_3$, 97% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.44$–7.40 (m, 6H; Ph), 7.35–7.22 (m, 9H; Ph), 5.80 (dddd, $J=17.0$, 10.2, 6.8, 6.8 Hz, 1H; C*H*=CH$_2$), 5.22 (d, $J=8.9$ Hz, 1H; NH), 5.03 (dd, $J=17.2$, 1.4 Hz, 1H; CH=CH$_E$H$_Z$), 4.96 (d, $J=10.2$ Hz, 1H; CH=CH$_E$H$_Z$), 3.85–3.79 (m; C*H*OH), 3.73–3.64 (m, 1H; CHN), 3.46 (dd, $J=9.2$, 4.1 Hz, 1H; CH_aH$_b$O), 3.19 (dd, $J=9.3$, 3.5 Hz, 1H; CH$_a$H$_b$O), 2.79 (br s, 1H; OH), 2.24–2.07 (m, 2H; 4-H), 1.68–1.52 (m, 2H; 3-H), 1.48 ppm (s, 9H; C(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=156.20$ (s, CO_2), 143.58 (s, Ph), 138.32 (d, =CH), 128.65, 128.14, 127.37 (3d, Ph), 114.99 (t, =CH$_2$), 87.34 (s, CPh$_3$), 79.54 (s, *C*(CH_3)$_3$), 72.21 (d, CHOH), 65.99 (t, CH$_2$O), 53.52 (d, CHN), 33.00 (t, C-3), 29.96 (t, C-4), 28.56 ppm (q, C(CH_3)$_3$); HRMS (FAB+): *m/z*: calcd for $C_{31}H_{38}NO_4^+$: 488.2795; found: 488.2853 $[M+H]^+$.

*Analytical data for (−)-(1*S*,2*R*)-**5a′***: Colorless rectangular plates; m.p. 99–101 °C; $[\alpha]_D^{20}=-7.0$ ($c=1.09$ in $CHCl_3$, 97% *ee*); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.45$–7.43 (m, 6H; Ph), 7.33 (t, $J=7.6$ Hz, 6H; Ph), 7.28–7.25 (m, 3H; Ph), 5.82 (dddd, $J=17.1$, 10.0, 7.7, 6.6 Hz, 1H; C*H*=CH$_2$), 5.08 (d, $J=9.1$ Hz, 1H; NH), 5.01 (d, $J=8.2$ Hz, 1H; CH=CH$_E$H$_Z$), 4.99 (d, $J=16.8$ Hz, 1H; CH=CH$_E$H$_Z$), 3.76–3.70 (m, 1H; CHN), 3.67 (ddd, $J=11.9$, 3.5, 3.5 Hz, 1H; CH_aH$_b$OH), 3.61 (ddd, $J=11.8$, 8.3, 3.1 Hz, 1H; CH$_a$H$_b$OH), 3.36 (dd, $J=9.4$, 3.5 Hz, 1H; CH_aH$_b$OCPh$_3$), 3.29 (dd, $J=9.5$, 3.7 Hz, 1H; CH$_a$H$_b$OCPh$_3$), 2.91 (dd, $J=8.0$, 4.7 Hz, 1H; OH), 2.12 (ddd, $J=13.9$, 8.5, 8.5 Hz, 1H; 3-H$_a$), 1.99 (ddd, $J=13.6$, 5.2, 5.2 Hz, 1H; 3-H$_b$), 1.85–1.79 (m, 1H; 2-H), 1.47 ppm (s, 9H; C(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=156.96$ (s, CO_2), 143.76 (s, Ph), 136.73 (d, =CH), 128.75, 128.06, 127.33 (3d, Ph), 116.70 (t, =CH$_2$), 86.79 (s, CPh$_3$), 79.91 (s, *C*(CH_3)$_3$), 63.32 (t, *C*H$_2$OCPh$_3$), 61.32 (t, CH$_2$OH), 51.49 (d, CHN), 41.83 (d, C-2), 32.73 (t, C-3), 28.54 ppm (q, C(CH_3)$_3$); HRMS (FAB+): *m/z*: calcd for $C_{31}H_{37}NNaO_4^+$: 510.2615; found: 510.2616 $[M+Na]^+$.

(+)-*tert*-Butyl {(1*R*,2*S*)-2-hydroxy-1-[(trityloxy)methyl]hex-5-en-1-yl}carbamate ((+)-(1*R*,2*S*)-5b) and (−)-*tert*-butyl {(1*S*,2*S*)-2-(hydroxymethyl)-1-[(trityloxy)methyl]pent-4-en-1-yl}-carbamate ((−)-(1*S*,2*S*)-5b′): The title compounds were prepared as described above for the preparation of (+)-(1*R*,2*R*)-**5a**. The reaction of the epoxide (−)-(1*R*,2′*R*)-**4b** (287 mg, 644 μmol) with allylmagnesium chloride was complete after 18 h according to TLC analysis (petroleum ether/diethyl ether 3×(3:1), R_f(**4b**)=0.22, R_f(**5b**)=0.16, R_f(**5b′**)=0.13, UV, $KMnO_4$, MPA). The crude product was subjected to flash chromatography on silica gel (4 g, petroleum ether/ethyl acetate 4:1) to give (+)-(1*R*,2*S*)-**5b** (262 mg, 83%) and (−)-(1*S*,2*S*)-**5b′** (8 mg, 2.5%).

*Analytical data for (+)-(1*R*,2*S*)-**5b***: Colorless needles; m.p. 105–106 °C; $[\alpha]_D^{20}=+4.5$ ($c=1.13$ in $CHCl_3$, 95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.44$–7.40 (m, 6H; Ph), 7.33–7.21 (m, 9H; Ph), 5.72 (dddd, $J=17.0$, 10.3, 6.6, 6.6 Hz, 1H; =CH), 5.37 (d, $J=7.5$ Hz, 1H; NH), 4.99–4.90 (m, 2H; =CH$_2$), 3.71–3.59 (m, 2H; CHN, C*H*OH), 3.51 (dd, $J=9.7$, 2.5 Hz, 1H; CH_aH$_b$O), 3.20 (dd, $J=9.8$, 3.2 Hz, CH$_a$H$_b$O), 2.71 (d, $J=8.1$ Hz, 1H; OH), 2.25–2.13 (m, 1H; 4-H$_a$), 2.07–1.94 (m, 1H; 4-H$_b$), 1.49 (s, 9H; C(CH_3)$_3$), 1.36–1.23 ppm (m, 2H; 3-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=155.89$ (s, CO_2), 143.50 (s, Ph), 138.23 (d, =CH), 128.62, 128.17, 127.42 (3d, Ph), 114.99 (t, =CH$_2$), 87.41 (s, CPh$_3$), 79.68 (s, *C*(CH_3)$_3$), 73.24 (d, CHOH), 63.40 (t, CH$_2$O), 54.02 (d, CHN), 33.43 (t, C-3), 30.13 (t, C-4), 28.61 ppm (q, C(CH_3)$_3$); elemental analysis calcd (%) for $C_{31}H_{37}NO_4$: C 76.36, H 7.65, N 2.87; found C 76.36, H 7.66, N 2.82; HRMS (FAB+): *m/z*: calcd for $C_{31}H_{37}NNaO_4^+$: 510.2615; found: 510.2614 $[M+Na]^+$.

*Analytical data for (−)-(1*S*,2*S*)-**5b′***: Colorless oil; $[\alpha]_D^{20}=-10.7$ ($c=0.65$ in $CHCl_3$, 95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.44$–7.40 (m, 6H; Ph), 7.33–7.20 (m, 9H; Ph), 5.65 (dddd, $J=16.7$, 10.2, 7.5, 6.5 Hz, 1H; C*H*=CH$_2$), 4.90 (d, $J=9.4$ Hz, 1H; CH=CH$_E$H$_Z$), 4.88 (d, $J=17.0$ Hz, 1H; CH=CH$_E$H$_Z$), 4.53 (d, $J=9.2$ Hz, 1H; NH), 4.21–4.10 (m, 1H; CHN), 3.62–3.51 (m, 1H; CH_aH$_b$OH), 3.49–3.41 (m, 1H; OH), 3.39–3.28 (m, 1H; CH$_a$H$_b$OH), 3.20 (d, $J=9.7$ Hz, 1H; CH_aH$_b$OCPh$_3$), 3.14 (d, $J=10.0$ Hz, 1H; CH$_a$H$_b$OCPh$_3$), 2.00–1.89 (m, 2H; 2-H, 3-H$_a$), 1.80–1.69 (m, 1H; 3-H$_b$), 1.45 ppm (s, 9H; C(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=157.12$ (s, CO_2), 143.76 (s, Ph), 136.68 (d, =CH), 128.77, 128.05, 127.30 (3d, Ph), 116.49 (t, =CH$_2$), 86.99 (s, CPh$_3$), 80.14 (s, *C*(CH_3)$_3$), 64.03 (t, *C*H$_2$OCPh$_3$), 62.73 (t, CH$_2$OH), 50.40 (d, CHN), 42.38 (d, C-2), 31.11 (t, C-3), 28.52 (q, C(CH_3)$_3$); HRMS (FAB+): *m/z*: calcd for $C_{31}H_{37}NNaO_4^+$: 510.2615; found: 510.2654 $[M+Na]^+$.

*Synthesis of (+)-(1*R*,2*S*)-**5b**) by means of Mitsunobu reaction/saponification*: A cooled (0 °C) solution of (+)-(1*R*,2*R*)-**5a** (36 mg, 74 μmol) in toluene (Tol; 1.5 mL) was treated with triphenylphosphine (39 mg, 150 μmol) and acetic acid (1 M in toluene, 150 μL, 150 μmol). After 15 min diisopropyl azodicarboxylate (DIAD) (30 μL, 150 μmol) was added to give a yellow solution, which became slightly turbid after some time. As TLC control (petroleum ether/ethyl acetate 3:1, R_f(**5a**)=0.41, R_f(acetate of **5b**)=0.49, PAA) still showed starting material after 30 min, further PPh$_3$ (39 mg), AcOH (150 μL), and DIAD (30 μL were added. This was repeated after 1.5, 3, and 5 h. The reaction was complete after 22 h. The reaction mixture was concentrated in vacuo and the residue subjected to flash chromatography on silica gel (4 g, petroleum ether/ethyl acetate 9:1). This gave 58 mg of a mixture of the acetate of **5b** and diisopropyl hydrazine-1,2-dicarboxylate, which was dissolved in methanol (6 mL). The solution was treated with K_2CO_3 (9 mg, 90 μmol) at room temperature (TLC: petroleum ether/ethyl acetate 3:1, R_f(acetate of **5b**)=0.49, R_f(**5b**)=0.41, PAA). After 1 h additional K_2CO_3 (6 mg, 60 μmol) was added. After 4 h the conversion was complete, and saturated aqueous NH_4Cl (3 mL) was added. The mixture was extracted with ethyl acetate (4×5 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was subjected to flash chromatography on silica gel (5 g, petroleum ether/ethyl acetate 4:1) to give the alcohol (+)-(1*R*,2*S*)-**5b** (31 mg, 86%). For analytical data, see the previous procedure.

General procedure 1 (GP1, cross-metathesis with the bis-carbonate 6): In a flame-dried Schlenk tube under an argon atmosphere Grubbs II catalyst (0.03–0.05 mmol) was added to a solution of the olefinic substrate (1 mmol) and **6** (5 mmol) in dry CH_2Cl_2 (20 mL). The mixture was stirred at room temperature until complete conversion was indicated by TLC analysis. Concentration of the mixture under reduced pressure and flash chromatography of the residue gave clean reaction products.

(−)-(*E*,6*S*,7*R*)-7-[(*tert*-Butoxycarbonyl)amino]-6-hydroxy-8-(trityloxy)-oct-2-en-1-yl methyl carbonate ((−)-(*E*,6*S*,7*R*)-7) and (+)-(*Z*,6*S*,7*R*)-7-[(*tert*-butoxycarbonyl)amino]-6-hydroxy-8-(trityloxy)oct-2-en-1-yl methyl

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carbonate ((+)-(*Z*,6*S*,7*R*)-7): Following GP1, Grubbs II catalyst (148 mg, 174 μmol) was added to a solution of alcohol (+)-(1*R*,2*S*)-**5b** (1.70 g, 3.49 mmol) and carbonate **6** (3.56 g, 17.4 mmol) in dry CH_2Cl_2 (60 mL), and the mixture was stirred at room temperature for 3.5 h when complete conversion of the substrate was detected by TLC control (petroleum ether/ethyl acetate 3:1, R_f(**5b**) = 0.31, R_f(**7**) = 0.16, $KMnO_4$, PAA). The mixture was filtered through a pad of Celite and the filtrate was concentrated in vacuo. The residue was subjected to flash chromatography on silica gel (86 g, petroleum ether/ethyl acetate 5:1 to ethyl acetate), which yielded an 89:11 mixture (1.97 g, 98%; ^{1}H NMR spectroscopy) of (−)-(*E*,6*S*,7*R*)-**7** and (+)-(*Z*,6*S*,7*R*)-**7** as a colorless oil. Separation of the diastereomers was accomplished by repeated preparative HPLC (petroleum ether/ethyl acetate 4:1, column: ProntoSIL, 250 × 20 mm, 5 μ silica gel, 15 mL min^{-1}, 90 bar). Analytically pure (−)-(*E*,6*S*,7*R*)-**7** (1.54 g, 76%) and (+)-(*Z*,6*S*,7*R*)-**7** (144 mg, 7%), both colorless oils, and a mixed fraction (211 mg, 10%) were obtained.

*Analytical data for (−)-(*E,6*S,7*R*)-**7***: Colorless oil; $[\alpha]_D^{20} = -10.1$ (*c* = 0.97 in acetone, 96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.39 (m, 6H; Ph), 7.33–7.21 (m, 9H; Ph), 5.72 (ddd, *J* = 15.3, 6.8, 6.8 Hz, 1H; 2-H), 5.51 (ddd, *J* = 15.1, 6.5, 6.5 Hz, 1H; 3-H), 5.37 (d, *J* = 7.5 Hz, 1H; NH), 4.54 (d, *J* = 6.2 Hz, 2H; CH_2OCO_2), 3.76 (s, 3H; CO_2CH_3), 3.66–3.58 (m, 2H; 6-H, 7-H), 3.51 (dd, *J* = 9.8, 2.6 Hz, 1H; $CH_aH_bOCPh_3$), 3.18 (dd, *J* = 9.8, 3.0 Hz, 1H; $CH_aH_bOCPh_3$), 2.76 (d, *J* = 8.1 Hz, 1H; OH), 2.26–2.15 (m, 1H; 4-H_a), 2.07–1.95 (m, 1H; 4-H_b), 1.49 (s, 9H; $C(CH_3)_3$), 1.34–1.25 ppm (m, 2H; 5-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.88 (s, NCO_2), 155.77 (s, OCO_2), 143.42 (s, Ph), 136.40 (d, C-3), 128.57, 128.17, 127.42 (3d, Ph), 123.83 (d, C-2), 87.39 (s, CPh_3), 79.72 (s, $C(CH_3)_3$), 73.09 (d, CHOH), 68.58 (t, CH_2OCO_2), 63.33 (t, CH_2OCPh_3), 54.81 (q, CO_2CH_3), 53.97 (d, CHN), 33.27 (t, C-5), 28.58 ppm (1t, 1q, C-4, C-$(CH_3)_3$); elemental analysis calcd (%) for $C_{34}H_{41}NO_7$: C 70.93, H 7.18, N 2.43; found C 71.12, H 7.29, N 2.44; HRMS (FAB+): *m*/*z*: calcd for $C_{34}H_{42}NO_7^+$: 576.2956; found: 576.2944 $[M+H]^+$.

*Analytical data for (+)-(*Z,6*S,7*R*)-**7***: Colorless oil; $[\alpha]_D^{20} = +1.7$ (*c* = 0.99 in $CHCl_3$, 96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.40 (m, 6H; Ph), 7.34–7.21 (m, 9H; Ph), 5.61–5.50 (m, 2H; CH=CH), 5.27 (d, *J* = 7.3 Hz, 1H; NH), 4.73–4.59 (m, 2H; CH_2OCO_2), 3.72 (s, 3H; CO_2CH_3), 3.68–3.60 (m, 2H; 6-H, 7-H), 3.46 (dd, *J* = 9.5, 2.7 Hz, 1H; $CH_aH_bOCPh_3$), 3.24 (dd, *J* = 9.7, 3.3 Hz, 1H; $CH_aH_bOCPh_3$), 2.83 (d, *J* = 6.2 Hz, 1H; OH), 2.24–2.17 (m, 2H; 4-H), 1.48 (s, 9H; $C(CH_3)_3$), 1.39–1.22 ppm (m, 2H; 5-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.91 (s, OCO_2), 155.88 (s, NCO_2), 143.54 (s, Ph), 135.16 (d, =CH), 128.63, 128.14, 127.39 (3d, Ph), 123.68 (d, =CH), 87.31 (s, CPh_3), 79.67 (s, $C(CH_3)_3$), 72.54 (d, CHOH), 63.74 (t, CH_2OCO_2), 63.26 (t, CH_2OCPh_3), 54.86 (q, CO_2CH_3), 54.24 (d, CHN), 33.62 (t, C-5), 28.59 (q, $C(CH_3)_3$), 24.00 ppm (t, C-4); HRMS (ESI+): *m*/*z*: calcd for $C_{34}H_{41}NNaO_7^+$: 598.2775; found: 598.2771 $[M+Na]^+$.

General procedure 2 (GP2, Ir-catalyzed allylic cyclization): Success with the following procedures requires dry THF (< 30 mg L^{-1} of H_2O, Karl–Fischer titration). A Schlenk tube was dried under argon with a heat gun and charged with a solution of $[\{IrCl(cod)\}_2]$ (13.4 mg, 0.02 mmol) and **L***(0.04 mmol) in dry THF (1 mL). Anhydrous TBD (11.1 mg, 0.08 mmol) was added, and the mixture was stirred for 5 min (**L2**) or 1 h (**L1**). Then the carbonate (1 mmol) and if necessary dry THF (3 mL) was added and the mixture was stirred for the time and at the temperature stated until TLC control indicated complete conversion. For workup, saturated aqueous NH_4Cl (4 mL) was added, and the mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, and the crude product was analyzed by GC with respect to the diastereomeric ratio. Pure products were obtained by flash chromatography on silica gel.

(−)-(1*R*)-1,4-Anhydro-5-[(*tert*-butoxycarbonyl)amino]-2,3,5-trideoxy-6-*O*-trityl-1-vinyl-D-*erythro*-hexitol ((−)-(1*R*)-D-*erythro*-8a): According to GP2, anhydrous TBD (2.0 mg, 14.6 μmol), was added to a solution of $[\{IrCl(cod)\}_2]$ (2.5 mg, 3.7 μmol) and (*S*,*S*,*aS*)-**L2** (4.4 mg, 7.3 μmol) in dry THF (300 μL), and the mixture was stirred for 5 min. Then a solution of the carbonate (−)-(*E*,6*S*,7*R*)-**7** (105 mg, 182 μmol) in dry THF (900 μL) was added, and the mixture was heated at reflux for 3 h when complete conversion was indicated by TLC (petroleum ether/ethyl acetate 3:1, R_f(**7**) = 0.19, R_f(**8a**) = 0.48, $KMnO_4$). After workup, the crude product was analyzed by HPLC (Chiralpak AD-H (*n*-hexane/*i*PrOH 95:5, flow 0.5 mL min^{-1}, RT, λ = 220 nm): t_R(**8a**) = 12.3, t_R(**8b**) = 21.0 min) with respect to the diastereomeric ratio (**8a**/**8b** = 98:2). The major diastereoisomer (−)-(1*R*)-D-*erythro*-**8a** (88 mg, 97%) was obtained after flash chromatography on silica gel (17 g, petroleum ether/diethyl ether 9:1 to 4:1) as a colorless oil. $[\alpha]_D^{20} = -21.7$ (*c* = 0.48 in $CHCl_3$, > 99% *ee*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49–7.48 (m, 6H; Ph), 7.33–7.30 (m, 6H; Ph), 7.26–7.23 (m, 3H; Ph), 5.75 (ddd, *J* = 17.0, 10.3, 6.5 Hz, 1H; C*H*=CH_2), 5.17 (d, *J* = 17.2 Hz, 1H; CH=CH_EH_Z), 5.03 (d, *J* = 10.1 Hz, 1H; CH=CH_EH_Z), 4.82 (d, *J* = 8.7 Hz, 1H; NH), 4.36–4.32 (m, 1H; 1-H), 4.16–4.12 (m, 1H; 4-H), 3.77 (brs, 1H; NCH), 3.49–3.46 (m, 1H; CH_aH_bO), 3.20–3.18 (m, 1H; CH_aH_b), 2.05–1.97 (m, 2H; 2-H_a, 3-H_a), 1.94–1.88 (m, 1H; 3-H_b), 1.65–1.58 (m, 1H; 2-H_b), 1.46 ppm (s, 9H; $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.68 (s, CO_2), 143.96 (s, Ph), 139.08 (d, =CH), 128.67, 127.73, 126.91 (3 d, Ph), 114.88 (t, =CH_2), 86.58 (s, CPh_3), 80.67 (d, C-1), 80.04 (s, $C(CH_3)_3$), 79.17 (d, C-4), 62.99 (t, CH_2O), 54.09 (d, CHN), 31.45 (t, C-2), 28.41 (t, C-3), 28.37 ppm (q, $C(CH_3)_3$); HRMS (FAB+): *m*/*z*: calcd for $C_{32}H_{37}NNaO_4^+$: 522.2616; found: 522.2661 $[M+Na]^+$.

(−)-(1*S*)-1,4-Anhydro-5-[(*tert*-butoxycarbonyl)amino]-2,3,5-trideoxy-6-*O*-trityl-1-vinyl-D-*erythro*-hexitol ((−)-(1*S*)-D-*erythro*-8b): According to GP2, anhydrous TBD (3.9 mg, 27.8 μmol) was added to a solution of $[\{IrCl(cod)\}_2]$ (4.7 mg, 7.0 μmol) and (*R*,*R*,*aR*)-**L2** (8.3 mg, 13.9 μmol) in dry THF (750 μL), and the mixture was stirred for 5 min. Then a solution of the carbonate (−)-(*E*,6*S*,7*R*)-**7** (188 mg, 327 μmol) in dry THF (1.5 mL) was added, and the mixture was heated at reflux for 3.5 h when complete conversion was indicated by TLC analysis (petroleum ether/ethyl acetate 3:1, R_f(**7**) = 0.19, R_f(**8b**) = 0.45, $KMnO_4$). After work up the crude product was analyzed by HPLC (Chiralpak AD-H (*n*-hexane/*i*PrOH 95:5, flow 0.5 mL min^{-1}, RT, λ = 220 nm): t_R(**8a**) = 12.3, t_R(**8b**) = 21.0 min) with respect to the diastereomeric ratio (**8a**/**8b** = 5:95). The major diastereomer (−)-(1*S*)-D-*erythro*-**8b** (148 mg, 91%) was obtained after flash chromatography on silica gel (15 g, petroleum ether/diethyl ether 9:1 to 4:1) as a colorless oil. $[\alpha]_D^{20} = -14.9$ (*c* = 0.32 in $CHCl_3$, > 99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.46 (m, 6H; Ph), 7.34–7.21 (m, 9H; Ph), 5.85 (ddd, *J* = 17.1, 10.4, 6.2 Hz, 1H; C*H*=CH_2), 5.23 (ddd, *J* = 17.1, 1.5, 1.5 Hz, 1H; CH=CH_EH_Z), 5.09 (ddd, *J* = 10.4, 1.4, 1.4 Hz, 1H; CH=CH_EH_Z), 4.86 (d, *J* = 8.7 Hz, 1H; NH), 4.34 (ddd, *J* = 7.2, 6.2, 6.2 Hz, 1H; 1-H), 4.27 (ddd, *J* = 7.2, 7.2, 7.2 Hz, 1H; 4-H), 3.76–3.68 (m, 1H; NCH), 3.49 (dd, *J* = 9.2, 3.7 Hz, 1H; CH_aH_bO), 3.15 (dd, *J* = 9.2, 3.3 Hz, 1H; CH_aH_bO), 2.13–2.01 (m, 2H; 2-H_a, 3-H_a), 1.93–1.80 (m, 1H; 3-H_b), 1.72–1.63 (m, 1H; 2-H_b), 1.45 ppm (s, 9H; $C(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.67 (s, CO_2), 143.96 (s, Ph), 139.20 (d, =CH), 128.68, 127.74, 126.93 (3d, Ph), 114.70 (t, =CH_2), 86.54 (s, CPh_3), 80.05 (d, C-1), 79.20 (s, $C(CH_3)_3$), 78.70 (d, C-4), 62.96 (t, CH_2O), 54.01 (d, CHN), 32.13 (t, C-2), 28.92 (t, C-3), 28.37 ppm (q, $C(CH_3)_3$); HRMS (FAB+): *m*/*z*: calcd for $C_{32}H_{37}NNaO_4^+$: 522.2616; found: 522.2604 $[M+Na]^+$. For HPLC data see (−)-(1*R*)-D-*erythro*-**8a**.

(+)-(*E*,6*S*,7*R*)-7-Amino-6,8-bis{[*tert*-butyl(dimethyl)silyl]oxy}oct-2-en-1-yl methyl carbonate ((+)-(*E*,6*S*,7*R*)-9): A solution of (−)-(*E*,6*S*,7*R*)-**7** (578 mg, 1.00 mmol) in CH_2Cl_2 (12 mL) was treated with trifluoroacetic acid (TFA; 12 mL, 162 mmol), and the yellow reaction mixture was stirred at room temperature. After 1 h all volatiles were removed under reduced pressure, and the yellow-brownish residue was dissolved in methanol (10 mL). The pale brown solution was concentrated under reduced pressure, and the residue was treated with diethyl ether (5 mL) and water (5 mL). The phases were separated and the organic phase was extracted repeatedly with water (5 × 5 mL). The combined aqueous phases were washed with diethyl ether (2 × 3 mL) and concentrated in vacuo to give the TFA salt of the amino diol as a colorless, highly viscous oil. This was treated with CH_2Cl_2 (20 mL), and the mixture was cooled to 0 °C. Imidazole (813 mg, 11.9 mmol) and *tert*-butyldimethylsilyl chloride (1.21 g, 8.04 mmol) were added, whereupon a white precipitate was formed. The ice bath was removed, and the mixture was allowed to warm to room temperature. After being stirred for 18 h, water (15 mL) was added. The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Analytically pure

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(+)-(*E*,6*S*,7*R*)-**9** (388 mg, 84% over two steps) was obtained after purification of the crude product by flash chromatography on silica gel (12 g, petroleum ether/ethyl acetate 3:1) as a colorless oil. $[\alpha]_D^{20}=+2.8$ ($c=1.10$ in $CHCl_3$, 96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=5.80$ (ddd, $J=15.4$, 6.6, 6.6 Hz, 1H; 3-H), 5.58 (ddddd, $J=15.3$, 6.5, 6.5, 1.3, 1.3 Hz, 1H; 2-H), 4.54 (d, $J=6.4$ Hz, 2H; CH_2OC), 3.75 (s, 3H; CO_2CH_3), 3.67 (ddd, $J=6.9$, 4.6, 4.6 Hz, 1H; CHOSi), 3.62 (dd, $J=9.8$, 5.1 Hz, 1H; CH_aH_bOSi), 3.43 (dd, $J=9.8$, 7.3 Hz, 1H; CH_aH_bOSi), 2.87 (ddd, $J=7.0$, 5.0, 5.0 Hz, 1H; CHN), 2.22–1.98 (m, 2H; 4-H), 1.69–1.56 (m, 1H; 5-H_a), 1.53–1.42 (m, 1H; 5-H_b), 1.33 (br s, 2H; NH_2), 0.87, 0.87 (2s, 18H; C-$(CH_3)_3$), 0.04 (s, 3H; $SiCH_3$), 0.03 ppm (s, 9H; $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=155.76$ (s, CO_2), 137.22 (d, C-3), 123.45 (d, C-2), 73.16 (d, CHOSi), 68.68 (t, CH_2OCO_2), 65.08 (t, CH_2OSi), 56.64 (d, CHN), 54.77 (q, CO_2CH_3), 31.33 (t, C-5), 27.90 (t, C-4), 26.01, 25.97 (2q, C(CH3)3), 18.34, 18.17 (2s, C(CH3)3), −4.24, −4.41, −5.26, −5.30 ppm (4q, $SiCH_3$); elemental analysis calcd (%) for $C_{22}H_{47}NO_5Si_2$: C 57.22, H 10.26, N 3.03; found C 57.29, H 10.30, N 2.98; HRMS (ESI+): *m*/*z*: calcd for $C_{22}H_{48}NO_5Si_2^+$: 462.3066; found: 462.3063 $[M+H]^+$.

(+)-(*Z*,6*S*,7*R*)-7-Amino-6,8-bis{[*tert*-butyl(dimethyl)silyl]oxy}oct-2-en-1-yl methyl carbonate ((+)-(*Z*,6*S*,7*R*)-9): This compound was prepared analogously to (+)-(*E*,6*S*,7*R*)-**9** from (+)-(*Z*,6*S*,7*R*)-**7** (129 mg, 224 μmol). Purification by flash chromatography on silica gel (3 g, petroleum ether/ethyl acetate 3:1) gave pure (+)-(*Z*,6*S*,7*R*)-**9** (60 mg, 58% over two steps) as a colorless oil. $[\alpha]_D^{20}=+3.7$ ($c=1.21$ in $CHCl_3$, 96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=5.68$ (ddd, $J=10.8$, 7.3, 7.3 Hz, 1H; 3-H), 5.55 (ddd, $J=11.1$, 6.7, 6.7 Hz, 1H; 2-H), 4.74–4.62 (m, 2H; CH_2OCO_2), 3.77 (s, 3H; CO_2CH_3), 3.72–3.66 (m, 1H; CHOSi), 3.66 (dd, $J=9.9$, 5.0 Hz, 1H; CH_aH_bOSi), 3.45 (dd, $J=9.9$, 7.3 Hz, 1H; CH_aH_bOSi), 2.90 (ddd, $J=7.2$, 5.0, 5.0 Hz, 1H; CHN), 2.31–2.20 (m, 1H; 4-H_a), 2.18–2.05 (m, 1H; 4-H_b), 1.70–1.58 (m, 1H; 5-H_a), 1.54–1.42 (m, 1H; 5-H_b), 1.40 (br s, 2H; NH_2), 0.89 (s, 18H; $C(CH_3)_3$), 0.06, 0.06 (2s, 6H; $SiCH_3$), 0.05 ppm (s, 6H; $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=155.88$ (s, CO_2), 135.90 (d, C-3), 123.08 (d, C-2), 73.28 (d, CHOSi), 65.20 (t, CH_2OSi), 63.74 (t, CH_2OC), 56.63 (d, CHN), 54.85 (q, CO_2CH_3), 32.13 (t, C-5), 26.06, 26.00 (2q, $C(CH_3)_3$), 23.31 (t, C-4), 18.40, 18.21 (2s, C-$(CH_3)_3$), −4.22, −4.39, −5.22, −5.26 ppm (4q, $SiCH_3$); elemental analysis calcd (%) for $C_{22}H_{47}NO_5Si_2$: C 57.22, H 10.26, N 3.03; found C 57.49, H 10.35, N 3.07; HRMS (ESI+): *m*/*z*: calcd for $C_{22}H_{48}NO_5Si_2^+$: 462.3066; found: 462.3067 $[M+H]^+$.

(+)-(2*R*,3*S*,6*R*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-({[*tert*-butyl-(dimethyl)silyl]oxy}methyl)-6-vinylpiperidine ((+)-(2*R*,3*S*,6*R*)-10a): According to GP2, anhydrous TBD (1.2 mg, 8.6 μmol) was added to a solution of $[\{IrCl(cod)\}_2]$ (1.5 mg, 2.2 μmol) and (*S*,*S*,*aS*)-**L2** (2.6 mg, 4.3 μmol) in dry THF (300 μL), and the mixture was stirred for 5 min. Then a solution of the carbonate (+)-(*E*,6*S*,7*R*)-**9** (50.0 mg, 108 μmol) in dry THF (700 μL) was added, and the mixture was stirred at room temperature for 6.5 h when TLC control (petroleum ether/ethyl acetate 1:1, R_f(**9**)=0.23, R_f(**10a**)=0.61, $KMnO_4$) showed complete conversion. After workup, the crude product was analyzed by GC with respect to the diastereomeric ratio (**10a**/**10b**=98:2). The major diastereomer (+)-(2*R*,3*S*,6*R*)-**10a** (34.6 mg, 89%) was obtained after flash chromatography on silica gel (5 g, petroleum ether/ethyl acetate 10:1) as a colorless oil. $[\alpha]_D^{20}=+38.8$ ($c=0.94$ in $CHCl_3$, >99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=5.81$ (ddd, $J=17.0$, 10.5, 6.4 Hz, 1H; CH=CH_2), 5.14 (d, $J=17.1$ Hz, 1H; CH=CH_EH_Z), 5.01 (d, $J=10.4$ Hz, 1H; CH=CH_EH_Z), 3.96 (dd, $J=9.5$, 2.9 Hz, 1H; CH_aH_bO), 3.47 (dd, $J=8.9$, 8.9 Hz, 1H; CH_aH_bO), 3.29 (ddd, $J=10.3$, 9.0, 4.6 Hz, 1H; 3-H), 3.12–3.06 (m, 1H; 6-H), 2.56 (ddd, $J=8.7$, 8.7, 3.0 Hz, 1H; 2-H), 2.05 (br s, 1H; NH), 1.96–1.89 (m, 1H; 4-H_a), 1.69 (ddd, $J=12.4$, 5.9, 2.9 Hz, 1H; 5-H_a), 1.50–1.35 (m, 1H; 4-H_b), 1.34–1.21 (m, 1H; 5-H_b), 0.87, 0.86 (2s, 18H; $C(CH_3)_3$), 0.04, 0.04, 0.02, 0.01 ppm (4s, 12H; $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=141.34$ (d, =CH), 114.09 (t, $=CH_2$), 70.05 (d, C-3), 64.81 (t, CH_2O), 64.08 (d, C-2), 58.45 (d, C-6), 34.45 (t, C-4), 31.70 (t, C-5), 26.09, 25.90 (2q, $C(CH_3)_3$), 18.47, 18.07 (2s, $C(CH_3)_3$), −3.94, −4.77, −5.21, −5.22 ppm (4q, $SiCH_3$); elemental analysis calcd (%) for $C_{20}H_{43}NO_2Si_2$: C 62.27, H 11.24, N 3.63; found C 62.31, H 11.24, N 3.68; HRMS (ESI+): *m*/*z*: calcd for $C_{20}H_{44}NO_2Si_2^+$: 386.2905; found: 386.2905 $[M+H]^+$. GC (achiral: HP-1, 200°C isothermal): t_R((+)-(2*R*,3*S*,6*R*)-**10a**)=15.1 min, t_R((+)-(2*R*,3*S*,6*S*)-**10b**)=16.1 min.

(+)-(2*R*,3*S*,6*S*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-({[*tert*-butyl-(dimethyl)silyl]oxy}methyl)-6-vinylpiperidine ((+)-(2*R*,3*S*,6*S*)-10b): Following GP2, a solution of $[\{IrCl(cod)\}_2]$ (1.5 mg, 2.2 μmol) and (*R*,*R*,*aR*)-**L2** (2.6 mg, 4.3 μmol) in dry THF (300 μL) was treated with anhydrous TBD (1.2 mg, 8.6 μmol), and the mixture was stirred for 5 min at room temperature. Then a solution of carbonate (+)-(*E*,6*S*,7*R*)-**9** (50.0 mg, 108 μmol) in dry THF (700 μL) was added, and the mixture was heated at 50°C for 1.25 h when conversion was complete according to TLC control (petroleum ether/ethyl acetate 1:1, R_f(**9**)=0.23, R_f(**10b**)=0.39, $KMnO_4$). After workup, the crude product was analyzed by GC with respect to the diastereomeric ratio (**10b**/**10a**=97:3). Purification of the crude product by flash chromatography on silica gel (5 g, petroleum ether/ethyl acetate 10:1) yielded the major diastereomer (+)-(2*R*,3*S*,6*S*)-**10b** (35.7 mg, 92%) as colorless oil. $[\alpha]_D^{20}=+48.5$ ($c=1.04$ in $CHCl_3$, >99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=5.99$ (ddd, $J=17.8$, 10.3, 5.0 Hz, 1H; CH=CH_2), 5.15 (ddd, $J=10.3$, 1.7, 1.7 Hz, 1H; CH=CH_EH_Z), 5.15 (ddd, $J=17.7$, 1.5, 1.4 Hz, 1H; CH=CH_EH_Z), 3.90 (dd, $J=9.4$, 3.8 Hz, 1H; CH_aH_bO), 3.55–3.50 (m, 1H; 6-H), 3.44 (dd, $J=9.4$, 8.1 Hz, 1H; CH_aH_bO), 3.39 (ddd, $J=9.8$, 8.5, 3.8 Hz, 1H; 3-H), 2.80 (ddd, $J=8.1$, 8.1, 3.7 Hz, 1H; 2-H), 1.96 (br s, 1H; NH), 1.79–1.71 (m, 3H; 4-H_a, 5-H), 1.59–1.45 (m, 1H; 4-H_b), 0.89, 0.87 (2s, 18H; $C(CH_3)_3$), 0.05 (s, 6H; $SiCH_3$), 0.03, 0.03 ppm (2s, 6H; $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=140.33$ (d, =CH), 114.97 (t, $=CH_2$), 70.10 (d, C-3), 64.76 (t, CH_2O), 58.26 (d, C-2), 53.00 (d, C-6), 29.99 (t, C-4), 28.56 (t, C-5), 26.07, 25.95 (2q, C-$(CH_3)_3$), 18.39, 18.14 (2s, $C(CH_3)_3$), −3.94, −4.72, −5.24 ppm (3q, $SiCH_3$); elemental analysis calcd (%) for $C_{20}H_{43}NO_2Si_2$: C 62.27, H 11.24, N 3.63; found C 62.28, H 11.24, N 3.60; HRMS (ESI+): *m*/*z*: calcd for $C_{20}H_{44}NO_2Si_2^+$: 386.2905; found: 386.2905 $[M+H]^+$. For GC data see (+)-(2*R*,3*S*,6*R*)-**10a**.

General procedure 3 (GP3, Cbz-protection): A solution of the piperidine (0.1 mmol) in CH_2Cl_2 (1 mL) was added to a solution of Na_2CO_3 (159 mg, 1.5 mmol) in H_2O (1.5 mL). The mixture was vigorously stirred and cooled to 0°C. Benzyl chloroformate (85 mg, 0.5 mmol) was added dropwise. After complete addition the ice bath was removed, and the mixture was allowed to warm to room temperature. When conversion was complete according to TLC, the mixture was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Pure products were obtained by flash chromatography on silica gel.

(+)-Benzyl (2*R*,3*S*,6*R*)-3-{[*tert*-butyl(dimethyl)silyl]oxy}-2-({[*tert*-butyl-(dimethyl)silyl]oxy}methyl)-6-vinylpiperidine-1-carboxylate ((+)-(2*R*,3*S*,6*R*)-11a): Following GP3, a solution of (+)-(2*R*,3*S*,6*R*)-**10a** (55.8 mg, 145 μmol) in CH_2Cl_2 (1.5 mL) was added to a solution of Na_2CO_3 (230 mg, 2.17 mmol) in H_2O (1.5 mL). The mixture was cooled to 0°C and benzyl chloroformate (123 mg, 721 μmol) was added dropwise. After complete addition the ice bath was removed, and the mixture was allowed to warm to room temperature. After 2.5 h conversion was complete according to TLC control (petroleum ether/diethyl ether 4:1, R_f(**10a**)=0.19, R_f(**11a**)=0.48), and the mixture was extracted with CH_2Cl_2 (4×3 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was subjected to flash chromatography on silica gel (5 g, petroleum ether/diethyl ether 20:1) to give pure (+)-(2*R*,3*S*,6*R*)-**11a** (73.1 mg, 97%) as a colorless oil. $[\alpha]_D^{20}=+26.2$ ($c=1.06$ in $CHCl_3$, >99% *ee*); ^{1}H NMR (300 MHz, $CHCl_3$): $\delta=7.38$–7.28 (m, 5H; Ph), 5.76 (ddd, $J=17.4$, 10.7, 4.9 Hz, 1H; =CH), 5.21–5.06 (m, 4H; CH_2Ph, $=CH_2$), 4.81 (br s, 1H; 6-H), 4.23–4.08 (m, 2H; 2-H, 3-H), 3.54–3.48 (m, 2H; CH_2OSi), 2.23 (dddd, $J=13.6$, 13.6, 6.2, 3.5 Hz, 1H; 5-H_a), 1.77 (dddd, $J=13.6$, 13.6, 2.7, 2.7 Hz, 1H; 4-H_a), 1.64–1.42 (m, 2H; 4-H_b, 5-H_b), 0.86 (s, 18H; $C(CH_3)_3$), 0.04 (s, 6H; $SiCH_3$), −0.01 ppm (br s, 6H; $SiCH_3$); ^{13}C NMR (75 MHz, $CHCl_3$): $\delta=156.56$ (s, CO_2), 147.35 (d, =CH), 137.06 (s, Ph), 128.52, 127.92, 127.85 (3d, Ph), 115.19 (t, $=CH_2$), 67.14 (t, CH_2Ph), 64.08 (d, C-3), 63.14 (t, CH_2OSi), 60.24 (d, C-2), 51.28 (d, C-6), 25.97, 25.91 (2q, $C(CH_3)_3$), 22.56 (t, C-4), 20.39 (t, C-5), 18.29, 18.17 (2s, $C(CH_3)_3$), −4.71, −4.80, −5.26, −5.47 ppm (4q, $SiCH_3$); elemental analysis calcd (%) for $C_{28}H_{49}NO_4Si_2$: C 64.69, H 9.50, N 2.69; found C 64.61, H 9.43, N 2.63; HRMS (ESI+): *m*/*z*: calcd for $C_{28}H_{49}NNaO_4Si_2^+$: 542.3092; found: 542.3087 $[M+Na]^+$.

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(+)-Benzyl (2*R*,3*S*,6*S*)-3-{[*tert*-butyl(dimethyl)silyl]oxy}-2-({[*tert*-butyl-(dimethyl)silyl]oxy}methyl)-6-vinylpiperidine-1-carboxylate ((+)-(2*R*,3*S*,6*S*)-11b): According to GP3, a solution of (+)-(2*R*,3*S*,6*S*)-**10b** (183 mg, 475 μmol) in CH_2Cl_2 (4.0 mL) was added to a solution of Na_2CO_3 (754 mg, 7.11 mmol) in H_2O (4.0 mL). The mixture was cooled to 0 °C and benzyl chloroformate (405 mg, 2.37 mmol) was added dropwise. When the addition was complete, the ice bath was removed, and the mixture was allowed to warm to room temperature. After 15 min the reaction was complete according to TLC analysis (petroleum ether/ethyl acetate 4:1, R_f(**10b**) = 0.31, R_f(**11b**) = 0.65, $KMnO_4$), and the mixture was extracted with CH_2Cl_2 (4 × 10 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (5 g, petroleum ether/diethyl ether 20:1) to give (+)-(2*R*,3*S*,6*S*)-**11b** (233 mg, 94 %) as a colorless oil. $[\alpha]_D^{20} = +10.7$ ($c = 0.99$ in $CHCl_3$, >99 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.36$–7.27 (m, 5H; Ph), 6.24 (ddd, $J = 17.3$, 10.3, 7.1 Hz, 1H; C*H*=CH$_2$), 5.16 (d, $J = 12.6$ Hz, 1H; CH_aH_bPh), 5.12–5.05 (m, 1H; CH=CH$_E H_Z$), 5.09 (d, $J = 12.6$ Hz, 1H; CH$_a H_b$Ph), 5.02 (ddd, J = 10.4, 1.8, 1.8 Hz, 1H; CH=CH$_E$H$_Z$), 4.24–4.20 (m, 2H; 3-H, 6-H), 4.00 (ddd, $J = 8.5$, 4.3, 3.9 Hz, 1H; 2-H), 3.73 (dd, $J = 9.6$, 4.5 Hz, 1H; CH_aH_bOSi), 3.56 (dd, $J = 9.5$, 9.5 Hz, 1H; CH$_a H_b$OSi), 1.98–1.87 (m, 1H; CH$_2$CH_aH_b), 1.84–1.61 (m, 3H; CH$_2$CH$_a H_b$), 0.87, 0.87 (2s, 18H; C(CH$_3$)$_3$), 0.05, 0.04 (2s, 6H; SiCH$_3$), 0.00 ppm (s, 6H; SiCH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 156.44$ (s, CO_2), 140.33 (d, =CH), 137.05 (s, Ph), 128.46, 127.95, 127.87 (3d, Ph), 113.63 (t, =CH$_2$), 66.85 (t, CH$_2$Ph), 65.55 (d, C-3), 62.86 (t, CH$_2$OSi), 60.91 (d, C-2), 55.12 (d, C-6), 26.15,§ 25.97,# 25.94,§ 25.90# (2×2q, C(*C*H$_3$)$_3$), 18.28, 18.10 (2s, *C*(CH$_3$)$_3$), −4.68, −4.79, −5.29, −5.47 ppm (4q, SiCH$_3$) (the CH$_3$ resonances of the *tert*-butyl groups appear as a pair of each two sharp (#) and two smaller and slightly broadened (§) signals); elemental analysis calcd (%) for $C_{28}H_{49}NO_4Si_2$: C 64.69, H 9.50, N 2.69; found C 64.77, H 9.53, N 2.67; HRMS (ESI+): *m*/*z*: calcd for $C_{28}H_{50}NO_4Si_2^+$: 520.3273; found: 520.3281 $[M+H]^+$.

(+)-Benzyl (2*R*,3*S*,6*R*)-3-Hydroxy-2-(hydroxymethyl)-6-vinylpiperidine-1-carboxylate ((+)-(2*R*,3*S*,6*R*)-12a): A solution of (+)-(2*R*,3*S*,6*R*)-**11a** (222 mg, 427 μmol) in methanol (1.0 mL) was treated with 20 % HCl/MeOH (2.0 mL, prepared from concentrated aqueous HCl (ca. 12 M, 0.4 mL) and methanol (1.6 mL)) and stirred at room temperature for 2.5 h when complete conversion was indicated by TLC control (petroleum ether/ethyl acetate 4:1, R_f(**11a**) = 0.63, R_f(**12a**) < 0.1, $KMnO_4$). $NaHCO_3$ was added in small portions until gas evolution ceased and the mixture was extracted with ethyl acetate (4 × 5 mL). The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (3 g, petroleum ether/ethyl acetate 1:1 to 1:2) to give the pure diol (+)-(2*R*,3*S*,6*R*)-**12a** (123 mg, 99 %) as a colorless oil. $[\alpha]_D^{20} = +28.0$ ($c = 0.68$ in $CHCl_3$, >99 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.37$–7.27 (m, 5H; Ph), 5.81 (ddd, $J = 17.4$, 10.6, 4.9 Hz, 1H; C*H*=CH$_2$), 5.17–5.09 (m, 2H; CH=C*H*$_2$), 5.16 (d, $J = 12.4$ Hz, 1H; CH_aH_bPh), 5.08 (d, $J = 12.4$ Hz, 1H; CH$_a H_b$Ph), 4.83–4.76 (m, 1H; 6-H), 4.35 (dd, $J = 7.3$, 7.3 Hz, 1H; 2-H), 4.08 (brs, 1H; C*H*OH), 3.59 (dd, $J = 10.9$, 6.8 Hz, 1H; CH_aH_bOH), 3.54 (dd, $J = 10.8$, 8.6 Hz, 1H; CH$_a H_b$OH), 3.19 (brs, 2H; OH), 2.25–2.12 (m, 1H; 5-H$_a$), 1.86–1.74 (m, 1H; 4-H$_a$), 1.68–1.60 ppm (m, 2H; 4-H$_b$, 5-H$_b$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 157.42$ (s, CO_2), 139.13 (d, =CH), 136.47 (s, Ph), 128.62, 128.15, 127.91 (3d, Ph), 115.79 (t, =CH$_2$), 67.74 (t, CH$_2$Ph), 64.13 (d, CHOH), 63.33 (t, CH$_2$OH), 60.41 (d, C-2), 51.58 (d, C-6), 22.15 (t, C-4), 20.60 ppm (t, C-5); HRMS (ESI+): *m*/*z*: calcd for $C_{16}H_{22}NO_4^+$: 292.1543; found: 292.1545 $[M+H]^+$.

(−)-Benzyl (2*R*,3*S*,6*S*)-3-hydroxy-2-(hydroxymethyl)-6-vinylpiperidine-1-carboxylate ((−)-(2*R*,3*S*,6*S*)-12b): This compound was prepared analogously to (+)-(2*R*,3*S*,6*R*)-**12a** from (+)-(2*R*,3*S*,6*S*)-**11b** (195 mg, 375 μmol). After 2.5 h, when the starting material was no longer detected by TLC control (petroleum ether/ethyl acetate 4:1, R_f(**11b**) = 0.65, R_f-(**12b**) < 0.1, $KMnO_4$), workup was carried out by addition of $NaHCO_3$ and extraction with ethyl acetate. The pure diol (−)-(2*R*,3*S*,6*S*)-**12b** (103 mg, 94 %) was obtained after purification by flash chromatography on silica gel (3 g, petroleum ether/ethyl acetate 1:1 to 1:2) as a colorless oil. $[\alpha]_D^{20} = -19.7$ ($c = 1.08$ in $CHCl_3$, >99 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.40$–7.29 (m, 5H; Ph), 5.78 (ddd, $J = 17.5$, 10.7, 3.6 Hz, 1H; C*H*=CH$_2$), 5.27 (ddd, $J = 10.7$, 2.4, 0.9 Hz, 1H; CH=CH$_E H_Z$), 5.20–5.12 (m, 1H; CH=CH$_E H_Z$), 5.16 (d, $J = 12.4$ Hz, 1H; CH_aH_bPh), 5.11 (d, J = 12.4 Hz, 1H; CH$_a H_b$Ph), 4.92–4.86 (m, 1H; 6-H), 4.62 (brs, 1H; CH$_2$O*H*), 4.13–3.99 (m, 2H; C*H*$_2$OH), 3.91–3.81 (m, 1H; C*H*OH), 3.19 (ddd, $J = 9.6$, 4.0, 3.0 Hz, 1H; 2-H), 3.11 (brs, 1H; CHO*H*), 1.98–1.85 (m, 2H; 4-H$_a$, 5-H$_a$), 1.82–1.58 ppm (m, 2H; 4-H$_b$, 5-H$_b$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 156.30$ (s, CO_2), 136.54 (d, =CH), 136.35 (s, Ph), 128.70, 128.31, 127.94 (3d, Ph), 117.15 (t, =CH$_2$), 67.58 (t, CH$_2$Ph), 67.09 (d, C-3), 61.17 (d, C-2), 60.08 (t, CH$_2$OH), 55.30 (d, C-6), 28.75 (t, C-4), 26.40 ppm (t, C-5); HRMS (ESI+): *m*/*z*: calcd for $C_{16}H_{22}NO_4^+$: 292.1543; found: 292.1546 $[M+H]^+$.

General procedure 4 (GP4, cross-metathesis): In a flame-dried Schlenk tube under an argon atmosphere, a solution of the piperidine derivative (0.1 mmol) and the olefin representing the side chain (0.3–1.0 mmol) in dry CH_2Cl_2 (1 mL) was treated with Grubbs II or Grubbs II–Hoveyda catalyst (1–10 μmol) and heated at reflux. If necessary, further portions of the catalyst and the side chain olefin were added until TLC control indicated complete or no further conversion (1–24 h). The mixture was concentrated and purified by flash chromatography on silica gel and, if necessary, by preparative HPLC.

(+)-Benzyl (2*R*,3*S*,6*R*)-3-hydroxy-2-(hydroxymethyl)-6-[(*E*)-10′-oxododec-1′-en-1′-yl]piperidine-1-carboxylate ((+)-(2*R*,3*S*,6*R*,*E*)-14a): Following GP4, Grubbs II–Hoveyda catalyst (2.0 mg, 3.2 μmol) was added to a solution of (+)-(2*R*,3*S*,6*R*)-**12a** (46.2 mg, 159 μmol) and **13** (145 mg, 797 μmol) in dry CH_2Cl_2 (1.5 mL), and the mixture was heated at reflux. An additional 5 portions of the catalyst (each 2.0 mg, 3.2 μmol) were added after intervals of 2 h each, and stirring was continued at reflux overnight. After 25 h no further conversion was detected by TLC control (ethyl acetate, R_f(**12a**) = 0.33, R_f(**14a**) = 0.39, $KMnO_4$), and the mixture was concentrated under reduced pressure. The residue was subjected to flash chromatography on silica gel (3 g, ethyl acetate) and subsequent preparative HPLC (ethyl acetate, column: ProntoSIL, 250 × 20 mm, 5 μ silica gel, 15 mL min^{-1}, 100 bar) to give pure (+)-(2*R*,3*S*,6*R*,*E*)-**14a** (40.8 mg, 58 %) as colorless needles (m.p. 50–51 °C); $[\alpha]_D^{20} = +41.7$ (c = 0.82 in $CHCl_3$, >99 % *ee*); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.34$–7.27 (m, 5H; Ph), 5.51 (ddd, $J = 14.9$, 6.8, 6.8 Hz, 1H; 2′-H), 5.36 (dd, $J = 15.6$, 5.2 Hz, 1H; 1′-H), 5.15 (d, $J = 12.3$ Hz, 1H; CH_aH_bPh), 5.05 (d, J = 12.3 Hz, CH$_a H_b$Ph), 4.74 (brs, 1H; 6-H), 4.32 (dd, $J = 7.1$, 7.1 Hz, 1H; 2-H), 4.10 (brs, 1H; 3-H), 3.57 (dd, $J = 10.7$, 6.0 Hz, 1H; CH_aH_bOH), 3.53 (dd, $J = 11.0$, 8.5 Hz, 1H; CH$_a H_b$OH), 3.32 (brs, 2H; OH), 2.40 (q, J = 7.7 Hz, 2H; C*H*$_2$CH$_3$), 2.37 (t, $J = 7.8$ Hz, 2H; 9′-H), 2.19–2.11 (m, 1H; 5-H$_a$), 1.95 (ddd, $J = 6.9$, 6.9, 6.9 Hz, 2H; 3′-H), 1.85–1.78 (m, 1H; 4-H$_a$), 1.65–1.60 (m, 1H; 4-H$_b$), 1.56–1.51 (m, 3H; 5-H$_b$, 8′-H), 1.31–1.20 (m, 8H; (CH$_2$)$_4$), 1.03 ppm (t, $J = 7.3$ Hz, 3H; CH$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 212.31$ (s, C=O), 157.28 (s, CO_2), 136.61 (s, Ph), 132.27 (d, C-2′), 130.38 (d, C-1′), 128.54, 128.05, 127.88 (3d, Ph), 67.56 (t, CH$_2$Ph), 64.15 (d, C-3), 63.44 (t, CH$_2$OH), 60.37 (d, C-2), 51.03 (d, C-6), 42.47 (t, C-9′), 35.99 (t, C-11′), 32.43 (t, C-3′), 29.27, 29.27, 29.10, 29.01 (4 t, C-4′, C-5′, C-6′, C-7′), 23.93 (t, C-8′), 22.10 (t, C-4), 21.35 (t, C-5), 7.94 ppm (q, CH$_3$); HRMS (ESI+): *m*/*z*: calcd for $C_{26}H_{39}NNaO_5^+$: 468.2720; found: 468.2717 $[M+Na]^+$.

(−)-Benzyl (2*R*,3*S*,6*S*)-3-hydroxy-2-(hydroxymethyl)-6-[(*E*)-10′-oxododec-1′-en-1′-yl]piperidine-1-carboxylate ((−)-(2*R*,3*S*,6*S*,*E*)-14b): Following GP4, a solution of (−)-(2*R*,3*S*,6*S*)-**12b** (39.0 mg, 134 μmol) and **13** (122 mg, 670 μmol) in dry CH_2Cl_2 (750 μL) was treated with Grubbs II–Hoveyda catalyst (2.5 mg, 4 μmol) and heated at reflux. A second and a third portion of the catalyst (each 2.5 mg, 4 μmol) was added after 2 h and 5 h reaction time, respectively. After 8.5 h the mixture was allowed to cool to room temperature, and stirring was continued overnight. After 24 h TLC control (ethyl acetate, R_f(**12b**) = 0.40, R_f(**14b**) = 0.47, $KMnO_4$) showed almost complete conversion. The mixture was concentrated in vacuo, and the residue was subjected to flash chromatography on silica gel (4 g, petroleum ether/ethyl acetate 1:1) and preparative HPLC (ethyl acetate, column: ProntoSIL, 250 × 20 mm, 5 μ silica gel, 15 mL min^{-1}, 54 bar) to give pure (−)-(2*R*,3*S*,6*S*,*E*)-**14b** (36.8 mg, 62 %) as a colorless oil together with some recovered starting material (−)-(2*R*,3*S*,6*S*)-**12b** (2.7 mg, 7 %). $[\alpha]_D^{20} = -41.3$ ($c = 1.43$ in $CHCl_3$, >99 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.37$–7.30 (m, 5H; Ph), 5.55 (dddd, $J = 15.6$, 6.8, 6.8, 1.8 Hz, 1H; 2′-H), 5.38 (dd, $J = 15.6$, 4.1 Hz, 1H; 1′-H), 5.14 (d, J =

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12.3 Hz, 1H; CH_aH$_b$Ph), 5.11 (d, J=12.3 Hz, 1H; CH$_a$$H_b$Ph), 4.85 (brs, 1H; 6-H), 4.61 (brs, 1H; CH$_2$OH), 4.08–4.00 (m, 2H; CH_2OH), 3.86–3.82 (m, 1H; 3-H), 3.22–3.17 (m, 1H; 2-H), 3.00 (brs, 1H; CHOH), 2.40 (q, J=7.7 Hz, 2H; CH_2CH$_3$), 2.38 (t, J=7.8 Hz, 2H; 9′-H), 2.02 (dt, J=7.0, 7.0 Hz, 2H; 3′-H), 1.94–1.90 (m, 1H; 4-H$_a$), 1.85–1.81 (m, 1H; 5-H$_a$), 1.75–1.62 (m, 2H; 4-H$_b$, 5-H$_b$), 1.58–1.52 (m, 2H; 8′-H), 1.37–1.30 (m, 2H; 4′-H), 1.30–1.22 (m, 6H; 5′-H, 6′-H, 7′-H), 1.04 ppm (t, J=7.3 Hz, 3H; CH$_3$); ^{13}C NMR (125 MHz, CDCl$_3$): δ=212.08 (s, C=O), 156.26 (s, CO$_2$), 136.47 (s, Ph), 133.69 (d, C-1′), 128.67, 128.25, 127.90 (3 d, Ph), 127.75 (d, C-2′), 67.45 (t, CH$_2$Ph), 67.27 (d, C-3), 60.96 (d, C-2), 60.15 (t, CH$_2$OH), 54.74 (d, C-6), 42.48 (t, C-9′), 35.99 (t, CH$_2$CH$_3$), 32.53 (t, C-3′), 29.30, 29.29, 29.17, 29.07, 28.80 (5 t, C-4, C-4′, C-5′, C-6′, C-7′), 27.03 (t, C-5), 23.97 (t, C-8′), 7.97 ppm (q, CH$_3$); elemental analysis calcd (%) for C$_{26}$H$_{39}$NO$_5$: C 70.08, H 8.82, N 3.14; found C 69.90, H 8.80, N 3.10; HRMS (ESI+): m/z: calcd for C$_{26}$H$_{39}$NNaO$_5^+$: 468.2720; found: 468.2719 [M+Na]$^+$.

General procedure 5 (GP5, catalytic hydrogenation on Pd(OH)$_2$/C): Under an atmosphere of hydrogen (1 bar) in a flame dried Schlenk tube, palladium hydroxide (ca. 10–20 wt% (dry) on activated charcoal, wet, ca. 50% H$_2$O) (5 mg, 3.6 μmol) was suspended in dry methanol (0.5 mL), and the mixture was stirred for 30 min. A solution of the olefin (0.1 mmol) in dry methanol (0.5 mL) was added and the mixture was stirred at room temperature until TLC control showed complete conversion (1–4 h). The mixture was filtered through a pad of silica gel, and the filtrate was concentrated under reduced pressure.

(+)-12-[(2′*S*,5′*S*,6′*R*)-5′-Hydroxy-6′-(hydroxymethyl)piperidin-2′-yl]dodecan-3-one ((+)-(2′*S*,5′*S*,6′*R*)-prosophylline; (+)-15a): According to GP5, a suspension of palladium hydroxide (2.5 mg) in methanol (400 μL) was stirred under an atmosphere of hydrogen (1 bar) for 30 min. Then a solution of (+)-(2*R*,3*S*,6*R*,*E*)-**14a** (24.9 mg, 55.9 μmol) in methanol (500 μL) was added, and the mixture was stirred at room temperature for 1 h when the starting compound was consumed according to TLC control (ethyl acetate, R_f(**14a**)=0.39, R_f(prosophylline)<0.1, KMnO$_4$). The mixture was filtered through a pad of Celite and the filtrate concentrated under reduced pressure to give a colorless oil, which was dissolved in ethyl acetate (5 mL). The resulting solution was washed with aqueous NaOH (2×2 mL, 1 N), and the aqueous layer was re-extracted with ethyl acetate (2×1 mL). The combined organic layers were dried over Na$_2$SO$_4$ and concentrated in vacuo to give pure (by NMR spectroscopy) (+)-(2′*S*,5′*S*,6′*R*)-prosophylline (17.4 mg, 99%) as a colorless solid showing physical properties that matched those reported.[14,17] Recrystallization from acetone afforded colorless crystals. M.p. 85.5–86 °C (ref. [17a]: 77–79 °C ((−)-prosophylline); ref. [17e]: 82–83 °C ((±)-prosophylline)); $[\alpha]_D^{20}$=+10.3 (c=1.30 in CHCl$_3$, >99% *ee*) (ref. [15a]: $[\alpha]_D^{26}$=−12.9 (c=2.54, CHCl$_3$ ((−)-prosophylline))); ^{1}H NMR (600 MHz, CDCl$_3$): δ=3.81 (dd, J=10.8, 4.5 Hz, 1H; CH_aH$_b$OH), 3.69 (dd, J=10.8, 5.4 Hz, 1H; CH$_a$$H_b$OH), 3.44 (ddd, J=10.0, 9.9, 4.5 Hz, 1H; 5′-H), 2.71 (brs, 3H; OH, NH), 2.54 (ddd, J=9.3, 4.8, 4.8 Hz, 1H; 6′-H), 2.53–2.48 (m, 1H; 2′-H), 2.41 (q, J=7.3 Hz, 2H; CH_2CH$_3$), 2.38 (t, J=7.3 Hz, 2H; 4-H), 2.04–2.00 (m, 1H; 4′-H$_a$), 1.75–1.71 (m, 1H; 3′-H$_a$), 1.57–1.52 (m, 2H; 5-H), 1.40–1.31 (m, 3H; 12-H, 4′-H$_b$), 1.31–1.22 (m, 12H; (CH$_2$)$_6$), 1.11 (dddd, J=13.5, 13.5, 10.9, 3.2 Hz, 1H; 3′-H$_b$), 1.03 ppm (t, J=7.4 Hz, 3H; CH$_3$); ^{13}C NMR (151 MHz, CDCl$_3$): δ=212.32 (s, C=O), 70.43 (d, C-5′), 64.47 (t, CH$_2$OH), 63.35 (d, C-6′), 56.14 (d, C-2′), 42.55 (t, C-4), 36.60 (t, C-12), 35.99 (t, C-2), 33.96 (t, C-4′), 31.15 (t, C-3′), 29.83, 29.60, 29.50, 29.48, 29.36, 26.29 [6t, (CH$_2$)$_6$), 24.04 (t, C-5), 7.98 ppm (q, CH$_3$); HRMS (ESI+): m/z: calcd for C$_{18}$H$_{36}$NO$_3^+$: 314.2690; found: 314.2691 [M+H]$^+$.

(+)-12-[(2′*R*,5′*S*,6′*R*)-5′-Hydroxy-6′-(hydroxymethyl)piperidin-2′-yl]dodecan-3-one ((+)-(2′*R*,5′*S*,6′*R*)-prosopinine (+)-15b): Following GP5, a suspension of palladium hydroxide (3.4 mg) in methanol (500 μL) was stirred under an atmosphere of hydrogen (1 bar) for 30 min. A solution of (−)-(2*R*,3*S*,6*S*,*E*)-**14b** (28.5 mg, 64.0 μmol) in methanol (750 μL) was added, and the mixture was stirred for 1 h when TLC analysis (ethyl acetate, R_f(**14b**)=0.45, R_f(**15b**)<0.1, KMnO$_4$) indicated complete consumption of the substrate. The mixture was filtered through a pad of Celite and all volatiles were evaporated to give analytically pure (+)-(2′*R*,5′*S*,6′*R*)-prosopinine (20.1 mg, quant.) as a colorless crystalline solid, the spectroscopic data of which were in accordance with the reported data.[11,15,58] Recrystallization from acetone afforded colorless needles (m.p. 100.0–100.5 °C; ref. [15b]: 96–99 °C ((−)-prosopinine (CHCl$_3$/Et$_2$O))). The relative configuration of the product was confirmed by X-ray crystal structural analysis. $[\alpha]_D^{20}$=+11.7 (c=0.70 in CHCl$_3$, >99% *ee*) (refs. [11,12b,13]: $[\alpha]_D^{20}$=+12 (c=0.01, CHCl$_3$)); ^{1}H NMR (600 MHz, CDCl$_3$): δ=3.74 (brs, 3H; NH, OH), 3.66 (dd, J=10.9, 7.1 Hz, 1H; CH_aH$_b$OH), 3.63 (dd, J=10.9, 5.0 Hz, 1H; CH$_a$$H_b$OH), 3.53 (ddd, J=6.6, 6.6, 3.8 Hz, 1H; 5′-H), 2.86 (ddd, J=6.0, 6.0, 6.0 Hz, 1H; 6′-H), 2.83–2.79 (m, 1H; 2′-H), 2.39 (q, J=7.3 Hz, 2H; CH_2CH$_3$), 2.36 (t, J=7.5 Hz, 2H; 4-H), 1.73–1.68 (m, 1H; 4′-H$_a$), 1.64–1.57 (m, 2H; 3′-H$_a$, 4′-H$_b$), 1.56–1.46 (m, 4H; 5-H, 12-H$_a$, 3′-H$_b$), 1.43–1.37 (m, 1H; 12-H$_b$), 1.30–1.19 (m, 12H; (CH$_2$)$_6$), 1.01 ppm (t, J=7.4 Hz, 3H; CH$_3$); ^{13}C NMR (151 MHz, CDCl$_3$): δ=212.33 (s, C=O), 67.45 (d, C-5′), 61.84 (t, CH$_2$OH), 58.14 (d, C-6′), 50.39 (d, C-2′), 42.50 (t, C-4), 35.94 (t, C-2), 33.05 (t, C-12), 29.67, 29.57, 29.45, 29.44, 29.30 (5t, CH$_2$), 28.24 (t, C-4′), 26.86 (t, C-3′), 26.40 (t, CH$_2$), 23.98 (t, C-5), 7.93 ppm (q, CH$_3$); HRMS (ESI+): m/z: calcd for C$_{18}$H$_{36}$NO$_3^+$: 314.2690; found: 314.2689 [M+H]$^+$.

(+)-Benzyl (2*R*,3*S*,6*R*)-3-hydroxy-6-[(*E*,11′*S*)-11′-hydroxydodec-1′-en-1′-yl]-2-(hydroxymethyl)piperidine-1-carboxylate ((+)-(2*R*,3*S*,6*R*,*E*,11′*S*)-17a): Following GP4, Grubbs II–Hoveyda catalyst (8.4 mg, 13.4 μmol) was added to a solution of (+)-(2*R*,3*S*,6*R*)-**12a** (80.0 mg, 275 μmol) and (+)-(*S*)-**16** (237 mg, 1.29 mmol) in dry CH$_2$Cl$_2$ (1.5 mL), and the mixture was heated at reflux. After 2 h TLC control (ethyl acetate, R_f(**12a**)=0.23, R_f(**17a**)=0.20, KMnO$_4$) still showed some starting material, and another portion of the catalyst (3.4 mg, 5.4 μmol) was added. After 5.5 h conversion was complete, and the mixture was concentrated in vacuo, and the residue subjected to flash chromatography on silica gel (3 g, petroleum ether/ethyl acetate 1:1 to ethyl acetate). The product obtained (105 mg, 85%) was still contaminated with unidentified side products and purified by repeated preparative HPLC (ethyl acetate, column: ProntoSIL, 250×20 mm, 5 μ silica gel, 15 mL min^{-1}, 58 bar) to furnish analytically pure (+)-(2*R*,3*S*,6*R*,*E*,11′*S*)-**17a** (41.5 mg, 34%) as a colorless oil. $[\alpha]_D^{20}$=+34.2 (c=1.18 in CHCl$_3$, >99% *ee*); ^{1}H NMR (500 MHz, CDCl$_3$): δ=7.36–7.28 (m, 5H; Ph), 5.52 (ddd, J=14.8, 7.1, 7.1 Hz, 1H; 2′-H), 5.38 (dd, J=15.5, 5.6 Hz, 1H; 1′-H), 5.16 (d, J=12.3 Hz, CH_aH$_b$Ph), 5.07 (d, J=12.6 Hz, 1H; CH$_a$$H_b$Ph), 4.75 (m, 1H; 6-H), 4.34–4.26 (m, 1H; 2-H), 4.10 (brs, 1H; 3-H), 3.77 (qt, J=6.0, 5.9 Hz, 1H; 11′-H), 3.62–3.51 (m, 2H; CH_2OH), 3.13 (brs, 2H; OH), 2.19–2.12 (m, 1H; 5-H$_a$), 2.03 (brs, 1H; OH), 1.96 (dt, J=7.0, 7.0 Hz, 2H; 3′-H), 1.86–1.79 (m, 1H; 4-H$_a$), 1.66–1.61 (m, 1H; 4-H$_b$), 1.58–1.52 (m, 1H; 5-H$_b$), 1.48–1.19 (m, 14H; (CH$_2$)$_7$), 1.16 ppm (d, J=6.3 Hz, 3H; CH$_3$); ^{13}C NMR (126 MHz, CDCl$_3$): δ=157.32 (s, CO$_2$), 136.61 (s, Ph), 132.46 (d, C-2′), 130.33 (d, C-1′), 128.59, 128.10, 127.94 (3d, Ph), 68.21 (d, C-11′), 67.61 (t, CH$_2$Ph), 64.19 (d, C-3), 63.49 (t, CH$_2$OH), 60.47 (d, C-2), 51.11 (d, C-6), 39.36 (t, C-10′), 32.40 (t, C-3′), 29.61, 29.58, 29.33, 29.10, 29.09, 25.79 (6t, CH$_2$), 23.51 (q, CH$_3$), 22.14 (t, C-4), 21.45 ppm (t, C-5); HRMS (ESI+): m/z: calcd for C$_{26}$H$_{41}$NNaO$_5^+$: 470.2877; found: 470.2879 [M+Na]$^+$.

(+)-(2*R*,3*S*,6*S*)-6-[(11′*S*)-11′-Hydroxydodecyl]-2-(hydroxymethyl)piperidin-3-ol ((+)-6-*epi*-prosopine; (+)-18a)): According to GP5, as suspension of palladium hydroxide (2.2 mg) in methanol (500 μL) was stirred for 30 min under an hydrogen atmosphere (1 bar). A solution of (+)-**17a** (23.6 mg, 52.8 μmol) in methanol (400 μL) was added, and the mixture was stirred at room temperature. After 3 h conversion was incomplete according to TLC (ethyl acetate, R_f(**17a**)=0.20, R_f(**18a**)<0.1), and another portion of the palladium catalyst (2.5 mg) was added. After being stirred for another 1 h, complete conversion was reached, and the mixture was filtered through a pad of Celite. Evaporation of all volatiles gave (+)-**18a** (16.5 mg, 99%) as a colorless oil. $[\alpha]_D^{20}$=+29.9 (c=0.84 in MeOH, >99% *ee*); ^{1}H NMR (600 MHz, CD$_3$OD): δ=3.94 (dd, J=11.5, 3.0 Hz, 1H; CH_aH$_b$OH), 3.74 (dd, J=11.5, 6.3 Hz, 1H; CH$_a$$H_b$OH), 3.72–3.68 (m, 1H; 11′-H), 3.54 (ddd, J=10.7, 10.2, 4.6 Hz, 1H; 3-H), 2.90–2.86 (m, 1H; 6-H), 2.79–2.76 (m, 1H; 2-H), 2.11–2.07 (m, 1H; 4-H$_a$), 1.99–1.95 (m, 1H; 5-H$_a$), 1.68–1.63 (m, 1H; 1′-H$_a$), 1.51–1.27 (m, 21H; (CH$_2$)$_9$, 1′-H$_b$, 4-H$_b$, 5-H$_b$), 1.14 ppm (d, J=6.2 Hz, 3H; CH$_3$); ^{13}C NMR (151 MHz, CD$_3$OD): δ=68.53 (d, C-11′), 67.26 (d, C-3), 64.68 (d, C-2), 60.90 (t, CH$_2$OH), 58.03 (d, C-6), 40.20 (t, C-10′), 34.98 (t, C-1′), 33.51 (t, C-4), 30.84, 30.75, 30.70, 30.65, 30.61, 30.55 (6t, CH$_2$), 29.13 (t, C-5), 26.90, 26.82 (2t, CH$_2$), 23.53 ppm (q, CH$_3$); HRMS (ESI+): m/z: calcd for C$_{18}$H$_{37}$NNaO$_3^+$: 338.2666; found: 338.2668 [M+Na]$^+$.

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(−)-Benzyl (2*R*,3*S*,6*S*)-3-hydroxy-6-[(*E*,11′*S*)-11′-hydroxydodec-1′-en-1′-yl]-2-(hydroxymethyl)piperidine-1-carboxylate ((−)-(2*R*,3*S*,6*S*,*E*,11′*S*)-17b): According to GP4, Grubbs II–Hoveyda catalyst (5.0 mg, 8.0 μmol) was added to a solution of (−)-**12b** (32.0 mg, 110 μmol) and (+)-(*S*)-**16** (59.0 mg, 320 μmol) in dry CH_2Cl_2 (600 μL). The solution was heated at reflux for 1 h when TLC control (ethyl acetate, R_f(**12b**) = 0.38, R_f(**17b**) = 0.32, R_f(**16**) = 0.58, $KMnO_4$) showed complete conversion. The mixture was concentrated in vacuo, and the residue was subjected to flash chromatography on silica gel (2 g, ethyl acetate) and subsequent preparative HPLC (ethyl acetate, column: ProntoSIL, 250 × 20 mm, 5 μ silica gel, 15 mL min^{-1}, 100 bar) to yield pure (−)-**17b** (28 mg, 57%) as a colorless oil. $[\alpha]_D^{20} = -38.6$ (c = 0.81 in $CHCl_3$, >99% *ee*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.30 (m, 5H; Ph), 5.55 (dddd, J = 15.5, 6.8, 6.8, 1.6 Hz, 1H; 2′-H), 5.39 (dd, J = 15.8, 4.0 Hz, 1H; 1′-H), 5.14 (d, J = 12.3 Hz, 1H; CH_aH$_b$Ph), 5.10 (d, J = 12.3 Hz, 1H; CH$_a$$H_b$Ph), 4.85 (brs, 1H; 6-H), 4.73 (brs, 1H; CH_2OH), 4.08–3.99 (m, 2H; CH_2OH), 3.85–3.80 (m, 1H; 3-H), 3.77 (qt, J = 6.0, 6.0 Hz, 1H; 11′-H), 3.34 (brs, 1H; 3-OH), 3.20–3.18 (m, 1H; 2-H), 2.02 (dt, J = 7.0, 7.0 Hz, 2H; 3′-H), 1.95–1.90 (m, 2H; 4-H$_a$, 11′-OH), 1.84–1.78 (m, 1H; 5-H$_a$), 1.74–1.62 (m, 2H; 4-H$_b$, 5-H$_b$), 1.49–1.22 (m, 14H; $(CH_2)_7$), 1.17 ppm (d, J = 6.0 Hz, 3H; CH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 156.25 (s, CO_2), 136.47 (s, Ph), 133.76 (d, C-2′), 128.65, 128.23, 127.88 (3d, Ph), 127.68 (d, C-1′), 68.15 (d, C-11′), 67.45 (t, CH_2Ph), 67.03 (d, C-3), 61.02 (d, C-2), 60.02 (t, CH_2OH), 54.74 (d, C-6), 39.42 (t, C-10′), 32.54 (d, C-3′), 29.68, 29.62, 29.43, 29.21, 29.20 (5t, CH_2), 28.82 (t, C-4), 27.05 (t, C-5), 25.83 (t, CH_2), 23.55 ppm (q, CH_3); HRMS (ESI+): m/z: calcd for $C_{26}H_{42}NO_5^+$: 448.3058; found: 448.3054 $[M+H]^+$.

(+)-(2*R*,3*S*,6*R*)-6-[(11′*S*)-11′-Hydroxydodecyl]-2-(hydroxymethyl)piperidin-3-ol ((+)-(2*R*,3*S*,6*R*,11′*S*)-prosopine; (+)-18b): According to GP5, a suspension of palladium hydroxide (2.6 mg) in methanol (100 μL) was stirred under an atmosphere of hydrogen (1 bar) for 30 min. Then a solution of (−)-**17b** (19.0 mg, 42.5 μmol) in methanol (250 μL) was added, and the mixture was stirred for 2 h when complete conversion was indicated by TLC control (ethyl acetate, R_f(**17b**) = 0.32, R_f(prosopine) < 0.1, $KMnO_4$). Filtration through cotton and a pad of Celite and evaporation of all volatiles gave (+)-(2*R*,3*S*,6*R*)-prosopine as colorless solid (13.4 mg, quant.), the analytical data of which agreed with the data reported in the literature.[11, 12b, 13, 58] Recrystallization from acetone gave fine colorless needles. M.p. 127.5–128.5 °C (ref. [12b]: 126–127 °C). $[\alpha]_D^{20} = +21.0$ (c = 1.00 in MeOH, >99% *ee*) (ref. [12b]: $[\alpha]_D^{20} = +25$ (c = 1, MeOH)); ^{1}H NMR (600 MHz, CD_3OD): δ = 3.83 (dd, J = 11.0, 4.2 Hz, 1H; CH_aH$_b$OH), 3.70 (qt, J = 6.3, 5.8 Hz, 1H; 11′-H), 3.56 (dd, J = 10.9, 7.8 Hz, 1H; CH$_a$$H_b$OH), 3.45 (ddd, J = 7.8, 7.5, 4.1 Hz, 1H; 3-H), 2.95–2.91 (m, 1H; 6-H), 2.83 (ddd, J = 7.5, 7.5, 4.2 Hz, 1H; 2-H), 1.82–1.78 (m, 1H; 4-H$_a$), 1.73–1.68 (m, 1H; 5-H$_a$), 1.67–1.58 (m, 3H; 1′-H$_a$, 4-H$_b$, 5-H$_b$), 1.54–1.48 (m, 1H; 1′-H$_b$), 1.45–1.29 (m, 18H; $(CH_2)_9$), 1.14 ppm (d, J = 6.2 Hz, 3H; CH_3); ^{13}C NMR (151 MHz, CD_3OD): δ = 68.56 (d, C-11′), 68.15 (d, C-3), 62.51 (t, CH_2OH), 59.07 (d, C-2), 52.07 (d, C-6), 40.22 (t, C-10′), 32.65 (t, C-1′), 30.84, 30.76, 30.72, 30.72, 30.71, 30.67 (6t, CH_2), 28.89 (t, C-4), 27.33, 27.25 (2t, C-5, CH_2), 26.91 (t, CH_2), 23.51 ppm (q, CH_3); HRMS (ESI+): m/z: calcd for $C_{18}H_{38}NO_3^+$: 316.2846; found: 316.2846 $[M+H]^+$.

(+)-*tert*-Butyl [(*R*)-1-methyl-3-oxopropyl]carbamate ((+)-(*R*)-21):[45] In a flame-dried Schlenk tube under argon, a solution of oxalyl chloride (800 μL, 9.3 mmol) in dry CH_2Cl_2 (10 mL) was cooled to −78 °C. Dry dimethyl sulfoxide (2.0 mL, 28 mmol) was added dropwise, and the solution was stirred at −78 °C for 40 min. Then a solution of (−)-(*R*)-**20** (1.19 g, 6.28 mmol) in dry CH_2Cl_2 (20 mL) was added dropwise. The solution was allowed to warm to −30 °C over a period of 4.5 h and stirred for 4.5 h. The mixture was then again cooled to −78 °C and NEt_3 (4.4 mL, 31 mmol) was added. After stirring for 30 min the cooling bath was removed, and stirring was continued overnight. The mixture was washed with saturated aqueous NH_4Cl (2 × 100 mL), and the combined aqueous layers were extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to give a yellow oil, which was subjected to flash chromatography on silica gel (5 g, petroleum ether/ethyl acetate 4:1, R_f(**20**) = 0.47, R_f(**21**) = 0.55 (ethyl acetate), $KMnO_4$) to give aldehyde (+)-(*R*)-**21** (1.10 g, 93%) as a colorless oil. $[\alpha]_D^{20} = +27.6$ (c = 1.12 in $CHCl_3$, 97% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.72 (t, J = 2.0 Hz, 1H; CHO), 4.73 (d, J = 6.0 Hz, 1H; NH), 4.16–4.03 (m, 1H; CHN), 2.65–2.49 (m, 2H; CH_2), 1.39 (s, 9H; $C(CH_3)_3$), 1.20 ppm (d, J = 6.8 Hz, 3H; CH_3CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.03 (d, CHO), 155.21 (s, CO_2), 79.65 (s, $C(CH_3)_3$), 50.66 (t, CH_2), 42.48 (d, CHN), 28.45 (q, $C(CH_3)_3$), 21.06 ppm (q, CH_3CH); HRMS (EI+): m/z: calcd for $C_8H_{14}NO_3^+$: 172.0968; found: 172.0974 $[M\text{-}CH_3]^+$.

(+)-*tert*-Butyl [(1*R*,3*R*)-3-hydroxy-1-methylhex-5-en-1-yl]carbamate ((+)-(1*R*,3*R*)-22) and (+)-*tert*-butyl [(1*R*,3*S*)-3-hydroxy-1-methylhex-5-en-1-yl]carbamate ((+)-3-*epi*-22): According to a general procedure,[46b] a flame-dried flask equipped with a coolable dropping funnel was charged with a solution of aldehyde (+)-(*R*)-**21** (3.017 g, 16.11 mmol) in dry diethyl ether (150 mL) and cooled to −100 °C. The dropping funnel was charged with a solution of (+)-Ipc_2B(allyl) (1 M in *n*-pentane, 20.0 mL, 20.0 mmol) in dry diethyl ether (150 mL) and cooled to −78 °C. The borane solution was added dropwise over a period of 30 min to the solution of the aldehyde, and the mixture was then allowed to warm to −45 °C over a period of 1.5 h. Methanol (30 mL), aqueous NaOH (3 M, 15 mL) and aqueous hydrogen peroxide (30%, 15 mL) were added to give a white suspension, which was allowed to warm up to room temperature overnight. After 18 h the phases were separated and the organic layer was washed with aqueous NaOH (1 M, 2 × 70 mL) and saturated aqueous NH_4Cl (2 × 70 mL). The combined aqueous layers were extracted with diethyl ether (3 × 100 mL), and the combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure to give the crude product, which was analyzed by GC with respect to the diastereomeric ratio ((+)-**22**/(+)-3-*epi*-**22** = 93:7). Flash chromatography on silica gel (19 g, petroleum ether/ethyl acetate 7:1 to 4:1 to 2:1, R_f(**22**) = 0.24, R_f(3-*epi*-**22**) = 0.11 (petroleum ether/ethyl acetate 3:1), $KMnO_4$) gave pure (+)-3-*epi*-**22** (317 mg, 8.6%) and pure (+)-(1*R*,3*R*)-**22** (415 mg, 11.2%), both colorless oils, together with a fraction of (+)-(1*R*,3*R*)-**22** (8.489 g), which was contaminated with degradation products of the chiral borane. This fraction was purified by slow sublimation of the borane impurities in a Kugelrohr distillation apparatus (0.2 mbar, 40–50 °C) to yield pure (+)-(1*R*,3*R*)-**22** (2.81 g, 76%) as a colorless oil, which crystallized over a period of a few days as colorless polyhedra (m.p. 39.5–40.5 °C) that were subjected to X-ray crystal structural analysis.

*Analytic data for (+)-(1*R*,3*R*)-**22***: $[\alpha]_D^{20} = +4.6$ (c = 0.92 in $CHCl_3$, >99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.85 (ddd, J = 17.2, 10.1, 7.1 Hz, 1H; =CH), 5.11–5.04 (m, 2H; $=CH_2$), 4.50 (d, J = 8.0 Hz, 1H; NH), 3.92 (brs, 2H; CHN, OH), 3.67 (brs, 1H; C*H*OH), 2.32–2.14 (m, 2H; 4-H), 1.57–1.30 (m, 2H; 2-H), 1.43 (s, 9H; $C(CH_3)_3$), 1.16 ppm (d, J = 6.7 Hz, CH_3CH); ^{13}C NMR (75, $CDCl_3$): δ = 156.97 (s, CO_2), 135.50 (d, =CH), 117.05 (t, $=CH_2$), 79.92 (s, $C(CH_3)_3$), 67.32 (d, CHOH), 45.70 (t, C-2), 43.45 (d, CHN), 41.54 (t, C-4), 28.49 (q, $C(CH_3)_3$), 21.69 ppm (q, CH_3CH); elemental analysis calcd (%) for $C_{12}H_{23}NO_3$: C 62.85, H 10.11, N 6.11; found C 62.84, H 10.26, N 6.07; HRMS (ESI+): m/z: calcd for $C_{12}H_{23}NNaO_3^+$: 252.1570; found: 252.1572 $[M+Na]^+$. GC (achiral: HP-1, 140 °C isothermal): t_R((+)-(1*R*,3*R*)-**22**) = 17.6 min, t_R((+)-3-*epi*-**22**). GC (chiral: β-CD, 125 °C isothermal): t_R((+)-(1*R*,3*R*)-**22**) = 42.0 min, t_R((−)-(1*S*,3*S*)-**22**) = 45.8 min.

*Analytical data for (+)-3-epi-**22***: $[\alpha]_D^{20} = +12.6$ (c = 1.00 in $CHCl_3$, 96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.81 (dddd, J = 17.4, 9.8, 7.5, 6.9 Hz, 1H; =CH), 5.15–5.07 (m, 2H; $=CH_2$), 4.61 (brs, 1H; NH), 3.82–3.69 (m, 2H; CHN, C*H*OH), 2.46 (brs, 1H; OH), 2.30 (ddd, J = 13.8, 6.5, 5.0 Hz, 1H; 4-H$_a$), 2.18 (ddd, J = 14.0, 7.5, 7.5 Hz, 1H; 4-H$_b$), 1.64–1.53 (m, 2H; 2-H), 1.43 (s, 9H; $C(CH_3)_3$), 1.16 ppm (d, J = 6.6 Hz, 3H; CH_3CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.83 (s, CO_2), 134.79 (d, =CH), 118.20 (t, $=CH_2$), 79.46 (s, $C(CH_3)_3$), 69.20 (d, CHOH), 45.20 (d, CHN), 44.31 (t, C-2), 42.39 (t, C-4), 28.55 (q, $C(CH_3)_3$), 21.95 ppm (q, CH_3CH); elemental analysis calcd (%) for $C_{12}H_{23}NO_3$: C 62.85, H 10.11, N 6.11; found C 62.69, H 10.08, N 5.97; HRMS (EI+): m/z: calcd for $C_{12}H_{23}NO_3^+$: 229.1673; found: 229.1672 $[M]^+$. For GC data see isomer (+)-(1*R*,3*R*)-**22**.

(+)-(*E*,5*R*,7*R*)-7-[(*tert*-Butoxycarbonyl)amino]-5-hydroxyoct-2-en-1-yl methyl carbonate ((+)-(*E*,5*R*,7*R*)-23) and (+)-(*Z*,5*R*,7*R*)-7-[(*tert*-butoxycarbonyl)amino]-5-hydroxyoct-2-en-1-yl methyl carbonate ((+)-(*Z*,5*R*,7*R*)-23): According to GP1, a solution of (+)-(1*R*,3*R*)-**22** (300 mg,

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1.308 mmol), **6** (1.30 g, 6.4 mmol) and Grubbs II catalyst (33 mg, 39 μmol) in dry CH_2Cl_2 (30 mL) was stirred at room temperature for 3.5 h when complete conversion was indicated by GC (HP-1; temperature program: isothermal 50 °C (1 min), heating rate 20 °C min^{-1} (10 min), isothermal 250 °C (14 min); t_R(**22**) = 8.90 min, t_R(**6**) = 8.12 min, t_R(**23**) = 12.47 min). The mixture was concentrated in vacuo and the residue subjected to flash chromatography on silica gel (21 g, petroleum ether/ethyl acetate 5:1 to 3:1, R_f(**22**) = 0.43, R_f(**6**) = 0.43, R_f(**23**) = 0.29 (petroleum ether/ethyl acetate 1:1), $KMnO_4$) to give **23** (359 mg, 86 %) as a 88:12 mixture of *E* and *Z* isomers (^{1}H NMR spectroscopy) as a colorless oil. Separation of the isomers was possible on a small scale by preparative HPLC (petroleum ether/ethyl acetate 3:1, column: ProntoSIL, 250 × 20 mm, 5 μ silica gel, 15 mL min^{-1}, 50 bar).

*Analytical data for (+)-(*E,*5*R*,7*R*)-**23***: Colorless needles; m.p. 63.5–64.5 °C; $[\alpha]_D^{20} = +10.6$ (*c* = 1.32 in $CHCl_3$, > 99 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.85 (ddd, *J* = 15.3, 7.1, 7.1 Hz, 1H; 3-H), 5.63 (ddd, *J* = 15.3, 6.4, 6.4 Hz, 1H; 2-H), 4.57 (dd, *J* = 6.4, 0.8 Hz, 2H; CH_2O), 4.49 (d, *J* = 8.7 Hz, 1H; NH), 4.13–4.07 (m, 1H; OH), 3.97–3.83 (m, 1H; CHN), 3.75 (s, 3H; CO_2CH_3), 3.69–3.58 (m, 1H; C*H*OH), 2.27 (ddd, *J* = 14.2, 6.8, 6.8 Hz, 1H; 4-H_a), 2.17 (ddd, *J* = 14.0, 6.8, 6.8 Hz, 1H; 4-H_b), 1.54–1.21 (m, 2H; 6-H), 1.42 (s, 9H; $C(CH_3)_3$), 1.15 ppm (d, *J* = 6.8 Hz, 3H; CH_3CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.04, 155.74 (2s, CO_2), 133.58 (d, C-3), 125.65 (d, C-2), 80.00 (s, $C(CH_3)_3$), 68.58 (t, CH_2O), 67.18 (d, CHOH), 54.80 (q, CO_2CH_3), 45.84 (t, C-6), 43.34 (d, CHN), 39.84 (t, C-4), 28.46 (q, $C(CH_3)_3$), 21.69 ppm (q, CH_3CH); elemental analysis calcd (%) for $C_{15}H_{27}NO_6$: C 56.77, H 8.57, N 4.41; found C 56.89, H 8.65, N 4.46; HRMS (ESI+): *m*/*z*: calcd for $C_{15}H_{28}NO_6^+$: 318.1911; found: 318.1913 $[M+H]^+$. For GC data see experimental procedure.

*Analytical data (+)-(*Z,*5*R*,7*R*)-**23***: Colorless oil; $[\alpha]_D^{20} = +6.6$ (*c* = 1.14 in $CHCl_3$, > 99 % *ee*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.77 (ddd, *J* = 10.8, 7.6, 7.6 Hz, 1H; 3-H), 5.65 (ddd, *J* = 11.0, 6.7, 6.7 Hz, 1H; 2-H), 4.72–4.65 (m, 2H; CH_2O), 4.48 (d, *J* = 8.3 Hz, 1H; NH), 4.09 (brs, 1H; OH), 3.95–3.87 (m, 1H; CHN), 3.76 (s, 3H; CO_2CH_3), 3.65 (brs, 1H; C*H*OH), 2.32 (ddd, *J* = 14.9, 7.5, 7.5 Hz, 1H; 4-H_a), 2.25 (ddd, *J* = 14.4, 7.0, 7.0 Hz, 1H; 4-H_b), 1.53 (ddd, *J* = 13.8, 10.9, 2.8 Hz, 1H; 6-H_a), 1.43 (s, 9H; $C(CH_3)_3$), 1.32 (dd, *J* = 11.9, 11.9 Hz, 1H; 6-H_b), 1.16 ppm (d, *J* = 6.7 Hz, 3H; CH_3CH); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 157.04 (s, NCO_2), 155.89 (s, OCO_2), 132.27 (d, C-3), 124.81 (d, C-2), 80.00 (s, $C(CH_3)_3$), 67.37 (d, CHOH), 63.88 (t, CH_2O), 54.86 (q, CO_2CH_3), 45.91 (t, C-6), 43.39 (d, CHN), 34.99 (t, C-4), 28.46 (q, $C(CH_3)_3$), 21.67 ppm (q, CH_3CH); HRMS (ESI+): *m*/*z*: calcd for $C_{15}H_{28}NO_6^+$: 318.1911; found: 318.1914 $[M+H]^+$. For GC data see experimental procedure.

(5*R*,7*R*)-7-Amino-5-hydroxyoct-2-en-1-yl methyl carbonate ((5*R*,7*R*)-24): A solution of (5*R*,7*R*)-**23** (*E*/*Z* = 91:9) (631 mg, 1.988 mmol) in CH_2Cl_2 (4.0 mL) was treated with trifluoracetic acid (4.0 mL) at room temperature. After 1.5 h, the solution was cooled to 0 °C and saturated aqueous $NaHCO_3$ (ca. 200 mL) was added until gas evolution had ceased. Aqueous NaOH (2 M) was added dropwise until pH 9–10 was reached. The mixture was carefully extracted with CH_2Cl_2 (15 × 50 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to give pure (NMR spectroscopy) (5*R*,7*R*)-**24** (*E*/*Z* = 91:9) (416 mg, 96 %) as a colorless oil, which was directly used in the next step.

(−)-(*E*,5*R*,7*R*)-7-Amino-5-hydroxyoct-2-en-1-yl methyl carbonate ((−)-(*E*,5*R*,7*R*)-24) and (*Z*,5*R*,7*R*)-7-amino-5-hydroxyoct-2-en-1-yl methyl carbonate ((*Z*,5*R*,7*R*)-24): Isomerically pure (−)-(*E*,5*R*,7*R*)-**24** (15 mg, 71 %) and isomerically enriched (*Z*,5*R*,7*R*)-**24** (*Z*/*E* > 90:10) (13 mg, 90 %) were synthesized in analogy to (5*R*,7*R*)-**24** from isomerically pure starting material (+)-(*E*,5*R*,7*R*)-**23** and isomerically enriched starting material (+)-(*Z*,5*R*,7*R*)-**23** (*Z*/*E* > 90:10), respectively.

*Analytical data for (−)-(*E,*5*R*,7*R*)-**24***: R_f(**24**) = 0.4 (CH_2Cl_2/MeOH 4:1); colorless oil; $[\alpha]_D^{20} = -2.5$ (*c* = 0.86 in $CHCl_3$, > 99 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.86 (ddd, *J* = 15.3, 7.1, 7.1 Hz, 1H; 3-H), 5.66 (ddd, *J* = 15.4, 6.4, 6.4 Hz, 1H; 2-H), 4.58 (dd, *J* = 6.5, 0.7 Hz, 2H; CH_2O), 4.02–3.95 (m, 1H; C*H*OH), 3.77 (s, 3H; CO_2CH_3), 3.45–3.31 (m, 1H; CHN), 2.73 (brs, 3H; NH_2, OH), 2.29 (ddd, *J* = 14.1, 7.0, 7.0 Hz, 1H; 4-H_a), 2.19 (ddd, *J* = 13.9, 6.7, 6.7 Hz, 1H; 4-H_b), 1.54 (ddd, *J* = 14.3, 8.4, 3.5 Hz, 1H; 6-H_a), 1.43 (ddd, *J* = 14.4, 6.5, 3.2 Hz, 1H; 6-H_b), 1.16 ppm (d, *J* = 6.6 Hz, 3H; CH_3CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.77 (s, CO_2), 133.65 (d, C-3), 125.78 (d, C-2), 68.65 (d, CHOH), 68.62 (t, CH_2O), 54.82 (q, CO_2CH_3), 44.82 (d, CHN), 42.12 (t, C-6), 40.78 (t, C-4), 23.39 ppm (q, CH_3CH); elemental analysis calcd (%) for $C_{10}H_{19}NO_4$: C 55.28, H 8.81, N 6.45; found C 55.57, H 8.87, N 6.33; HRMS (ESI+): *m*/*z*: calcd for $C_{10}H_{20}NO_4^+$: 218.1387; found: 218.1387 $[M+H]^+$.

*Analytical data for (*Z,*5*R*,7*R*)-**24***: R_f(**24**) = 0.4 (CH_2Cl_2/MeOH 4:1); colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.78 (ddd, *J* = 10.9, 7.0, 7.0 Hz, 1H; 3-H), 5.67 (ddd, *J* = 11.2, 6.3, 6.3 Hz, 1H; 2-H), 4.71 (d, *J* = 6.1 Hz, 2H; CH_2O), 4.05–3.93 (m, 1H; C*H*OH), 3.78 (s, 3H; CO_2CH_3), 3.47–3.33 (m, 1H; CHN), 2.74 (brs, 3H; NH_2, OH), 2.44–2.19 (m, 2H; 4-H), 1.58 (ddd, *J* = 14.5, 7.8, 3.6 Hz, 1H; 6-H_a), 1.45 (ddd, *J* = 14.3, 6.4, 3.5 Hz, 1H; 6-H_b), 1.17 ppm (d, *J* = 6.5 Hz, 3H; CH_3CH).

(−)-(2*R*,4*S*,6*R*)-2-Methyl-6-vinylpiperidin-4-ol ((−)-(2*R*,4*S*,6*R*)-25a): Following GP2, anhydrous TBD (30.0 mg, 216 μmol) was added to a solution of [{IrCl(cod)}$_2$] (36.2 mg, 53.9 μmol) and (*S*,*S*,*aS*)-**L2** (64.6 mg, 108 μmol) in dry THF (3.0 mL). After 5 min, a solution of the carbonate (5*R*,7*R*)-**24** (*E*/*Z* = 9:1) (585 mg, 2.69 mmol) in dry THF (2.0 mL) was added, and the mixture was stirred at room temperature for 6 h when the reaction was complete according to TLC (CH_2Cl_2/MeOH 4:1, R_f(**24**) = 0.4, R_f(**25a**) = 0.3, R_f(**25b**) = 0.3, $KMnO_4$). The mixture was concentrated in vacuo and analyzed by GC with respect to the ratio of diastereomers ((−)-**25a**/(+)-**25b** = 98:2). Purification by flash chromatography on silica gel (3 g, CH_2Cl_2/MeOH 4:1 to 3:1) gave (−)-**25a** (342 mg, 90 %) as a colorless solid. An analytically pure sample was obtained by sublimation under reduced pressure, which gave (−)-**25a** as colorless needles (m.p. 82–83 °C) that were suitable for X-ray crystal structural analysis. $[\alpha]_D^{20} = -4.7$ (*c* = 0.34 in acetone, > 99 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.82 (ddd, *J* = 17.1, 10.5, 6.6 Hz, 1H; =CH), 5.16 (ddd, *J* = 17.3, 1.3, 1.3 Hz, 1H; =CH_EH$_Z$), 5.04 (ddd, *J* = 10.4, 1.1, 1.1 Hz, 1H; =CH_EH$_Z$), 3.69 (dddd, *J* = 11.1, 11.1, 4.6, 4.6 Hz, 1H; C*H*OH), 3.20–3.13 (m, 1H; 6-H), 2.80–2.69 (m, 1H; 2-H), 2.11 (brs, 2H; NH, OH), 2.01–1.90 (m, 2H; 3-H_a, 5-H_a), 1.22–0.99 (m, 2H; 3-H_b, 5-H_b), 1.13 ppm (d, *J* = 6.2 Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.28 (d, =CH), 114.96 (t, =CH_2), 68.99 (d, CHOH), 57.74 (d, C-6), 50.26 (d, C-2), 43.33, 41.16 (2t, C-3, C-5), 22.36 ppm (q, CH_3); elemental analysis calcd (%) for $C_8H_{15}NO$: C 68.04, H 10.71, N 9.92; found C 67.87, H 10.70, N 9.62; HRMS (EI+): *m*/*z*: calcd for $C_8H_{15}NO^+$: 141.1148; found: 141.1142 $[M]^+$; GC (achiral HP-1, 90 °C isothermal): t_R((−)-(2*R*,4*S*,6*R*)-**25a**) = 15.5 min, t_R((+)-(2*R*,4*S*,6*S*)-**25b**) = 18.2 min.

(+)-(2*R*,4*S*,6*S*)-2-Methyl-6-vinylpiperidin-4-ol (25b): According to GP2, anhydrous TBD (11.9 mg, 85.6 μmol) was added to a solution of [{IrCl(cod)}$_2$] (14.4 mg, 21.4 μmol) and (*R*,*R*,*aR*)-**L2** (25.7 mg, 42.9 μmol) in dry THF (1.0 mL). After 5 min a solution of the carbonate (5*R*,7*R*)-**24** (*E*/*Z*=9:1) (233 mg, 1.07 mmol) in dry THF (1.5 mL) was added and the mixture was stirred at room temperature for 6 h until the reaction was complete according to TLC (CH_2Cl_2/MeOH 4:1, R_f(**24**) = 0.4, R_f(**25a**) = 0.3, R_f(**25b**) = 0.3, $KMnO_4$). The mixture was concentrated and analyzed by GC with respect to the ratio of diastereomers ((+)-**25b**:(−)-**25a** = 94:6). Purification by flash chromatography on silica gel (2 g, CH_2Cl_2/MeOH 5:1 to 3:1) gave (+)-**25b** (113 mg, 74 %) as a brownish solid. An analytically pure sample was obtained by sublimation under reduced pressure, which gave (+)-**25b** as a colorless solid (m.p. 38–40 °C). $[\alpha]_D^{20} = +69.2$ (*c* = 0.27 in acetone, > 99 % *ee*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.97 (ddd, *J* = 17.3, 10.8, 5.6 Hz, 1H; =CH), 5.13 (ddd, *J* = 17.4, 1.4, 1.4 Hz, 1H; =CH_EH$_Z$), 5.12 (ddd, *J* = 10.5, 1.4, 1.4 Hz, 1H; CH=CH_EH$_Z$), 3.84 (dddd, *J* = 11.0, 11.0, 4.5, 4.5 Hz, 1H; C*H*OH), 3.80–3.76 (m, 1H; 6-H), 3.01–2.94 (m, 1H; 2-H), 2.05–1.98 (m, 3H; 5-H_a, OH, NH), 1.95–1.91 (m, 1H; 3-H_a), 1.58 (ddd, *J* = 12.4, 11.3, 5.5 Hz, 1H; 5-H_b), 1.10–1.02 (m, 1H; 3-H_b), 1.08 ppm (d, *J* = 6.4 Hz, 3H; CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.06 (d, =CH), 115.20 (t, =CH_2), 65.52 (d, CHOH), 54.46 (d, C-6), 44.93 (d, C-2), 44.18 (t, C-3), 38.68 (t, C-5), 22.76 ppm (q, CH_3); HRMS (EI+): *m*/*z*: calcd for $C_8H_{15}NO^+$: 141.1148; found: 141.1167 $[M]^+$. For GC data see (−)-(2*R*,4*S*,6*R*)-**25a**.

(−)-Benzyl (2*R*,4*S*,6*R*)-4-Hydroxy-2-methyl-6-vinylpiperidine-1-carboxylate ((−)-(2*R*,4*S*,6*R*)-26a): Following GP3, a solution of (−)-(2*R*,4*S*,6*R*)-**25a** (53.3 mg, 377 μmol) in CH_2Cl_2 (2 mL) was cooled to 0 °C with an ice bath and treated with a solution of Na_2CO_3 (590 mg, 5.62 mmol) in H_2O (1.5 mL) and benzyl chloroformate (265 μL, 1.86 mmol). The ice bath

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was removed and the heterogeneous mixture was vigorously stirred for 3 h when TLC (CH_2Cl_2/MeOH 4:1, R_f(**25a**) = 0.3, R_f(**26a**) = 0.77, $KMnO_4$) showed complete conversion. The mixture was extracted with CH_2Cl_2 (3×3 mL), and the combined extracts were dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography on silica gel (3 g, petroleum ether/ethyl acetate 3:1 to 2:1) yielded pure (−)-**26a** (95.7 mg, 92%) as a colorless oil. $[\alpha]_D^{20} = -16.4$ ($c = 0.73$ in MeOH, >99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.39$–7.28 (m, 5H; Ph), 6.16 (ddd, $J = 17.1$, 10.4, 6.6 Hz, 1H; C*H*=CH$_2$), 5.15 (ddd, $J = 17.0$, 1.2, 1.2 Hz, 1H; CH=CH$_E$H$_Z$), 5.14 (s, 2H; CH_2Ph), 5.07 (ddd, $J = 10.4$, 1.3, 1.3 Hz, 1H; CH=CH$_E$H$_Z$), 4.85–4.78 (m, 1H; 6-H), 4.36 (ddq, $J = 7.1$, 7.1, 4.2 Hz, 1H; 2-H), 4.09 (dddd, $J = 5.9$, 5.9, 4.3, 4.3 Hz, 1H; 4-H), 2.13–1.95 (m, 2H; 3-H$_a$, 5-H$_a$), 1.88 (dddd, $J = 14.5$, 5.5, 4.0, 1.1 Hz, 1H; 5-H$_b$), 1.84 (br s, 1H; OH), 1.67 (dddd, $J = 13.9$, 6.1, 4.4, 1.1 Hz, 1H; 3-H$_b$), 1.38 ppm (d, $J = 7.0$ Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 155.92$ (s, CO_2), 141.47 (d, =CH), 136.94 (s, Ph), 128.56, 128.02, 127.92 (3d, Ph), 115.11 (t, =CH_2), 67.23 (t, CH_2Ph), 65.10 (d, CHOH), 52.04 (d, C-6), 46.27 (d, C-2), 36.91 (t, C-3), 35.77 (t, C-5), 23.68 ppm (q, CH_3); elemental analysis calcd (%) for $C_{16}H_{21}NO_3$: C 69.79, H 7.69, N 5.09; found C 69.85, H 7.64, N 4.86; HRMS (EI+): *m/z*: calcd for $C_{16}H_{22}NO_3^+$: 276.1594; found: 276.1593 $[M+H]^+$.

(−)-Benzyl (2*R*,4*S*,6*R*)-4-(acetyloxy)-2-methyl-6-vinylpiperidine-1-carboxylate ((−)-(2*R*,4*S*,6*R*)-27a): A solution of (−)-**26a** (106 mg, 385 μmol) in pyridine (700 μL) was treated with acetic anhydride (300 μL, 3.17 mmol) at room temperature. After 1 h TLC (ethyl acetate, R_f(**26a**) = 0.33, R_f(**27a**) = 0.57, $KMnO_4$) still showed some starting material. More pyridine (100 μL) and acetic anhydride (100 μL, 1.06 mmol) were added, and stirring was continued overnight. After 19 h conversion was complete, and the mixture was cooled to 0°C. Water (2 mL) and ethyl acetate (5 mL) were added, the phases were separated, and the aqueous layer was extracted with ethyl acetate (3×10 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (3 g, petroleum ether/ethyl acetate 4:1) to give (−)-**27a** (106 mg, 87%) as a colorless oil. $[\alpha]_D^{20} = -24.3$ ($c = 0.87$ in $CHCl_3$, >99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.39$–7.29 (m, 5H; Ph), 6.07 (ddd, $J = 17.1$, 10.5, 6.6 Hz, 1H; C*H*=CH$_2$), 5.17–5.04 (m, 3H; CHOAc, CH=C*H*$_2$), 5.15 (s, 2H; CH_2Ph), 4.89–4.82 (m, 1H; 6-H), 4.42 (qdd, $J = 7.1$, 7.1, 3.3 Hz, 1H; 2-H), 2.07–2.02 (m, 2H; 5-H), 2.04 (s, 3H; CH_3CO_2), 1.97 (ddd, $J = 14.4$, 7.3, 4.0 Hz, 1H; 3-H$_a$), 1.81 (dddd, $J = 14.4$, 4.9, 3.5, 1.2 Hz, 1H; 3-H$_b$), 1.35 ppm (d, $J = 7.0$ Hz, 3H; C*H*$_3$CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.49$ (s, CH_3CO_2), 155.83 (s, NCO_2), 140.69 (d, =CH), 136.89 (s, Ph), 128.61, 128.10, 128.03 (3d, Ph), 115.34 (t, =CH_2), 67.34 (t, CH_2Ph), 67.25 (d, CHOAc), 51.35 (d, C-6), 45.65 (d, C-2), 33.34 (t, C-3), 32.23 (t, C-5), 22.95 (q, *C*H$_3$CH), 21.62 ppm (q, *C*H$_3$CO$_2$); elemental analysis calcd (%) for $C_{18}H_{23}NO_4$: C 68.12, H 7.30, N 4.41; found C 68.02, H 7.35, N 4.48; HRMS (FAB+): *m/z*: calcd for $C_{18}H_{24}NO_4^+$: 318.1700; found: 318.1695 $[M+H]^+$.

(−)-Benzyl (2*R*,4*S*,6*R*)-4-(acetyloxy)-2-methyl-6-[(*E*)-non-1′-en-1′-yl]piperidine-1-carboxylate ((−)-(2*R*,4*S*,6*R*)-28a): According to GP4, a mixture of (−)-(2*R*,4*S*,6*R*)-**27a** (61.4 mg, 194 μmol), 1-nonene (150 μL, 869 μmol) (500 μL) and Grubbs II catalyst (8.2 mg, 9.7 μmol) in dry CH_2Cl_2 was heated at reflux. After 3 h TLC (petroleum ether/ethyl acetate 3:1, R_f(**27a**) = 0.42, R_f(**28a**) = 0.53, MPA) indicated incomplete conversion and 1-nonene (150 μL, 869 μmol) together with a second portion of the catalyst (8.0 mg, 9.4 μmol) were added. After additional 2 h no further conversion was detected, and the mixture was cooled to room temperature and concentrated under reduced pressure. The residue was subjected to flash chromatography on silica gel (12 g, petroleum ether/ethyl acetate 9:1) and subsequent preparative HPLC (petroleum ether/ethyl acetate 9:1, column: ProntoSIL, 250×20 mm, 5 μ silica gel, 20 mL min^{-1}, 70 bar) to give pure (−)-**28a** (56.8 mg, 71%) as a colorless oil together with some starting material (−)-**27a** (13.8 mg, 22%). $[\alpha]_D^{20} = -8.9$ ($c = 1.06$ in $CHCl_3$, >99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.35$–7.28 (m, 5H; Ph), 5.68 (dddd, $J = 15.4$, 7.0, 1.1, 1.1 Hz, 1H; 1′-H), 5.52 (dddd, $J = 15.4$, 6.6, 6.6, 1.0 Hz, 1H; C-2′), 5.17 (d, $J = 12.4$ Hz, 1H; C*H*$_a$H$_b$Ph), 5.11 (d, $J = 12.4$ Hz, 1H; CH$_a$*H*$_b$Ph), 5.05 (dddd, $J = 4.5$, 4.5, 4.5, 4.5 Hz, 1H; CHOAc), 4.81 (ddd, $J = 6.0$, 5.9, 4.8 Hz, 1H; 6-H), 4.40 (qdd, $J = 7.1$, 7.1, 3.3 Hz, 1H; 2-H), 2.05 (s, 3H; CH_3CO_2), 2.01–1.91 (m, 5H; 3-H$_a$, 5-H, 3′-H), 1.80 (ddd, $J = 14.3$, 4.1, 4.0 Hz, 1H; 3-H$_b$), 1.40–1.19 (m, 10H; $(CH_2)_5$), 1.35 (d, $J = 7.2$ Hz, 3H; C*H*$_3$CH), 0.87 ppm (t, $J = 6.8$ Hz, 3H; C*H*$_3$CH$_2$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.34$ (s, CH_3CO_2), 155.69 (s, NCO_2), 136.95 (s, Ph), 132.11, 131.95 (2d, CH=CH), 128.50, 127.96, 127.93 (3d, Ph), 67.40 (d, CHOAc), 67.13 (t, CH_2Ph), 50.78 (d, C-6), 45.51 (d, C-2), 33.36 (t, C-3), 32.71, 32.36 (2t, C-5, CH_2), 31.91, 29.22, 29.19, 29.18 (4t, CH_2), 22.95 (q, *C*H$_3$CH), 22.73 (t, CH_2), 21.54 (q, *C*H$_3$CO$_2$), 14.17 ppm (q, *C*H$_3$CH$_2$); elemental analysis calcd (%) for $C_{25}H_{37}NO_4$: C 72.26, H 8.97, N 3.37; found C 72.06, H 9.09, N 3.34; HRMS (FAB+): *m/z*: calcd for $C_{25}H_{38}NO_4^+$: 416.2795; found: 416.2843 $[M+H]^+$.

(−)-(2*R*,4*S*,6*S*)-2-Methyl-6-nonylpiperidin-4-yl acetate ((−)-(2*R*,4*S*,6*S*)-29a): In a Schlenk tube under hydrogen atmosphere (1 bar), a suspension of rhodium (5 wt% (dry) on charcoal, wet, Degussa type G106B/W) (7.0 mg) in dry methanol (500 μL) was stirred for 30 min. A solution of (−)-**28a** (28.1 mg, 67.6 μmol) in dry methanol (1.5 mL) was added, and the mixture was stirred at room temperature for 1.5 h when TLC control (petroleum ether/ethyl acetate 3:1, R_f(**28a**) = 0.41, R_f(**29a**) < 0.1, $KMnO_4$) showed complete conversion. The mixture was filtered through a pad of Celite, and the filtrate was concentrated in vacuo. Flash chromatography of the residue on silica gel (1 g, ethyl acetate) furnished analytically pure (−)-(2*R*,4*S*,6*S*)-**29a** (17.6 mg, 92%) as a colorless oil. $[\alpha]_D^{20} = -6.7$ ($c = 0.81$ in acetone, >99% *ee*); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 4.74$ (dddd, $J = 11.3$, 11.3, 4.7, 4.7 Hz, 1H; CHOAc), 2.72 (dqd, $J = 11.2$, 6.2, 2.3 Hz, 1H; 2-H), 2.58 (dddd, $J = 11.1$, 6.4, 6.4, 2.1 Hz, 1H; 6-H), 2.00 (s, 3H; CH_3CO_2), 1.98–1.91 (m, 2H; 3-H$_a$, 5-H$_a$), 1.45 (br s, 1H; NH), 1.42–1.35 (m, 2H; 1′-H), 1.33–1.20 (m, 14H; $(CH_2)_7$), 1.12–1.02 (m, 2H; 3-H$_b$, 5-H$_b$), 1.09 (d, $J = 6.4$ Hz, 3H; C*H*$_3$CH), 0.85 ppm (t, $J = 7.0$ Hz, 3H; C*H*$_3$CH$_2$); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 170.72$ (s, CO_2), 71.93 (d, CHOAc), 54.79 (d, C-6), 50.12 (d, C-2), 39.94 (t, C-3), 37.84 (t, C-5), 36.94 (t, C-1′), 31.99, 29.83, 29.65, 29.63, 29.41, 26.05, 22.78 (7t, $(CH_2)_7$), 22.53 (q, *C*H$_3$CH), 21.48 (q, *C*H$_3$CO$_2$), 14.21 ppm (q, *C*H$_3$CH$_2$); elemental analysis calcd (%) for $C_{17}H_{33}NO_2$: C 72.03, H 11.73, N 4.94; found C 71.80, H 11.69, N 4.68; HRMS (EI+): *m/z*: calcd for $C_{17}H_{33}NO_2^+$: 283.2511; found: 283.2531 $[M]^+$.

(+)-(2*R*,4*S*,6*S*)-2-Methyl-6-nonylpiperidin-4-ol ((+)-241D; (+)-30a): A solution of (−)-**29a** (16.0 mg, 56.5 μmol) in methanol (400 μL) was treated with methanolic NaOH (1 M, 400 μL, 400 μmol) at room temperature for 15 min until starting material was not detected by TLC control (ethyl acetate/MeOH 5:1, R_f(**29a**) = 0.48, R_f((+)-241D) = 0.10, $KMnO_4$). Water (1 mL) was added, and the mixture was repeatedly extracted with CH_2Cl_2 (4×2 mL). The combined organic phases were washed with H_2O (1×1 mL) and dried over Na_2SO_4. Evaporation of the solvent gave virtually pure (+)-241D (13.4 mg, 98%) as a colorless solid. An analytically pure sample was obtained after flash chromatography on silica gel (100 mg, ethyl acetate to ethyl acetate/MeOH 5:1) as a colorless solid (m.p. 106–107°C), the spectroscopic properties of which were in full accordance with the literature.[38–40] Recrystallization from ethyl acetate by addition of petroleum ether at 0°C furnished (+)-241D as colorless needles. M.p. 108–109°C (ref. [40a]: 108–109°C). $[\alpha]_D^{20} = +5.9$ ($c = 0.65$ in MeOH, >99% *ee*) (ref. [40d]: $[\alpha]_D^{20} = +6.5$ ($c = 1.20$ in MeOH)); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.66$ (dddd, $J = 11.0$, 11.0, 4.6, 4.6 Hz, 1H; C*H*OH), 2.71 (dqd, $J = 11.1$, 6.3, 2.3 Hz, 1H; 2-H), 2.56 (dddd, $J = 11.0$, 6.4, 6.4, 2.2 Hz, 1H; 6-H), 2.01–1.93 (m, 4H; 3-H$_{eq}$, 5-H$_{eq}$, NH, OH), 1.49–1.37 (m, 2H; 1′-H), 1.36–1.21 (m, 14H; $CH_{2(n\text{-nonyl})}$), 1.14 (d, $J = 6.4$ Hz, 3H; C*H*$_3$CH), 1.05 (ddd, $J = 11.6$, 11.6, 11.6 Hz, 1H; 3-H$_{ax}$), 1.00 (ddd, $J = 11.5$, 11.5, 11.5 Hz, 1H; 5-H$_{ax}$), 0.88 ppm (t, $J = 7.0$ Hz, 3H; C*H*$_3$CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 69.43$ (d, CHOH), 55.02 (d, C-6), 50.36 (d, C-2), 43.86 (t, C-3), 41.63 (t, C-5), 36.73 (t, C-1′), 32.04, 29.87, 29.71, 29.69, 29.46, 26.15 (6t, $CH_{2(n\text{-nonyl})}$), 22.81 (t, *C*H$_2$CH$_3$), 22.41 (q, *C*H$_3$CH), 14.26 ppm (q, *C*H$_3$CH$_2$); HRMS (FAB+): *m/z*: calcd for $C_{15}H_{32}NO^+$: 242.2478; found: 242.2453 $[M+H]^+$.

(−)-Benzyl (2*R*,4*S*,6*S*)-4-Hydroxy-2-methyl-6-vinylpiperidine-1-carboxylate ((−)-(2*R*,4*S*,6*S*)-26b): According to GP3, a solution of (+)-**25b** (16.6 mg, 118 μmol) in CH_2Cl_2 (1.0 mL) was cooled to 0°C and treated with a solution of Na_2CO_3 (187 mg, 1.76 mmol) in H_2O (1.0 mL) and benzyl chloroformate (84 μL, 0.59 mmol). The cooling bath was removed, and the mixture was vigorously stirred for 4.5 h when TLC control

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(CH_2Cl_2/MeOH 4:1, R_f(**25b**) = 0.3, R_f(**26b**) = 0.69, $KMnO_4$) showed complete conversion. The mixture was extracted with CH_2Cl_2 (3×3 mL), and the combined extracts were dried over Na_2SO_4 and concentrated in vacuo. The residue was subjected to flash chromatography on silica gel (1 g, petroleum ether/ethyl acetate 2:1) to give (−)-**26b** (30.6 mg, 94%) as a colorless oil. $[\alpha]_D^{20} = -9.6$ ($c = 0.74$ in MeOH, >99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.37$–7.27 (m, 5H; Ph), 5.79 (ddd, $J = 17.2$, 10.6, 4.2 Hz, 1H; C*H*=CH_2), 5.17–5.02 (m, 4H; CH=CH_2, CH_2Ph), 4.75–4.70 (m, 1H; 6-H), 4.08 (dddd, $J = 9.8$, 6.6, 6.6, 3.5 Hz, 1H; C*H*OH), 3.98 (qdd, $J = 6.7$, 5.0, 5.0 Hz, 1H; 2-H), 2.28 (ddd, $J = 13.8$, 7.2, 3.0 Hz, 1H; 5-H_a), 2.15 (ddd, $J = 14.6$, 6.1, 4.9 Hz, 1H; 3-H_a), 2.06 (brs, 1H; OH), 1.90 (ddd, $J = 13.8$, 9.6, 5.4 Hz, 1H; 5-H_b), 1.56 (ddd, $J = 14.6$, 4.9, 3.9 Hz, 1H; 3-H_b), 1.44 ppm (d, $J = 6.8$ Hz, 3H; CH_3); ^{13}C NMR (300 MHz, $CDCl_3$): $\delta = 155.96$ (s, CO_2), 138.60 (d, =CH), 136.89 (s, Ph), 128.52, 127.99, 127.93 (3 d, Ph), 114.81 (t, =CH_2), 67.01 (t, CH_2Ph), 63.20 (d, CHOH), 53.18 (d, C-6), 47.65 (d, C-2), 38.22 (t, C-3), 35.62 (t, C-5), 22.44 ppm (q, CH_3); elemental analysis calcd (%) for $C_{16}H_{21}NO_3$: C 69.79, H 7.69, N 5.09; found C 69.50, H 7.79, N 4.92; HRMS (EI+): *m/z*: calcd for $C_{16}H_{21}NO_3^+$: 275.1516; found: 275.1521 $[M]^+$.

(+)-Benzyl (2*R*,4*S*,6*S*)-4-(acetyloxy)-2-methyl-6-vinylpiperidine-1-carboxylate ((+)-(2*R*,4*S*,6*S*)-27b): This compound was prepared from (−)-(2*R*,4*S*,6*S*)-**26b** analogously to (−)-(2*R*,4*S*,6*R*)-**27a** (30.6 mg, 111 μmol) using pyridine (500 μL) and acetic anhydride (200 μL, 2.11 mmol). After 16 h workup and purification by flash chromatography on silica gel (2 g, petroleum ether/ethyl acetate 4:1) furnished (+)-**27b** (34.4 mg, 97%) as a colorless oil. R_f(**27b**) = 0.61 (petroleum ether/ethyl acetate 1:1); $[\alpha]_D^{20} = +2.7$ ($c = 1.00$ in MeOH, >99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.35$–7.27 (m, 5H; Ph), 5.82 (ddd, $J = 17.2$, 10.6, 4.1 Hz, 1H; C*H*=CH_2), 5.18–5.02 (m, 5H; CH=CH_2, CH_2Ph, CHOAc), 4.71 (ddd, $J = 8.9$, 5.3, 2.1 Hz, 1H; 6-H), 4.07 (qdd, $J = 6.6$, 4.6, 4.6 Hz, 1H; 2-H), 2.40 (ddd, $J = 14.0$, 7.8, 3.0 Hz, 1H; 5-H_a), 2.25 (ddd, $J = 15.2$, 6.7, 5.2 Hz, 1H; 3-H_a), 2.03 (s, 3H; CH_3CO_2), 1.98 (ddd, $J = 14.2$, 9.2, 5.2 Hz, 1H; 5-H_b), 1.65 (ddd, $J = 15.3$, 3.9, 2.9 Hz, 1H; 3-H_b), 1.39 ppm (d, $J = 6.9$ Hz, 3H; CH_3CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.58$ (s, CH_3CO_2), 155.71 (s, NCO_2), 138.38 (d, =CH), 136.88 (s, Ph), 128.54, 128.03, 127.99 (3 d, Ph), 115.09 (t, =CH_2), 67.06 (t, CH_2Ph), 66.07 (d, CHOAc), 52.36 (d, C-6), 47.06 (d, C-2), 34.08 (t, C-3), 32.04 (t, C-5), 22.16 (q, CH_3CH), 21.44 ppm (q, CH_3CO_2); elemental analysis calcd (%) for $C_{18}H_{23}NO_4$: C 68.12, H 7.30, N 4.41; found C 68.02, H 7.48, N 4.45; HRMS (EI+): *m/z*: calcd for $C_{18}H_{23}NO_4^+$: 317.1622; found: 317.1646 $[M]^+$.

(−)-Benzyl (2*R*,4*S*,6*S*)-4-(acetyloxy)-2-methyl-6-[(*E*)-non-1′-en-1′-yl]piperidine-1-carboxylate ((−)-(2*R*,4*S*,6*S*)-28b): According to GP4, a solution of (+)-**27b** (15.0 mg, 47.3 μmol), 1-nonene (80 μL, 0.51 mmol) and Grubbs II catalyst (4.0 mg, 4.7 μmol) in dry CH_2Cl_2 was heated at reflux for 8 h when no further conversion was detected by TLC (petroleum ether/ethyl acetate 3:1, R_f(**27b**) = 0.46, R_f(**28b**) = 0.62, MPA). The mixture was concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (2 g, petroleum ether/ethyl acetate 9:1) to give (−)-**28b** (9.0 mg, 46%) as a colorless oil Additionally some starting material (+)-**27b** (8.0 mg, 53%) was recovered. An analytically pure sample was obtained by preparative HPLC (petroleum ether/ethyl acetate 9:1, column: ProntoSIL, 250×20 mm, 5 μ silica gel, 20 mL min^{-1}, 60 bar). $[\alpha]_D^{20} = -7.1$ ($c = 0.75$ in $CHCl_3$, >99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.35$–7.28 (m, 5H; Ph), 5.48 (dddd, $J = 15.3$, 6.3, 6.3, 1.1 Hz, 1H; 2′-H), 5.38 (dd, $J = 15.4$, 4.1 Hz, 1H; 1′-H), 5.17 (d, $J = 12.3$ Hz, 1H; C$H_a$$H_b$Ph), 5.12–5.04 (m, CHOAc), 5.10 (d, $J = 12.5$ Hz, 1H; $CH_a$$H_b$Ph), 4.67 (brs, 1H; C-6), 4.04 (qdd, $J = 6.6$, 4.6, 4.6 Hz, 1H; 2-H), 2.35 (ddd, $J = 13.8$, 7.8, 2.9 Hz, 1H; 5-H_a), 2.26 (ddd, $J = 15.2$, 6.5, 5.0 Hz, 1H; 3-H_a), 2.03 (s, 3H; CH_3CO_2), 2.02–1.90 (m, 3H; 5-H_b, 3′-H), 1.64 (ddd, $J = 15.2$, 3.9, 3.0 Hz, 1H; 3-H_b), 1.38 (d, $J = 6.9$ Hz, 3H; CH_3CH), 1.35–1.20 (m, 10H; $(CH_2)_5$), 0.88 ppm (t, $J = 6.7$ Hz, 3H; CH_3CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.64$ (s, CH_3CO_2), 155.72 (s, NCO_2), 137.00 (s, Ph), 131.67 (d, C-2′), 129.65 (d, C-1′), 128.53, 127.98, 127.98 (3 d, Ph), 66.95 (t, CH_2Ph), 66.31 (d, CHOAc), 51.85 (d, C-6), 46.97 (d, C-2), 34.24 (t, C-3), 32.58 (t, C-5), 32.32 (t, C-3′), 31.91, 29.28, 29.28, 29.23, 22.77 (5t, $(CH_2)_5$), 22.17 (q, CH_3CH), 21.48 (q, CH_3CO_2), 14.21 ppm (q, CH_3CH_2); two signals coincide at 127.98 ppm (d, Ph) and 29.28 ppm (t, CH_2); elemental analysis calcd (%) for $C_{25}H_{37}NO_4$: C 72.26, H 8.97, N 3.37; found C 72.15, H 8.96, N 3.42; HRMS (EI+): *m/z*: calcd for $C_{25}H_{37}NO_4^+$: 415.2717; found: 415.2719 $[M]^+$.

(+)-(2*R*,4*S*,6*R*)-2-Methyl-6-nonylpiperidin-4-yl acetate ((+)-(2*R*,4*S*,6*R*)-29b): According to GP5, a suspension of palladium hydroxide (4.5 mg) in dry methanol (500 μL) was stirred for 30 min under an atmosphere of hydrogen (1 bar). A solution of (−)-**28b** (13.2 mg, 31.8 μmol) in dry methanol (1.2 mL) was added, and the mixture was stirred for 50 min when conversion was complete according to TLC (petroleum ether/ethyl acetate 3:1, R_f(**28b**) = 0.57, R_f(**29b**) < 0.1, $KMnO_4$). The mixture was filtered through a pad of Celite, concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (1 g, ethyl acetate to ethyl acetate/MeOH 10:1), which furnished (+)-**29b** (8.5 mg, 94%) as a colorless oil. $[\alpha]_D^{20} = +21.0$ ($c = 0.38$ in $CHCl_3$, >99% *ee*); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 4.98$ (dddd, $J = 10.4$, 10.4, 4.5, 4.5 Hz, 1H; CHOAc), 3.15–3.11 (m, 1H; 6-H), 3.04–2.98 (m, 1H; 2-H), 2.02 (s, 3H; CH_3CO_2), 1.97 (d, $J = 12.6$ Hz, 1H; 3-H_a), 1.81 (d, $J = 12.6$ Hz, 1H; 5-H_a), 1.63 (ddd, $J = 12.3$, 11.0, 5.1 Hz, 1H; 5-H_b), 1.62–1.54 (m, 1H; C$H_a$$H_b$), 1.49–1.40 (m, 1H; $CH_a$$H_b$), 1.34–1.22 (m, 15H; $(CH_2)_7$, NH), 1.17 (ddd, $J = 11.4$, 10.9, 10.9 Hz, 1H; 3-H_b), 1.10 (d, $J = 6.4$ Hz, 3H; CH_3CH), 0.87 ppm (t, $J = 7.0$ Hz, 3H; CH_3CH_2); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 170.74$ (s, CO_2), 68.88 (d, CHOAc), 51.87 (d, C-6), 44.22 (d, C-2), 39.69 (t, C-3), 34.80 (t, C-5), 32.50, 32.02, 29.74, 29.72, 29.70, 29.44, 26.99, 22.81 (8t, $(CH_2)_8$), 22.58 (q, CH_3CH), 21.57 (q, CH_3CO_2), 14.24 ppm (q, CH_3CH_2); elemental analysis calcd (%) for $C_{17}H_{33}NO_2$: C 72.03, H 11.73, N 4.94; found C 71.74, H 11.73, N 4.86; HRMS (ESI+): *m/z*: calcd for $C_{17}H_{34}NO_2^+$: 284.2584; found: 284.2589 $[M+H]^+$.

(+)-(2*R*,4*S*,6*R*)-2-Methyl-6-nonylpiperidin-4-ol ((+)-6-*epi*-241D; (+)-30b): A solution of (+)-(2*R*,4*S*,6*R*)-**29b** (6.5 mg, 23 μmol) in methanol (1 mL) was treated with methanolic NaOH (1 M, 1 mL, 1 mmol) at room temperature for 15 min when no starting material was detected by TLC (ethyl acetate/MeOH 5:1, R_f(**29b**) = 0.38, R_f(**30b**) < 0.1, $KMnO_4$). Aqueous NH_4Cl (1 mL) and H_2O (1 mL) were added, and the mixture was extracted with ethyl acetate (4×3 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (600 mg, ethyl acetate to ethyl acetate/MeOH 5:1) gave (+)-6-*epi*-241D (5.2 mg, 95%) as colorless needles (m.p. 88.5–89.5 °C), suitable for X-ray crystal structural analysis, which confirmed the relative configuration of the compound. $[\alpha]_D^{20} = +10.0$ ($c = 0.57$ in MeOH, >99% *ee*); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 3.87$ (dddd, $J = 10.7$, 10.7, 4.5, 4.5 Hz, 1H; C*H*OH), 3.13–3.10 (m, 1H; 6-H), 2.94–2.88 (m, 1H; 2-H), 1.97–1.93 (m, 1H; 3-H_a), 1.88–1.84 (m, 1H; 5-H_a), 1.82 (brs, 2H; NH, OH), 1.55–1.45 (m, 1H; 1′-H_a), 1.48 (ddd, $J = 11.9$, 11.6, 5.2 Hz, 1H; 5-H_b), 1.44–1.38 (m, 1H; 1′-H_b), 1.30–1.22 (m, 14H; $CH_{2(n\text{-nonyl})}$), 1.08 (d, $J = 6.3$ Hz, 3H; CH_3CH), 1.03 (ddd, $J = 11.4$, 11.4, 11.4 Hz, 1H; 3-H_b), 0.87 ppm (t, $J = 7.0$ Hz, 3H; CH_3CH_2); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 65.71$ (d, CHOH), 52.50 (d, C-6), 44.27 (d, C-2), 44.16 (t, C-3), 38.65 (t, C-5), 32.44 (t, C-1′), 32.02, 29.76, 29.76, 29.71, 29.45, 27.16 (6t, $CH_{2(n\text{-nonyl})}$), 22.91 (t, CH_2CH$_3$), 22.81 (q, CH_3CH), 14.25 ppm (q, CH_3CH_2); HRMS (ESI+): *m/z*: calcd for $C_{15}H_{32}NO^+$: 242.2478; found: 242.2483 $[M+H]^+$.

(+)-Benzyl (2*R*,4*S*,6*R*)-4-(acetyloxy)-2-formyl-6-methyliperidine-1-carboxylate ((+)-(2*R*,4*S*,6*R*)-31): A solution of (−)-**27a** (106 mg, 333 μmol) in CH_2Cl_2/MeOH (4:1, 2.5 mL) was treated with a small amount of Sudan® III red as indicator, and the resulting red mixture was cooled to −78 °C. Ozone was bubbled through for 3 min when the red color disappeared. Dimethylsulfide (ca. 200 μL, ca. 2.7 mmol) was added and stirring was continued for 10 min at −78 °C. Then the mixture was allowed to warm to room temperature and stirring was continued for 1 h. Volatiles were removed under reduced pressure, and the crude product was subjected to flash chromatography on silica gel (5 g, petroleum ether/ethyl acetate 4:1 to 3:1, R_f(**27a**) = 0.62, R_f(**31**) = 0.52 (petroleum ether/ethyl acetate 1:1), $KMnO_4$), which gave aldehyde (+)-(2*R*,4*S*,6*R*)-**31** (99 mg, 93%) as a colorless oil. $[\alpha]_D^{20} = +2.9$ ($c = 1.03$ in $CHCl_3$, >99% *ee*); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 9.67$ (s, 1H; CHO), 7.37–7.30 (m, 5H; Ph), 5.20 (d, $J = 12.3$ Hz, 1H; C$H_a$$H_b$Ph), 5.17 (d, $J = 12.3$ Hz, $CH_a$$H_b$Ph), 5.07 (dddd, $J = 3.4$, 3.4, 3.4, 3.4 Hz, 1H; CHOAc), 4.70 (d, $J = 7.2$ Hz, 1H; 2-H), 4.46 (qdd, $J = 7.0$, 7.0, 1.6 Hz, 1H; 6-H), 2.61 (d, $J = 14.7$ Hz, 1H; 3-H_a), 1.96 (s, 3H; CH_3CO_2), 1.89–1.84 (m, 2H; 3-H_b, 5-H_a), 1.79 (d, $J =$

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14.7 Hz, 1H; 5-H_b), 1.29 ppm (d, J=7.1 Hz, 3H; CH_3CH); ^{13}C NMR (126 MHz, $CDCl_3$): δ=201.28 (d, CHO), 169.98 (s, CH_3CO_2), 156.01 (s, NCO_2), 136.29 (s, Ph), 128.63, 128.27, 128.05 (3d, Ph), 67.79 (t, CH_2Ph), 65.90 (d, CHOAc), 57.37 (d, C-2), 45.39 (d, C-6), 32.52 (t, C-5), 27.41 (t, C-3), 21.71 (q, CH_3CH), 21.29 ppm (q, CH_3CO_2); HRMS (ESI+): m/z: calcd for $C_{17}H_{22}NO_5^+$: 320.1493; found: 320.1498 $[M+H]^+$.

Benzyl (2*R*,4*S*,6*R*)-4-(acetyloxy)-2-methyl-6-(prop-1′-en-1′-yl)piperidine-1-carboxylate ((2*R*,4*S*,6*R*)-32): A solution of potassium hexamethyldisilazane (KHMDS; 0.5 M in toluene, 830 μL, 415 μmol) was added dropwise at 0 °C to a suspension of ethyltriphenylphosphonium bromide (149 mg, 401 μmol) in dry THF (1.5 mL) to give an initially yellow solution, which was stirred at 0 °C for 30 min when the color changed to red. A solution of the aldehyde (+)-**31** (44.6 mg, 140 μmol) in dry THF (2.0 mL) was added dropwise, and stirring was continued for 1.5 h at 0 °C until TLC (petroleum ether/ethyl acetate 3:1, R_f(**31**)=0.15, R_f(**32**)=0.30, MPA) showed complete conversion. Brine (2 mL) was added, and the mixture was extracted with ethyl acetate (4×5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was subjected to flash chromatography on silica gel (4 g, petroleum ether/ethyl acetate 4:1) to give (2*R*,4*S*,6*R*)-**32** (37.6 mg, 81%) as a 87:13 mixture of *Z* and *E* isomers (^{1}H NMR spectroscopy), which could not be separated; colorless oil. Analytical data refers to this mixture: ^{1}H NMR (*E* isomer, 500 MHz, $CDCl_3$): δ=7.36–7.28 (m, 5H; Ph), 5.75 (ddq, J=10.9, 9.3, 1.7 Hz, 1H; C*H*=CHCH$_3$), 5.43 (dqd, J=10.8, 6.9, 1.2 Hz, 1H; =C*H*CH$_3$), 5.18–5.10 (m, 3H; 6-H, CH_2Ph), 5.06 (dddd, J=4.7, 4.7, 4.4, 4.2 Hz, 1H; CHOAc), 4.42 (qdd, J=7.1, 7.1, 3.2 Hz, 1H; 2-H), 2.04 (s, 3H; CH_3CO_2), 2.03–1.97 (m, 2H; CH_2), 1.91–1.85 (m, 1H; CH_2), 1.84–1.77 (m, 1H; CH_2), 1.59 (dd, J=7.0, 1.6 Hz, 3H; =CHC*H*$_3$), 1.39 ppm (d, J=7.0 Hz, 3H; C*H*$_3$CHN); ^{13}C NMR (126 MHz, $CDCl_3$): δ=170.43 (s, CH_3CO_2), 155.63 (s, NCO_2), 136.87 (s, Ph), 133.00 (d, *C*H=CHCH$_3$), 128.52, 128.02, 128.01 (3 d, Ph), 124.75 (d, =*C*HCH$_3$), 67.27 (d, CHOAc), 67.25 (t, CH_2Ph), 46.55 (d, C-6), 45.47 (d, C-2), 33.33, 33.33 (2 t, CH_2), 23.06 (q, *C*H$_3$CHN), 21.58 (q, *C*H$_3$CO$_2$), 12.60 ppm (q, *C*H$_3$CH=CH); two signals (t, CH_2) coincide at 33.33 ppm; elemental analysis calcd (%) for $C_{19}H_{25}NO_4$: C 68.86, H 7.60, N 4.23; found C 68.69, H 7.69, N 4.27; HRMS (FAB+): m/z: calcd for $C_{19}H_{26}NO_4^+$: 332.1856; found: 332.1884 $[M+H]^+$.

(−)-(2*R*,4*S*,6*S*)-2-Methyl-6-propylpiperidin-4-yl acetate ((−)-(2*R*,4*S*,6*S*)-33): Following GP5, a suspension of palladium hydroxide (6.8 mg) in dry methanol (0.5 mL) was stirred for 30 min under an atmosphere of hydrogen (1 bar). A solution of (2*R*,4*S*,6*R*)-**32** (21.0 mg, 63.4 μmol) in dry methanol (1.2 mL) was added, and the mixture was stirred for 1 h when TLC control (petroleum ether/ethyl acetate 3:1, R_f(**32**)=0.40, R_f(**33**)< 0.1, $KMnO_4$) showed complete conversion. The mixture was filtered through a pad of silica gel and concentrated under reduced pressure to give (−)-(2*R*,4*S*,6*S*)-**33** (11.0 mg, 87%) as a colorless oil. An analytically pure sample was obtained by flash chromatography on silica gel (1 g, ethyl acetate). $[\alpha]_D^{20}$=−3.0 (c=0.75 in $CHCl_3$, >99% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.76 (dddd, J=11.3, 11.3, 4.7, 4.7 Hz, 1H; CHOAc), 2.75 (dqd, J=11.1, 6.2, 2.0 Hz, 1H; 2-H), 2.67–2.58 (m, 1H; 6-H), 2.03 (s, 3H; CH_3CO_2), 2.01–1.91 (m, 2H; 3-H_a, 5-H_a), 1.45–1.30 (m, 5H; CH_2CH_2, NH), 1.16–1.01 (m, 2H; 3-H_b, 5-H_b), 1.11 (d, J=6.4 Hz, 3H; C*H*$_3$CH), 0.91 ppm (t, J=6.9 Hz, 3H; C*H*$_3$CH$_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.66 (s, CO_2), 71.58 (d, CHOAc), 54.59 (d, C-6), 50.28 (d, C-2), 39.59 (t, C-3), 38.69 (t, CH_2), 37.40 (t, C-5), 22.19 (q, *C*H$_3$CH), 21.43 (q, *C*H$_3$CO$_2$), 19.15 (t, CH_2), 14.19 ppm (q, *C*H$_3$CH$_2$); HRMS (EI+): m/z: calcd for $C_{11}H_{21}NO_2^+$: 199.1572; found: 199.1615 $[M]^+$; GC (chiral: β-CD, 145 °C isothermal): t_R((−)-(2*R*,4*S*,6*S*)-**33**)=50.5 min, t_R((+)-(2*S*,4*R*,6*R*)-**33**)=56.4 min.

(+)-(2*R*,4*S*,6*S*)-2-Methyl-6-propylpiperidin-4-ol ((+)-34): A solution of (−)-(2*R*,4*S*,6*S*)-**33** (15.0 mg, 75.4 μmol) in methanol (0.5 mL) was treated with methanolic NaOH (1 M, 0.5 mL, 0.5 mmol) at room temperature for 30 min until TLC control (ethyl acetate/MeOH 4:1, R_f(**33**)=0.34, R_f(**34**)=0.16, $KMnO_4$) showed complete consumption of the starting material. The mixture was concentrated in vacuo, and the residue was treated with CH_2Cl_2 (1 mL) and H_2O (1 mL). The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (4×1 mL). The combined organic layers were washed with H_2O (2 mL), dried over Na_2SO_4 and concentrated in vacuo to give pure (NMR spectroscopy) (+)-**34** (10.0 mg, 85%) as a colorless solid. An analytically pure sample was obtained after purification by flash chromatography on silica gel (ethyl acetate to ethyl acetate/MeOH 10:1) as colorless polyhedra (m.p. 94–95 °C; ref. [47]: 88–89 °C ((±)-**34**, (ethyl acetate))), suitable for X-ray crystal structural analysis. $[\alpha]_D^{20}$=+8.8 (c=0.43 in MeOH, >99% *ee*); ^{1}H NMR (500 MHz, $CDCl_3$): δ=3.63 (dddd, J=11.0, 11.0, 4.6, 4.6 Hz, 1H; C*H*OH), 2.68 (dqd, J=11.0, 6.3, 2.3 Hz, 1H; 2-H), 2.58–2.53 (m, 1H; 6-H), 1.98–1.90 (m, 2H; 3-H_a, 5-H_a), 1.85 (br s, 2H; NH, OH), 1.43–1.30 (m, 4H; CH_2CH_2), 1.11 (d, J=6.3 Hz, 3H; C*H*$_3$CH), 1.05–0.93 (m, 2H; 3-H_b, 5-H_b), 0.90 ppm (t, J=7.1 Hz, 3H; C*H*$_3$CH$_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=69.34 (d, CHOH), 54.66 (d, C-6), 50.28 (d, C-2), 44.00 (t, C-3), 41.78 (t, C-5), 39.06 (t, *C*H$_2$CH$_2$CH$_3$), 22.55 (q, *C*H$_3$CH), 19.29 (t, *C*H$_2$CH$_3$), 14.28 ppm (*C*H$_3$CH$_2$); HRMS (ESI+): m/z: calcd for $C_9H_{20}NO^+$: 158.1539; found: 158.1539 $[M+H]^+$.

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