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Amino Aldehydes

Iridium-Catalyzed Asymmetric Allylic Substitutions with Bulky Amines/Oxidative Double Bond Cleavage – Entry into the Reetz Synthesis of Amino Alcohols

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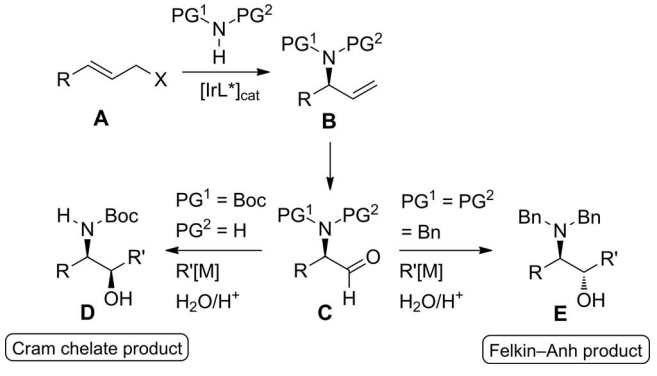
Abstract: Branched allylic amines were prepared by Ir-catalyzed enantioselective allylic aminations with the bulky N-nucleophiles $HN(Boc)_2$ and $HNBn_2$. The products were transformed into *N*-protected amino aldehydes, which were either reduced or coupled diastereoselectively with organometallic compounds to give vicinal amino alcohols. A formal synthesis of the neurokinin receptor antagonist (+)-L-733060 was carried out as an application.

Introduction

Many natural products, drugs, and peptidomimetics are β-amino alcohols.[1] Particularly versatile procedures for the synthesis of β-amino alcohols were developed by Reetz and coworkers, who have shown that reactions between organometallic compounds and α-amino aldehydes can display high diastereoselectivity controlled by N-protecting groups.[2,3] Thus, *N*-Boc-α-amino aldehydes preferentially proceed under chelate control to give *syn*-β-amino alcohols, whereas *N*,*N*-dibenzylamino aldehydes, which contain sterically shielded nitrogen atoms, do not form chelated intermediates and preferentially yield *anti*-β-amino alcohols (Scheme 1).



Scheme 1. Diastereoselective syntheses of *syn*- and *anti*-β-amino alcohols.

The Reetz approach relies almost exclusively on α-amino aldehydes derived from natural amino acids as starting materials. In view of the limited set of substituents and the preference for L enantiomers of this compound class, it appears desirable to broaden the structural space.

We have now investigated the preparation of *N*-protected α-amino aldehydes by oxidation of branched allylic amines, which can be prepared by Ir-catalyzed allylic amination. This approach is obvious, but there were challenges involved: (a) preparation of allylamines with very bulky *N*-protecting groups by Ir-catalyzed allylic substitution has so far not been sufficiently investigated, and (b) oxidative cleavage of the double bond required conditions that would not give rise to racemization or deterioration of the resulting sensitive α-amino aldehydes.

Oxidative cleavage of the double bond in branched allylic amination products has previously been carried out with $RuCl_3$/$NaIO_4$, to give protected amino acids.[4,6c] To the best of our knowledge, aldehydes or alcohols have so far only been prepared from allylic *alkylation* products by ozonolysis followed by reduction.[5]

Results and Discussion

The Boc-protected allylic amines were prepared with excellent selectivities by treatment of $HN(Boc)_2$ with allylic carbonates **1** under "salt-free" reaction conditions (Table 1).[6] The catalysts were either prepared in situ by adding a base (DMAP) to a mixture of $[Ir(dbcot)Cl]_2$ and the phosphoramidite **L2**[7,8] (Figure 1) or by mixing isolated (π-allyl)Ir complex **C1** with DBU.[9] Enantiomeric excesses were determined after partial deprotection by treatment either with TFA (compounds **4a**–**f**) or with KOH/ethanol (compound **4g**) to give the mono-Boc-protected amines **4**.[10] Use of dbcot as ancillary ligand is advantageous because of generally superior regioselectivity.

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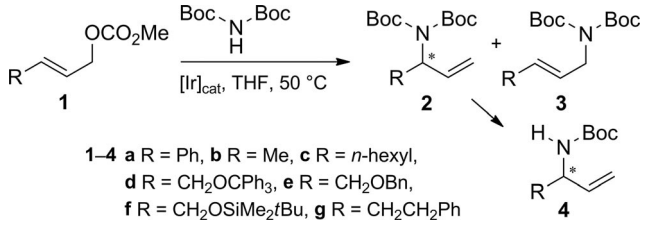
Table 1. Ir-catalyzed asymmetric allylic substitution with $HN(Boc)_2$ as pronucleophile.



1–4 **a** R = Ph, **b** R = Me, **c** R = *n*-hexyl, **d** R = CH_2OCPh_3, **e** R = CH_2OBn, **f** R = CH_2OSiMe_2tBu, **g** R = CH_2CH_2Ph

Entry	1	Catalyst[a]	Time [h]	Yield[c] [%]	**2**/**3**[d]	*ee*[e] [%]
1	**1a**	A	2	87	92:8	99
2[b]	**1b**	A	1	84	99:1	98
3	**1c**	A	20	69	94:6	98
4	**1d**	A	1	85	94:6	99
5[b]	**1e**	B	2.5	76	92:8	93
6[b]	**1f**	B	4	73	93:7	89
7	**1g**	B	2.5	78	98:2	98

[a] Catalyst A: **C1** (1–2 mol-%), DBU (8 mol-%). Catalyst B: $[Ir(dbcot)Cl]_2$ (2 mol-%). **L2** (4 mol-%) and DMAP (8 mol-%). [b] *ent*-**L2** was used. [c] Isolated yields of **2**. [d] Determined by ^1H NMR examination of the crude products. [e] Determined by chiral HPLC examination of carbamates **4**.

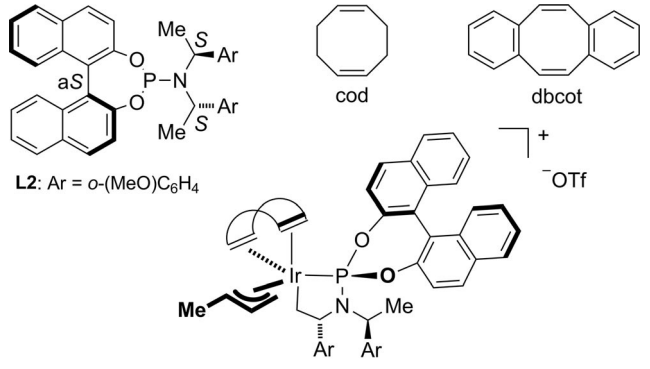


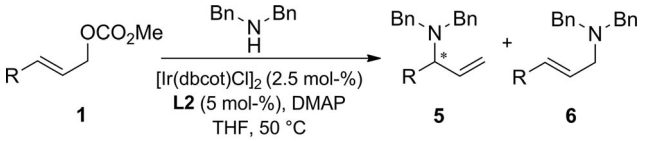
Figure 1. Ligands and (π-allyl)Ir complex **C1** used in this work.

The *N*,*N*-dibenzyl-allylamines **5a**–**g** were similarly obtained with good to high selectivities by enantioselective Ir-catalyzed allylic amination with $HNBn_2$ as nucleophile (Table 2).[11] The catalysts were prepared in situ as described above.

Representative examples of allylic derivatives **4** and **5** were converted into β-amino alcohols **8** or **9** via aldehydes **7** (Scheme 2). Both ozonolysis and dihydroxylation by treatment with OsO_4 (cat.)/NMO and subsequent periodide cleavage were probed as oxidation procedures. The latter procedure gave superior results. Racemization was minimal because purification was possible at the diol stage; the aldehydes were sufficiently pure for further steps. For precise assessment of racemization, aldehydes were reduced to the amino alcohols **8** or **9** with $NaBH_4$ at room temperature (yields: 74–98 %, 87–98 % *ee*, Schemes 3, 4).

Ozonolysis furnished less satisfactory results because purification of the aldehydes by column chromatography was necessary for *ee* determination or addition of organometallic compounds, and this led to partial racemization.

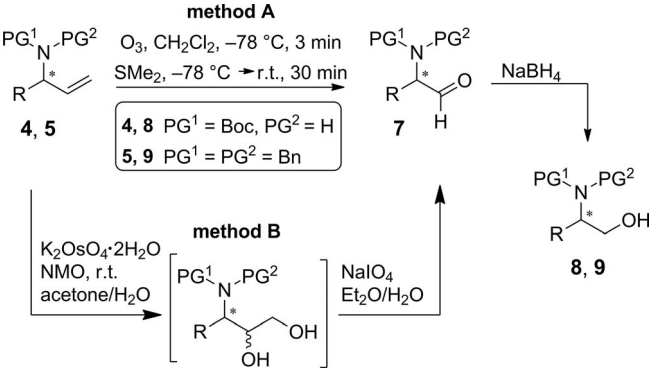
Table 2. Ir-catalyzed asymmetric allylic substitution with $HNBn_2$ as pronucleophile.



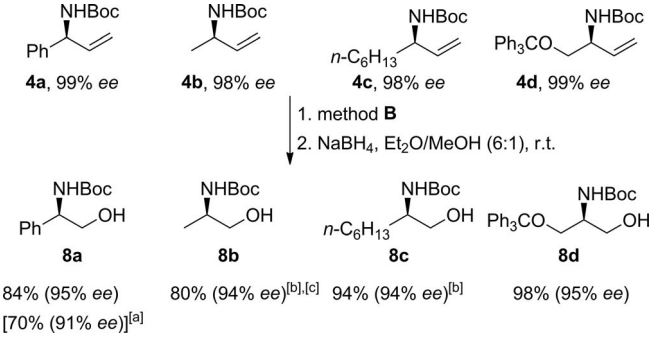
1, **5**, **6** **a** R = Ph, **b** R = Me, **c** R = *n*-hexyl, **d** R = CH_2OCPh_3, **e** R = CH_2OBn, **f** R = CH_2OSiMe_2tBu, **g** R = CH_2CH_2Ph

Entry	1	Time [h]	Yield[a] [%]	**5**/**6**[b]	*ee*[c] [%]
1[d]	**1a**	0.5	89	96:4	99
2[f]	**1b**	2	88	98:2	94
3	**1c**	2.5	74	82:18	96
4[f]	**1d**	2.5	73	84:16	91
5[d],[e]	**1e**	6	71	86:14	95
6	**1f**	3.5	82	86:14	97[g]
7	**1g**	3	65	75:25	94

[a] Isolated yields of **5**. [b] Determined by ^1H NMR examination of the crude products. [c] Determined by chiral HPLC. [d] 4 mol-% of Ir were used. [e] *ent*-**L2** was used. [f] Reaction was performed at 40 °C. [g] Determined by chiral HPLC after *O*-deprotection.

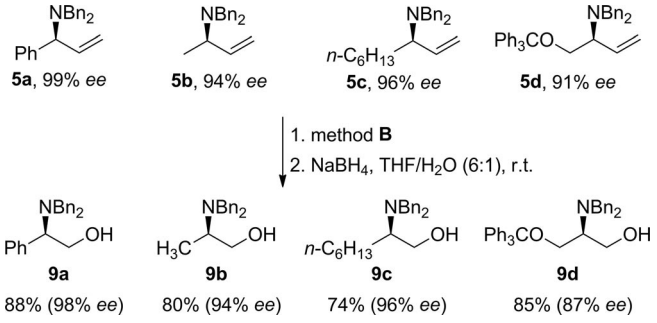


Scheme 2. Preparation of β-amino alcohols **8** and **9** by oxidative cleavage/reduction.



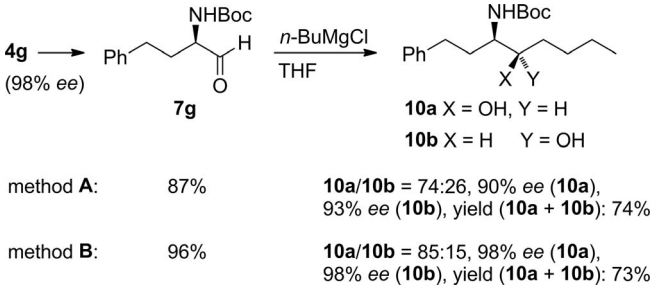
Scheme 3. Preparation of *N*-Boc-amino alcohols. [a] Compound **4a** (97 % *ee*) was used in conjunction with Method **A**. [b] *ee* was determined after transformation into the 4-nitrobenzoate. [c] Compound *ent*-**4b** was used.

To test the oxidation procedure in conjunction with the Reetz method, reactions between Grignard compounds and aldehydes derived from allylic derivatives **4a** or **4g** were carried out. In the latter case, the aldehyde **7g** (Scheme 5) was prepared from **4g** by both Method **A** and Method **B**. The aldehyde



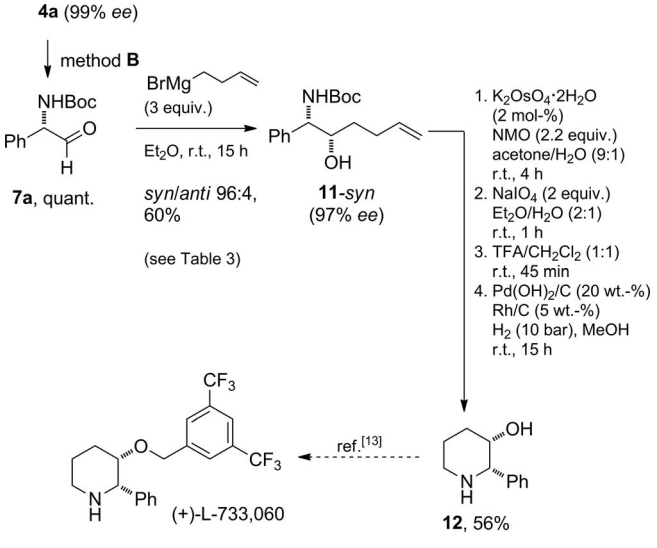
Scheme 4. Preparation of *N*,*N*-dibenzylamino alcohols.

obtained by the latter procedure was sufficiently pure for the *ee* (97 %) to be determined reliably by HPLC. Treatment with *n*BuMgCl/THF was carried out with the crude aldehyde after fast workup and furnished the amino alcohols **10** with up to 98 % *ee*. The results given in Scheme 5 clearly demonstrate that oxidation procedure **B** is the superior procedure. The preference for the *syn*-amino alcohol **10a** was as anticipated according to the results of the Reetz group.[3]



Scheme 5. Addition of a Grignard reagent to the aldehyde **7g**.

As an application in medicinal chemistry, we prepared the piperidine derivative **12** (Scheme 6), which has been used as an intermediate in the syntheses of the neurokinin receptor antagonist (+)-L-733060.[12,13] This example is of interest because the starting aldehyde **7a** is particularly prone to racemization. The amide **4a** was transformed into the aldehyde **7a** by Method **B**; the aldehyde was treated with but-3-en-1-ylmagnesium bromide at room temperature, initially in THF as solvent. The product **11** was obtained with satisfactory diastereoselectivity (92:8), but with a considerably diminished *ee* of 77 % (Table 3). Fortunately, results were much improved by use of Et_2O as solvent (Table 3, Entry 1).



Scheme 6. Addition of but-3-en-1-ylmagnesium bromide to the aldehyde **7a** and synthesis of (2*S*,3*S*)-2-phenylpiperidin-3-ol (**12**).

Table 3. Addition of but-3-en-1-ylmagnesium bromide to the aldehyde **7a** (see Scheme 6).

Entry	Solvent	*syn*/*anti*[a]	Yield [%][b]	*ee* **11**-*syn*[c]
1	Et_2O	96:4	62 (60)	97
2	THF	92:8	51 (49)	77
3	Et_2O/THF	96:6	48	n.d.

[a] Determined by HPLC examination of the crude product. [b] Refers to overall yields, with the isolated yields of **11** in parentheses. [c] Determined by chiral HPLC.

Further steps in the synthesis of **12** (Scheme 6) involved chromatographic isolation of pure **11**-*syn*, oxidative cleavage of the double bond (Method **B**), deprotection by treatment with TFA, and reductive amination (H_2/Pd/C) to give (2*S*,3*S*)-2-phenylpiperidin-3-ol (**12**) in 56 % yield over four steps.

Conclusions

In summary, Ir-catalyzed asymmetric allylic substitutions with the particularly bulky (pro)nucleophiles $HN(Boc)_2$ and $HNBn_2$ proceed with excellent yields and enantioselectivities. The branched products were subjected to oxidative double bond cleavage, preferably by dihydroxylation followed by periodate treatment to give *N*-protected α-amino aldehydes with a high degree of conservation of enantiomeric excess, as determined either directly or after reduction to alcohols with $NaBH_4$. By use of methods developed by Reetz et al., two representative *N*-Boc-α-amino aldehydes were treated with Grignard reagents to give *syn*-β-amino alcohols with *ee* ≥ 97 %. As an application, a synthesis of (2*S*,3*S*)-2-phenylpiperidin-3-ol (**12**), an intermediate in the syntheses of the non-peptide substance P antagonist (+)-L-733060, was carried out.

Experimental Section

General: All reactions requiring exclusion of air and moisture were performed in dried glassware under argon. Absolute solvents were purchased from Sigma–Aldrich. But-3-enylmagnesium bromide was purchased from Acros Organics as a 0.5 M solution in THF. For addition reactions with this compound in Et_2O, THF was evaporated off and the Grignard reagent was dissolved again in Et_2O. Catalytic hydrogenations were carried out with an autoclave Roth model II. Ozonolysis was carried out with a Fischer Ozone-Generator Modell 503. Macherey–Nagel Polygram Sil G/UV precoated sheets were used for TLC; spots were visualized with aqueous $KMnO_4$ solution or under UV. Macherey–Nagel silica gel 60 was used for flash chromatography. Preparative HPLC was carried out with a Gilson 305 instrument coupled with a Knauer UV/Vis filter photometer and a silica gel Latek column (250 × 21 mm, 5 μm). ^1H NMR spectra were recorded with Bruker DRX 200, Avance 300, Avance II 400, or Av-

ance 500 instruments. Chemical shifts are reported in δ units (ppm) relative to the solvent residual peak or TMS; coupling constants are given in Hertz. ^{13}C NMR spectra were recorded with Bruker Avance 300, Avance II 400, or Avance 500 instruments. Chemical shifts are reported in δ units (ppm) relative to the solvent residual peak. High-resolution mass spectra were recorded with Bruker ApexQe FT-ICR (ESI$^+$), ZAB-2F (EI$^+$), or JEOL JMS-700 (FAB$^+$) instruments. Optical rotations were measured at 20 °C with a Perkin–Elmer 341 instrument. Enantiomeric excesses were determined with a HP 1100 liquid chromatograph and chiral Daicel columns (Chiralpak AD-H, AS-H, OD-H, OJ-H, IB, 250 × 4.6 mm, 5 µm); diastereomeric ratios were determined with a silica gel column from Merck (LiChroCART, 250 × 4.6 mm, 7 µm). Melting points (m.p.) were determined with a Büchi Tottoli apparatus and are not corrected.

General Procedure 1 – Iridium-Catalyzed Allylic Substitutions with Catalyst Activation in situ: Success with the following procedures requires dry THF (<35 µg of H_2O mL^{-1}, Karl Fischer titration). Under argon, in a heat-gun-dried Schlenk tube, a solution of $[Ir(dbcot)Cl]_2$ (2–2.5 mol-%), **L2** or *ent*-**L2** (4–5 mol-%), and DMAP (8 mol-%) in dry THF (0.4 M with respect to the carbonate) was stirred for 5–10 min at room temperature until a white precipitate had formed at the glass wall above the solution. The allylic carbonate **1** (1.0 equiv.) and, after a further 5 min, $HN(Boc)_2$ (1.2 equiv.) or $HNBn_2$ (1.5 equiv.) were added, and the mixture was stirred at the stated temperature and for the stated time until TLC monitoring (petroleum ether/ethyl acetate, $KMnO_4$) indicated complete conversion. The solvent was removed under reduced pressure, and the residue was analyzed with respect to content of branched and linear product by ^1H NMR spectroscopy. The pure reaction products were obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate).

General Procedure 2 – Iridium-Catalyzed Allylic Substitutions with (π-Allyl)Ir-Complex C1 as Catalyst: Success with the following procedures requires dry THF (<35 µg of H_2O mL^{-1}, Karl Fischer titration). Under argon, in a heat-gun-dried Schlenk tube, (π-Allyl)Ir complex **C1** (1–2 mol-%) and DBU (8 mol-%) were dissolved in dry THF (0.4 M with respect to the carbonate). The allylic carbonate **1** (1.0 equiv.) and, after a further 5 min, $HN(Boc)_2$ (1.1 equiv.) were added, and the mixture was stirred at 50 °C and for the stated time until TLC monitoring (petroleum ether/ethyl acetate, $KMnO_4$) indicated complete conversion. The solvent was removed under reduced pressure, and the residue was analyzed with respect to content of branched and linear product by ^1H NMR spectroscopy. The pure reaction products were obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate).

General Procedure 3 – Mono-Boc Removal: Except in the case of **2d**, a solution of the di-Boc-protected amine **2** (1.0 equiv.) in CH_2Cl_2 (0.1 M) was treated dropwise with TFA (1.5 equiv.) at room temperature. The mixture was stirred for 1.5 h until TLC monitoring (petroleum ether/ethyl acetate, $KMnO_4$) showed complete conversion of the starting material. The solvent was removed in vacuo, and the crude product was subjected to flash column chromatography on silica gel (petroleum ether/ethyl acetate).

General Procedure 4/A – Ozonolysis: Ozone was bubbled through a cooled (–78 °C) solution of a branched allylic amine derivative **4** or **5** (1.0 equiv.) and a small amount of Sudan® III in CH_2Cl_2 (0.1 M) until the red color of the solution disappeared. Then O_2 was bubbled through for further 3 min, SMe_2 (10 equiv.) was added, and the mixture was stirred first for 10 min at –78 °C and then for 30 min at room temperature. The solvent was removed in vacuo, and the residue was subjected to flash chromatography on silica gel (petroleum ether/ethyl acetate) to give the corresponding α-amino aldehyde **7**.

General Procedure 4/B – Dihydroxylation/Periodide Cleavage: A solution of a branched allylic amine derivative **4** or **5** (1.0 equiv.) in acetone (0.1 M) at room temperature was treated dropwise with a mixture of $K_2OsO_4{\cdot}2\,H_2O$ (2.5 mol-%) and NMO (2.2 equiv.) in water (1:10 of acetone volume used). When complete conversion was reached (16 h, TLC monitoring, petroleum ether/ethyl acetate, $KMnO_4$), $Na_2S_2O_4$ was added, and the mixture was stirred for 30 min. Subsequently, the solution was filtered through a pad of Celite®, the solvent was removed from the filtrate in vacuo, and the residue was dissolved in Et_2O/H_2O (2:1, 0.1 M). Then $NaIO_4$ (2.1 equiv.) was added, and the mixture was vigorously stirred at room temperature until TLC monitoring (1–2 h, petroleum ether/ethyl acetate, $KMnO_4$) showed complete conversion. Phosphate buffer/Et_2O (1:1) was added, and the aqueous layer was separated and extracted twice with Et_2O. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated in vacuo to give the corresponding α-amino aldehyde **7**. The crude product was directly used for further reactions without analysis (unless otherwise mentioned).

General Procedure 5 – Reduction of Crude α-Amino Aldehydes 7 to Give α-Amino Alcohols 8: A crude α-amino aldehyde **7** (1.0 equiv.) was dissolved in Et_2O/MeOH (6:1, 0.02 M), and $NaBH_4$ (2.0 equiv.) was added. The mixture was stirred at room temperature until TLC monitoring (petroleum ether/ethyl acetate, $KMnO_4$) showed complete conversion. Water was added, and the mixture was extracted three times with ethyl acetate. The combined organic layers were dried with Na_2SO_4. The solvent was removed under reduced pressure to give the crude product, which was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate) to afford the α-amino alcohol **8**.

General Procedure 6 – Reduction of Crude α-Amino Aldehydes 7 to Give α-Amino Alcohols 9: The crude α-amino aldehyde **7** (1.0 equiv.) was dissolved in THF/H_2O (6:1, 0.2 M), and $NaBH_4$ (1.5 equiv.) was added. The mixture was stirred at room temperature until TLC monitoring (petroleum ether/ethyl acetate, $KMnO_4$) showed complete conversion (15 min). Water was added, and the mixture was extracted three times with ethyl acetate. The combined organic layers were dried with Na_2SO_4. The solvent was removed under reduced pressure to give the crude product, which was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate) to afford α-amino alcohol **9**.

(–)-Di-*tert*-butyl [(1*S*)-1-Phenylprop-2-en-1-yl]imidodicarbonate (2a): This compound was prepared as described in General Procedure 2; yield 580 mg (1.74 mmol), 87 %, colorless oil, 99 % *ee* (determined after mono-Boc removal), **2a**/**3a** = 92:8. $[\alpha]_D^{20}$ (99 % *ee*) = –36.6 [*c* = 1.0, $CHCl_3$, (*S*)], ref.[14] $[\alpha]_D^{20}$ (99 % *ee*) = +49.1 [*c* = 1.16, $CHCl_3$, (*R*)]. The analytical data were in agreement with the literature.

[(2*E*)-3-Phenylprop-2-en-1-yl]imidodicarbonate (3a): The analytical data were in agreement with the literature.[14]

(–)-Di-*tert*-butyl [(1*S*)-1-Methylprop-2-en-1-yl]imidodicarbonate (2b): This compound was prepared as described in General Procedure 2; yield 456 mg (1.68 mmol), 84 %, colorless solid, m.p. 30–33 °C, 98 % *ee* (determined after mono-Boc removal), **2b**/**3b** = 99:1. $[\alpha]_D^{20}$ (95 % *ee*) = +9.5 [*c* = 1.03, $CHCl_3$, (*R*)]. ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.39 (d, *J* = 6.9 Hz, 3 H), 1.48 (s, 18 H), 4.76–4.85 (m, 1 H), 5.07 (d, *J* = 10.5 Hz, 1 H), 5.13 (d, *J* = 17.4 Hz, 1 H), 6.00 (ddd, *J* = 17.1, 10.4, 5.5 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 18.1, 28.2,

54.2, 82.3, 115.0, 139.2, 153.0 ppm. HRMS (ESI$^+$) calcd. for $C_{17}H_{35}N_2O_4$ [M + Me_3NH]$^+$ 331.2597; found 331.2592.

Di-*tert*-butyl (2*E*)-But-2-en-1-ylimidodicarbonate (3b): The analytical data were in agreement with the literature.[15]

(–)-Di-*tert*-butyl [(1*R*)-1-Hexylprop-2-en-1-yl]imidodicarbonate (2c): This compound was prepared as described in General Procedure 2; yield 471 mg (1.38 mmol), 69 %, colorless oil, 98 % *ee* (determined after mono-Boc removal), **2c**/**3c** = 94:6. $[\alpha]_D^{20}$ (95 % *ee*) = +2.6 [*c* = 1.00, $CHCl_3$, (*S*)]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.87 (t, *J* = 6.8 Hz, 3 H), 1.23–1.34 (m, 8 H), 1.48 (s, 18 H), 1.63–1.73 (m, 1 H), 1.79–1.90 (m, 1 H), 4.56–4.65 (m, 1 H), 5.09 (td, *J* = 10.3, 1.3 Hz, 1 H), 5.15 (td, *J* = 17.3, 1.4 Hz, 1 H), 6.00 (ddt, *J* = 17.2, 10.3, 6.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.2, 22.7, 26.5, 28.2, 29.1, 31.9, 32.6, 59.3, 82.2, 116.2, 138.2, 153.2 ppm. HRMS (ESI$^+$) calcd. for $C_{19}H_{35}NO_4Na$ [M + Na]$^+$ 364.2464; found 364.2465.

Di-*tert*-butyl (2*E*)-Non-2-en-1-ylimidodicarbonate (3c): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.87 (t, *J* = 6.8 Hz, 3 H), 1.23–1.37 (m, 8 H), 1.49 (s, 18 H), 2.00 (q, *J* = 6.9, 6.8 Hz, 2 H), 4.09 (d, *J* = 6.0 Hz, 2 H), 5.40–5.50 (m, 1 H), 5.55–5.65 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.1, 22.6, 28.8, 29.2, 31.7, 28.1, 32.2, 48.0, 82.0, 125.1, 133.9, 152.4 ppm. HRMS (ESI$^+$) calcd. for $C_{19}H_{35}NO_4Na$ [M + Na]$^+$ 364.2464; found 364.2464.

(+)-Di-*tert*-butyl [(2*S*)-1-(Trityloxy)but-3-en-2-yl]imidodicarbonate (2d): This compound was prepared as described in General Procedure 2; yield 450 mg (0.85 mmol), 85 %, colorless solid, m.p. 140–143 °C, ref.[6d] 143–146 °C, 99 % *ee* (determined after mono-Boc removal), **2d**/**3d** = 94:6. $[\alpha]_D^{20}$ (99 % *ee*) = +24.5 [*c* = 1.12, $CHCl_3$, (*S*)], ref.[6d] $[\alpha]_D^{20}$ (97 % *ee*) = +25.7 [*c* = 0.97, $CHCl_3$, (*S*)]. The analytical data were in agreement with the literature.

Di-*tert*-butyl [(2*E*)-4-(Trityloxy)but-2-en-1-yl]imidodicarbonate (3d): The analytical data were in agreement with the literature.[6d]

(–)-Di-*tert*-butyl {(1*R*)-1-[(Benzyloxy)methyl]prop-2-en-1-yl}-imidodicarbonate (2e): This compound was prepared as described in General Procedure 1; yield 122 mg (0.32 mmol), 76 %, colorless oil, 93 % *ee* (determined after mono-Boc removal), **2e**/**3e** = 92:8. $[\alpha]_D^{20}$ (93 % *ee*) = –10.4 [*c* = 1.01, $CHCl_3$, (*R*)]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.48 (s, 18 H), 3.70 (dd, *J* = 9.8, 6.4 Hz, 1 H), 3.88 (dd, *J* = 9.8, 8.2 Hz, 1 H), 4.52 (d, *J* = 12.0 Hz, 1 H), 4.56 (d, *J* = 12.0 Hz, 1 H), 4.96–5.05 (m, 1 H), 5.18 (td, *J* = 10.6, 1.2 Hz, 1 H), 5.25 (td, *J* = 17.4, 1.2 Hz, 1 H), 5.96 (ddd, *J* = 17.1, 10.5, 6.1 Hz, 1 H), 7.22–7.36 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.2, 58.1, 70.7, 72.9, 82.4, 117.5, 127.6, 127.7, 128.4, 134.8, 138.5, 153.1 ppm. HRMS (ESI$^+$) calcd. for $C_{21}H_{31}NO_5Na$ [M + Na]$^+$ 400.2100; found 400.2093.

Di-*tert*-butyl [(2*E*)-4-(Benzyloxy)but-2-en-1-yl]imidodicarbonate (3e): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.50 (s, 18 H), 3.97–4.04 (m, 2 H), 4.15–4.22 (m, 2 H), 4.50 (s, 2 H), 5.66–5.84 (m, 2 H), 7.24–7.38 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.2, 47.6, 70.2, 72.0, 82.5, 127.7, 127.8, 128.5, 128.9, 129.2, 138.4, 152.5 ppm. HRMS (ESI$^+$) calcd. for $C_{21}H_{31}NO_5Na$ [M + Na]$^+$ 400.2100; found 400.2093.

(–)-Di-*tert*-butyl [(1*R*)-1-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-prop-2-en-1-yl]imidodicarbonate (2f): This compound was prepared as described in General Procedure 1; yield 108 mg (0.27 mmol), 73 %, colorless oil, 89 % *ee* (determined after mono-Boc removal), **2f**/**3f** = 93:7. $[\alpha]_D^{20}$ (89 % *ee*) = –8.2 [*c* = 1.02, $CHCl_3$, (*R*)]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.04 (s, 6 H), 0.88 (s, 9 H), 1.49 (s, 18 H), 3.76 (dd, *J* = 9.9, 6.4 Hz, 1 H), 4.00 (dd, *J* = 9.9, 8.5 Hz, 1 H), 4.78–4.84 (m, 1 H), 5.16 (td, *J* = 10.5, 1.4 Hz, 1 H), 5.18 (td, *J* = 17.4, 1.4 Hz, 1 H), 5.92 (ddd, *J* = 17.4, 10.5, 6.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = –5.2, 18.4, 26.0, 28.2, 60.9, 63.9, 82.2, 117.4, 134.7, 153.2 ppm. HRMS (ESI$^+$) calcd. for $C_{20}H_{39}NO_5SiNa$ [M + Na]$^+$ 424.2495; found 424.2488.

Di-*tert*-butyl ((2*E*)-4-{[*tert*-Butyl(dimethyl)-silyl]oxy}but-2-en-1-yl)imidodicarbonate (3f): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.06 (s, 6 H), 0.90 (s, 9 H), 1.49 (s, 18 H), 4.13–4.17 (m, 4 H), 5.65–5.77 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = –5.1, 18.5, 26.1, 28.2, 47.6, 63.3, 82.4, 125.6, 132.2, 152.4 ppm. HRMS (ESI$^+$) calcd. for $C_{20}H_{39}NO_5SiNa$ [M + Na]$^+$ 424.2495; found 424.2489.

(–)-Di-*tert*-butyl [(1*R*)-1-(2-Phenylethyl)prop-2-en-1-yl]imidodicarbonate (2g): This compound was prepared as described in General Procedure 1; yield 384 mg (1.06 mmol), 78 %, colorless oil, 98 % *ee* (determined after mono-Boc removal), **2g**/**3g** = 98:2. $[\alpha]_D^{20}$ (98 % *ee*) = –0.4 [*c* = 1.03, $CHCl_3$, (*R*)], ref.[16] $[\alpha]_D^{20}$ (93 % *ee*) = –0.5 [*c* = 1.09, $CHCl_3$, (*S*)]. The analytical data were in agreement with the literature.

Di-*tert*-butyl [(2*E*)-5-Phenylpent-2-en-1-yl]imidodicarbonate (3g): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.49 (s, 18 H), 2.34 (dt, *J* = 7.3, 6.9 Hz, 1 H), 2.68 (t, *J* = 7.3 Hz, 2 H), 4.10 (dd, *J* = 5.9, 0.8 Hz, 1 H), 5.51 (dtt, *J* = 15.3, 6.0, 1.2 Hz, 1 H), 5.67 (dt, *J* = 15.4, 6.7 Hz, 1 H), 7.13–7.31 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 28.2, 34.2, 35.8, 48.0, 82.3, 126.0, 126.0, 128.4, 128.5, 132.8, 141.9, 152.6 ppm. HRMS (ESI$^+$) calcd. for $C_{21}H_{31}NO_4Na$ [M + Na]$^+$ 384.2151; found 384.2148.

(–)-*tert*-Butyl [(1*S*)-1-Phenylprop-2-en-1-yl]carbamate (4a): This compound was prepared as described in General Procedure 3; yield 551 mg (2.36 mmol), 96 %, colorless solid, m.p. 56–57 °C, ref.[14] 54–55 °C. $[\alpha]_D^{20}$ (99 % *ee*) = –64.4 [*c* 1.00, $CHCl_3$, (*S*)], ref.[14] $[\alpha]_D^{20}$ (99 % *ee*) = +62.2 [*c* = 1.00, $CHCl_3$, (*R*)]. The analytical data were in agreement with the literature.

(–)-*tert*-Butyl [(1*S*)-1-Methylprop-2-en-1-yl]carbamate (4b): This compound was prepared as described in General Procedure 3; yield 126 mg (0.74 mmol), 95 %; colorless solid, m.p. 56–57 °C. $[\alpha]_D^{20}$ (98 % *ee*) = –4.9 [*c* = 1.09, $CHCl_3$, (*S*)], ref.[17] $[\alpha]_D^{20}$ = –6.3 [*c* = 1.2, $CHCl_3$, (*S*)]. The analytical data were in agreement with the literature.

(–)-*tert*-Butyl [(1*R*)-1-Hexylprop-2-en-1-yl]carbamate (4c): This compound was prepared as described in General Procedure 3; yield 80.5 mg (0.33 mmol), 97 %, colorless oil. $[\alpha]_D^{20}$ (98 % *ee*) = –12.4 [*c* = 1.55, $CHCl_3$, (*R*)]. HPLC (Chiralpak AS-H, *n*-hexane/2-propanol 99.5:0.5, flow 0.5 mL min^{-1}, room temp., λ = 205 nm), t_R[(–)-(*R*)-**4c**] = 12.8 min, t_R[(+)-(*S*)-**4c**] = 16.9 min. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.87 (t, *J* = 6.9 Hz, 3 H), 1.20–1.36 (m, 8 H), 1.40–1.54 (m, 2 H), 1.44 (s, 9 H), 4.07 (br. s, 1 H), 4.44 (br. s, 1 H), 5.06 (td, *J* = 10.4, 1.3 Hz, 1 H), 5.13 (td, *J* = 17.2, 1.3 Hz, 1 H), 5.73 (ddd, *J* = 17.1, 10.4, 5.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.2, 22.7, 25.8, 28.5, 29.2, 31.9, 35.4, 52.9, 79.3, 114.3, 139.3, 155.5 ppm. HRMS (ESI$^+$) calcd. for $C_{14}H_{27}NO_2Na$ [M + Na]$^+$ 264.1939; found 264.1934.

(–)-*tert*-Butyl (*S*)-[1-(Trityloxy)but-3-en-2-yl]carbamate (4d): A solution of **2d** (185 mg, 0.35 mmol) in a mixture of toluene (1 mL) and EtOH (10 mL) was treated with KOH (39.2 mg, 0.51 mmol). Then the mixture was stirred under reflux until TLC monitoring showed complete conversion [petroleum ether/diethyl ether (10:1); R_f(**2d**) = 0.38, R_f(**4d**) = 0.23, $KMnO_4$]. The solvent was removed in vacuo, and the crude product was subjected to flash column chromatography on silica gel [petroleum ether/diethyl ether (20:1)] to give **4d** (133.8 mg, 0.31 mmol, 89 %) as a colorless oil. $[\alpha]_D^{20}$ (99 % *ee*) = –18.5 [*c* = 1.05, $CHCl_3$, (*S*)]. HPLC (Chiralpak AD-H, *n*-hexane/2-propanol 95:5, flow 0.5 mL min^{-1}, room temp., λ = 220 nm), t_R[(+)-(*R*)-**4d**] = 12.6 min, t_R[(–)-(*S*)-**4d**] = 15.2 min. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.48 (s, 18 H), 3.20–3.26 (m, 2 H), 4.42 (br. s, 1 H), 4.87 (br. s, 1 H), 5.23 (td, *J* = 10.0, 1.5 Hz, 1 H), 5.29 (td, *J* = 17.3, 1.3 Hz, 1 H), 5.94 (ddd, *J* = 17.1, 10.5, 5.0 Hz, 1 H), 7.27–7.30 (m, 3 H), 7.34–7.37 (m, 6 H), 7.48–7.50 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$,

125 MHz): δ = 28.5, 52.9, 65.7, 79.5, 86.6, 115.6, 127.2, 127.9, 128.8, 136.7, 143.9, 155.5 ppm. HRMS (ESI$^+$) calcd. for $C_{28}H_{31}NNaO_3$ [M + Na]$^+$ 452.2196; found 452.2198.

(+)-*tert*-Butyl {(1*R*)-1-[(Benzyloxy)methyl]prop-2-en-1-yl}carbamate (4e): This compound was prepared as described in General Procedure 3; yield 76.9 mg (0.28 mmol), 97 %, colorless oil. $[\alpha]_D^{20}$ (93 % *ee*) = +32.2 [*c* = 1.01, $CHCl_3$, (*R*)], ref.[10a]: $[\alpha]_D^{20}$ (98 % *ee*) = +30.9 [*c* = 0.62, $CHCl_3$, (*R*)]. The analytical data were in agreement with the literature.

(–)-*tert*-Butyl [(1*S*)-1-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-prop-2-en-1-yl]carbamate (4f): This compound was prepared as described in General Procedure 3; yield 22.7 mg (75.3 μmol), 38 %, colorless oil. $[\alpha]_D^{20}$ (89 % *ee*) = –32.2 [*c* = 0.77, $CHCl_3$, (*S*)], ref.[18] $[\alpha]_D^{20}$ (98 % *ee*) = –35.0 [*c* = 1.05, $CHCl_3$, (*S*)]. The analytical data were in agreement with the literature.

(–)-*tert*-Butyl [(1*R*)-1-(2-Phenylethyl)prop-2-en-1-yl]carbamate (4g): This compound was prepared as described in General Procedure 3; yield 27.4 mg (105 μmol), 98 %, colorless solid, m.p. 76–77 °C. $[\alpha]_D^{20}$ (98 % *ee*) = –25.3 [*c* = 1.04, $CHCl_3$, (*R*)], ref.[19] $[\alpha]_D^{20}$ (90 % *ee*) = +22.5 [*c* = 1.9, $CHCl_3$, (*S*)]. HPLC (Chiralpak OD-H, *n*-hexane/2-propanol 95:5, flow 0.8 mL min^{-1}, room temp., λ = 210 nm), t_R[(–)-(*R*)-**4g**] = 7.6 min, t_R[(+)-(*S*)-**4g**] = 10.7 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.45 (s, 9 H), 1.70–1.92 (m, 2 H), 2.56–2.75 (m, 2 H), 4.15 (br. s, 1 H), 4.47 (br. s, 1 H), 5.12 (d, *J* = 10.4 Hz, 1 H), 5.18 (d, *J* = 17.2 Hz, 1 H), 5.78 (ddd, *J* = 17.0, 10.4, 5.6 Hz, 1 H), 7.13–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 28.6, 32.3, 37.1, 52.8, 79.5, 114.9, 126.11, 128.5, 128.6, 138.9, 141.8, 155.5 ppm. HRMS (ESI$^+$) calcd. for $C_{32}H_{46}N_2O_4Na$ [2 M + Na]$^+$ 545.3355; found 545.3348.

(–)-(1*S*)-*N*,*N*-Dibenzyl-1-phenylprop-2-en-1-amine (5a): This compound was prepared as described in General Procedure 1; yield 151 mg (0.48 mmol), 89 %; colorless oil, 99 % *ee*, **5a**/**6a** = 96:4. $[\alpha]_D^{20}$ (99 % *ee*) = –111 [*c* = 1.03, $CHCl_3$, (*S*)], ref.[11] $[\alpha]_D^{20}$ (95 % *ee*) = –111 [*c* = 1.06, $CHCl_3$, (*S*)]. The analytical data were in agreement with the literature.

(2*E*)-*N*,*N*-Dibenzyl-3-phenylprop-2-en-1-amine (6a): The analytical data were in agreement with the literature.[11]

(+)-(2*R*)-*N*,*N*-Dibenzylbut-3-en-2-amine (5b): This compound was prepared as described in General Procedure 1; yield 341 mg (1.36 mmol), 88 %, colorless oil, 94 % *ee*, **5b**/**6b** = 98:2. $[\alpha]_D^{20}$ (94 % *ee*) = +13.4 [*c* = 0.53, $CHCl_3$, (*R*)], ref.[20] $[\alpha]_D^{20}$ = –11.6 [*c* = 8.3, $CHCl_3$, (*S*)]. The analytical data were in agreement with the literature.

(*E*)-*N*,*N*-Dibenzylbut-2-en-1-amine (6b): The analytical data were in agreement with the literature.[21]

(–)-(3*R*)-*N*,*N*-Dibenzylnon-1-en-3-amine (5c): This compound was prepared as described in General Procedure 1; yield 120 mg (0.37 mmol), 74 %; colorless oil, 96 % *ee*, **5c**/**6c** 82:18. $[\alpha]_D^{20}$ (96 % *ee*) = –15.0 [*c* = 1.01, $CHCl_3$, (*R*)]. HPLC (Chiralpak OD-H, *n*-hexane/2-propanol 95:5, flow 0.5 mL min^{-1}, room temp., λ = 210 nm), t_R[(+)-(*S*)-**5c**] = 5.1 min, t_R[(–)-(*R*)-**5c**] = 6.2 min. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.88 (t, *J* = 6.9 Hz, 3 H), 1.15–1.32 (m, 7 H), 1.34–1.51 (m, 2 H), 1.64–1.77 (m, 1 H), 2.97–3.05 (m, 1 H), 3.38 (d, *J* = 13.8 Hz, 2 H), 3.81 (d, *J* = 13.8 Hz, 2 H), 5.03 (ddd, *J* = 17.2, 2.1, 0.8 Hz, 1 H), 5.26 (ddd, *J* = 10.3, 2.1, 0.4 Hz, 1 H), 5.81 (ddd, *J* = 17.2, 10.3, 8.6 Hz, 1 H), 7.19–7.42 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.3, 22.8, 26.6, 29.4, 32.0, 32.2, 53.8, 61.0, 117.6, 126.8, 128.3, 128.8, 136.9, 140.8 ppm. HRMS (ESI$^+$) calcd. for $C_{23}H_{32}N$ [M + H]$^+$ 322.2535; found 322.2528.

(2*E*)-*N*,*N*-Dibenzylnon-2-en-1-amine (6c): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.85–0.92 (m, 3 H), 1.22–1.40 (m, 8 H), 2.00–2.07 (m, 2 H), 3.02 (d, *J* = 5.9 Hz, 2 H), 3.58 (s, 4 H), 5.52 (td, *J* = 15.4, 5.9 Hz, 1 H), 5.60 (td, *J* = 15.5, 6.2 Hz, 1 H), 7.20–7.42 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.2, 22.8, 29.0, 29.5, 31.9, 32.6, 55.7, 57.8, 126.9, 127.2, 128.3, 129.0, 134.4, 140.1 ppm. HRMS (ESI$^+$) calcd. for $C_{23}H_{32}N$ [M + H]$^+$ 322.2535; found 322.2529.

(–)-(2*S*)-*N*,*N*-Dibenzyl-1-(trityloxy)but-3-en-2-amine (5d): This compound was prepared as described in General Procedure 1; yield 191 mg (0.38 mmol), 73 %, colorless oil, 91 % *ee*, **5d**/**6d** = 84:16. $[\alpha]_D^{20}$ (91 % *ee*) = –45.0 [*c* = 0.95, $CHCl_3$, (*S*)], ref.[22] $[\alpha]_D^{20}$ (97 % *ee*) = +56.2 [*c* = 0.93, $CHCl_3$, (*R*)]. The analytical data were in agreement with the literature.

(2*E*)-*N*,*N*-Dibenzyl-4-(trityloxy)but-2-en-1-amine (6d): The analytical data were in agreement with the literature.[22]

(+)-(2*R*)-*N*,*N*-Dibenzyl-1-(benzyloxy)but-3-en-2-amine (5e): This compound was prepared as described in General Procedure 1; yield 52.7 mg (0.15 mmol), 71 %, colorless oil, 95 % *ee*, **5e**/**6e** = 86:14. $[\alpha]_D^{20}$ (95 % *ee*) = –27.2 [*c* = 1.07, $CHCl_3$, (*S*)]. HPLC (Chiralpak IB, *n*-hexane/2-propanol 99:1, flow 0.5 mL min^{-1}, room temp., λ = 210 nm), t_R[(+)-(*R*)-**5e**] = 9.2 min, t_R[(–)-(*S*)-**5e**] = 11.4 min. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.42–3.50 (m, 1 H), 3.57 (d, *J* = 13.9 Hz, 2 H), 3.64 (dd, *J* = 9.8, *J* = 6.5 Hz, 1 H), 3.76 (dd, *J* = 9.8, 6.2 Hz, 1 H), 3.83 (d, *J* = 13.9 Hz, 2 H), 4.50 (s, 2 H), 5.23 (ddd, *J* = 17.3, 1.7, 1.2 Hz, 1 H), 5.34 (ddd, *J* = 10.7, 1.8, 1.0 Hz, 1 H), 5.93 (ddd, *J* = 17.5, 10.5, 7.5 Hz, 1 H), 7.18–7.44 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 54.6, 60.1, 71.5, 73.1, 118.6, 126.9, 127.6, 127.7, 128.3, 128.4, 128.7, 135.0, 138.6, 140.5 ppm. HRMS (ESI$^+$) calcd. for $C_{25}H_{28}NO$ [M + H]$^+$ 358.2171; found 358.2166.

(2*E*)-*N*,*N*-Dibenzyl-4-(benzyloxy)but-2-en-1-amine (6e): The analytical data were in agreement with the literature.[23]

(–)-(2*S*)-*N*,*N*-Dibenzyl-1-{[*tert*-butyl(dimethyl)silyl]oxy}but-3-en-2-amine (5f): This compound was prepared as described in General Procedure 1; yield 139 mg (0.36 mmol), 82 %, colorless oil, 97 % *ee* (determined after TBS removal with TBAF), **5f**/**6f** = 86:14. $[\alpha]_D^{20}$ (97 % *ee*) = +7.4 [*c* = 1.02, $CHCl_3$, (*R*)], ref.[24] $[\alpha]_D^{20}$ = +5.5 [*c* = 1.00, $CHCl_3$, (*R*)]. The analytical data were in agreement with the literature.

(2*E*)-*N*,*N*-Dibenzyl-4-{[*tert*-butyl(dimethyl)silyl]-oxy}but-2-en-1-amine (6f): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.08 (2 × s, 6 H), 0.92 (s, 9 H), 3.07 (d, *J* = 4.7 Hz, 2 H), 3.58 (s, 4 H), 4.18 (d, *J* = 3.7 Hz, 2 H), 5.68–5.83 (m, 2 H), 7.20–7.44 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = –5.0, 18.6, 26.1, 55.0, 57.9, 63.7, 126.9, 127.8, 128.3, 128.9, 132.6, 139.8 ppm. HRMS (ESI$^+$) calcd. for $C_{24}H_{36}NOSi$ [M + H]$^+$ 382.2566; found 382.2562.

(–)-(3*R*)-*N*,*N*-Dibenzyl-5-phenylpent-1-en-3-amine (5g): This compound was prepared as described in General Procedure 1; yield 81.2 mg (0.24 mmol), 65 %, colorless oil, 94 % *ee*, **5g**/**6g** = 75:25. $[\alpha]_D^{20}$ (94 % *ee*) = +27.7 [*c* = 1.03, $CHCl_3$, (*S*)]. HPLC (Chiralpak IB, *n*-hexane/2-propanol 99.9:0.1, flow 1.0 mL min^{-1}, room temp., λ = 210 nm), t_R[(+)-(*S*)-**5g**] = 7.3 min, t_R[(–)-(*R*)-**5g**] = 7.8 min. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.79 (dddd, *J* = 13.6, 10.7, 6.9, 5.5 Hz, 1 H), 2.04 (dddd, *J* = 13.4, 10.8, 7.5, 5.8 Hz, 1 H), 2.55 (ddd, *J* = 13.9, 10.8, 5.4 Hz, 1 H), 2.81 (ddd, *J* = 13.9, 10.7, 5.8 Hz, 1 H), 3.09–3.17 (m, 1 H), 3.42 (d, *J* = 13.8 Hz, 2 H), 3.85 (d, *J* = 13.8 Hz, 2 H), 5.09 (ddd, *J* = 17.2, 2.0, 0.8 Hz, 1 H), 5.32 (ddd, *J* = 10.6, 2.2, 0.5 Hz, 1 H), 5.88 (ddd, *J* = 17.2, 10.3, 8.6 Hz, 1 H), 7.09–7.45 (m, 15 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 33.1, 34.3, 53.9, 60.8, 118.1, 125.7, 126.9, 128.3, 128.4, 128.5, 128.9, 136.3, 140.5, 142.8 ppm. HRMS (ESI$^+$) calcd. for $C_{25}H_{28}N$ [M + H]$^+$ 342.2222; found 342.2217.

(2*E*)-*N*,*N*-Dibenzyl-5-phenylpent-2-en-1-amine (6g): The analytical data were in agreement with the literature.[23]

(+)-*tert*-Butyl [(1*S*)-2-Oxo-1-phenylethyl]carbamate (7a): This compound was prepared as described in General Procedure 4/B; yield 118 mg (0.44 mmol), quant., colorless oil. $[\alpha]_D^{20}$ (99 % *ee* according to the starting material) = +214, [*c* = 1.08, $CHCl_3$, (*S*)], ref.[25a] $[\alpha]_D^{20}$ = +272 [*c* = 0.9, CH_2Cl_2, (*S*)]. The analytical data were in agreement with the literature.[25b]

(–)-*tert*-Butyl [(1*R*)-1-Formyl-3-phenylpropyl]carbamate (7g): This compound was prepared as described in General Procedure 4/A; yield 124 mg (0.47 mmol), 87 %. It was also prepared as described in General Procedure 4/B; yield 243 mg (0.92 mmol), 96 %, colorless oil, 97 % *ee*. $[\alpha]_D^{20}$ (97 % *ee*) = –62.3 [*c* = 0.92, $CHCl_3$, (*R*)]. HPLC (Chiralpak OD-H, *n*-hexane/2-propanol 96:4, flow 0.8 mL min^{-1}, λ = 210 nm), t_R[(–)-(*R*)-**7g**] = 29.2 min, t_R[(+)-(*S*)-**7g**] = 33.6 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.46 (s, 9 H), 1.80–1.97 (m, 1 H), 2.10–2.34 (m, 1 H), 2.61–2.80 (m, 2 H), 4.24 (br. s, 1 H), 5.08 (br. s, 1 H), 7.12–7.35 (m, 5 H), 9.55 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 28.4, 31.0, 31.6, 59.7, 80.3, 126.5, 128.6, 128.8, 140.7, 155.7, 199.6 ppm. HRMS (ESI$^+$) calcd. for $C_{15}H_{21}NO_3Na$ [M + Na]$^+$ 286.1419; found 286.1415.

(–)-*tert*-Butyl [(1*R*)-2-Hydroxy-1-phenylethyl]carbamate (8a): This compound was prepared as described in General Procedure 4/A plus General Procedure 5: **4a** (97 % *ee*) was used, yield 106 mg (0.45 mmol), 70 %, 91 % *ee*. This compound was also prepared as described in General Procedure 4/B plus General Procedure 5: **4a** (99 % *ee*) was used, yield 89.6 mg (0.38 mmol), 84 %, colorless oil, 95 % *ee*. $[\alpha]_D^{20}$ (94 % *ee*) = –27.9 [*c* = 1.03, $CHCl_3$, (*R*)], ref.[26] $[\alpha]_D^{25}$ = –31.3 [*c* = 0.4, $CHCl_3$, (*R*)]. The analytical data were in agreement with the literature.

(–)-*tert*-Butyl [(2*S*)-1-Hydroxypropan-2-yl]carbamate (8b): This compound was prepared as described in General Procedure 4/B plus General Procedure 5: *ent*-**4b** (98 % *ee*) was used, yield 51.8 mg (0.30 mmol), 80 %, yellowish oil, 94 % *ee* (determined after conversion into the *p*-nitrobenzoate ester), $[\alpha]_D^{20}$ (96 % *ee*) = +3.6 [*c* = 1.0, $CHCl_3$, (*R*)], ref.[27] $[\alpha]_D^{20}$ = +8.6 [*c* = 0.8, $CHCl_3$, (*R*)]. HPLC (Chiralpak OD-H, *n*-hexane/2-propanol 95:5, flow 1.0 mL min^{-1}, λ = 254 nm), t_R[(*R*)-*p*-nitrobenzoate ester **8b**] = 14.6 min, t_R[(*S*)-*p*-nitrobenzoate ester **8b**] = 18.0 min. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.12 (d, *J* = 17.3 Hz, 3 H), 1.42 (s, 9 H), 3.15 (br. s, 1 H), 3.46–3.49 (m, 1 H), 3.58–3.60 (m, 1 H), 3.72 (br. s, 1 H), 4.80 (br. s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 17.4, 28.5, 48.5, 66.9, 79.6, 156.4 ppm. HRMS (EI$^+$) calcd. for $C_7H_{14}O_3N$ [M – CH_3]$^+$ 160.0974; found 160.0981.

(+)-*tert*-Butyl [(2*R*)-1-Hydroxyoctan-2-yl]carbamate (8c): This compound was prepared as described in General Procedure 4/B plus General Procedure 5: **4c** (98 % *ee*) was used, yield 135 mg (0.55 mmol), 94 %, colorless oil, 94 % *ee* (determined after conversion into the *p*-nitrobenzoate ester). $[\alpha]_D^{20}$ (94 % *ee*) = +16.4 [*c* = 1.00, $CHCl_3$, (*R*)]. HPLC (Chiralpak AD-H, *n*-hexane/2-propanol 97:3, flow 1.0 mL min^{-1}, λ = 254 nm), t_R[(*R*)-*p*-nitrobenzoate ester **8c**] = 30.4 min, t_R[(*S*)-*p*-nitrobenzoate ester **8c**] = 37.0 min. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.86 (t, *J* = 6.2 Hz, 3 H), 1.26–1.33 (m, 10 H), 1.43 (s, 9 H), 2.85 (br. s, 1 H), 3.50–3.52 (m, 1 H), 3.59–3.3.65 (m, 2 H), 4.67 (br. s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.1, 22.7, 26.1, 28.5, 29.3, 31.6, 31.8, 52.9, 66.0, 79.6, 156.7 ppm. HRMS (EI$^+$) calcd. for $C_{13}H_{27}NNaO_3$ [M + Na]$^+$ 268.1893; found 268.1881.

(–)-*tert*-Butyl [(2*S*)-1-Hydroxy-3-(trityloxy)propan-2-yl]carbamate (8d): This compound was prepared as described in General Procedure 4/B plus General Procedure 5: **4d** (99 % *ee*) was used, yield 106 mg (0.24 mmol), 98 %, colorless oil, 95 % *ee*. $[\alpha]_D^{20}$ (95 % *ee*) = –2.3 [*c* = 1.00, $CHCl_3$, (*S*)]. HPLC (Chiralpak OD-H, *n*-hexane/2-propanol 95:5, flow 1.0 mL min^{-1}, λ = 215 nm), t_R[(+)-(*R*)-**8d**] = 12.1 min, t_R[(–)-(*S*)-**8d**] = 16.8 min. ^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 1.43 (s, 9 H), 2.34 (br. s, 1 H), 3.21–3.22 (m, 2 H), 3.63–3.67 (m, 1 H), 3.70–3.77 (m, 2 H), 5.04 (br. s, 1 H), 7.24–7.27 (m, 3 H), 7.30–7.33 (m, 6 H), 7.42–7.44 (m, 6 H) ppm. ^{13}C NMR (CD_2Cl_2, 125 MHz): δ = 28.5, 52.6, 63.9, 64.0, 79.7, 87.2, 127.6, 128.3, 128.9, 144.2, 156.3 ppm. HRMS (ESI$^+$) calcd. for $C_{27}H_{31}NNaO_4$ [M + Na]$^+$ 456.2145; found 456.2158.

(+)-(2*R*)-2-[Bis(phenylmethyl)amino]-2-phenylethanol (9a): This compound was prepared as described in General Procedure 4/B plus General Procedure 6: **5a** (99 % *ee*) was used, yield 107 mg (0.34 mmol), 88 %, colorless oil, 98 % *ee*. $[\alpha]_D^{20}$ (98 % *ee*) = +148 [*c* = 0.52, $CHCl_3$, (*R*)]. HPLC (Chiralpak AD-H, *n*-hexane/2-propanol 88:12, flow 0.7 mL min^{-1}, room temp., λ = 210 nm), t_R[(–)-(*S*)-**9a**] = 11.3 min, t_R[(+)-(*R*)-**9a**] = 12.1 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.02 (br. s, 1 H), 3.15 (d, *J* = 13.4 Hz, 2 H), 3.61 (dd, *J* = 10.7, 5.2 Hz, 1 H), 3.9 (d, *J* = 13.4 Hz, 2 H), 3.94 (m, 12 H), 4.14 (dd, *J* = 11.3, 10.7 Hz, 1 H), 7.23–7.45 (m, 15 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 53.5, 60.5, 63.0, 127.3, 128.1, 128.3, 128.6, 129.0, 129.3, 135.1, 139.1 ppm. HRMS (EI$^+$) calcd. for $C_{22}H_{24}NO$ [M + H]$^+$ 318.1852; found 318.1852.

(–)-(2*R*)-2-[Bis(phenylmethyl)amino]propan-1-ol (9b): This compound was prepared as described in General Procedure 4/B plus General Procedure 6: **5b** (94 % *ee*) was used, yield 61 mg (0.24 mmol), 80 %, colorless oil, 94 % *ee*. $[\alpha]_D^{20}$ (94 % *ee*) = –62.3 [*c* = 0.68, $CHCl_3$ (*R*)]. HPLC (Chiralcel OD-H, *n*-hexane/2-propanol 90:10, flow 0.7 mL min^{-1}, λ = 205 nm), t_R[(–)-(*R*)-**9b**] = 8.8 min, t_R[(+)-(*S*)-**9b**] = 11.9 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.90 (d, *J* = 6.9 Hz, 3 H), 2.86–3.04 (m, 1 H), 3.03 (br. s, 1 H), 3.25 (dd, *J* = 10.7, 4.9 Hz, 1 H), 3.28 (d, *J* = 13.4 Hz, 2 H), 3.39 (dd, *J* = 11.3, 10.6 Hz, 1 H), 3.74 (d, *J* = 13.4 Hz, 2 H), 7.13–7.27 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 7.6, 51.9, 53.2, 61.7, 126.2, 127.5, 128.0, 138.2 ppm. HRMS (EI$^+$) calcd. for $C_{17}H_{21}NO$ [M]$^+$ 255.1623; found 255.1604.

(–)-(2*R*)-2-[Bis(phenylmethyl)amino]octan-1-ol (9c): This compound was prepared as described in General Procedure 4/B plus General Procedure 6: **5c** (96 % *ee*) was used, yield 123 mg (0.38 mmol), 74 %, colorless oil, 96 % *ee*. $[\alpha]_D^{20}$ (96 % *ee*) = –79.1 [*c* = 0.47, $CHCl_3$, (*R*)]. The analytical data were in agreement with the literature.[28]

(+)-(2*S*)-2-[Bis(phenylmethyl)amino]-3-(trityloxy)propan-1-ol (9d): This compound was prepared as described in General Procedure 4/B plus General Procedure 6: **5d** (91 % *ee*) was used, yield 109 mg (0.21 mmol), 85 %, colorless oil, 87 % *ee*. $[\alpha]_D^{20}$ (87 % *ee*) = +65.5 [*c* = 0.4, $CHCl_3$ (*S*)], ref.[29] $[\alpha]_D^{20}$ = +58.4 [*c* = 1.0, $CHCl_3$ (*S*)]. HPLC (Chiralcel OD-H, *n*-hexane/2-propanol 95:5, flow 0.7 mL min^{-1}, λ = 200 nm), t_R[(–)-(*R*)-**9d**] = 10.2 min, t_R[(+)-(*S*)-**9d**] = 14.2 min. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.83 (br. s, 1 H), 3.11 (br. s, 2 H), 3.35 (m, 4 H), 3.48 (br. s, 1 H), 3.68 (d, *J* = 12.5 Hz, 2 H), 7.13–7.26 (m, 19 H), 7.37 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 54.0, 58.9, 59.8, 60.3, 87.3, 127.2, 128.0, 128.5, 128.7, 129.0, 139.5, 143.8 ppm. HRMS (EI$^+$) calcd. for $C_{36}H_{36}NO_2$ [M + H]$^+$ 514.2743; found 514.2740.

(+)-*tert*-Butyl [(1*R*,2*R*)-2-Hydroxy-1-(2-phenylethyl)hexyl]carbamate (10a) and (+)-*tert*-Butyl [(1*R*,2*S*)-2-Hydroxy-1-(2-phenylethyl)hexyl]carbamate (10b): Under argon, *n*-BuMgCl (2.0 M in THF, 295 µL, 0.59 mmol) was added to a cooled (0 °C) solution of **7g** (51.6 mg, 0.20 mmol, obtained by General Procedure 4/B, 98 % *ee*) in dry THF (2 mL). After addition the mixture was allowed to warm to room temperature and stirred overnight (15 h). Then water (5 mL) and Et_2O (5 mL) were added, and the aqueous layer was separated and extracted with Et_2O (3 × 5 mL). The combined organic layers were dried with Na_2SO_4 and filtered through a pad of Celite®, the solvent was removed in vacuo, and the ratio of dia-

stereoisomers was determined by analytical HPLC [silica gel, *n*-hexane/2-propanol (99:1), flow 0.8 mL min^{-1}] of the crude product (**10a/10b** = 85:15). The diastereoisomers were separated by preparative HPLC [petroleum ether/ethyl acetate (5:1); R_f(**10a**) = 0.21, R_f(**10b**) = 0.18, $Ce(SO_4)_2$] to give **10a** (38.5 mg, 0.12 mmol, 60 %, 98 % *ee*) as a colorless oil and **10b** (8.1 mg, 25.2 µmol, 13 %, 98 % *ee*) as a colorless solid (m.p. 118–122 °C).

Compound 10a: $[\alpha]_D^{20}$ (90 % *ee*) = +8.7 [*c* = 1.02, $CHCl_3$, (1*R*,2*R*)]. HPLC (Chiralpak IB, *n*-hexane/2-propanol 95:5, flow 0.8 mL min^{-1}, λ = 210 nm), t_R[(+)-(1*R*,2*R*)-**10a**] = 8.2 min, t_R[(–)-(1*S*,2*S*)-**10a**] = 14.3 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.89 (t, *J* = 7.0 Hz, 3 H), 1.22–1.39 (m, 4 H), 1.45 (s, 9 H), 1.86 (dd, *J* = 15.2, 7.8 Hz, 2 H), 2.03 (br. s, 1 H), 2.57–2.80 (m, 2 H), 3.42–3.65 (m, 2 H), 4.76 (d, *J* = 9.1 Hz, 1 H), 7.14–7.32 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1, 22.8, 28.0, 28.5, 32.8, 34.2, 34.8, 54.3, 73.9, 79.4, 126.0, 128.5, 142.1, 156.6 ppm. HRMS (ESI^+) calcd. for $C_{19}H_{32}NO_3$ $[M + H]^+$ 322.2382; found 322.2377.

Compound 10b: $[\alpha]_D^{20}$ (93 % *ee*) = +16.3 [*c* = 1.00, $CHCl_3$, (1*R*,2*S*)]. HPLC (Chiralpak IB, *n*-hexane/2-propanol 95:5, flow 0.8 mL min^{-1}, λ = 210 nm), t_R[(+)-(1*R*,2*S*)-**10b**] = 7.0 min, t_R[(–)-(1*S*,2*R*)-**10b**] = 10.0 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.88 (t, *J* = 7.0 Hz, 3 H), 1.20–1.44 (m, 4 H), 1.46 (s, 9 H), 1.56–1.74 (m, 1 H), 1.75–1.90 (m, 1 H), 2.29 (br. s, 1 H), 2.55–2.69 (m, 1 H), 2.70–2.84 (m, 1 H), 3.50–3.75 (m, 2 H), 4.73 (d, *J* = 8.0 Hz, 1 H), 7.14–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1, 22.8, 28.3, 28.6, 31.3, 32.8, 33.1, 55.2, 74.9, 79.7, 126.1, 128.5, 128.6, 141.9, 156.6 ppm. HRMS (ESI^+) calcd. for $C_{19}H_{32}NO_3$ $[M + H]^+$ 322.2382; found 322.2378.

(+)-*tert*-Butyl [(1*S*,2*S*)-2-Hydroxy-1-phenylhex-5-en-1-yl]-carbamate (11): Under argon, but-3-enylmagnesium bromide (1.0 M in Et_2O, 600 µL, 0.60 mmol) was added to a solution of **7a** (47.1 mg, 0.20 mmol, obtained by General Procedure 4/B) in dry Et_2O (1.4 mL), and the mixture was stirred at room temperature overnight (15 h). Then water (3 mL), brine (3 mL), and Et_2O (5 mL) were added, and the aqueous layer was separated and extracted with Et_2O (3 × 5 mL). The combined organic layers were dried with Na_2SO_4 and filtered through a pad of Celite®, the solvent was removed in vacuo, and the ratio of diastereoisomers was determined by analytical HPLC [silica gel, *n*-hexane/2-propanol (99:1), flow 0.8 mL min^{-1}] of the crude product (**11**-*syn*/**11**-*anti* = 96:4). The crude product was subjected to flash chromatography on silica gel [petroleum ether/ethyl acetate (5:1); R_f(**11**-*syn*) = 0.16, R_f(**11**-*anti*) = 0.09, $KMnO_4$] to give **11**-*syn* (35.0 mg, 0.12 mmol, 60 %, 97 % *ee*) as a colorless oil and **11**-*anti* (1.1 mg, 3.8 µmol, 2 %) as a colorless solid (m.p. 118–122 °C, ref.[30] 100–102 °C).

Compound 11-*syn*: $[\alpha]_D^{20}$ (95 % *ee*) = +6.6 [*c* = 1.02, $CHCl_3$, (1*S*,2*S*)]. HPLC (Chiralcel OD-H, *n*-hexane/2-propanol 97:3, flow 0.8 mL min^{-1}, λ = 210 nm), t_R[(+)-(1*S*,2*S*)-**11**] = 11.2 min, t_R[(–)-(1*R*,2*R*)-**11**] = 12.9 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.42 (s, 9 H), 1.54–1.73 (m, 2 H), 1.94 (br. s, 1 H), 2.12–2.31 (m, 2 H), 3.84 (br. s, 1 H), 4.66 (br. s, 1 H), 4.96–5.06 (m, 2 H), 5.37 (d, *J* = 8.5 Hz, 1 H), 5.81 (tdd, *J* = 16.9, 10.2, 6.7 Hz, 1 H), 7.25–7.37 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 28.5, 30.2, 33.1, 58.7, 74.8, 79.9, 115.3, 126.6, 127.6, 128.9, 138.2, 141.0, 156.2 ppm. HRMS (ESI^+) calcd. for $C_{17}H_{26}NO_3$ $[M + H]^+$ 292.1913; found 292.1909.

Compound 11-*anti*: $[\alpha]_D^{20}$ (95 % *ee*) = +10.0 [*c* = 0.35, $CHCl_3$, (1*S*,2*R*)]. The analytical data were in agreement with the literature.[30]

(+)-(2*S*,3*S*)-2-Phenylpiperidin-3-ol (12): A solution of K_2OsO_4•2 H_2O (0.7 mg, 1.9 µmol) and NMO (50 wt.-% in H_2O, 46 µL, 0.22 mmol) in water (160 µL) was added dropwise to a solution of **11**-*syn* (29.3 mg, 0.10 mmol) in acetone (1.4 mL). Complete conversion was reached after 4 h at room temperature [petroleum ether/ethyl acetate (1:1); R_f(**11**-*syn*) = 0.48, R_f(diol) = 0.10, UV]. $Na_2S_2O_4$ (35 mg) was added, the mixture was stirred for 30 min and then filtered through a pad of Celite®, and the solvent was removed in vacuo. The crude product was dissolved in Et_2O/H_2O (2:1, 3 mL). $NaIO_4$ (43.0 mg, 0.20 mmol) was added, and the mixture was vigorously stirred for 1 h at room temperature [TLC monitoring: petroleum ether/ethyl acetate (1:1); R_f(aldehyde) = 0.35, $KMnO_4$]. Water (5 mL) and ethyl acetate (5 mL) were added, and the aqueous layer was separated and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated in vacuo. Then, the yellowish solid was dissolved in CH_2Cl_2 (0.5 mL)/trifluoroacetic acid (500 µL, 6.50 mmol), and the mixture was stirred for 45 min at room temperature. The solvent was removed in vacuo, and the residue was dissolved in MeOH (1.5 mL), before addition of a mixture of $Pd(OH)_2$/C (5.8 mg, 20 wt.-%) and Rh/C (1.5 mg, 5 wt.-%). The black suspension was placed in an autoclave and stirred for 15 h under H_2 (10 bar). The mixture was filtered through a pad of Celite® (ethyl acetate), and NaOH (1 M, 5 mL) was added to the filtrate. The aqueous layer was separated and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated in vacuo. The crude product was subjected to flash chromatography on silica gel [petroleum ether/triethylamine/methanol (80:15:5); R_f(**12**) = 0.15, UV] to give **12** (9.9 mg, 55.9 mmol, 56 %) as colorless needles (m.p. 86–88 °C, ref.[13] 90–93 °C). $[\alpha]_D^{20}$ (97 % *ee* according to the starting material) = +50.1 [*c* = 0.42, $CHCl_3$, (2*S*,3*S*)], ref.[13] $[\alpha]_D^{23}$ = +66.4 [*c* = 0.62, $CHCl_3$, (2*S*,3*S*)]. The analytical data were in agreement with the literature.

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