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Rearrangement Reactions leading to Optically Active α,α-Disubstituted Primary Allylamines

Martin Hennum,[a] Hege Hortemo Odden,[a] [‡] and Lise-Lotte Gundersen*[a]

Abstract: Synthetic routes to α,α-disubstituted allylamines have been examined. Racemic compounds were conveniently prepared by thermal Overman rearrangements of primary allyl alcohols with trisubstituted double bonds, but rearrangement of these substrates by the only commercially available compound known to catalyze enantioselective Overman rearrangements, the cobalt oxazoline palladacycle (*R*)-COP-Cl, failed. Instead optically active secondary allyl alcohols with trisubstituted double bonds, obtained by CBS-mediated reduction of the corresponding methyl ketones, were synthesized and converted to α,α-disubstituted allylamines via a thermal Overman rearrangement or an allyl cyanate to isocyanate rearrangement. High chiral transfer (90-99%) was obtained with both reaction sequences, but the chemical yields were greatly improved when the allyl cyanate to isocyanate rearrangement were employed.

Introduction

We have previously shown that 7,8,9,10-tetrahydro-[1,4]diazepino-[1,2,3-*gh*]purine (Fig. 1), the heterocyclic part in marine natural products called asmarines,[1,2] can be synthesized with a ring-closing metathesis (RCM) as a key-step.[3] A retrosynthetic analysis of asmarine H is shown in Fig. 1. 7-Alkenyl-6-halopurines are easily available by base or ruthenium mediated rearrangements of the corresponding 7-allylpurine,[3,4] but synthesis of the α,α-disubstituted allylamine building block is expected to be a major challenge.

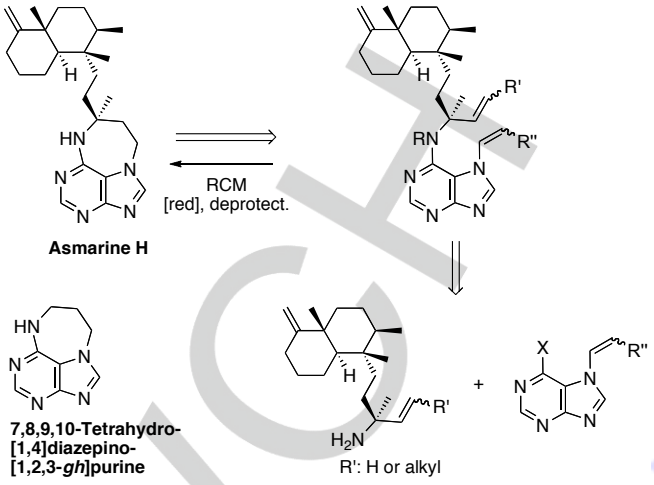

Figure 1. Structure of 7,8,9,10-tetrahydro-[1,4]diazepino-[1,2,3-*gh*]purine and a retrosynthetic analysis of asmarine H.

There are relatively few examples of α,α-disubstituted primary allylamines, except α-substituted vinyglycines or cyclic compounds, the in the literature. These amines have been synthesized as racemates from α,α-disubstituted propargyl halides by reaction with ammonia followed by partial reduction of the triple bond,[5] non-regioselective ring opening of 2-methyl-2-vinyloxirane,[6] Pd-catalyzed formal [3,3] rearrangement of allylic N-PMP trifluoroacetimidates,[7] addition of organosamarium reagents to acrylonitrile,[8] addition of vinyl Grignard reagents to sulfinylimines,[9] cycloaddition of bis(methoxycarbonyl)sulfur diimide with alkenes followed by a [2,3] sigmatropic rearrangement,[10] Pd-catalyzed hydroamination of 1,3-dienes with hydrazines followed by reduction of the hydrazine product or quite regioselective Pd-catalyzed allylic alylation of ammonia synthons,[11] and last but not least the Overman rearrangement of allylic alcohols,[12] and related rearrangements of allylic cyanates.[13]

Few of the methods listed above are applicable for the synthesis of optically active α,α-disubstituted allylamines. Pd-catalyzed regio- and enantioselective ring opening of isoprene monoxide with primary amines has been achieved,[14] enantioselective Pd-mediated aza-Claisen rearangements[15] and Pd-catalyzed enantioselective decarboxylative cycloaddition of vinylene carbonates with isocyanates or imines followed by hydrolysis of the oxazilidinone formed[16] are reported. Vinyllithium addition to a chiral 1,3 oxazolidine followed by reductive removal of the N-substituent also gives optically active α,α-disubstituted primary allylamines.[17] This last methodology is restricted to synthesis of compounds where one of the α-substituents is CF_3. We herein report and compare several strategies for the synthesis of α,α-disubstituted allylamines; useful building blocks in organic synthesis and model substances for the amines required in asmarine synthesis.

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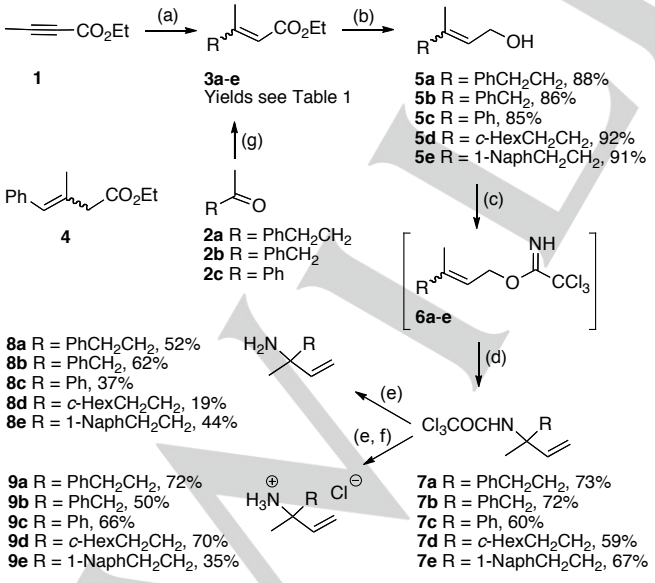
Results and Discussion

Our first approach to α,α-disubstituted allylamines was the Overman rearrangement,[12] since also transition metal mediated asymmetric versions of this reaction are known.[18] Scheme 1 presents synthesis of racemic amines with the thermal Overman rearrangement as the key-step. Esters **3** were synthesized either by a conjugated copper-mediated addition of Grignard reagents to the alkynes **1**[15a,19] or by a Horner-Wadsworth-Emmons (HWE) olefination of ketones **2** (Scheme 1, Table 1). The total yields of compounds **3** from the methods tried varied greatly with the structure of the starting material. The HWE reaction on ketone **2b** in the presence of DBU and $CsCO_3$ resulted only in a low yield of the desired product **3b**. Instead compound **4**,[20] where the double bond had migrated into conjugation with the phenyl ring was formed as the major product. Changing the base to NaH, however, allowed isolation of the desired α,β-unsaturated ester **3b** in 93% yield. The ketones needed for the synthesis of esters **3d** and **3e** by the HWE reaction were not commercially available and these esters were only prepared from alkyne **1**. In general addition of Grignard reagents to the alkyne **1** in the presence of CuI, LiCl and TMSCl resulted in very high *E*-selectivity compared with the other strategies. The α,β-unsaturated esters **3** were conveniently reduced to the allylic alcohols **5** by DIBAL-H. The *E/Z* ratio in the starting material was conserved in the product and there were no indications that the isomers of **3** reacted with a significantly different rate. Alcohols **5** were converted to the corresponding trichloroacetimidates **6**, employing a modified procedure of that previously used to generate imidate **6c**.[12e] The imidates **6** were, due to their low stability, reacted directly to the amides **7** by a thermal Overman rearrangement. Finally the amides **7** were hydrolyzed to the racemic allylic amines **8**. Best yields were in most cases obtained when the amines were isolated as their HCl salts **9**.



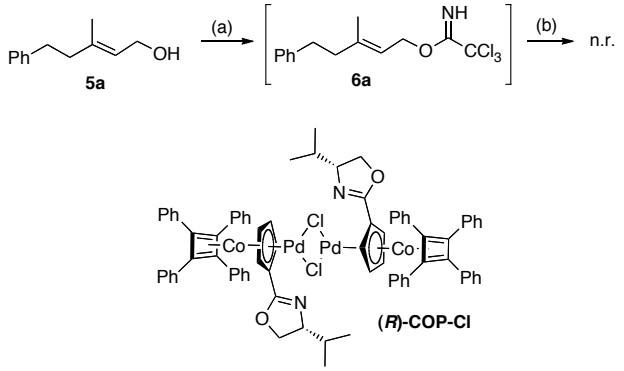
Scheme 1. (a) Meth. A or B, see Table 1; (b) DIBAL-H, CH_2Cl_2 or toluene, -78 °C; (c) 1. NaH, 2. Cl_3CCN, THF, 0 °C; (d) Na_2CO_3, xylenes, Δ; (e) NaOH(aq), EtOH, 40 °C; (f) HCl (aq); (g) Meth. D or E, see Table 1.

Table 1. Synthesis of compounds **3**.

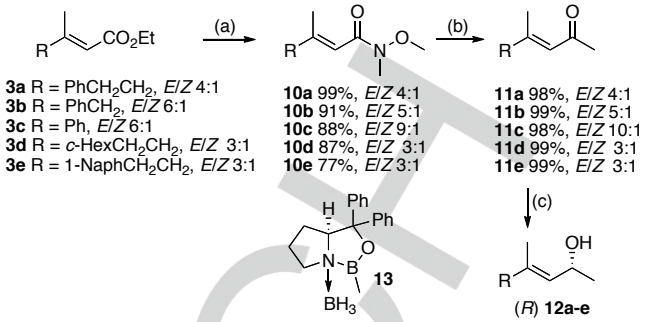
Entry	Starting material	R	Reaction conditions	Yield [%] **3**[a]	*E*/*Z*[b]
1	**1**	$Ph(CH_2)_2$	A[c]	90, **3a**	75:25
2	**1**	$Ph(CH_2)_2$	B[d]	72, **3a**	97:3
3	**2a**	$Ph(CH_2)_2$	C[e]	60, **3a**	3:1
4	**2a**	$Ph(CH_2)_2$	D[f]	95, **3a**	4:1
5	**1**	$PhCH_2$	A	62, **3b**	9:1
6	**1**	$PhCH_2$	B	56, **3b**	>99:1
7	**2b**	$PhCH_2$	C	12, **3b**[g]	2:1
8	**2b**	$PhCH_2$	D	93, **3b**	6:1
9	**1**	Ph	A	88, **3c**	62:38
10	**1**	Ph	B	57, **3c**	>99:1
11	**2c**	Ph	C	73, **3c**	6:1
12	**2c**	Ph	D	89, **3c**	6:1
13	**1**	*c*-$Hex(CH_2)_2$	A	69, **3d**	56:44
14	**1**	*c*-$Hex(CH_2)_2$	B	73, **3d**	89:11
15	**1**	1-$Naph(CH_2)_2$	A	75, **3e**	62:38
16	**1**	1-$Naph(CH_2)_2$	B	70, **3e**	>99:1

[a] Isolated yield. [b] From ^{1}H NMR. [c] RMgX, CuI, TMEDA, THF, -78 °C. [d] RMgX, CuI, LiCl, TMSCl, THF, -78 °C. [e] $(EtO)_2POCH_2CO_2Et$, DBU, CsCO. [f] $(EtO)_2POCH_2CO_2Et$, NaH, THF. [g] Compound **4** (*E*/*Z*: 9:8) was also observed. The ^{1}H NMR data of the *E*-isomer, were in good agreement with those reported before.[20]

Next we examined the possibility for an enantioselective Overman rearrangement of imidates **6**. The only known examples of aza-Claisen rearrangements in the presence of chiral catalysts, leading to optically active α,α-disubstituted allylamines, include reaction of *N*-substituted trifluoroacetimidates catalyzed by a ferrocenyl imidazoline palladacycle,[15] or by a palladacycle combined with the chiral TRIP anion.[21] However neither the ferrocenyl imidazoline palladacycles nor the TRIP compound are commercially available. Enantioselective Overman rearrangement of imidates from disubstituted alkenes have been catalyzed by cobalt oxazoline palladacycles (COP) including the commercially available (*R*)-COP-Cl.[18] Unfortunately, no rearrangement took place at all, when the *in situ* generated imidate **6a** was reacted with this catalyst following conditions previously employed for rearrangement of imidates from disubstituted alkenes (Scheme 2).[18c] Raising the temperature to 55 °C did not improve the reaction.



Scheme 2. (a) 1. NaH, 2. Cl_3CCN, THF, 0 °C; (b) (R)-COP-Cl (2.8 mol%), CH_2Cl_2, 38 °C, 7 days.



Scheme 3. (a) HNMeOMe•HCl, *t*-BuMgBr, THF, 0 °C; (b) MeMgBr THF, -30 °C; (c) See Table 2.

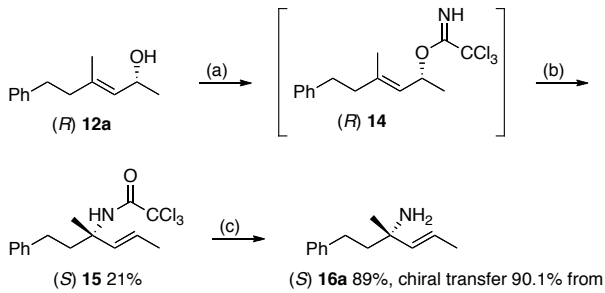
There are many examples of thermal enantioselective Overman rearrangements of imidates from optically active alcohols,[22] and we turned to another route to optically active α,α-disubstituted allylamines; enantioselective reduction of ketones to optically active allylic alcohols followed by conversion to an imidate via a [3,3] rearrangement (Schemes 3-4). The esters **3** were converted to ketones **11**, via the corresponding Weinreb amide **10**, according to a literature procedure for synthesis of ketones **11a** and **11c** (Scheme 3).[23] The ketones were first isolated as *E*/*Z* mixtures as shown in Scheme 3 and we observed that *E*-ketones **11** partly isomerized to the *Z*-isomer upon storage. In the planned reaction sequence pure *E*-isomers of alcohols **12** were desired and the *E* and *Z* isomers of ketones **11** were separated just before the next step was carried out. Unfortunately, we were not able to isolate the ketone **11b** as the *E*-isomer only. Asymmetric reduction was first attempted employing BINAL-H[24] generated from lithium aluminum hydride and equimolar amounts of (*R*)-BINOL and EtOH. At its best, the reaction gave the alcohol **12a** in 78% chemical yield from ketone **11a**, but the method was not reproducible with respect to %ee. The literature also points out that generation of the reducing agent can be difficult.[24] Instead we turned to CBS-mediated reduction. However, we found, as also reported by others,[25] the results not to be fully reproducible when commercially available (*R*) 2-methyl-CBS-oxazaborolidine was used due to impurities present and limited stability of the reagent. Instead we synthesized the stable (*S*) oxazaborolidine-borane complex **13** (Scheme 3) by literature methods.[26] The ketones were reduced both with a catalytic amount of borane **13** together with BH_3•SMe_2 and with a stoichiometric amount of borane **13** only (Table 2). Using **13** as a stoichiometric reagent gave higher enantiomeric excess and generally better yield compared to when complex **13** was used as a catalyst. The (*R*) configuration and %ee of alcohols **12** were determined by Mosher ester analysis using both ^{19}F and ^{1}H-NMR.[27]

Table 2. CBS-mediated reduction of compounds **11**

Entry	Starting material	Reaction conditions	Yield **12**[a,b] [%]	ee [%] **12**[c]
1	**11a**	A[d]	88[e]	91[e]
2	**11a**	B[f]	87	96
3	**11b**[g]	A	87[h]	82
4	**11b**[i]	B	71[j]	92
5	**11c**	A	94	88
6	**11c**	B	98	94
7	**11d**	A	84	86
8	**11d**	B	89	93
9	**11e**	A	87	86
10	**11e**	B	89	88

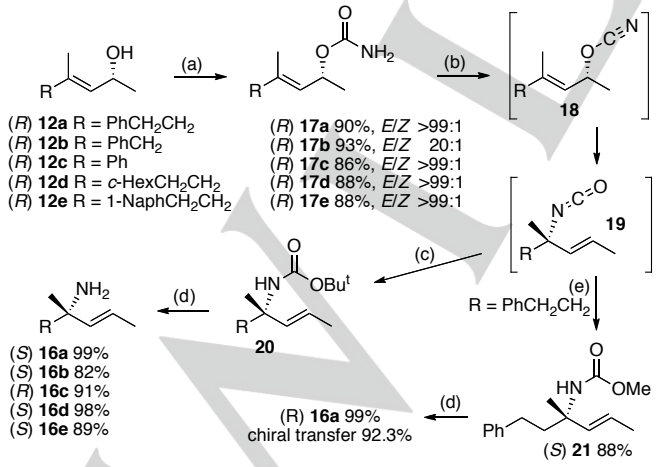
[a] Isolated yield. [b] Isolated as pure *E*-isomer unless otherwise stated. [c] Determined from the corresponding Mosher esters. [d] Comp. **13** (0.2 equivs.), BH_3•SMe_2 (0.5 equivs.), THF, -20 °C. [e] The ketone was added over a period of 12 h. [f] Comp. **13** (1.5 equivs.), THF, -78 °C - r.t. [g] 24:1 mixture of the *E*- and *Z*-isomer. [h] Isolated as a 20:1 mixture of the *E*- and *Z*-isomer. [i] 35:1 mixture of the *E*- and *Z*-isomer. [j] Isolated as a 33:1 mixture of the *E*- and *Z*-isomer.

Overman rearrangement of the imidate **14** from alcohol **12a** is shown in Scheme 4. The reaction occurred with reasonable chiral transfer,[28] but the chemical yield was disappointingly low, compared to what was achieved with the related primary allylic alcohols **5** (Scheme 1).



Scheme 4. (a) CCl_3CN, DBU, CH_2Cl_2; (b) Na_2CO_3, xylenes, 120 °C; (c) NaOH (6M), EtOH 40 °C.

Instead, we transformed the alcohols **12** to carbamates **17** and examined the allyl cyanate to isocyanate rearrangement (Scheme 5, Table 3).[13] The carbamates **17** were converted to cyanates **18**, which spontaneously rearranged to the isocyanates **19**, by treatment with TFAA and base.[29] The isocyanates **19** were reacted further to carbamates **20** by a $MoO_2Cl_2(DMF)_2$ catalyzed reaction with *t*-BuOH.[30] The use of *t*-BuOLi[31] instead of the Mo-catalyst in the second step of the synthesis of carbamate **20a** and / or PPh_3, CBr_4 and Et_3N[31,32] for the generation of the cyanate **18a** resulted in almost the same chiral transfer but somewhat reduced chemical yields. The carbamates **19** were hydrolyzed under basic conditions[33] to give the free amines in excellent yields and with very good chiral transfer. Carbamate cleavage with aqueous HCl or TFA in CH_2Cl_2, or by treatment with TMSI in CH_2Cl_2[34] was unsuccessful due to the formation of elimination products. Isocyanate **19a**, generated from carbamate **17a** by treatment with PPh_3, CBr_4 and Et_3N, could also be converted to carbamate **21** when reacted with Bu_3SnOMe.[32] The overall yield of the target allylamine **16a** from carbamate **17a** and chiral transfer (92.3%) were comparable of what was achieved with the conditions described above and in Table 3 using less toxic reagents.



Scheme 5. 1. $Cl_3CCONCO$, CH_2Cl_2, 0 °C, 2. K_2CO_3(aq), MeOH; (b) See Table 3; (c) See Table 3; (d) *t*-BuOK, KOH, THF, 55 °C; (e) Bu_3SnOMe, MeOH.

Table 3. Rearrangement of carbamates **17** to carbamates **20**.

Entry	Starting material	Reaction conditions for generating cyanate **18**	Reaction conditions for converting **19** to **20**	Yield [%] **20**[a,b]	Chiral transfer [%][c]
1	**17a**	A[d]	B[e]	84	99.9
2	**17a**	A	C[f]	78	97.9
3	**17a**	D[g]	C	67	98.3
4	**17b**	A	B	84	91.8
5	**17c**	A	B	88	95.7
6	**17d**	A	B	60	95.2
7	**17e**	A	B	87	98.9

[a] Isolated yield. [b] Only the *E*-isomer was formed. [c] Calculated from the ratios of the starting alcohol **12** and the final free amine **16**, both determined from the corresponding Mosher esters. [d] TFAA, Et_3N, CH_2Cl_2, -78 °C - r.t. [e] cat. $MoO_2Cl_2(DMF)_2$, *t*-BuOH, CH_2Cl_2. [f] *t*-BuOLi, *t*-BuOH, THF, -15 °C. [g] PPh_3, CBr_4, Et_3N, CH_2Cl_2, -28 °C.

Allyl cyanates are believed to rearrange to isocyanates via a concerted cyclic transition state as shown in Figure 2 and transfer of chirality generally occurs with very high selectivity.[13b] The *E*-isomer of the cyanate **18** was expected to rearrange via transition state A and not transition state B where the two methyl groups are occupying pseudo-axial positions. Unfortunately, is was not possible to prepare carbamate **17b** as pure *E*-isomer and minor amounts of the (*E*,*R*) isocyanate **19b** could be formed by rearrangement of the (*Z*,*R*) cyanate **18b** via the favored transition state A'. This might explain why the synthesis of amine **16b** occurred with slightly lower chiral transfer compared to the other examples (Table 3). Likewise, if some *E* to *Z* isomerization of the carbamates **17** or cyanates **18** took place in solution before the rearrangement, this would also result in reduced chiral transfer.

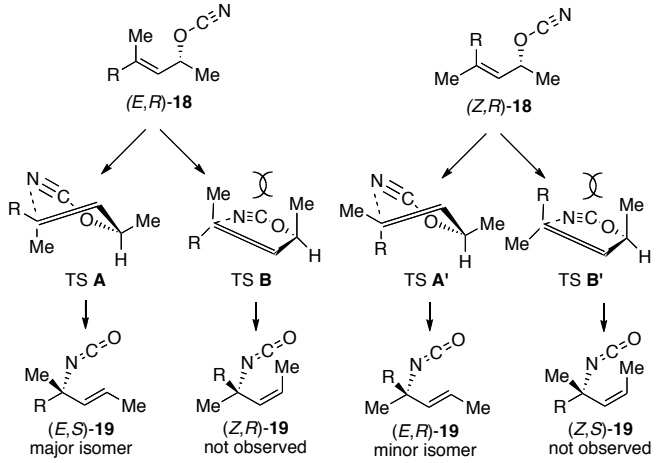
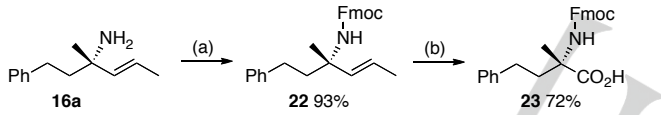


Figure 2. Rearrangement of the *E*- and *Z* isomers of cyanate **18** via the favored transition states **A** / **A'** and the more strained transition states **B** / **B'**.[13b]

The expected absolute configuration (*S*) was confirmed for the amine **16a** the following way: Compound **16a** was converted to the corresponding Fmoc ester **22**, which was subjected to ozonylysis and oxidation (Scheme 6). The carboxylic acid **23** thus formed showed (+) rotation, whereas the (*R*) enatiomer of compound **23** previously is reported to be the (-) form.[15a]



Scheme 6. (a) FmocCl, $NaHCO_3$(aq), CH_2Cl_2; (b) 1. O_3, CH_2Cl_2, -78 °C, 2. DMS, CH_2Cl_2, -78 °C, 3. $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, *t*-BuOH, H_2O.

Conclusions

Racemic α,α-disubstituted allylamines where conveniently prepared by thermal Overman rearrangements of primary allylic alcohols with trisubstituted double bonds, but enantioselective rearrangement of these substrates catalyzed by the commercially available chiral cobalt oxazoline palladacycle, (*R*)-COP-Cl, failed. Optically active secondary allylic alcohols with trisubstituted double bonds, obtained by CBS-mediated reduction of the corresponding methyl ketones, were converted to the corresponding α,α-disubstituted allylamines via a thermal Overman rearrangement or an allyl cyanate to isocyanate rearrangement. The Overman reaction utilizes less expensive reagents and constitutes of one step less than the rearrangement of allyl cyanate, but the chemical yield in the Overman rearrangement was low. The allyl cyanate to isocyanate rearrangement gave target products with high chemical yields and a very good chiral transfer ranging from 92 to 99%. When the sequence was carried out with carbamates available as pure *E*-isomers, the chiral transfer was 95% or above. Various reaction conditions for the generation of the cyanate and conversion of the rearrangement product to a stable carbamate were compared. Best results were obtained when the cyanate was generated by treatment of the corresponding carbamate with TFAA and Et_3N and the isocyanate was trapped with *t*-BuOH in the presence of a catalytic amount of $MoO_2Cl_2(DMF)_2$. We envisage that the methodology described here in can be applied in syntheses of a wide variety of optically active α,α-disubstituted allylamines including building blocks for the synthesis of asmarines and analogs (cf. Fig. 1).

Experimental Section

General remarks: ^{1}H NMR spectra were recorded at 600 MHz with a Bruker AV 600 instrument, at 400 MHz with a Bruker AVII 400 instrument or at 300 MHz with a Bruker DPX instrument. The decoupled ^{13}C NMR spectra were recorded at 150, 100 or 75 MHz. using instruments mentioned above. Mass spectra under electron impact conditions were recorded on a VG Prospec instrument at 70 eV ionizing voltage. Mass spectra under electron-spray condition were recorded on a Bruker Maxis II ETD or a Micromass Q-Tof-2 instrument. All mass spectra are presented as *m/z* (% rel. int.). HRMS-EI and HRMS-ESI were performed with the instruments mentioned above. Melting points were determined with a Büchi Melting Point B-545 apparatus and are uncorrected. Flash chromatography was performed on silica gel (Merck no. 09385). Optical rotations were measured on a Perkin-Elmer 341 polarimeter. %ee for compounds **12**, **16** and **17** were determined by Mosher ester analysis[27] and the %ee for compounds **19** were assumed to be the same as for the corresponding compounds **16**. CuI and LiCl were dried at high vacuum at 120 °C for 24 h. Et_3N, TMSCl, toluene and xylenes were distilled from CaH_2. Dry CH_2Cl_2 and THF were obtained from solvent purification system, MB SPS-800 from MBraun. Compounds available by literature methods: $MoO_2Cl_2(DMF)_2$[35] and (*S*)-1-methyl-3,3-diphenyltetrahydro-1*H*,3*H*-pyrrolo[1,2-*c*][1,3,2]oxazaborole BH_3 adduct **13**.[26]

Synthesis of compounds 3 from alkyne 1, alternative 1: A mixture of CuI (583 mg, 3.06 mmol) and LiCl (133 mg, 3.14 mmol) in dry THF (20 mL) was stirred under N_2-atm. at ambient temperatures until the salts were dissolved; ca. 30 min. The solution was cooled to -78 °C and the alkyne **1** (3.00 mmol) followed by TMSCl (0.50 mL, 4.0 mmol) and Grignard reagent in THF (7.2 mmol) were added. After 1 h the reaction was quenched by addition of sat. aq NH_4Cl (20 mL). The solution was heated to ambient temperature and extracted with EtOAc (3× 25 mL) and washed with water (25 mL) and brine (25 mL). The organic layer was dried ($MgSO_4$) and evaporated. The product was purified by flash chromatography.

Synthesis of compounds 3 from alkyne 1, alternative 2: CuI (664 mg, 3.49 mmol) was dissolved in THF (9 mL) and cooled to -40 °C under Ar-atm. before addition of TMEDA (1.26 mL, 8.45 mmol). The Grignard reagent in THF (3.0 mmol) was added and the mixture was stirred at -40 °C for 10 min. The reaction mixture was cooled to -78 °C, the alkyne **1** (2.70 mmol) was added and the reaction was stirred at -78 °C for 2 h. The reaction was quenched with addition of methanol (10 mL) followed by sat. aq $(NH_4)_2SO_4$ (10 mL). The mixture was heated to ambient temperature and extracted with EtOAc (3× 25 mL) and washed with water (25 mL) and brine (25 mL). The organic layer was dried ($MgSO_4$) and evaporated. The crude product was purified by flash chromatography.

Synthesis of compounds 3 from ketones 2, alternative 1: To a mixture of triethyl phosphonoacetate (2.24 g, 10.0 mmol), 1,8-diazabicycloundec-7-ene (152 mg, 1.00 mmol) and $CsCO_3$ (1.95 g, 10.1 mmol) was added ketone **2** (5.00 mmol) and the resulting mixture was stirred at ambient temperature under N_2 atm. for 18 h. The reaction was quenched with water (25 mL) and extracted with a 1:2 mixture of EtOAc-hexane (3× 20 mL). The combined organic extracts were dried ($MgSO_4$), and evaporated. The crude product was purified by flash chromatography.

Synthesis of compounds 3 from ketones 2, alternative 2: Triethyl phosphonoacetate (5.95 mL, 30.0 mmol) was added dropwise to a suspension of ca. 60 % NaH (1.12 g, ca. 28.0 mmol) in THF (15 mL) at 0 °C under Ar-atm. The mixture was warmed to ambient temperatures and stirred for 30 min. Acetophenone (2.33 mL, 20.0 mmol) was added and the solution was stirred for 20 h and subsequently quenched with sat. aq. NH_4Cl (20 mL). The mixture was extracted with ethyl acetate (3× 20 mL) and the combined organic extracts were dried ($MgSO_4$), and evaporated. The crude products were purified by flash chromatography.

Ethyl-3-methyl-5-phenylpent-2-enoate (3a): EtOAc-hexane (1:19) was used as eluent for flash chromatography; yield and *E*/*Z* ratio, see Table 1, pale yellow liquid. ^{1}H NMR (600 MHz, $CDCl_3$, *E*-isomer): δ = 1.26 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.19 (d, *J* = 0.6 Hz, 3 H, CH_3), 2.42 (t, *J* = 7.8 Hz, 2 H, CH_2), 2.77 (t, *J* = 7.8 Hz, 2 H, PhC$\underline{H}_2$), 4.13 (q, *J* = 7.2 Hz, 2 H, OCH_2), 5.67 (q, *J* = 0.6 Hz, 1 H, =CH), 7.12–7.28 (m, 5 H, Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, *E*-isomer): δ = 14.3 (CH_3), 18.9 (CH_3), 33.9 (Ph$\underline{C}H_2$), 42.7 (CH_2), 59.5 (OCH_2), 116.0 (=CH), 126.1 (CH in Ph), 128.3 (2× CH in Ph), 128.5 (2× CH in Ph), 141.1 (C in Ph), 158.9 ($CH_3\underline{C}$=), 166.7 (CO) ppm. MS (EI): *m*/*z* (%) = 218 (5) $[M]^+$, 173 (14), 144 (24), 91 (100). HRMS (EI) calcd. for $C_{14}H_{18}O_2$ $[M]^+$ 218.1307; found 218.1208. The NMR data were in good agreement with those reported before.[36]

Ethyl 3-methyl-4-phenylbut-2-enoate (3b): EtOAc-hexane (1:9) was used as eluent for flash chromatography; yield and *E*/*Z* ratio, see Table 1, pale yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$, *E*-isomer): δ = 1.27 (m, 3 H, CH_3, overlap with signal from *Z*-isomer), 2.11 (d, *J* = 1.2 Hz, 3 H, CH_3), 3.41 (s, 2 H, CH_2), 4.09–4.19 (m, 2 H in OCH_2, overlap with signal from *Z*-isomer), 5.67 (br s, 1 H, =CH), 7.14–7.31 (m, 5 H, Ph, overlap with signal from *Z*-isomer) ppm. ^{1}H NMR (300 MHz, $CDCl_3$, *Z*-isomer): δ = 1.27 (m, 3 H, CH_3, overlap with signal from *E*-isomer), 1.77 (d, *J* = 1.2 Hz, 3 H, CH_3), 4.01 (s, 2 H, CH_2), 4.09–4.19 (m, 2 H in OCH_2, overlap with signal from *E*-isomer), 5.67 (br s, 1 H, =CH), 7.14–7.31 (m, 5 H, Ph, overlap with signal from *Z*-isomer) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, *E*-isomer): δ = 14.3 (CH_3), 18.6 (CH_3), 47.0 (CH_2), 59.6 (OCH_2), 117.2 (=CH), 126.7 (CH in Ph), 128.5 (2× CH in Ph), 129.1 (2× CH in Ph), 137.8 (C in Ph), 158.2 ($CH_3\underline{C}$=), 166.7 (CO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, *Z*-isomer): δ = 14.3 (CH_3), 24.5 (CH_3), 38.8 (CH_2), 59.7 (OCH_2), 117.1 (=CH), 126.2 (CH in Ph), 128.4 (2× CH in Ph), 128.9 (2× CH in Ph), 138.9 (C in Ph), 157.5 ($CH_3\underline{C}$=), 166.5 (CO) ppm. MS (EI): *m*/*z* (%) = 204 (100) $[M]^+$, 159 (89), 158 (94), 131 (99), 91 (62). HRMS (EI) calcd. for $C_{13}H_{16}O_2$ $[M]^+$ 204.1150; found 204.1153. The NMR data were in good agreement with those reported before.[37]

Ethyl 3-phenylbut-2-enoate (3c): EtOAc-hexane (1:9) was used as eluent for flash chromatography; yield and *E*/*Z* ratio, see Table 1, pale yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$, *E*-isomer): δ = 1.30 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.56 (d, *J* = 1.5 Hz, 3 H, CH_3), 4.20 (q, *J* = 7.2 Hz, 2 H, CH_2), 6.12 (q, *J* = 1.5 Hz, 1 H, =CH), 7.17–7.58 (m, 5 H Ph) ppm. ^{1}H NMR (300 MHz, $CDCl_3$, *Z*-isomer): δ = 1.06 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.16 (d, *J* = 1.5 Hz, 3 H, CH_3), 3.98 (q, *J* = 7.2 Hz, 2 H, CH_2), 5.89 (q, *J* = 1.5 Hz, 1 H, =CH), 7.17–7.58 (m, 5 H, Ph, overlapping with Ph signals from the *E*-isomer) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, *E*-isomer): δ = 14.3 (CH_3), 17.9 (CH_3), 59.8 (CH_2), 117.2 (=CH), 126.8 (2× CH in Ph), 127.9 (2× CH in Ph), 128.9 (CH in Ph), 142.2 ($CH_3\underline{C}$=), 155.5 (C in Ph), 166.8 (CO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, *Z*-isomer): δ = 13.9 (CH_3), 27.1 (CH_3), 59.7 (CH_2), 117.8 (=CH), 126.3 (2× CH in Ph), 127.7 (CH in Ph), 128.5 (2× CH in Ph), 140.9 ($CH_3\underline{C}$=), 155.3 (C in Ph), 165.9 (CO) ppm. MS (EI): *m*/*z* (%) = 190 (92) $[M]^+$, 161 (33), 145 (100), 115 (43), 91 (16). HRMS (EI) calcd. for $C_{12}H_{14}O_2$ $[M]^+$ 190.0994; found 190.0989. The NMR data of were in good agreement with those reported before.[36]

Ethyl 5-cyclohexyl-3-methylpent-2-enoate (3d): EtOAc-hexane (1:49) was used as eluent for flash chromatography; yield and *E*/*Z* ratio, see Table 1, pale yellow liquid. ^{1}H NMR (600 MHz, $CDCl_3$, *E*-isomer): δ = 0.85–0.88 (m, 2 H, *c*-hex), 1.13–1.35 (m, 10 H, *c*-hex and CH_3 in Et), 1.63–1.69 (m, 5 H, *c*-hex), 2.09–2.13 (m, 5 H, CH_2 and CH_3), 4.12 (q, *J* = 7.2 Hz, 2 H, OCH_2), 5.63 (s, 1 H, CH=) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, *E*-isomer): δ = 14.3 (CH_3), 18.8 (CH_3), 26.3 (CH_2 in *c*-hex), 26.6 (CH_2 in *c*-hex), 33.2 (CH_2 in *c*-hex), 35.1 (CH_2), 37.3 (CH in *c*-hex), 38.4 (CH_2), 59.4 (OCH_2), 115.2 (CH=), 160.9 (C=), 167.0 (CO) ppm. MS (EI): *m*/*z* (%) = 224 (14) $[M]^+$, 179 (58), 128 (100). HRMS (EI) calcd. for $C_{14}H_{24}O_2$ $[M]^+$ 224.1776; found 224.1784.

Ethyl 3-methyl-5-(naphtalene-1-yl)pent-2-enoate (3e): EtOAc-hexane (1:49) was used as eluent for flash chromatography; yield and *E*/*Z* ratio, see Table 1, pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$, *E*-isomer): δ = 1.28 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.73 (s, 3H, CH_3), 2.54–2.58 (m, 2 H, CH_2), 3.21–3.25 (m, 2 H, CH_2), 4.16 (q, *J* = 7.2 Hz, 2 H, OCH_2), 5.76 (s, 1 H, CH=), 7.29–7.53 (m, 4 H in Ar), 7.71 (d, *J* = 8.4 Hz, 1 H, Ar), 7.85 (d, *J* = 7.6 Hz, 1 H, Ar), 7.99 (d, *J* = 8.4 Hz, 1 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, *E*-isomer): δ = 14.3 (CH_3), 19.0 (CH_3), 31.2 (CH_2), 42.0 (CH_2), 59.6 (OCH_2), 115.9 (CH=), 123.4 (CH in Ar), 125.6 (CH in Ar), 125.6 (CH in Ar), 125.9 (CH in Ar), 126 (CH in Ar), 126.9 (CH in Ar), 128.9 (CH in Ar), 131.6 (C in Ar), 133.9 (C in Ar), 137.2 (C in Ar), 159.1 (C=), 167.5 (CO) ppm. MS (EI): *m*/*z* (%) = 268 (22) $[M]^+$, 141 (100), 115 (11). HRMS (EI) calcd. for $C_{18}H_{20}O_2$ $[M]^+$ 268.1463; found 268.1464. ^{1}H NMR data of the *E*-isomer, are in good agreement with those reported before.[37]

Synthesis of allyl alcohols 5 by DIBAL-H reduction of esters 3, alternative 1: Ester **3a**, **3d** or **3e** (6.33 mmol) was dissolved in dry CH_2Cl_2 (17 mL) and cooled to -78 °C under N_2-atm. DIBAL-H (16.8 mL, 1 M in hexanes, 16.8 mmol) was added to the solution. The reaction mixture was stirred at -78 °C for 1 h and quenched by dropwise addition of 1M HCl. The mixture was extracted with CH_2Cl_2 (2× 25 mL), the combined organic extract were washed with water (20 mL), dried ($MgSO_4$) and evaporated. The crude products were considered pure as judged by NMR and used without further purification in the next step.

3-Methyl-5-phenylpent-2-en-1-ol (5a): Colorless liquid (982 mg, 88%). The starting material and product were pure *E*-isomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (br s, 1 H, OH), 1.56 (s, 3H, CH_3), 2.31 (m, 2 H, PhC$\underline{H}_2$), 2.73 (m, 2 H, CH_2), 4.12 (m, 2 H, OCH_2), 5.39–5.41 (m, 1 H, =CH), 7.15–7.27 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.4 (CH_3), 34.4 (CH_2), 41.3 (CH_2), 59.3 (OCH_2), 123.9 (=CH), 125.8 (CH in Ph), 128.3 (2× CH in Ph), 128.3 (2× CH in Ph), 139.1 ($CH_3\underline{C}$=), 141.9 (C in Ph) ppm. MS (ESI): *m*/*z* (%) = 183 (100) $[M + Li]^+$. HRMS (ESI) calcd. for $C_{12}H_{16}LiO$ $[M + Li]^+$ 183.1361; found 183.1370. The NMR data were in good agreement with those reported before.[38]

5-Cyclohexyl-3-methylpent-2-en-1-ol (5d): Colorless liquid (1.06 g, 92%). The starting material and product were pure *E*-isomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84–0.91 (m, 2 H, *c*-hex), 1.10–1.31 (m, 7 H, *c*-hex and CH_2), 1.61–2.02 (m, 7 H, *c*-hex and CH_3), 4.10–4.14 (m, 2 H, OCH_2), 5.35–5.40 (m, 1 H, CH=) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.3 (CH_3), 26.3 (CH_2 in *c*-hex), 26.7 (CH_2 in *c*-hex), 33.3 (CH_2 in *c*-hex), 35.5 (CH_2), 36.9 (CH_2), 37.4 (CH in *c*-hex), 59.4 (OCH_2), 122.8 (CH=), 140.7 (C-3) ppm. MS (EI): *m*/*z* (%) = 182 (9) $[M]^+$, 164 (6), 96 (100), 71 (70). HRMS (EI) calcd. for $C_{12}H_{22}O$ $[M]^+$ 182.1671; found 182.1675.

3-Methyl-5-(naphtalene-1-yl)pent-2-en-1-ol (5e): Colorless liquid (1.30 g, 91%). The starting material and product were pure *E*-isomers. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.12 (s, 1 H, OH), 1.79 (s, 3 H, CH_3), 2.44 (m, 2 H, CH_2), 3.19 (m, 2 H, CH_2), 4.16 (m, 2 H, CH_2), 5.45 (m, 1 H, CH=), 7.30–7.50 (m, 4 H, Ar), 7.70 (d, *J* = 7.8 Hz, 1 H, Ar), 7.84 (d, *J* = 7.8 Hz, 1 H, Ar), 8.02 (d, *J* = 8.0 Hz, 1 H, Ar) ppm. ^{13}C NMR (150 MHz, $CDCl_3$,): δ = 16.5 (CH_3), 31.6 (CH_2), 40.6 (CH_2), 59.4 (OCH_2), 123.6 (CH=), 123.8 (CH in Ar), 125.4 (CH in Ar), 125.5 (CH in Ar), 125.8 (CH in Ar), 125.9 (CH in Ar), 126.7 (CH in Ar), 128.8 (CH in Ar), 131.8 (C in Ar), 133.9 (C in Ar), 138.1 (C in Ar), 139.4 (C=) ppm. MS (EI): *m*/*z* (%) = 226 (18) $[M]^+$, 208 (23), 141 (100). HRMS (EI) calcd. for $C_{16}H_{18}O$ $[M]^+$ 226.1358; found 226.1361. ^{1}H NMR data of the *E*-isomer, are in good agreement with those reported before.[39]

Synthesis of allyl alcohols 5 by DIBAL-H reduction of esters 3, alternative 2: Ester **3b** or **3c** (6.53 mmol) were dissolved in dry toluene (35 mL) under N_2-atm. and cooled to -78 °C. DIBAL-H (20 mL, 1 M sol. in hexanes, 20 mmol) was added dropwise and the solution was stirred for 2 h. before the reaction was quenched by pouring it into sat. aq. potassium sodium tartrate (60 mL). The water phase was extracted with ethyl acetate (3× 30 mL) and the combined organic phases were washed with water (30 mL) and brine (30 mL), dried ($MgSO_4$) and evaporated. The crude product was purified by flash chromatography.

3-Methyl-4-phenylbut-2-en-1-ol (5b): EtOAc-hexane (1:3) was used as eluent for flash chromatography to give **5b** (910 mg, 86%) as a pale yellow liquid. *E*/*Z* ratio in starting material and product was 86:14. ^{1}H NMR (600 MHz, $CDCl_3$, *E*-isomer): δ = 1.22 (br s, 1 H, OH), 1.61 (s, 3 H, CH_3), 3.31 (s, 2 H, CH_2), 4.17 (d, *J* = 6.0 Hz, 2 H, OCH_2), 5.46–5.49 (m, 1 H, CH=), 7.13–7.30 (m, 5 H, Ph) ppm. ^{1}H NMR (600 MHz, $CDCl_3$, *Z*-isomer): δ = 1.22 (br s, 1 H, OH), 1.67 (s, 3 H, CH_3), 3.41 (s, 2 H, CH_2), 4.26 (d, *J* = 6.0 Hz, 2 H, OCH_2), 5.57–5.59 (m, 1 H, CH=), 7.13–7.30 (m, 5 H, Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, *E*-isomer): δ = 16.1 (CH_3), 46.0 (CH_2), 59.4 (OCH_2), 125.3 (CH=), 126.2 (2× CH in Ph), 128.4 (CH in Ph), 128.9 (2× CH in Ph), 138.9 (C=), 139.4 (C in Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, *Z*-isomer): δ = 23.4 (CH_3), 38.0 (CH_2), 59.3 (OCH_2), 125.2 (CH=), 126.1 (CH in Ph), 128.3 (2× CH in Ph), 128.5 (2× CH in Ph) ppm, two signals were hidden. MS (ESI): *m*/*z* (%) = 169 (100) $[M + Li]^+$. HRMS (ESI) calcd. for $C_{11}H_{14}O$ $[M + Li]^+$ 169.12005; found 169.1219. The NMR data were in good agreement with those reported before.[40]

3-Phenylbut-2-en-1-ol (5c): EtOAc-hexane (1:3) was used as eluent for flash chromatography to give **5c** (823 mg, 85%) as a pale yellow liquid. *E*/*Z* ratio in starting material and product was 88:12. ^{1}H NMR (300 MHz, $CDCl_3$, *E*-isomer): δ = 1.78 (br s, 1 H, OH), 2.06 (br s, 3 H, CH_3), 4.34 (m, 2 H, CH_2), 5.92–5.99 (m, 1 H, CH=), 7.17–7.41 (m, 5 H, Ph) ppm. ^{1}H NMR (300 MHz, $CDCl_3$, *Z*-isomer): δ = (br s, 1 H, OH), 2.06 (br s, 3 H, CH_3), 4.05 (m, 2 H, CH_2), 5.66–5.72 (m, 1 H, CH=), 7.17–7.41 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, *E*-isomer): δ = 16.4 (CH_3), 60.3 (CH_2), 126.2 (2× CH in Ph), 126.9 (CH=), 128.6 (CH in Ph), 128.7 (2× CH in Ph), 138.2 (C=), 143.3 (C in Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, *Z*-isomer): δ = 25.7 (CH_3), 60.7 (CH_2), 126.5 (CH=), 127.6 (2× CH in Ph), 127.7 (CH in Ph), 128.2 (2× CH in Ph) ppm, two signals were hidden. MS (EI): *m*/*z* (%) = 148 (32) $[M]^+$, 133 (100), 105 (74), 91 (59), 77 (37). HRMS (EI) calcd. for $C_{10}H_{12}O$ $[M]^+$ 148.0888; found 148.0892. The ^{1}H NMR data of both isomers were in good agreement with those reported before.[41]

General procedure for the synthesis of amides 7: To a mixture of NaH (231 mg, ca. 60% dispersion in mineral oil, ca. 5.77 mmol) in dry THF (12 mL) under N_2-atm. was added the allylic alcohol **5** (2.34 mmol) in THF (2 mL). The mixture was cooled to 0 °C before trichloroacetonitrile (0.28 mL, 2.8 mmol) was added and the reaction was stirred for 2 h at 0 °C. The mixture was warmed to ambient temperature, filtered through a silica gel pad and evaporated. The intermediate **6** was dissolved in xylenes (35 mL) and after addition of Na_2CO_3 (90 mg, 0.86 mmol), the mixture was stirred at reflux for 24 h. The reaction was cooled to ambient temperature, evaporated and the residue purified by flash chromatography.

2,2,2-Trichloro-N-(3-methyl-5-phenylpent-1-en-3-yl)acetamide (7a): EtOAc-hexane (1:3) was used as eluent for flash chromatography to give **7a** (548 mg, 73%) as a yellow wax. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (s, 3 H, CH_3), 2.10–2.14 (m, 1 H, H_A in CH_2), 2.19–2.24 (m, 1 H, H_B in CH_2), 2.58–2.60 (m, 2 H, CH_2), 5.20 (d, *J* = 17.4 Hz, 1 H, H_A in =CH_2), 5.24 (d, *J* = 10.8 Hz, 1 H, H_B in =CH_2), 5.97 (dd, *J* = 17.4, 10.8 Hz, 1 H, CH=), 6.61 (s, 1 H, NH), 7.16–7.28 (m, 5 H, Ph) ppm. ^{13}C NMR (150 MHz $CDCl_3$): δ = 24.1 (CH_3), 30.3 (CH_2), 40.5 (CH_2), 58.7 (CN), 93.2 (CCl_3), 113.8 (CH_2=), 126.1 (2× CH in Ph), 128.4 (2× CH in Ph), 128.6 (CH in Ph), 141.2 (CH=), 141.3 (C in Ph), 160.0 (CO) ppm. MS (ESI): *m*/*z* (%) = 268 (100) $[M + Li]^+$. HRMS (ESI) calcd. for $C_{14}H_{16}Cl_3NO$ $[M + Li]^+$ 326.0458; found 326.0465.

2,2,2-Trichloro-N-(2-methyl-1-phenylbut-3-en-2-yl)acetamide (7b): EtOAc-hexane (1:3) was used as eluent for flash chromatography to give **7b** (517 mg, 72%) as a yellow wax. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (s, 3 H, CH_3), 3.04 (d, *J* = 13.0 Hz, 1 H, H_A in CH_2), 3.19 (d, *J* = 13.0 Hz, 1 H, H_B in CH_2), 5.09 (d, *J* = 17.2 Hz, 1 H, H_A in =CH_2), 5.19 (d, *J* = 10.8 Hz, 1 H, H_B in =CH_2), 6.00 (dd, *J* = 17.2, 10.8 Hz, 1 H, CH=), 6.53 (s, 1 H NH), 7.13–7.29 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.4 (CH_3), 44.5 (CH_2), 58.7 (CN), 113.9 (CH_2=), 127.1 (CH in Ph), 128.3 (2× CH in Ph), 130.7 (2× CH in Ph), 135.7 (C in Ph), 141.0 (CH=), 160.3 (C=) ppm, CCl_3 signal was hidden. MS (ESI): *m*/*z* (%) = 312/310/308/306 (3/34/94/100) $[M + H]^+$. HRMS (ESI) calcd. for $C_{13}H_{14}Cl_3NO$ $[M + Li]^+$ 312.0301; found 312.0288.

2,2,2-Trichloro-N-(2-phenylbut-3-en-2-yl)acetamide (7c): EtOAc-hexane (1:9) was used as eluent for flash chromatography to give **7c** (411 mg, 60%) as a pale yellow wax. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.87 (s, 3 H, CH_3), 5.22 (d, *J* = 17.2 Hz, 1 H, H_A in =CH_2), 5.31 (d, *J* = 10.8 Hz, 1 H, H_B in =CH_2), 6.26 (dd, *J* = 17.2, 10.8 Hz, 1 H, CH=), 6.97 (s 1 H, NH), 7.24–7.36 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.9 (CH_3), 61.6 (CN), 93.6 (CCl_3), 115.2 (CH_2=), 125.8 (2× CH in Ph), 128.1 (CH in Ph), 129.2 (2× CH in Ph), 140.9 (CH=), 143.5 (C in Ph), 160.3 (CO) ppm. MS (ESI): *m*/*z* (%) = 304/302/300/298 (3/30/92/100) $[M + Li]^+$. HRMS (ESI) calcd. for $C_{12}H_{12}Cl_3NO$ $[M + Li]^+$ 298.0145; found 298.0132. NMR data were in good agreement with those reported before.[12e]

2,2,2-Trichloro-N-(5-cyclohexyl-3-methylpent-1-en-3-yl)acetamide (7d): EtOAc-hexane (1:3) was used as eluent for flash chromatography to give **7d** (451 mg, 59%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87–0.89 (m, 2 H, *c*-hex), 1.11–1.24 (m, 7 H, *c*-hex and CH_2), 1.46 (s, 3 H, CH_3), 1.61–1.69 (m, 4 H, *c*-hex), 1.76–1.86 (m, 2 H, CH_2), 5.12 (d, *J* = 17.4 Hz, 1 H, H_A in =CH_2), 5.16 (d, *J* = 10.8 Hz, 1 H, H_B in =CH_2), 5.89 (dd, *J* = 17.4, 10.8 Hz, 1 H, CH=), 6.55 (s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.8 (CH_3), 26.3 (2× CH_2 in *c*-hex), 26.6 (CH_2 in *c*-hex), 31.2 (CH_2), 33.3 (2× CH_2 in *c*-hex), 36.3 (CH_2), 37.8 (CH in *c*-hex) 58.7 (CN), 93.3 (CCl_3), 113.4 (CH_2=), 141.4 (CH=), 160.1 (CO) ppm. MS (EI): *m*/*z* (%) = 332/330/328/326 (4/40/98/100) $[M + H]^+$, 256 (53), 214 (52), 165 (74). HRMS (EI) calcd. for $C_{14}H_{22}Cl_3NO$ $[M]^+$ 325.0767; found 325.0773.

2,2,2-Trichloro-N-[3-methyl-5-(naphthalen-1-yl)pent-1-en-3-yl]acetamide (7e): EtOAc-hexane (1:3) was used as eluent for flash chromatography to give **7e** (512 mg, 59%) as a pale yellow wax. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.62 (s, 3 H, CH_3), 2.21–2.37 (m, 1 H, H_A in CH_2), 2.32–2.38 (m, 1 H, H_B in CH_2), 3.05–3.07 (m, 2 H, CH_2), 5.27 (d, *J* = 17.3

Hz, 1 H, H_A in $=CH_2$), 5.31 (d, J = 10.8 Hz, 1 H, H_B in $=CH_2$), 6.05 (dd, J = 17.3, 10.8 Hz, 1 H, CH=), 6.71 (s, 1 H, NH, 1H), 7.31–7.53 (m, 2 H, Ar), 7.70 (d, J = 8.0 Hz, 1 H, Ar), 7.83 (d, J = 8.0 Hz, 1 H, Ar), 7.96 (d, J = 8.0 Hz, 1 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.2 (CH_3), 27.5 (CH_2), 39.9 (CH_2), 58.9 (CN), 114.0 (CH_2=), 123.5 (CH in Ar), 125.6 (CH in Ar), 125.7 (CH in Ar), 126.1 (CH in Ar), 126.2 (CH in Ar), 126.9 (CH in Ar), 128.9 (CH in Ar), 131.7 (C in Ar), 133.9 (C in Ar), 137.4 (C in Ar), 141.2 (CH=), 160.3 (CO) ppm, CCl_3 signal was hidden. MS (EI): m/z (%) = 375/373/371/369 (1/7/21/22) $[M]^+$, 208 (38), 141(100). HRMS (EI) calcd. for $C_{18}H_{18}Cl_3NO$ $[M]^+$ 369.0454; found 369.0447.

General procedure for the hydrolysis of amides 7, and isolation of products as free amines 8: A mixture of amide **7** (0.794 mmol), NaOH (3.8 mL, 6 M, 23 mmol) and EtOH (4 mL) was stirred at 40 °C for 24 h. The reaction mixture was extracted with diethyl ether (2× 10 mL). The combined organic layers were washed with water (10 mL), dried ($MgSO_4$) and evaporated. The crude product was purified by flash chromatography.

3-Methyl-5-phenylpent-1-en-3-amine (8a): EtOAc was used as eluent for flash chromatography to give **8a** (72 mg, 52%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (s, 3 H, CH_3), 1.37 (s, 2 H, NH_2), 1.67–1.76 (m, 2 H, CH_2), 2.55–2.61 (m, 2 H, CH_2), 5.04 (dd, J = 10.6, 1.1 Hz, 1H, H_A in $=CH_2$), 5.13 (dd, J = 17.4, 1.1 Hz, 1 H, H_B in $=CH_2$), 5.95 (dd, J = 17.4, 10.6 Hz, 1 H, CH=), 7.15–7.28 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.5 (CH_3), 30.7 (CH_2), 45.1 (CH_2), 53.7 (CN), 111.0 (CH_2=), 125.7 (CH in Ph), 128.3 (2× CH in Ph), 128.3 (2× CH in Ph), 142.6 (C in Ph), 147.1 (CH=) ppm. MS (ESI): m/z (%) = 176 (100) $[M + H]^+$. HRMS (ESI) calcd. for $C_{12}H_{17}N$ $[M + H]^+$ 176.1439; found 176.1443.

2-Methyl-1-phenylbut-3-en-2-amine (8b): EtOH-EtOAc (1:3) was used as eluent for flash chromatography to give **8b** (79 mg, 62%) as a yellow wax. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (s, 3 H, CH_3), 2.74 (d, J = 13.0 Hz, 1 H, H_A in CH_2), 2.69 (d, J = 13.0 Hz, 1 H, H_B in CH_2), 4.97 (dd, J = 10.6, 1.0 Hz, 1 H, H_A in $=CH_2$), 5.00 (dd, J = 17.4, 1.0 Hz, 1 H, H_B in $=CH_2$), 5.96 (dd, J = 17.4, 10.6 Hz, 1 H, CH=), 7.14–7.28 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.3 (CH_3), 49.6 (CH_2), 54.1 (CN), 110.9 (CH_2=), 126.3 (CH in Ph), 127.9 (2× CH in Ph), 130.6 (2× CH in Ph), 137.5 (C in Ph), 146.9 (CH=) ppm. MS (ESI): m/z (%) = 162 (100) $[M + H]^+$. HRMS (ESI) calcd. for $C_{11}H_{15}N$ $[M + H]^+$ 162.1283; found 162.2435.

2-Phenylbut-3-en-2-amine (8c): EtOH-EtOAc (1:3) was used as eluent for flash chromatography to give **8c** (51 mg, 44%) as a yellow wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, CH_3), 5.22 (d, J = 17.4 Hz, 1 H, H_A in $=CH_2$), 5.31 (d, J = 10.8 Hz, 1 H, H_B in $=CH_2$), 6.26 (dd, J = 17.4, 10.8 Hz, 1 H, CH=), 7.25–7.86 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.4 (CH_3), 61.2 (CN), 114.8 (CH_2=), 125.4 (2× CH in Ph), 127.7 (CH in Ph), 128.8 (2× CH in Ph), 140.5 (CH=), 143.1 (C in Ph) ppm. MS (EI): m/z (%) = 147 (83) $[M]^+$, 133 (100), 115 (66), 91 (59), 77 (37). HRMS (EI) calcd. for $C_{10}H_{13}N$ $[M]^+$ 147.1048; found 147.1054. NMR data were in good agreement with those reported before.[12e]

5-Cyclohexyl-3-methylpent-1-en-3-amine (8d): EtOH-EtOAc (1:1) was used as eluent for flash chromatography to give **8d** (27 mg, 19%) as a yellow wax. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83–0.88 (m, 2 H, *c*-hex), 1.06–1.28 (m, 10 H, CH_3, *c*-hex and NH_2), 1.38–1.42 (m, 2 H, CH_2), 1.60–1.68 (m, 6 H, *c*-hex), 4.95 (d, J = 10.8, 1 H, H_A in $=CH_2$), 5.04 (d, J = 17.1, 1 H, H_B in $=CH_2$), 5.85 (dd, J = 17.1, 10.8 Hz, 1 H, CH=) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (2× CH_2 in *c*-hex), 26.7 (CH_2 in *c*-hex), 28.3 (CH_3), 31.7 (CH_2), 33.4 (2× CH_2 in *c*-hex), 38.1 (CH in *c*-hex), 40.5 (CH_2), 53.6 (CN), 110.4 (CH_2=), 147.6 (CH=) ppm. MS (ESI): m/z (%) = 182 (100) $[M + H]^+$. HRMS (ESI) calcd. for $C_{12}H_{23}N$ $[M + H]^+$ 182.1916; found 182.1914.

3-Methyl-5-(naphthalene-1-yl)pent-1-en-3-amine (8e): EtOH-EtOAc (1:3) was used as eluent for flash chromatography to give **8e** (79 mg, 44%) as a yellow wax. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, CH_3), 1.69 (s, 2 H, NH_2), 1.83–1.84 (m, 1 H, H_A in CH_2), 1.86–1.87 (m, 1 H H_B in CH_2), 3.05 (t, J = 8.0 Hz, 2 H, CH_2), 5.12 (d, J = 10.4 Hz, 1 H, H_A in $=CH_2$), 5.22 (d, J = 17.2 Hz, 1 H, H_B in $=CH_2$), 6.03 (dd, J = 17.2, 10.4 Hz, 1H, =CH), 7.30 (d, J = 6.8 Hz, 1 H, CH in Ar), 7.31–7.37 (m, 1 H, CH in Ar), 7.44–7.49 (m, 2 H, 2 × CH in Ar), 7.68 (d, J = 8.0 Hz, 1 H, CH in Ar), 7.83 (d, J = 7.6 Hz, 1 H, CH in Ar), 8.00 (d, J = 8.0 Hz, 1 H, CH in Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.8 (CH_2), 28.4 (CH_3), 44.2 (CH_2), 54.1 (CN), 111.4 ($=CH_2$), 123.7 (CH in Ar), 125.6 (CH in Ar), 125.6 (CH in Ar), 125.7 (CH in Ar), 125.8 (CH in Ar), 126.5 (CH in Ar), 128.8 (CH in Ar), 131.8 (C in Ar), 133.9 (C in Ar), 138.7 (C in Ar), 146.7 (=CH) ppm. MS (EI): m/z (%) = 225 (8) $[M]^+$, 208 (46), 141 (41), 70 (100). HRMS (EI) calcd. for $C_{16}H_{19}N$ $[M]^+$ 225.1517; found 225.1520.

General procedure for the hydrolysis of amides 7, and isolation of products as ammonium chlorides 9: The hydrolysis was carried out as described for the synthesis of free amines **8** above. The reaction mixture was extracted with CH_2Cl_2 (2× 10 mL), acidified with aq. HCl (0.95 mL, 1 M, 1.1 eq.), dried ($MgSO_4$) and evaporated. The product was isolated by crystallization / precipitation from acetone-hexane.

3-Methyl-5-phenylpent-1-en-3-aminium chloride (9a): Yellow waxy solid (121 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.54 (s, 3 H, CH_3), 2.03–2.05 (m, 1 H, H_A in CH_2), 2.14–2.18 (m, 1 H, H_B in CH_2), 2.63–2.68 (m, 1 H, H_A in $PhCH_2$), 2.71–2.76 (m, 1 H, H_B in $PhCH_2$), 5.25 (d, J = 10.8 Hz, 1 H, H_A in $=CH_2$), 5.46 (d, J = 17.4 Hz, 1 H, H_B in $=CH_2$), 5.89 (dd, J = 17.4, 10.8, Hz, 1 H, =CH), 7.13–7.20 (m, 5 H, Ph), 8.79 (s, 3 H, NH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 24.2 (CH_3), 30.1 ($PhCH_2$), 41.4 (CH_2), 58.3 (CN), 116.9 ($=CH_2$), 126.1 (CH in Ph), 128.3 (2× CH in Ph), 128.4 (2× CH in Ph), 137.9 (=CH), 140.6 (C in Ph) ppm. MS (ESI): m/z (%) = 176 (100) $[M]^+$. HRMS (ESI) calcd. for $C_{12}H_{18}N$ $[M]^+$ 176.1434; found 176.1443. NMR data were in good agreement with those reported for the (*R*)-enantiomer before.[15b]

2-Methyl-1-phenylbut-3-en-2-aminium chloride (9b): Beige needles (78 mg, 50%), m.p. 158–160 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53 (s, 3 H, CH_3), 3.16 (br s, 2 H, CH_2), 5.30 (d, J = 10.4 Hz, 1 H, H_A in $=CH_2$), 5.32 (d, J = 16.4 Hz, 1 H, H_B in $=CH_2$), 5.94 (m, 1 H, =CH), 7.19–7.26 (m, 5 H, Ph), 8.71 (s, 3 H, NH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.9 (CH_3), 45.7 (CH_2), 58.7 (CN), 117.1 ($=CH_2$), 127.3 (CH in Ph), 128.3 (2× CH in Ph), 130.8 (2× CH in Ph), 134.0 (C in Ph), 137.5 (=CH) ppm. MS (ESI): m/z (%) = 162 (100) $[M]^+$. HRMS (ESI) calcd. for $C_{11}H_{16}N$ $[M]^+$ 162.1283; found 162.1288.

2-Phenylbut-3-en-2-aminium chloride (9c): Beige waxy solid (96 mg, 66%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.84 (s, 3 H, CH_3), 5.31 (d, J = 10.8 Hz, 1 H, H_A in $=CH_2$), 5.38 (d, J = 17.4 Hz, 1 H, H_B in $=CH_2$), 6.05 (dd, J = 17.4, 10.8 Hz, 1 H, =CH), 7.24–7.53 (m, 5 H, Ph), 9.12 (s, 3 H, NH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.2 (CH_3), 60.4 (CN), 116.6 ($=CH_2$), 126.1 (2× CH in Ph), 128.3 (CH in Ph), 128.7 (2× CH in Ph), 138.6 (=CH), 139.2 (C in Ph) ppm. MS (ESI): m/z (%) = 148 (1) $[M]^+$, 147 (11), 132 (100), 120 (44). HRMS (EI) calcd. for $C_{10}H_{14}N$ $[M - H]^+$ 147.1048; found 147.1054.

5-Cyclohexyl-3-methylpent-1-en-3-aminium chloride (9d): Yellow waxy solid (121 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82–0.87 (m, 2 H, CH_2 in *c*-hex), 1.14–1.24 (m, 11 H, NH_3, CH_3, 3 H in *c*-hex, CH_2), 1.45–1.49 (m, 2 H, CH_2), 1.59–1.70 (m, 4 H, 2× CH_2 in *c*-hex), 5.01 (d, J = 10.8 Hz, 1 H, H_A in $=CH_2$), 5.09 (d, J = 17.2 Hz, 1 H, H_B in $=CH_2$), 5.84 (dd, J = 17.2, 10.8 Hz, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (2× CH_2 in *c*-hex), 26.7 (CH_2 in *c*-hex), 27.1 (CH_3), 31.5 (CH_2), 33.4 (2× CH_2 in *c*-hex), 38.1 (CH in *c*-hex), 39.8 (CH_2), 54.4 (CN), 117.7

(=CH_2), 145.7 (=CH) ppm. MS (ESI): *m*/*z* (%) = 182 (100) $[M]^+$. HRMS (EI) calcd. for $C_{12}H_{24}N$ $[M]^+$ 182.1909; found 182.1914. NMR data were in good agreement with those reported for the (*R*)-enantiomer before.[15a]

3-Methyl-5-(naphthalen-1-yl)pent-1-en-3-aminium chloride (9e): Yellow waxy solid (73 mg, 35%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, CH_3), 1.79–1.86 (m, 2 H, CH_2), 3.02–3.06 (m, 2 H, CH_2), 5.12 (d, *J* = 10.8 Hz, 1 H, H_A in =CH_2), 5.21 (d, *J* = 17.6 Hz, 1 H, H_B in =CH_2), 6.03 (dd, *J* = 17.6, 10.8 Hz, 1 H, =CH), 7.30 (d, *J* = 6.4 Hz, 1 H, CH in Ar), 7.34–7.38 (m, 1 H, CH in Ar), 7.43–7.50 (m, 2 H, 2× CH in Ar), 7.68 (d, *J* = 8.0 Hz, 1 H, CH in Ar), 7.83 (d, *J* = 7.6 Hz, 1 H, CH in Ar), 7.99 (d, *J* = 8.4 Hz, 1 H, CH in Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$,): δ = 27.9 (CH_2), 28.6 (CH_3), 44.4 (CH_2), 53.9 (CN), 111.3 (=CH_2), 123.7 (CH in Ar), 125.4 (CH in Ar), 125.6 (CH in Ar), 125.7 (CH in Ar), 125.8 (CH in Ar), 126.5 (CH in Ar), 128.8 (CH in Ar), 131.8 (C in Ar), 133.9 (C in Ar), 138.8 (C in Ar), 147.1 (=CH) ppm. MS (EI): *m*/*z* (%) = 225 (4) $[M - H]^+$, 208 (45), 141 (67), 70 (100); HRMS (EI) calcd. for $C_{16}H_{20}N$ $[M - H]^+$ 225.1517; found 225.1520.

***N*-Methoxy-*N*,3-dimethyl-5-phenylpent-2-enamide (10a):** *N,O*-dimethylhydroxylamine hydrochloride (3.26 g, 33.5 mmol) was added to a solution of ester **3a** (4.05 g, 18.6 mmol) in dry THF (50 mL) under Ar-atm. The suspension was cooled to 0 °C and *t*-BuMgCl (34.2 mL, 65.1 mmol, 1.9 M in ether) was added. The solution was stirred for 30 min at ambient temperature and subsequently quenched with sat. aq. NH_4Cl (20 mL). The mixture was extracted with EtOAc (3× 20 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography eluting with EtOAc-hexane (0-50% EtOAc) to give **10a** (4.30 g, 99%) as a colorless oil, *E/Z* ratio 4:1. The NMR data for the major isomer are given. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.16 (d, *J* = 1.4 Hz, 3 H, CH_3C=), 2.40–2.50 (m, 2 H, CH_2), 2.74–2.83 (m, 2 H, CH_2Ph), 3.15 (s, 3 H, CH_3N), 3.52 (s, 3 H, CH_3O), 6.05 (s, 1 H, CH=), 7.10–7.20 (m, 3 H, Ph), 7.22–7.30 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.7 ($\underline{C}H_3C$=), 32.2 (CH_3N), 33.9 (CH_2Ph), 42.7 (CH_2), 61.3 (CH_3O), 114.5 (CH=), 126.0 (CH in Ph), 128.3 (2× CH in Ph), 128.4 (2× CH in Ph), 141.2 (C in Ph), 155.0 (C=), 167.9 (CO) ppm. MS (EI): *m*/*z* (%) = 218 (8) $[M - CH_3]^+$, 173 (15), 172 (7), 145 (11), 144 (24), 129 (7), 91 (100). HRMS (EI) calcd. for $C_{14}H_{19}NO_2$ $[M - CH_3]^+$ 218.1181; found 218.1307.

***N*-Methoxy-*N*,3-dimethyl-4-phenylbut-2-enamide (10b):** The title compound was synthesized in 18.3 mmol scale otherwise as described for **10a** above. EtOAc-hexane (0-50% EtOAc) was used as eluent for flash chromatography to give **10b** (3.70 g, 91%) as a colorless oil, *E/Z* ratio 5:1. The NMR data for the major isomer are given. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.10 (s, 3 H, CH_3C=), 3.21 (s, 3 H, CH_3N), 3.47 (s, 2 H, CH_2), 3.64 (s, 3 H, CH_3O), 6.13 (s, 1 H, CH=), 6.94–7.44 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.6 ($\underline{C}H_3C$=), 32.2 (CH_3N), 47.2 (CH_2), 61.4 (CH_3O), 115.8 (CH=), 126.5 (CH in Ph), 128.4 (2× CH in Ph), 129.1 (2× CH in Ph), 138.3 (C in Ph), 154.7 (C=), 168.0 (CO) ppm. MS (EI): *m*/*z* (%) = 204 (89) $[M - CH_3]^+$, 159 (81), 158 (82), 131 (100), 130 (72), 129 (52), 115 (33) 91 (70). HRMS (EI) calcd. for $C_{14}H_{20}NO_2$ $[M - CH_3]^+$ 204.1025; found 204.1144.

***N*-Methoxy-*N*-methyl-3-phenylbut-2-enamide (10c):** The title compound was synthesized in 17.6 mmol scale otherwise as described for **10a** above. EtOAc-hexane (0-50% EtOAc) was used as eluent for flash chromatography to give **10c** (3.16 g, 88%) as a colorless oil, *E/Z* ratio 9:1. The NMR data for the major isomer are given. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.51 (s, 3 H, CH_3C=), 3.25 (s, 3 H, CH_3N), 3.69 (s, 3 H, CH_3O), 6.55 (s, 1 H, CH=), 7.27–7.42 (m, 3 H, Ph), 7.42–7.52 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.0 ($\underline{C}H_3C$=), 32.4 (CH_3N), 61.6 (CH_3O), 116.0 (CH=), 126.3 (CH in Ph), 128.5 (2× CH in Ph), 128.9 (2× CH in Ph), 143.0 (C in Ph), 152.3 (C=), 168.0 (CO) ppm. MS (EI): *m*/*z* (%) = 190 (82) $[M - CH_3]^+$, 161 (32), 145 (100), 144 (40), 117 (33), 115 (48), 91 (22). HRMS (EI) calcd. $C_{12}H_{15}NO_2$ $[M - CH_3]^+$ 190.0868; found 190.0998. NMR data were in good agreement with those reported before.[23]

5-Cyclohexyl-*N*-methoxy-*N*,3-dimethylpent-2-enamide (10d): The title compound was synthesized in 5.89 mmol scale otherwise as described for **10a** above. EtOAc-hexane (0-50% EtOAc) was used as eluent for flash chromatography to give **10d** (1.22 g, 87%) as a colorless oil, *E/Z* ratio 3:1. The NMR data for the major isomer are given. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82–0.92 (m, 2 H, *c*-hex), 1.09–1.25 (m, 4 H, *c*-hex), 1.29–1.36 (m, 2 H, *c*-hex-CH_2), 1.56–1.74 (m, 5 H, *c*-hex), 2.09 (d, *J* = 1.3 Hz, 3 H, CCH_3), 2.11–2.13 (m, 2 H, *c*-hex-$CH_2\underline{CH_2}$), 3.17 (s, 3 H, NCH_3), 3.65 (s, 3 H, OCH_3), 6.07 (s, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.7 ($\underline{C}H_3C$=), 26.3 (*c*-hex), 26.6 (*c*-hex), 32.3 (NCH_3), 33.3 (*c*-hex), 35.3 (*c*-hex-CH_2), 37.3 (*c*-hex), 38.5 (*c*-hex-$CH_2\underline{CH_2}$), 61.4 (OCH_3), 113.6 (=CH), 157.3 (C=), 168.2 (CO). MS (EI): *m*/*z* (%) = 224 (23) $[M - CH_3]^+$, 179 (52), 178 (9), 151 (100), 88 (13) ppm. HRMS (EI) calcd. for $C_{14}H_{25}NO_2$ $[M - CH_3]^+$ 224.1651; found 224.1612.

***N*-Methoxy-*N*,3-dimethyl-5-(naphthalen-1-yl)pent-2-enamide (10e):** The title compound was synthesized in 18.1 mmol scale otherwise as described for **10a** above. EtOAc-hexane (0-40% EtOAc) was used as eluent for flash chromatography to give **10e** (1.70 g, 77%) as a colorless oil, *E/Z* ratio 3:1. The NMR data for the major isomer are given. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.24 (d, *J* = 0.8 Hz, 3 H, CH_3C=), 2.57–2.61 (m, 2 H, CH_2C=), 3.17 (s, 3 H, NCH_3), 3.24–3.28 (m, 2 H, $ArCH_2$), 3.50 (s, 3 H, OCH_3), 6.09 (s, 1 H, =CH), 7.30 (d, *J* = 6.7 Hz, 1 H, Ar), 7.36–7.39 (m, 1 H, Ar), 7.45–7.54 (m, 2 H, Ar), 7.70 (d, *J* = 8.0 Hz, 1 H, Ar), 7.84 (d, *J* = 8.1 Hz, 1 H, Ar), 8.01 (d, *J* = 8.2 Hz, 1 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.8 ($\underline{C}H_3C$=), 31.2 ($ArCH_2$), 32.3 (NCH_3), 42.0 (CH_2C=), 61.3 (OCH_3), 114.5 (=CH), 123.4 (CH in Ar), 125.5 (CH in Ar), 125.5 (CH in Ar), 125.9 (CH in Ar), 126.0 (CH in Ar), 126.8 (CH in Ar), 128.8 (CH in Ar), 131.6 (C in Ar), 133.9 (C in Ar), 137.3 (C in Ar), 155.5 (C=), 167.3 (CO) ppm. MS (EI): *m*/*z* (%) = 268 (7) $[M - CH_3]^+$, 223 (21), 195 (9), 129 (7) 141 (100). HRMS (EI) calcd. for $C_{18}H_{21}NO_2$ $[M - CH_3]^+$ 268.1338; found 268.1375.

4-Methyl-6-phenylhex-3-en-2-one (11a): The Weinreb amide **10a** (6.41 g, 27.5 mmol) in dry THF (25 mL) was cooled to -30 °C under Ar-atm. MeMgBr (12.5 mL, 27.6 mmol, 2.2 M in ether) was added and the solution was stirred for 1 h. Sat. aq. NH_4Cl (20 mL) was added and the mixture was extracted with EtOAc (3× 20 mL). The combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography eluting with EtOAc-hexane (0-5% EtOAc) to give **10a** (5.09 g, 98%) as a colorless oil, *E/Z* ratio 4:1. The pure *E*-isomer was isolated by flash chromatography just before use in the synthesis of compound **12a**. The NMR data for the major isomer are given. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.17 (s, 3 H, CH_3CO), 2.20 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 2.40–2.48 (m, 2 H, CH_2), 2.78–2.85 (m, 2 H, CH_2Ph), 6.06 (q, *J* = 1.3 Hz, 1 H, CH=), 7.16–7.27 (m, 3 H, Ph), 7.27–7.35 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.7 ($\underline{C}H_3C$=), 31.7 ($\underline{C}H_3CO$), 34.4 (CH_2Ph), 35.9 (CH_2), 124.4 (CH=), 125.9 (CH in Ph), 128.3 (2× CH in Ph), 128.5 (2× CH in Ph), 141.7 (C in Ph), 158.2 (C=), 198.1 (CO) ppm. MS (EI): *m*/*z* (%) = 188 (18) $[M]^+$, 173 (16), 145 (22), 130 (9), 91 (100), 65 (9). HRMS (EI) calcd. for $C_{13}H_{16}O$ $[M]^+$ 188.1201; found 188.1200. NMR data were in good agreement with those reported before.[23]

4-Methyl-5-phenylpent-3-en-2-one (11b): The title compound was synthesized in 16.8 mmol scale otherwise as described for **11a** above. EtOAc-hexane (0-5% EtOAc) was used as eluent for flash chromatography to give **11b** (2.89 g, 99%), colorless oil, *E/Z* ratio 5:1. The NMR data for the major isomer are given. ^{1}H NMR (400 MHz,

$CDCl_3$): δ = 2.07 (d, *J* = 1.2 Hz, 3 H, CH_3C=), 2.16 (s, 3 H, CH_3CO), 3.40 (s, 2 H, CH_2), 6.05 (q, *J* = 1.2 Hz, 1 H, CH=), 7.10–7.17 (m, 2 H, Ph), 7.17–7.35 (m, 3 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.7 ($\underline{C}H_3C$=), 31.9 ($\underline{C}H_3CO$), 38.9 (CH_2), 124.9 (CH=), 126.2 (CH in Ph), 128.4 (2× CH in Ph), 129.0 (2× CH in Ph), 138.9 (C in Ph), 156.0 (C=), 198.3 (CO) ppm. MS (EI): *m*/*z* (%) = 174 (100) $[M]^+$, 159 (45), 144 (15), 141 (14), 131 (94), 115 (18), 91 (57). HRMS (EI) calcd. for $C_{12}H_{14}O$ $[M]^+$ 174.1045; found 174.1045. NMR data were in good agreement with those reported before.[42]

4-Phenylpent-3-en-2-one (11c): The title compound was synthesized in 15.2 mmol scale otherwise as described for **11a** above. EtOAc-hexane (0-5% EtOAc) was used as eluent for flash chromatography to give **11c** (2.37 g, 98%) as a colorless oil, *E*/*Z* ratio 10:1. The NMR data for the major isomer are given. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3CO), 2.52 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 6.49 (q, *J* = 1.3 Hz, 1 H, CH=), 7.32–7.40 (m, 3 H, Ph), 7.44–7.50 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.3 ($\underline{C}H_3C$=), 32.2 ($\underline{C}H_3CO$), 124.5 (CH=), 126.4 (2× CH in Ph), 128.5 (2× CH in Ph), 129.0 (CH in Ph), 142.5 (C=), 153.8 (C in Ph), 198.8 (CO) ppm. MS (EI): *m*/*z* (%) = 160 (75) $[M]^+$, 159 (100), 145 (92), 117 (60), 115 (60), 91 (24). HRMS (EI) calcd. for $C_{11}H_{12}O$ $[M]^+$ 160.0888; found 160.0886. NMR data were in good agreement with those reported before.[23]

6-Cyclohexyl-4-methylhex-3-en-2-one (11d): The title compound was synthesized in 5.10 mmol scale otherwise as described for **11a** above. *c*-Hexane-TBME (0-5% TBME) was used as eluent for flash chromatography to give **11d** (981 mg, 99%) as a colorless oil, *E*/*Z* ratio 3:1. The NMR data for the major isomer are given. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83–0.92 (m, 2 H, *c*-hex), 1.10–1.21 (m, 4 H, *c*-hex), 1.30–1.35 (m, 2 H, *c*-hex-CH_2), 1.65–1.70 (m, 5 H, *c*-hex), 2.09 (t, *J* = 8.0 Hz, 2 H, *c*-hex-$CH_2C\underline{H}_2$), 2.09 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 2.14 (s, 3 H, $COCH_3$), 6.04 (q, *J* = 1.3 Hz, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.3 ($\underline{C}H_3C$=), 26.3 (*c*-hex), 26.6 (*c*-hex), 31.7 ($CO\underline{C}H_3$), 33.3 (*c*-hex), 35.3 (*c*-hex-$\underline{C}H_2$), 37.4 (*c*-hex), 38.7 (*c*-hex-$CH_2\underline{C}H_2$), 123.3 (=CH), 159.4 (C=), 198.8 (CO) ppm. MS (EI): *m*/*z* (%) = 194 (67) $[M]^+$, 179 (32), 151 (100). HRMS (EI) calcd. for $C_{13}H_{22}O$ $[M]^+$ 194.1671; found 194.1667.

4-Methyl-6-(naphthalen-1-yl)hex-3-en-2-one (11e): The title compound was synthesized in 10.0 mmol scale otherwise as described for **11a** above. EtOAc-hexane (0-5% EtOAc) was used as eluent for flash chromatography to give **11e** (2.36 g, 99%) as a colorless oil, *E*/*Z* ratio 3:1. The NMR data for the major isomer are given. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, $COCH_3$), 2.25 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 2.52–2.56 (m, 2 H, CH_2C=), 3.21 (m, 2 H, $ArCH_2$), 6.07 (q, *J* = 1.3 Hz, 1 H, =CH), 7.29 (d, *J* = 7.2 Hz, 1 H, Ar), 7.40 (dd, *J* = 8.2, 7.0 Hz, 1 H, Ar), 7.47–7.56 (m, 2 H, Ar), 7.73 (d, *J* = 8.1 Hz, 1 H, Ar), 7.87 (d, *J* = 8.0 Hz, 1 H, Ar), 8.01 (d, *J* = 8.2 Hz, 1 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4 ($\underline{C}H_3C$=), 31.1 ($CO\underline{C}H_3$), 31.7 ($Ar\underline{C}H_2$), 42.1 ($\underline{C}H_2C$=), 123.3 (CH in Ar), 123.9 (=CH), 125.5 (CH in Ar), 125.5 (CH in Ar), 125.9 (CH in Ar), 125.9 (CH in Ar), 126.9 (CH in Ar), 128.9 (CH in Ar), 131.5 (C in Ar), 133.8 (C in Ar), 137.0 (C in Ar), 157.2 (C=), 198.7 (CO) ppm. MS (EI): *m*/*z* (%) = 238 (22) $[M]^+$, 223 (9), 195 (18), 141 (100), 83 (7). HRMS (EI) calcd. for $C_{17}H_{18}O$ $[M]^+$ 238.1358; found 238.1361.

(*R*,*E*)-4-Methyl-6-phenylhex-3-en-2-ol (12a): Oxazaborolidine-borane complex **13** (253 mg, 0.870 mmol) was added to dry THF (5 mL) under Ar-atm. The solution was cooled to -78 °C and ketone **11a** (109 mg, 0.580 mmol), freshly isolates as pure *E*-isomer, was added. After addition of the ketone, the solution was immediately placed in a water / ethyleneglycol bath at -20 ºC and stirred for 1h. The reaction mixture was quenched with careful addition of MeOH (2 mL) at -20 ºC. When evolution of H_2-gas no longer could be observed, the reaction mixture was warmed to ambient temperatures and stirred for an additional 20 min. The reaction mixture was concentrated under reduced pressure and MeOH (10 mL) was added. The reaction mixture was again concentrated under reduced pressure and the crude product was purified by flash chromatography eluting with EtOAc-hexane (0-20% EtOAc) to give **12a** (96 mg, 87%) as a colorless oil. $[\alpha]^{20}_D$ = +20.5 (*c* = 1.1, $CHCl_3$, 96% ee) [lit. (*S*,*E*) **12a**[43] $[\alpha]^{20}_D$ = -11.0 (*c* = 2.05, $CHCl_3$, 98% ee)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.30 (br s, 1 H, OH), 1.72 (s, 3 H, CH_3C=), 2.18–2.34 (m, 2 H, CH_2Ph), 4.47–4.62 (m, 1 H, CHO), 5.17–5.20 (m, 1 H, CH=), 7.15–7.19 (m, 3 H, Ph), 7.25–7.29 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.7 ($\underline{C}H_3C$=), 23.7 (CH_3), 34.4 (CH_2Ph), 41.4 (CH_2), 64.8 (OCH), 126.0 (CH in Ph), 128.4 (2× CH in Ph), 128.5 (2× CH in Ph), 129.8 (CH=), 137.0 (C=), 142.1 (C in Ph) ppm. MS (EI): *m*/*z* (%) = 190 (2) $[M]^+$, 172 (25), 157 (18), 132 (35), 129 (11), 91 (100), 85 (49), 65 (13). HRMS (EI) $C_{13}H_{18}O$ requires 190.1358, found 190.1362. HRMS (EI) calcd. for $C_{13}H_{18}O$ $[M]^+$ 190.1358; found 190.1362. NMR data were in good agreement with those reported for (*S*,*E*) **12a**.[43]

(*R*,*E*)-4-Methyl-5-phenylpent-3-en-2-ol (12b): The title compound was synthesized in 1.21 mmol scale otherwise as described for **12a** above. EtOAc-hexane (0-20% EtOAc) was used as eluent for flash chromatography to give **12b** (152 mg, 71%) as a colorless oil, *E*/*Z* ratio 33:1. $[\alpha]^{20}_D$ = +21.0 (*c* = 0.10, $CHCl_3$, 92% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (d, *J* = 6.3 Hz, 3 H, $CHC\underline{H}_3$), 1.60 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 3.27 (s, 2 H, $PhCH_2$), 4.52–4.64 (m, 1 H, $C\underline{H}OH$), 5.31 (dd, *J* = 8.5, 1.3 Hz, 1 H, =CH), 7.06–7.36 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 ($CH\underline{C}H_3$), 23.6 ($\underline{C}H_3C$=), 46.0 ($PhCH_2$), 64.8 (CHOH), 126.1 (=CH), 128.3 (CH in Ph), 128.9 (2× CH in Ph), 131.0 (2× CH in Ph) 136.8 (C=), 139.5 (C in Ph) ppm. MS (EI): *m*/*z* (%) = 161 (4) $[M - CH_3]^+$, 158 (18), 143 (63), 118 (72), 91 (66), 85 (100). HRMS (ESI) calcd. for $C_{12}H_{16}O$ $[M + Na]^+$ 199.1099; found 199.1102. NMR data were in good agreement with those reported for *rac*. (*E*)-**12b**.[44]

(*R*,*E*)-4-Phenylpent-3-en-2-ol (12c): The title compound was synthesized in 4.47 mmol scale otherwise as described for **12a** above. EtOAc-hexane (0-25% EtOAc) was used as eluent for flash chromatography to give **12c** (729 mg, 98%) as a colorless oil. $[\alpha]^{20}_D$ = +28.5 (*c* = 1.0, $CHCl_3$, 94% ee) [lit.[45] $[\alpha]_D$ = +30.6 (*c* = 1.9, EtOH, 98% ee); lit.[46] $[\alpha]^{23}_D$ = +26.9 (*c* = 1.9, EtOH, 98% ee)]. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.33 (d, *J* = 6.3 Hz, 3 H, $CHC\underline{H}_3$), 1.52 (s, 1 H, OH), 2.09 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 4.70–4.79 (m, 1 H, $C\underline{H}OH$), 5.79 (dq, *J* = 8.3, 1.3, Hz, 1 H, =CH), 7.22–7.33 (m, 3 H, Ph), 7.37–7.40 (m, 2 H, Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 16.1 ($\underline{C}H_3C$=), 23.5 ($CH\underline{C}H_3$), 65.2 (CHOH), 125.8 (2× CH in Ph), 127.2 (CH in Ph), 128.2 (2× CH in Ph), 131.9 (=CH), 136.2 (C=), 142.9 (C in Ph) ppm. MS (EI): *m*/*z* (%) = 162 (14) $[M]^+$, 147 (100), 129 (65). HRMS (EI) calcd. for $C_{11}H_{14}O$ $[M]^+$ 162.1045; found 162.1044. NMR data were in good agreement with those reported before.[45,46]

(*R*,*E*)-6-Cyclohexyl-4-methylhex-3-en-2-ol (12d): The title compound was synthesized in 0.263 mmol scale otherwise as described for **12a** above. EtOAc-hexane (0-20% EtOAc) was used as eluent for flash chromatography to give **12d** (45.8 mg, 89%) as a colorless oil. $[\alpha]^{20}_D$ = +11.8 (*c* = 0.1, $CHCl_3$, 93% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86–0.95 (m, 2 H, *c*-hex), 1.14–1.33 (m, 6 H, *c*-hex, *c*-hex-CH_2), 1.25 (d, *J* = 6.2 Hz, 3 H, $CHC\underline{H}_3$), 1.62–1.77 (m, 5 H, *c*-hex), 1.69 (d, *J* = 1.3 Hz, 3 H, $C\underline{H}_3C$=), 2.00 (t, *J* = 8.0 Hz, 2 H, $C\underline{H}_2C$=), 4.56–4.63 (m, 1 H, $C\underline{H}OH$), 5.22 (dq, *J* = 8.5, 1.3 Hz, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.4 ($\underline{C}H_3C$=), 23.7 ($CH\underline{C}H_3$), 26.38 (*c*-hex), 26.39 (*c*-hex), 26.7 (*c*-hex), 33.3 (*c*-hex), 33.4 (*c*-hex), 35.5 (*c*-hex-$\underline{C}H_2$), 36.8 ($\underline{C}H_2C$=), 37.5 (*c*-hex), 64.8 (CHOH), 128.6 (=CH), 138.5 (C=) ppm. MS (ESI): *m*/*z* (%) = 219 (100) $[M + Na]^+$. HRMS (ESI) calcd. for $C_{13}H_{24}O$ $[M + Na]^+$ 219.1725; found 219.1728.

(*R,E*)-4-Methyl-6-(naphthalen-1-yl)hex-3-en-2-ol (12e): The title compound was synthesized in 0.764 mmol scale otherwise as described for **12a** above. EtOAc-hexane (0-15% EtOAc) was used as eluent for flash chromatography to give **12e** (163 mg, 89%) as a colorless oil. $[\alpha]^{20}_D$ = +13.1 (*c* = 1.0, $CHCl_3$, 88% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (d, *J* = 6.3 Hz, 3 H, CHC$\underline{H}_3$), 1.78 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 2.40 (t, *J* = 8.2 Hz, 2 H, CH_2C=), 3.17 (t, *J* = 8.2 Hz, 2 H, ArCH_2), 4.47–4.66 (m, 1 H, CHOH), 5.21 (dq, *J* = 8.6, 1.3 Hz, 1 H, =CH), 7.29 (dd, *J* = 7.2, 1.2 Hz, 1 H, Ar), 7.37 (t, *J* = 7.8 Hz, 1 H, Ar), 7.42–7.54 (m, 2 H, Ar), 7.70 (d, *J* = 8.2 Hz, 1 H, Ar), 7.84 (dd, *J* = 7.8, 1.5 Hz, 1 H, Ar), 8.01 (dd, *J* = 8.2, 1.5 Hz, 1 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.7 ($\underline{C}H_3$C=), 23.6 (CH$\underline{C}H_3$), 31.5 (Ar$\underline{C}H_2$), 40.5 ($\underline{C}H_2$C=), 64.8 (CHOH), 123.6 (CH in Ar), 125.4 (CH in Ar), 125.5 (CH in Ar), 125.8 (CH in Ar), 125.9 (CH in Ar), 126.7 (CH in Ar), 128.8 (CH in Ar), 129.6 (=CH), 131.8 (C in Ar), 133.9 (C in Ar), 137.1 (C=), 138.1 (C in Ar) ppm. MS (ESI): *m*/*z* (%) = 263 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{17}H_{20}O$ [M + Na]$^+$ 263.1412; found 263.1420.

General procedure for the reduction of ketones 11 with catalytic amounts of oxazaborolidine-borane complex 13:

Oxazaborolidine-borane complex **13** (385 mg, 1.32 mmol) was dissolved in dry THF (3 mL) under Ar-atm. and cooled to -20 ºC. Ketone **11**, freshly isolates as pure *E*-isomer, (6.62 mmol, in 4 mL THF) and BH_3•SMe_2 (0.314 mL, 3.31 mmol in 4 mL THF) were simultaneously added over a period of 2 h using a syringe pump. After the addition was completed, the mixture was stirred for 1 h and quenched with careful addition of MeOH (10 mL) at -20 ºC. When evolution of H_2-gas no longer could be observed, the reaction mixture was warmed to ambient temperatures and stirred for an additional 20 min. The reaction mixture was concentrated under reduced pressure and MeOH (10 mL) was added. The reaction mixture was again concentrated under reduced pressure and the crude product was purified by flash chromatography. The yields and % ee are given in Table 2.

(*S,E*)-2,2,2-trichloro-*N*-(3-methyl-1-phenylhex-4-en-3-yl)acetamide (15): 1,8-Diazabicyclo[5.4.0]undec-7-ene (0.0280 mL, 0.187 mmol) was added to a solution of compound **12a** (176 mg, 0.926 mmol) in CH_2Cl_2 (5 mL) under Ar-atm. The mixture was cooled to 0 ºC and trichloroacetonitrile (0.140 mL, 1.40 mmol) was added over a period of 5 min. After stirring for 1 h, the mixture was concentrated under reduced pressure and the crude trichloroacetimidate was filtered through a short plug (4 cm) of silica, eluting with 2% EtOAc in hexanes (40 mL). Solvents were evaporated under reduced pressure and the residue was dissolved in xylenes (20 mL). Na_2CO_3 (19.6 mg, 0.185 mmol) was added and the mixture was stirred for 20 h under Ar-atm. at 130 ºC. The mixture was concentrated under reduced pressure and the crude product was purified by flash chromatography eluting with EtOAc-hexanes (0-15% EtOAc) to give **15** (65.8 mg, 21%) as a pale yellow wax. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53 (s, 1 H, CH_3), 1.75 (d, *J* = 5.1 Hz, 3 H, CH_3), 2.05–2.25 (m, 2 H, CH_2), 2.55–2.59 (m, 2 H, C$\underline{H}_2$Ph), 5.62–5.66 (m, 2 H, CH=CH), 7.14–7.17 (m, 3 H, Ph), 7.24–7.28 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9 ($\underline{C}H_3$CH=), 24.5 (CH_2Ph), 30.5 (CH_3), 40.8 (CH_2), 58.3 (CN), 93.3 (CCl_3), 124.9 ($CH_3\underline{C}H$=), 126.0 (CH in Ph), 128.4 (2× CH in Ph), 128.5 (2× CH in Ph), 134.3 (CH=), 141.5 (C in Ph), 160.1 (CO) ppm. MS (ESI): *m*/*z* (%) = 356 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{15}H_{18}Cl_3NO$ [M + Na]$^+$ 356.0352, found 356.0349.

(*S,E*)-3-Methyl-1-phenylhex-4-en-3-amine (16a): Potassium *tert*-butoxide (371 mg, 3.31 mmol) and finely grounded KOH (92.8 mg, 1.65 mmol) was added to a solution of compound **20a** (239 mg, 0.827 mmol) in THF (5 mL) under Ar-atm. The mixture was heated to 55 ºC and stirred for 18 h. The reaction mixture was concentrated under reduced pressure. Methyl *tert*-butyl ether (5 mL) and water (5 mL) was added and the aqueous phase was extracted with methyl *tert*-butyl ether (3× 5 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give **16a** (148 mg, 95%) as a colorless oil. $[\alpha]^{20}_D$ = +15.6 (*c* = 1.0, $CHCl_3$, 88% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (s, 3 H, CH_3), 1.47 (s, 2 H, NH_2), 1.58–1.89 (m, 5 H, CH_3C= and CH_2), 2.48–2.72 (m, 2 H, CH_2Ph), 5.43–5.68 (m, 2 H, 2× CH=), 7.06–7.40 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8 ($\underline{C}H_3$CH=), 28.9 (CH_2Ph), 30.9 (CH_3), 45.6 (CH_2), 53.0 (CNH_2), 121.6 ($\underline{C}$H=CH_3) 125.6 (CH in Ph), 128.3 (4× CH in Ph), 139.9 C-$\underline{C}$H=), 142.7 (C in Ph) ppm. MS (EI) *m/z* (rel. int.) 147 (17), 131 (13), 129 (11), 122 (14), 105 (69), 91 (100), 77 (35). MS (ESI): *m*/*z* (%) = 190 (100) [M + H]$^+$. HRMS (ESI) calcd. for $C_{13}H_{19}N$ [M + Na]$^+$ 212.1415; found 212.1417.

(*S,E*)-2-Methyl-1-phenylpent-3-en-2-amine (16b): The title compound was synthesized in 0.247 mmol scale otherwise as described for **16a** above to give **16b** (35.4 mg, 82%) as a colorless oil. $[\alpha]^{20}_D$ = +16.5 (*c* = 1.0, $CHCl_3$, 67% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14 (s, 3 H, CCH_3) 1.16 (s, 2 H, NH_2), 1.66 (dd, *J* = 6.3, 1.5 Hz, 3 H, =CHC$\underline{H}_3$), 2.67 (s, 2 H, $PhCH_2$), 5.33–5.46 (m, 1 H, =C$\underline{H}$CH$_3$), 5.55 (dq, *J* = 15.5, 1.5 Hz, 1 H, C$\underline{H}$=CHCH$_3$), 7.11–7.17 (m, 2 H, Ph), 7.18–7.28 (m, 3 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8 ($\underline{C}H_3$CH=), 28.9 (CH_2Ph), 30.9 (CH_3), 45.6 (CH_2), 53.0 (CNH_2), 121.6 ($\underline{C}$H=CH_3) 125.6 (CH in Ph), 128.3 (4× CH in Ph), 139.9 C-$\underline{C}$H=), 142.7 (C in Ph) ppm. MS (EI) *m/z* (rel. int.) 147 (17), 131 (13), 129 (11), 122 (14), 105 (69), 91 (100), 77 (35). MS (ESI): *m*/*z* (%) = 198 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{12}H_{17}N$ [M + Na]$^+$ 198.1259; found 198.1259.

(*R,E*)-2-Phenylpent-3-en-2-amine (16c): The title compound was synthesized in 0.609 mmol scale otherwise as described for **16a** above to give **16c** (89.4 mg, 91%) as a colorless oil. $[\alpha]^{20}_D$ = +29.7 (*c* = 1.0, $CHCl_3$, 80% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 (s, 3 H, CCH_3), 1.59 (s, 2 H, NH_2), 1.70 (dd, *J* = 6.3, 1.5 Hz, 3 H, =CHC$\underline{H}_3$), 5.57 (dq, *J* = 15.5, 6.3 Hz, 1 H, =C$\underline{H}$CH$_3$), 5.72 (dq, *J* = 15.5, 1.5 Hz, 1 H, C$\underline{H}$=CHCH$_3$), 7.17–7.22 (m, 1 H, Ph), 7.27–7.34 (m, 2 H, Ph), 7.43–7.47 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.7 (=CH$\underline{C}$H$_3$), 30.5 (C$\underline{C}$H$_3$), 56.1 (CNH_2), 121.7 (=$\underline{C}$HCH$_3$), 125.5 (2× CH in Ph), 126.3 (CH in Ph), 128.1 (2× CH in Ph), 140.4 ($\underline{C}$H=CHCH$_3$), 148.6 (C in Ph) ppm. MS (ESI): *m*/*z* (%) = 184 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{11}H_{15}N$ [M + Na]$^+$ 184.1102; found 184.1101.

(*S,E*)-1-Cyclohexyl-3-methylhex-4-en-3-amine (16d): The title compound was synthesized in 0.102 mmol scale otherwise as described for **16a** above to give **16d** (19.5 mg, 98%) as a colorless oil. $[\alpha]^{20}_D$ = +12.4 (*c* = 0.9, $CHCl_3$, 77% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79–0.90 (m, 2 H, *c*-hex), 1.08–1.24 (m, 6 H, *c*-hex, *c*-hex-C$\underline{H}_2$), 1.10 (s, 3 H, =CHC$\underline{H}_3$), 1.31–1.40 (m, 2 H, *c*-hex -CH_2C$\underline{H}_2$), 1.58–1.73 (m, 5 H, *c*-hex), 1.66 (d, *J* = 4.7 Hz, 3 H, CCH_3), 5.43–5.46 (m, 4 H, 2× CH= and NH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5 (=CH$\underline{C}$H$_3$), 26.1 (*c*-hex), 26.4 (*c*-hex), 28.4 (C$\underline{C}$H$_3$), 31.5 (*c*-hex-CH_2), 33.1 (*c*-hex), 38.0 (*c*-hex), 40.0 (*c*-hex-CH_2C$\underline{H}_2$), 52.5 (CNH_2), 120.6 (=$\underline{C}$HCH$_3$), 140.2 (C$\underline{C}$H=) ppm. MS (ESI): *m*/*z* (%) = 218 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{13}H_{25}N$ [M + Na]$^+$ 218.1885; found 218.1884.

(*S,E*)-3-Methyl-1-(naphthalen-2-yl)hex-4-en-3-amine (16e): The title compound was synthesized in 0.252 mmol scale otherwise as described for **16a** above to give **16e** (39.9 mg, 89%) as a colorless oil. $[\alpha]^{20}_D$ = +13.5 (*c* = 1.0, $CHCl_3$, 84% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (s, 3 H, CCH_3), 1.47 (s, 2 H, NH_2), 1.73–1.77 (m, 3 H, =CHC$\underline{H}_3$), 1.77–1.85 (m, 2 H, ArCH_2C$\underline{H}_2$), 2.99–3.07 (m, 2 H, ArCH_2), 5.56–5.67 (m, 2 H, 2× CH=), 7.27–7.40 (m, 2 H, Ar), 7.41–7.52 (m, 2 H, Ar), 7.68 (d, *J* = 8.2 Hz, 1 H, Ar), 7.82 (d, *J* = 7.6 Hz, 1 H, Ar), 7.99 (d, *J* = 8.2 Hz, 1 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8 (=CH$\underline{C}$H$_3$), 28.0 (Ar$\underline{C}$H$_2$), 28.9 (C$\underline{C}$H$_3$), 44.9 (Ar$CH_2\underline{C}H_2$), 53.3 (CNH_2), 121.9 (=$\underline{C}$HCH$_3$), 123.7 (CH in Ar), 125.4 (CH in Ar), 125.6 (CH in Ar), 125.7 (CH in Ar), 125.8 (CH in Ar),

126.5 (CH in Ar), 128.8 (CH in Ar), 131.8 (C in Ar), 133.9 (C in Ar), 138.9 (C in Ar), 139.9 (CH=$CHCH_3$) ppm. MS (ESI): *m*/*z* (%) = 262 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{17}H_{21}N$ [M + Na]$^+$ 262.1572; found 262.1569.

Synthesis of compound 16a, alternative 2: A mixture of amide **15** (65.9 mg, 0.197 mmol), NaOH (2 mL, 6M, 12 mmol) and EtOH (3 mL) was stirred at 40 °C for 24 h. The reaction mixture was extracted with diethyl ether (2× 10 mL). The combined organic layers were washed with water (10 mL), dried ($MgSO_4$) and evaporated. The crude product was purified by flash chromatography eluting with EtOH-EtOAc (1:3) to give **16a** (33.1 mg, 89%) as a colorless oil.

(*R,E*)-4-Methyl-6-phenylhex-3-en-2-yl carbamate (17a): Trichloroacetyl isocyanate (0.885 mL, 7.48 mmol) was added over a period of 1 min to a stirred solution of compound **12a** (712 mg, 3.75 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C under Ar-atm. After stirring for 10 min, the mixture was concentrated under reduced pressure. MeOH (10 mL) and aqueous K_2CO_3 (2.0 M, 15 mL) were added and the mixture was stirred 18 h at ambient temperatures. MeOH was removed under reduced pressure and the remaining aqueous residue was extracted with CH_2Cl_2 (3× 30 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure and the crude product was purified by flash chromatography eluting with EtOAc-hexane (0-40% EtOAc) to give **17a** (787 mg, 90%) as colorless crystals, m.p. 54–56 °C. $[\alpha]^{20}_D$ = +13.9 (*c* = 1.0, $CHCl_3$, 96% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (d, *J* = 6.4 Hz, 3 H, $CHCH_3$), 1.75 (s, 3 H, CH_3C=), 2.28 (t, *J* = 8.0 Hz, 2 H, CH_2), 2.64–2.77 (m, 2 H, CH_2Ph), 4.69 (s, 2 H, NH_2), 5.13 (d, *J* = 8.7 Hz, 1 H, CH=), 5.48 (dq, *J* = 8.7, 6.4 Hz, 1 H, OCH), 7.12–7.20 (m, 3 H, Ph), 7.22–7.29 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.8 (CH_3C=), 21.0 ($CHCH_3$), 34.2 (CH_2Ph), 41.2 (CH_2), 68.8 (OCH), 125.3 (CH=), 125.7 (CH in Ph), 128.2 (2× CH in Ph), 128.4 (2× CH in Ph), 138.7 (C in Ph), 156.6 (CO) ppm. MS (EI): *m*/*z* (%) 173 (23) [M - NH_2CO_2]$^+$, 172 (74), 157 (58), 143 (31), 129 (16), 91 (100), 81 (13). MS (ESI): *m*/*z* (%) = 256 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{14}H_{19}NO_2$ [M + Na]$^+$ 256.1313; found 256.1318.

(*R*)-4-Methyl-5-phenylpent-3-en-2-yl carbamate (17b): The title compound was synthesized in 0.811 mmol scale otherwise as described for **17a** above. EtOAc-hexane (0-40% EtOAc) was used as eluent for flash chromatography to give **17b** (165 mg, 93%) as colorless crystals, *E*/*Z* ratio 20:1, m.p. 62–64 °C. $[\alpha]^{20}_D$ = +26.5 (*c* = 0.98, $CHCl_3$, 92% ee), The NMR data for the major isomer are given. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (d, *J* = 6.4 Hz, 3 H, $CHCH_3$), 1.64 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 3.28 (s, 2 H, $PhCH_2$), 4.53 (br s, 2 H, NH_2), 5.24 (dd, *J* = 8.6, 1.3 Hz, 1 H, =CH), 5.49 (dq, *J* = 8.6, 6.3 Hz, 1 H, OCH), 7.11–7.30 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.5 ($CHCH_3$), 21.1 (CH_3C=), 45.9 ($PhCH_2$), 68.9 (CHO), 126.1 (=CH), 126.8 (CH in Ph), 128.3 (2× CH in Ph), 128.9 (2× CH in Ph), 138.5 (C=), 139.3 (C in Ph), 156.4 (CO) ppm. MS (ESI): *m*/*z* (%) = 242 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{13}H_{17}NO_2$ [M + Na]$^+$ 242.1157; found 242.1155.

(*R,E*)-4-Phenylpent-3-en-2-yl carbamate (17c): The title compound was synthesized in 5.67 mmol scale otherwise as described for **17a** above. EtOAc-hexane (0-40% EtOAc) was used as eluent for flash chromatography to give **17c** (834 mg, 86%) as colorless crystals, m.p. 85–88 °C. $[\alpha]^{20}_D$ = +33.6 (*c* = 1.0, $CHCl_3$, 94% ee). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.36 (d, *J* = 6.3 Hz, 3 H, $CHCH_3$), 2.12 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 4.59 (s, 2 H, NH_2), 5.61–5.69 (m, 1 H, CHO), 5.71 (dq, *J* = 8.7, 1.3, Hz, 1 H, =CH), 7.22–7.32 (m, 3 H, Ph), 7.35–7.40 (m, 2 H, Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 16.4 (CH_3C=), 21.0 ($CHCH_3$), 69.1 (CHO), 125.9 (2× CH in Ph), 127.3 (CH in Ph), 127.6 (=CH), 128.2 (2× CH in Ph), 137.9 (C=), 142.7 (C in Ph), 156.4 (CO) ppm. MS (EI): *m*/*z* (%) = 289 (0.2) [M]$^+$, 233 (12), 184 (16), 173 (11), 172 (18), 157 (10), 128 (100), 91 (22), 84 (42). HRMS (ESI) calcd. for $C_{12}H_{15}NO_2$ [M + Na]$^+$ 228.1000; found 228.0994.

(*R,E*)-6-Cyclohexyl-4-methylhex-3-en-2-yl carbamate (17d): The title compound was synthesized in 1.62 mmol scale otherwise as described for **17a** above. EtOAc-hexane (0-40% EtOAc) was used as eluent for flash chromatography to give **17d** (341 mg, 88%) as colorless crystals, m.p. 51–54 °C. $[\alpha]^{20}_D$ = +15.2 (*c* = 1.0, $CHCl_3$, 93% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79–0.91 (m, 2 H, *c*-hex), 1.09–1.29 (m, 6 H, *c*-hex, *c*-hex-CH_2), 1.25 (d, *J* = 6.2 Hz, 3 H, $CHCH_3$), 1.59–1.72 (m, 5 H, *c*-hex), 1.68 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 1.97 (t, *J* = 8.0 Hz, 2 H, CH_2C=), 4.48 (br s, 2 H, NH_2), 5.12 (dd, *J* = 8.8, 1.3 Hz, 1 H, =CH), 5.47 (m, 1 H, OCH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.7 (CH_3C=), 21.1 ($CHCH_3$), 26.4 (*c*-hex), 26.4 (*c*-hex), 26.7 (*c*-hex), 33.3 (*c*-hex), 33.4 (*c*-hex), 35.4 (*c*-hex-CH_2), 36.8 (CH_2C=), 37.4 (*c*-hex), 69.0 (OCH), 124.3 (=CH), 140.4 (C=), 156.4 (CO) ppm. MS (ESI): *m*/*z* (%) = 262 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{18}H_{21}NO_2$ [M + Na]$^+$ 306.1470; found 306.1481.

(*R,E*)-4-Methyl-6-(naphthalen-1-yl)hex-3-en-2-yl carbamate (17e): The title compound was synthesized in 0.443 mmol scale otherwise as described for **17a** above. EtOAc-hexane (0-30% EtOAc) was used as eluent for flash chromatography to give **17e** (111 mg, 88%) as colorless crystals, m.p. 66–70 °C. $[\alpha]^{20}_D$ = +11.3 (*c* = 0.55, $CHCl_3$, 88% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (d, *J* = 6.4 Hz, 3 H, $CHCH_3$), 1.82 (d, *J* = 1.3 Hz, 3 H, CH_3C=), 2.41 (t, *J* = 8.0 Hz, 2 H, CH_2C=), 3.04–3.29 (m, 2 H, $ArCH_2$), 4.49 (br s, 2 H, NH_2), 5.17 (d, *J* = 8.5 Hz, 1 H, =CH), 5.43–5.59 (m, 1 H, OCH), 7.28 (d, *J* = 6.8 Hz, 1 H, Ar), 7.36 (t, *J* = 8.2 Hz, 1 H, Ar), 7.41–7.56 (m, 2 H, Ar), 7.69 (d, *J* = 8.2 Hz, 1 H, Ar), 7.83 (d, *J* = 7.8 Hz, 1 H, Ar), 8.01 (d, *J* = 8.2 Hz, 1 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.9 (CH_3C=), 21.0 ($CHCH_3$), 31.5 ($ArCH_2$), 40.5 (CH_2C=), 68.9 (CHO), 123.7 (CH in Ar), 125.3 (CH in Ar), 125.4 (CH in Ar), 125.5 (CH in Ar), 125.8 (CH in Ar), 126.0 (=CH), 126.6 (CH in Ar), 128.8 (CH in Ar), 131.8 (C in Ar), 133.9 (C in Ar), 138.0 (C=), 139.0 (C in Ar), 156.4 (CO) ppm. MS (ESI): *m*/*z* (%) = 306 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{18}H_{21}NO_2$ [M + Na]$^+$ 306.1470; found 306.1481.

(*S,E*)-*tert*-Butyl (3-methyl-1-phenylhex-4-en-3-yl)carbamate (20a): Triethylamine (0.547 mL, 3.93 mmol) was added to a solution of carbamate **17a** (229 mg, 0.983 mmol) in dry CH_2Cl_2 (10 mL) under Ar-atm. The mixture was cooled to -78 ºC and trifluoroacetic anhydride (0.208 mL, 1.47 mmol) was added over a period of 2 min. The reaction mixture was stirred 1 h at -78 ºC and warmed to ambient temperatures. After stirring for 20 min, the reaction mixture was concentrated under reduced pressure. The residue was redissolved in a minimal amount of dry CH_2Cl_2 and filtered through a short silica pad (2 cm), eluting with CH_2Cl_2 (10 mL). *tert*-BuOH (0.937 mL, 9.83 mmol) and $MoCl_2O_2(DMF)_2$ (6.76 mg, 0.0197 mmol) was added under Ar-atm. and the mixture was stirred for 18 h at ambient temperatures. The reaction mixture was concentrated under reduced pressure and the crude product was purified by flash chromatography eluting with EtOAc-hexane (0-10% EtOAc) to give **20a** (239 mg, 84%) as a colorless oil. $[\alpha]^{20}_D$ = +14.3 (*c* = 1.1, $CHCl_3$, 88% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (s, 3 H, CH_3CN), 1.43 (s, 9 H, *t*-Bu), 1.70 (d, *J* = 4.7 Hz, 3 H, CH_3C=), 1.94–2.08 (m, 2 H, CH_2), 2.53 (t, *J* = 8.5 Hz, 2 H, CH_2Ph), 4.53 (s, 1 H, NH), 5.53–5.55 (m, 2 H, 2× CH=), 7.15–7.20 (m, 3 H, Ph), 7.21–7.28 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.6 (CH_3C=), 25.3 (CH_3CN), 28.3 (3× CH_3 in *t*-Bu), 30.4 (CH_2Ph), 41.5 (CH_2), 55.5 (CN), 78.6 (C in *t*-Bu), 122.7 (CH_3C=), 125.5 (CH in Ph), 128.1 (2× CH in Ph), 128.2 (2× CH in Ph), 136.4 (NCCH=), 142.2 (C in Ph), 154.1 (CO) ppm. MS (EI): *m*/*z* (%) = 289 (0.2) [M]$^+$, 233 (12), 184 (16), 173 (11), 172 (18), 157 (10), 128 (100), 91 (22), 84 (42). HRMS (ESI) calcd. for $C_{18}H_{17}NO_2$ [M + Na]$^+$ 289.2042; found 289.2041.

(*S*,*E*)-*tert*-Butyl 2-methyl-1-phenylpent-3-en-2-ylcarbamate (20b): The title compound was synthesized in 0.525 mmol scale otherwise as described for **20a** above. EtOAc-hexane (0-10% EtOAc) was used as eluent for flash chromatography to give **20b** (121 mg, 84%) as a colorless oil. $[\alpha]^{20}_D$ = +15.4 (*c* = 0.30, $CHCl_3$, 67% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 3 H, CH_3CN), 1.48 (s, 9 H, *t*-Bu), 1.72 (dd, *J* = 6.3, 1.6 Hz, 3 H, =CHC$\underline{H}_3$), 2.96 (d, *J* = 13.2 Hz, 1 H, $PhCH_2$), 3.16 (d, *J* = 13.2 Hz, 1 H, $PhCH_2$), 4.40 (br s, 1 H, NH), 5.42–5.53 (m, 1 H, =C$\underline{H}$CH$_3$), 5.66 (dd, *J* = 15.2, 1.6 Hz, 1 H, C$\underline{H}$=CHCH$_3$), 7.14–7.19 (m, 2 H, Ph), 7.21–7.32 (m, 3 H, Ph) ppm. ^{13}C NMR (C100 MHz, $CDCl_3$): δ = 17.8 (=CH$\underline{C}$H$_3$), 25.6 ($\underline{C}$H$_3$CN), 28.5 (3× CH_3 in *t*-Bu), 44.8 ($PhCH_2$), 55.9 (CN), 78.8 (C in *t*-Bu), 123.0 (=$\underline{C}$HCH$_3$), 126.2 (CH in Ph), 127.8 (2× CH in Ph), 130.8 (2× CH in Ph), 136.4 ($\underline{C}$H=CHCH$_3$), 137.5 (C in Ph), 154.5 (CO) ppm. MS (ESI): *m*/*z* (%) = 298 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{17}H_{25}NO_2$ [M + Na]$^+$ 298.1783; found 298.1787.

(*R*,*E*)-*tert*-Butyl 2-phenylpent-3-en-2-ylcarbamate (20c): The title compound was synthesized in 3.77 mmol scale otherwise as described for **20a** above. EtOAc-hexane (0-15% EtOAc) was used as eluent for flash chromatography to give **20c** (868 mg, 88%) as a colorless oil. $[\alpha]^{20}_D$ = +26.1 (*c* = 1.0, $CHCl_3$, 80% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 9 H, *t*-Bu), 1.69 (s, 3 H, CH_3CN), 1.71 (dd, *J* = 6.5, 1.7 Hz, 3 H, =CHC$\underline{H}_3$), 4.93 (s, 1 H, NH), 5.50 (dq, *J* = 15.6, 6.5 Hz, 1 H, =C$\underline{H}$CH$_3$), 5.84 (dd, *J* = 15.6, 1.7 Hz, 1 H, C$\underline{H}$=CHCH$_3$), 7.16–7.22 (m, 1 H, Ph), 7.26–7.32 (m, 1 H, Ph), 7.33-7.37 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8 (=CH$\underline{C}$H$_3$), 27.1 ($\underline{C}$H$_3$CN), 28.3 (3× CH_3 in *t*-Bu), 58.8 (CN), 79.1 (C in *t*-Bu), 124.2 (=$\underline{C}$HCH$_3$), 125.6 (2× CH in Ph), 126.5 (CH in Ph), 128.1 (2× CH in Ph), 136.3 ($\underline{C}$H=CHCH$_3$), 146.1 (C in Ph) 154.8 (CO) ppm. MS (ESI): *m*/*z* (%) = 284 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{16}H_{23}NO_2$ [M + Na]$^+$ 284.1626; found 284.1624.

(*S*,*E*)-*tert*-Butyl 1-cyclohexyl-3-methylhex-4-en-3-ylcarbamate (20d): The title compound was synthesized in 0.829 mmol scale otherwise as described for **20a** above. EtOAc-hexane (0-10% EtOAc) was used as eluent for flash chromatography to give **20d** (163 mg, 67%) as a colorless oil. $[\alpha]^{20}_D$ = +10.5 (*c* = 0.9, $CHCl_3$, 77% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79–0.89 (m, 2 H, *c*-hex), 1.05–1.21 (m, 6 H, *c*-hex, *c*-hex-CH_2), 1.29 (s, 3 H, CH_3CN), 1.40 (s, 9 H, *t*-Bu), 1.52–1.70 (m, 10 H, *c*-hex, *c*-hex-$CH_2C\underline{H}_2$, =CHC$\underline{H}_3$), 4.43 (br s, 1 H, NH), 5.44–5.47 (m, 2 H, 2× CH=) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9 (=CH$\underline{C}$H$_3$), 25.2 ($\underline{C}$H$_3$CN), 26.4 (*c*-hex), 26.7 (*c*-hex), 28.5 (3× CH_3 in *t*-Bu), 31.4 (*c*-hex-CH_2), 33.5 (*c*-hex), 37.5 (*c*-hex), 38.0 (*c*-hex-$CH_2\underline{C}H_2$), 55.7 (CN), 78.7 (C in *t*-Bu), 122.5 (=$\underline{C}$HCH$_3$), 136.9 (C$\underline{C}$H=), 154.5 (CO) ppm. MS (ESI): *m*/*z* (%) = 318 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{18}H_{33}NO_2$ [M + Na]$^+$ 318.2409; found 318.2406.

(*S*,*E*)-*tert*-Butyl 3-methyl-1-(naphthalen-1-yl)hex-4-en-3-ylcarbamate (20e): The title compound was synthesized in 0.435 mmol scale otherwise as described for **20a** above. EtOAc-hexane (0-10% EtOAc) was used as eluent for flash chromatography to give **20e** (128 mg, 87%) as a colorless oil. $[\alpha]^{20}_D$ = +11.2 (*c* = 1.37, $CHCl_3$, 84% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (s, 3 H, CH_3CN), 1.47 (s, 9 H, *t*-Bu), 1.75 (d, *J* = 5.0 Hz, 3 H, =CHC$\underline{H}_3$), 2.06–2.20 (m, 2 H, $ArCH_2C\underline{H}_2$), 3.00 (t, *J* = 8.6 Hz, 2 H, $ArCH_2$), 4.63 (br s, 1 H, NH), 5.59–5.67 (m, 2 H, 2× CH=), 7.30 (d, *J* = 7.0 Hz, 1 H, Ar), 7.36 (t, *J* = 7.6 Hz, 1 H, Ar), 7.41–7.52 (m, 2 H, Ar), 7.68 (d, *J* = 8.3 Hz, 1 H, Ar), 7.82 (d, *J* = 7.9 Hz, 1 H, Ar), 8.03 (d, *J* = 8.3 Hz, 1 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9 (=CH$\underline{C}$H$_3$), 25.6 ($\underline{C}$H$_3$CN), 27.8 (Ar$\underline{C}$H$_2$), 28.5 (3× CH_3 in *t*-Bu), 40.9 ($ArCH_2\underline{C}H_2$), 55.9 (CN), 79.0 (C in *t*-Bu), 123.2 (=$\underline{C}$HCH$_3$), 123.9 (CH in Ar), 125.4 (CH in Ar), 125.6 (CH in Ar), 125.8 (CH in Ar), 126.0 (CH in Ar), 126.5 (CH in Ar), 128.7 (CH in Ar), 131.9 (C in Ar), 133.9 (C in Ar), 136.6 ($\underline{C}$H=CHCH$_3$), 138.6 (C in Ar), 154.4 (CO) ppm. MS (ESI): *m*/*z* (%) = 362 (100) [M + Na]$^+$. HRMS (ESI) calcd. for $C_{22}H_{29}NO_2$ [M + Na]$^+$ 362.2096; found 362.2094.

Synthesis of compound 20a, alternative 2: Triethylamine (0.451 mL, 3.24 mmol) was added to a solution of carbamate **17a** (0.189 g, 0.809 mmol) in dry CH_2Cl_2 (5 mL) under Ar-atm. The mixture was cooled to -78 ºC and trifluoroacetic anhydride (0.171 mL, 1.21 mmol) was added over a period of 2 min. The reaction mixture was stirred 1 h at -78 ºC and warmed to ambient temperatures. After stirring for 20 min, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in a minimal amount of dry CH_2Cl_2 and filtered through a short silica pad (2 cm), eluting with CH_2Cl_2 (10 mL). The mixture was concentrated under reduced pressure and the crude isocyanate was dissolved THF (5 mL) and cooled to -15 ºC. *tert*-BuOH (3.60 mL, 37.7 mmol) and lithium *tert*-butoxide (0.890 mL, 1M in THF) was added and the mixture was stirred for 2 h. Sat. aq. NH_4Cl (20 mL) was added and the mixture was extracted with EtOAc (3× 20 mL). The combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography eluting with EtOAc-hexane (0-10% EtOAc) to give **20a** (199 mg, 85%) as a colorless oil.

Synthesis of compound 20a, alternative 3: Carbamate **17a** (784 mg, 3.36 mmol), triphenylphosphine (1.32 g, 5.04 mmol) and triethylamine (938 mg, 6.72 mmol) was subsequently added to dry CH_2Cl_2 (18 mL) under Ar-atm. and the solution was cooled to -28 °C. Carbon tetrabromide (1.67 g, 5.04 mmol) dissolved in CH_2Cl_2 (2 mL) was added dropwise over a period of 1 min and the solution was stirred at -28 °C for 1 h. Heptane (50 mL) was added and the suspension was warmed to ambient temperature. Aq. $KHSO_4$ (1 M, 20 mL) was added and the mixture was vigorously stirred for 20 min. The phases were separated and the aqueous phase was extracted with heptane (2× 10 mL). The combined organic phases were dried ($MgSO_4$), concentrated under reduced pressure to ca. 2/3 of its original volume and filtered through a plug of cotton. The solution was further concentrated to give the intermediate isocyanate as a pale yellow oil. THF (15 mL) and *tert*-BuOH (5 mL) was added and the solution was cooled to -15 ºC. Lithium *tert*-butoxide (3.36 mL, 1 M in THF) was added and the solution was stirred for 1 h. Sat. aq. NH_4Cl (20 mL) and water (10 mL) were added and the mixture was extracted with Et_2O (30 mL) and CH_2Cl_2 (3× 20 mL). The combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash column chromatography eluting with EtOAc-hexane (0-30 % EtOAc) to give **20a** (651 mg, 67%) as a colorless oil.

(*S*,*E*)-Methyl (3-methyl-1-phenylhex-4-en-3-yl)carbamate (21): Carbamate **17a** (224 mg, 0.961 mmol) and triphenylphosphine (755 mg, 2.88 mmol) were dissolved in toluene (10 mL) and concentrated under reduced pressure. The resulting solid was dissolved in dry CH_2Cl_2 (15 mL), and triethylamine (582 mg, 5.76 mmol) was added. The solution was cool to 0 °C under Ar-atm. and carbon tetrabromide (956 mg, 2.88 mmol) in CH_2Cl_2 (10 mL) was added. The solution was stirred at 0 °C for 20 min. Tributyltin methoxide (302 µL, 1.06 mmol) in MeOH (9 mL) was added and the solution was stirred for 12 h at ambient temperature. The reaction mixture was diluted with Et_2O (50 mL) and washed with aq. $KHSO_4$ (1 M, 2× 20 mL), sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL). The solution was concentrated under reduced pressure and the resulting residue was dissolved in a solution of KF in acetonitrile (1 M, 15 mL). After stirring for 1 h, the suspension was diluted with Et_2O (50 mL) and filtered. The filtrate was washed with water (2× 10 mL) and brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by flash column chromatography eluting with EtOAc-hexane (0-30% EtOAc) to give **21** (651 mg, 67%) as a colorless oil. $[\alpha]^{20}_D$ = +12.1 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (s, 3 H, CH_3CN), 1.72 (d, *J* = 4.1 Hz, 3 H, CH_3C=), 1.95–2.10 (m, 2 H, CH_2), 2.55 (t, *J* = 8.6 Hz, 2 H, CH_2Ph), 3.61 (s, 3 H, CH_3O), 4.68 (s, 1 H, NH), 5.54-5.59 (m, 2 H, 2× CH=), 7.13–7.18 (m, 3 H, Ph), 7.21–7.29 (m, 2 H, Ph)

ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9 ($\underline{C}H_3C$=), 25.1 ($\underline{C}H_3CN$), 30.5 (CH_2Ph), 41.6 (CH_2), 51.6 (CH_3O), 55.9 (CN), 123.6 ($CH_3\underline{C}$=), 125.7 (CH in Ph), 128.3 (2× CH in Ph), 128.4 (2× CH in Ph), 136.0 (NC$\underline{C}$H=), 142.2 (C in Ph), 155.2 (CO) ppm. MS (EI): *m*/*z* (%) = 247 (1) $[M]^+$, 172 (17), 157 (15), 142 (100), 129 (6), 110 (10), 99 (5), 91 (30). HRMS (EI) calcd. for $C_{15}H_{21}NO_2$ $[M]^+$ 247.1572; found 247.1572.

(*R,E*)-3-Methyl-1-phenylhex-4-en-3-ylcarbamic acid 9*H*-fluoren-9-ylmethyl ester (22): Compound **16a** (68.0 mg, 0.359 mmol) was added to a mixture of CH_2Cl_2 (10 mL) and sat. aq. $NaHCO_3$ (10 mL). 9-Fluorenylmethylchloroformate (111 mg, 0.431 mmol) was added and the reaction mixture was stirred at ambient temperature for 18 h. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2× 10 mL). The combined organic extracts were dried ($MgSO_4$), concentrated under reduced pressure and the crude product was purified by flash column chromatography eluting with EtOAc-hexane (0-30% EtOAc) to give **22** (138 mg, 93%) as a colorless oil. $[\alpha]^{20}_D$ = +8.2 (*c* = 0.99, $CHCl_3$, 72% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 3 H, CCH_3), 1.70 (s, 3 H, =$CHCH_3$), 1.92–2.10 (m, 2 H, $PhCH_2C\underline{H}_2$), 2.44–2.61 (m, 2 H, $PhCH_2$), 4.19 (t, *J* = 6.6 Hz, 1 H, $OCH_2C\underline{H}$ in Fmoc), 4.38 (d, *J* = 6.6 Hz, 2 H, CH_2 in Fmoc), 4.72 (s, 1 H, NH), 5.45–5.61 (m, 2 H, 2× CH=), 7.09–7.19 (m, 3 H, Ph), 7.20–7.33 (m, 4 H, Ph and Fmoc), 7.37 (t, *J* = 7.3 Hz, 2 H, Fmoc), 7.58 (d, *J* = 7.3 Hz, 2 H, Fmoc), 7.74 (d, *J* = 7.5 Hz, 2 H, Fmoc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9 (=$CH\underline{C}H_3$), 25.1 ($C\underline{C}H_3$), 30.5 ($PhCH_2$), 41.6 ($PhCH_2\underline{C}H_2$), 47.4 ($OCH_2\underline{C}H$ in Fmoc), 56.0 (CNH), 65.9 ($O\underline{C}H_2CH$ in Fmoc), 119.9 (2× CH in Fmoc), 123.7 (=$\underline{C}HCH_3$), 125.0 (2× CH in Fmoc), 125.8 (CH in Ph), 127.0 (2× CH in Fmoc), 127.6 (2× CH in Fmoc), 128.3 (CH in Ph), 128.4 (CH in Ph), 135.9 ($\underline{C}H$=$CHCH_3$), 141.3 (C in Fmoc), 142.1 (C in Ph), 144.1 (C in Fmoc), 154.5 (CO) ppm. MS (EI): *m*/*z* (%) = 196 (24), 178 (24), 166 (74), 165 (100), 139 (11), 115 (10). HRMS (ESI) calcd. for $C_{28}H_{29}NO_2$ $[M + Na]^+$ 434.2096; found 434.2095.

(*S*)-2-({[(9*H*-Fluoren-9-yl)methoxy]carbonyl}amino)-2-methyl-4-phenylbutanoic acid (23): Compound **22** (51.7 mg, 0.126 mmol, 72% ee) was dissolved in dry CH_2Cl_2 (10 mL) and cooled to -78 °C. Ozone was bubbled through the solution until a blue color appeared. The solution was purged with nitrogen until the color disappeared, before dimethylsulfide (0.92 mL, 12.9 mmol) was added. After additional 30 min. at -78 °C, the solution was warmed to ambient temperature and the solvent was removed under reduced pressure. The residue was dissolved in *tert*-BuOH (5 mL) and 2-methyl-2-butene (0.5 mL). Sodium chlorite (114 mg, 1.26 mmol) and sodium dihydrogenphosphate (45.4 mg, 0.378 mmol) dissolved in water (2 mL) was added over a period of 5 min. and the reaction mixture was stirred at ambient temperature for 2 h. Subsequently, aqueous HCl (0.1 M, 5 mL) was added and the mixture was extracted with methyl *tert*-butyl ether (3× 10 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), concentrated under reduced pressure and the crude product was purified by flash column chromatography eluting with AcOH-MeOH-CH_2Cl_2 (1:2:97) to give **23** (38.4 mg, 74%) as a colorless oil. $[\alpha]^{20}_D$ = +11.7 (*c* = 1.07, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.65 (s, 3 H, CH_3), 2.20 (br s, 1 H, $PhCH_2C\underline{H}_2$), 2.49 (br s, 2 H, $PhCH_2$), 2.59 (br s, 1 H, $PhCH_2C\underline{H}_2$), 4.21 (t, *J* = 6.4 Hz, 1 H, CH in Fmoc), 4.40 (br s, 2 H, CH_2 in Fmoc), 5.62 (br s, 1 H, NH), 7.09–7.18 (m, 2 H, Ph), 7.20-7.41 (m, 7 H, Ph and Fmoc), 7.58 (d, *J* = 7.4 Hz, 2 H, Fmoc), 7.74 (d, *J* = 7.5 Hz, 2 H, Fmoc) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.5 (CH_3), 30.5 ($PhCH_2$), 38.1 ($PhCH_2\underline{C}H_2$), 47.2 ($\underline{C}HCH_2$ in Fmoc), 59.7 (CN), 66.6 (CH_2 in Fmoc), 120.0 (2× CH in Fmoc), 125.0 (2× CH in Fmoc), 126.0 (CH in Ph), 127.1 (2× CH in Fmoc), 127.7 (2× CH in Fmoc), 128.4 (2× CH in Ph), 128.4 (2× CH in Ph), 140.8 (C in Ph), 141.3 (C in Fmoc), 143.8 (C in Fmoc), 154.6 (CO in Fmoc), 178.3 (COOH) ppm. MS (ESI): *m*/*z* (%) = 438 (100) $[M + Na]^+$. HRMS (ESI) calcd. for $C_{26}H_{25}NO_4$ $[M + Na]^+$ 438.1681; found 438.1679. The spectroscopic data where in good agreement with those reported for the (*R*) enantiomer before.[15a]

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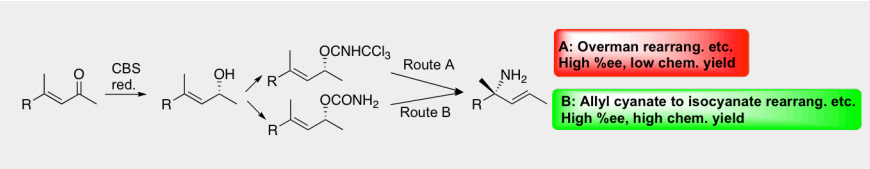

Optically active α,α-disubstituted primary allylamines from allylic alcohols prepared by CBS-reduction, employing either an Overman- or an allyl cyanate to isocyanate rearrangement as a key-step. The target amines were formed in high %ee in both cases, but the chemical yield was substantially higher in the allyl cyanate to isocyanate rearrangement

Asymmetric synthesis

*Martin Hennum, Hege Hortemo Odden, Lise-Lotte Gundersen**

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Rearrangement Reactions leading to Optically Active α,α-Disubstituted Primary Allylamines