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Synthesis of Enantiopure Benzyl Homoallylamines by Indium-Mediated Barbier-Type Allylation Combined with Enzymatic Kinetic Resolution: Towards the Chemoenzymatic Synthesis of N-Containing Heterocycles

Ari Hietanen,[a][‡] Tiina Saloranta,[b][‡] Sara Rosenberg,[b] Evelina Laitinen,[b] Reko Leino,*[b] and Liisa T. Kanerva*[a]

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Barbier-type indium-mediated allylations of different *N*,*N*-(dimethylsulfamoyl)-protected aldimines with a number of allyl bromides followed by high-yielding deprotection afforded allylic amines in good to excellent yields. The racemic amines were then subjected to enzymatic kinetic resolution in order to obtain the corresponding (*S*)-amines and (*R*)-amides. When acyl donors with a terminal double bond were applied in the enzymatic kinetic resolution, the product amide could be converted into unsaturated lactams in a straightforward manner by utilizing ring-closing metathesis. Furthermore, the enantiopure (*S*)-1-phenylbut-3-enylamine was converted into the corresponding diallylamine, which was subjected to ring-closing metathesis to yield a substituted dehydropiperidine mimicking a number of natural products.

Introduction

Chiral benzylamines are important intermediates in the synthesis of biologically and pharmaceutically relevant targets. Thus, the development of synthetic strategies towards such moieties is of considerable academic as well as industrial importance in both fine chemical and pharmaceutical industries. In particular, chiral benzylamines have emerged as fragments in some neuroactive pharmaceutical ingredients. For example, the parasympathomimetic (*S*)-rivastigmine has been adopted in the clinical treatment of dementia associated with Alzheimer's disease.[1] Moreover, the synthesis of N-containing heterocycles such as piperidines,[2] lactams[3] and derivatives thereof is of topical interest due to the frequent occurrence of such moieties in biologically active small molecules, whether of natural or synthetic origin, and peptidomimetics. Figure 1 illustrates representative examples of each of these compound classes.[4]

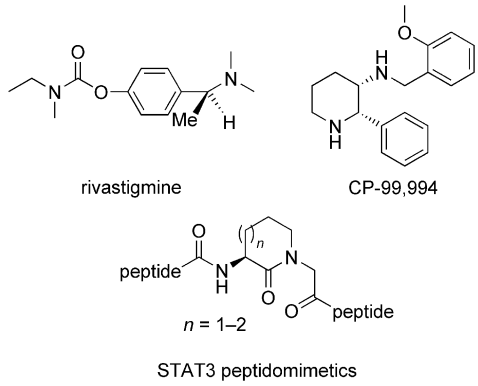

Figure 1. Examples of bioactive chiral benzylamines, piperidines and lactams.

Recently, we briefly described an efficient and high-yielding procedure for the synthesis of racemic homoallylamines by utilization of Barbier-type allylation of an *N*,*N*-dimethylsulfamoyl-protected aldimine followed by subsequent deprotection by transamination.[5] A series of *N*,*N*-dimethylsulfamoyl-protected aldimines have also been utilized in Pd-catalyzed allylations to produce various protected amines in good to excellent yields.[6] In the present work, we further examine the Barbier-type allylation of the *N*,*N*-dimethylsulfamoyl-protected aldimines and extend the product scope to amines with different electronic and steric properties (Figure 2).

Similar homoallylic amines have been synthesized previously in an enantioselective manner by utilizing chiral induction from the protective group,[7a] enantiodifferentiation by addition of cinchona alkaloids,[7b] or in the presence of a chiral ligand in catalytic allylations.[7c] Herein, we report a methodology to produce the enantiomers of bifunctional

[a] Institute of Biomedicine/Department of Pharmacology, Drug Development and Therapeutics/Laboratory of Synthetic Drug Chemistry,
University of Turku, 20014 Turku, Finland
Fax: +358-2-333-7955
E-mail: lkanerva@utu.fi
[b] Laboratory of Organic Chemistry,
Åbo Akademi Univeristy, 20500 Åbo, Finland
Fax: +358-2-215-4866
E-mail: reko.leino@abo.fi
[‡] A. Hietanen and T. Saloranta contributed equally to this work
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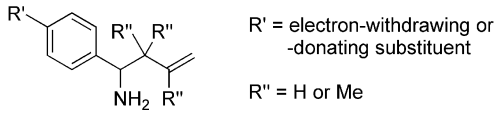


Figure 2. General structure of homoallylamines prepared in present work with variations in electronic and steric properties.

homoallylbenzylamines *rac*-**3a**–**e** (Figure 3) using the lipase-catalyzed *N*-acylation of the more reactive (*R*)-amines in racemates. Racemic 1-phenylbut-3-en-1-amine (*rac*-**3a**) was selected as a model substrate for the enzymatic studies throughout the work.

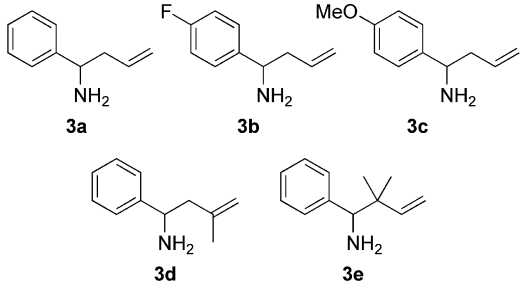
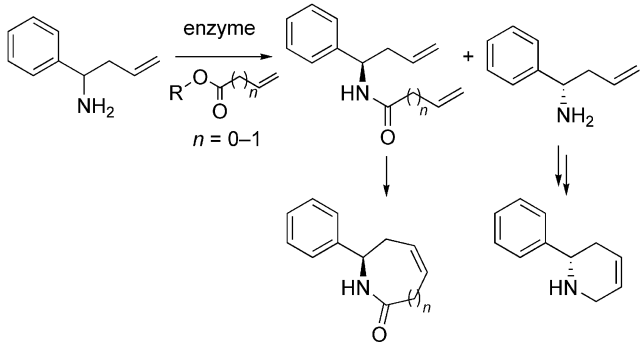


Figure 3. Homoallylbenzylamines prepared in the present work for enzymatic kinetic resolution.

Finally, we have also explored the utilization of the enantiopure homoallylic amines for the synthesis of N-containing heterocycles by olefin metathesis. The approach is schematically illustrated in Scheme 1. By utilization of acyl donors with a terminal double bond, the enzymatically produced (*R*)-amides can be converted into the corresponding unsaturated lactams by ring-closing metathesis, a strategy previously used in the synthesis of lactones.[8] Therefore, this approach directly utilizes the enhanced molecular functionality and increases the attractiveness of the kinetic resolution method. Furthermore, conversion of the enzymatically less reactive (*S*)-amines into the corresponding diallylic compounds provides precursors for ring-closing metathesis to yield substituted dehydropiperidines.



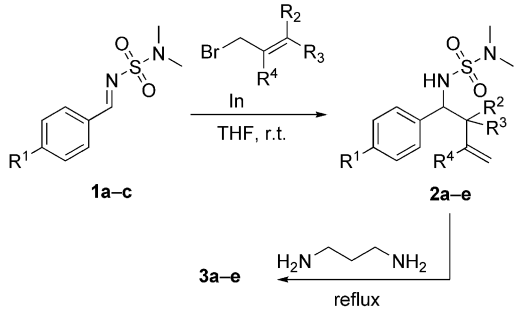
Scheme 1. Synthesis of enantiopure N-containing heterocycles via a chemoenzymatic pathway.

Results and Discussion

Synthesis of Homoallylic Amines

In our previous work, the synthesis of racemic homoallylbenzylamine *rac*-**3a** via Barbier-type allylation of the precursor aldimine was briefly explored.[5] In the present work, the substrate scope of this reaction was successfully extended to cover also substituted benzaldimines with electron-withdrawing (**1b**) and electron-donating (**1c**) *para*-substituents to prepare the racemic amines **3b** and **3c** (Figure 3, Table 1). In addition, sterically demanding allylating agents methallyl bromide and prenyl bromide were utilized to synthesize the products **3d** and **3e**, respectively. The indium-mediated allylations of aldimines **1a**–**c** were performed in anhydrous THF giving full conversions in all cases except with the bulkier prenyl bromide reagent as allylating agent (Table 1, Entry 5, step 1).

Table 1. Synthesis of homoallylic amine series.[a]



Entry	Product	R^1	R^2	R^3	R^4	Conv. [%][b]	Yield [%][c]
1	*rac*-**3a**	H	H	H	H	100/100	71/91
2	*rac*-**3b**	F	H	H	H	100/100	68/68
3	*rac*-**3c**	OMe	H	H	H	100/100	68/90
4	*rac*-**3d**	H	H	H	Me	100/100	65/76
5	*rac*-**3e**	H	Me	Me	H	75/100	27/83

[a] Allylations were performed at room temp. on 4–11-mmol scale with 3 equiv. of indium and allylating agent, respectively. [b] Conversion as determined by ^{1}H NMR spectroscopy (step 1/step 2). [c] Isolated yields (step 1/step 2).

In our previous work,[5] it was shown that the *N*,*N*-dimethylsulfamoyl group is smoothly removed by transamination with 1,3-diaminopropane under conventional reflux conditions. Here, the same protocol was utilized to deprotect all modified substrates **2b**–**e**. The method proved its feasibility and the desired allylic amines **3a**–**e** were obtained in good to excellent yields (Table 1, step 2).

Enzymatic Kinetic Resolution of Homoallylic Amines

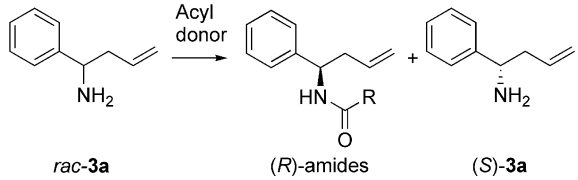
Enzymatic kinetic resolution of racemic amines is typically based on reactions between a primary or, less frequently, a secondary amine and a suitable acyl donor in organic solvents.[9,10] Lipases (E.C. 3.1.1.3) in general, and *Burkholderia cepacia* lipase (as a lipase PS-D preparation on Celite) and *Candida antarctica* lipases A (as adsorbed on Celite in the presence of sucrose[11]) and B (CAL-B as a Novozym 435 preparation) in particular, are useful biocatalysts for the enantioselective *N*-acylation of amino groups since they only rarely can split an amide bond other than

that in β-lactams, and accordingly cause the transformation of the amide back into the amine.[12,13] It has been suggested that the resonance stabilization of normal amide functionalities makes amides stable toward lipases.[13c] Another issue related to amide stability is the intrinsic reactivity of the acyl donor. High enough reactivity is pivotal to enable reasonable reaction rates while too high reactivity can lead to chemical *N*-acylation parallel with the enzymatic one. Moreover, irreversible acyl donors, vinyl and isopropenyl esters (common with alcoholic substrates), are inappropriate with amine substrates due to possible imine formation with acetaldehyde and acetone, tautomerization products from the liberated vinyl and isopropenyl alcohols, respectively.

For developing a procedure for the enzymatic kinetic resolution, *rac*-**3a** (0.1 M) was first subjected to lipase screening (see the lipases in the Exp. Section) using commercial lipase preparations (25 mg mL^{-1}) and ethyl methoxyacetate (5 equiv. corresponding to 6 vol.-% of the acyl donor) in *tert*-butyl methyl ether (TBME) dried with molecular sieves (4 Å). The potential of Subtilisin Carlsberg (a serine protease) and acylase I to acylate *rac*-**3a** was also tested. Acyl activated ethyl methoxyacetate was chosen as it was reported to work well in the CAL-B-catalyzed acylation of amines.[14] The activation is mainly due to a weak hydrogen bond between the β-oxygen atom of the methoxyacetate moiety of the acyl-enzyme intermediate and the amine hydrogen of the reactive amine counterpart on the mechanistic pathway of serine hydrolases.[15] CAL-A was by far the most reactive but virtually a non-enantioselective catalyst while lipase PS-D [$ee^{(R)\text{-amide}}$ = 95% at 30% conversion] and CAL-B [$ee^{(R)\text{-amide}}$ = 92% at 35% conversion] both showed reactivity with relatively good enantioselectivity. Other enzymes in the test set were completely inefficient. A possible chemical background reaction was excluded by performing the reaction under the same conditions except in the absence of an enzyme. However, the ammonium salt between the substrate and methoxyacetic acid (hydrolysis product of the acyl donor) precipitated and lowered the rate and selectivity of the resolution. Changing the solvent from ethers (TBME or diisopropyl ether) to toluene (dried on molecular sieves) more than halved the water content (from more than 90 ppm to about 40 ppm), and precipitation was not visually detectable any more with lipase PS-D. This effect is in accordance with our earlier experience of lipase PS-D causing less hydrolysis of hydrolyzable compounds than CAL-B (Novozym 435) when used in organic solvents,[16] and might explain the better selectivity of lipase PS-D vs. CAL-B.

At this point, attention was paid to the nature of the acyl donor and to the reaction conditions in order to increase reactivity and enantioselectivity. The commonly used alkyl-activated acyl donors, 2,2,2-trifluoroethyl acetate and butanoate, resulted in fast but completely non-selective acylation of *rac*-**3a** (0.1 M) with lipase PS-D (25 mg mL^{-1}) in toluene. The ability of normal esters (6 vol.-%, Entries 1–4) to enantioselectively acylate *rac*-**3a** indicated isopropyl acetate to have some potential (Entry 4) (Table 2). With increasing isopropyl acetate content enantioselectivity increased (Entries 4–7). When ethyl methoxyacetate content was increased, conversion after 3 d was enhanced at the expense of enantioselectivity (Entries 13, 19 and 22). Accordingly, working at low ethyl methoxyacetate content or in neat isopropyl acetate was shown to be favorable. Attempts to neutralize the possibly formed methoxyacetic (Entries 14 and 20) or acetic acid (Entry 8) by performing the reaction in the presence of triethylamine affected the outcome only at high ethyl methoxyacetate contents. Attempts to keep the system dry by adding molecular sieves into the reaction mixture were more productive, and excellent *E* values could be calculated when the reaction proceeded in neat isopropyl acetate (water content 60 ppm) or with ethyl methoxyacetate (6 vol.-%, equals to 5 equiv.) in toluene (water content 40 ppm) (Entries 9 and 15). In addition, considerable reactivity enhancement was gained. In order to further increase reactivity, the enzyme content was increased from 25 mg mL^{-1} to 50 mg mL^{-1} (Entries 11 and 17). Larger amounts of the enzyme did not boost reactivity higher. Increasing the temperature above room temperature negatively affected enantioselectivity with isopropyl acetate (Entries 16–18).

Table 2. Screening of acyl donors (0.5 M) for the acylation of *rac*-**3a** (0.1 M) with lipase PS-D (25 mg mL^{-1}) in toluene at room temperature; reaction time 3 d.



rac-**3a** (*R*)-amides (*S*)-**3a**

Entry	Acyl donor/[vol.-%]	Conv. [%]	$ee^{(R)\text{-amide}}$ [%]	$ee^{(S)\text{-}3}$ [%] (E)[g]
1	ethyl acetate/6	11	10	1
2	ethyl propanoate/6	1	43	<1
3	ethyl butanoate/6	6	2	<1
4	isopropyl acetate/6	3	78	2
5	isopropyl acetate/20	5	87	5
6	isopropyl acetate/50	19	95	23
7	isopropyl acetate/100	31	95	42
8	isopropyl acetate/100[a]	32	95	44
9	isopropyl acetate/100[b]	31	99	45 (200)
10	isopropyl acetate/100[c,d]	38	98	59 (200)
11	isopropyl acetate/100[c]	45	99	82 (200)
12	isopropyl acetate/100[c,e]	48	96	87 (100)
13	ethyl methoxyacetate/6	14	95	16
14	ethyl methoxyacetate/6[a]	17	96	20
15	ethyl methoxyacetate/6[b]	44	99	76 (200)
16	ethyl methoxyacetate/6[c,d]	42	99	73 (200)
17	ethyl methoxyacetate/6[c]	45	99	82 (200)
18	ethyl methoxyacetate/6[c,e,f]	50	97	97 (200)
19	ethyl methoxyacetate/20	29	91	37
20	ethyl methoxyacetate/20[a]	38	94	58
21	ethyl methoxyacetate/20[b]	57	75	99
22	ethyl methoxyacetate/50	34	76	39

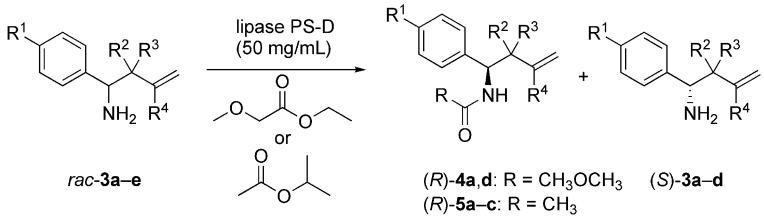
[a] Et_3N (0.1 M) was added. [b] Molecular sieves (4 Å) were added. [c] 50 mg mL^{-1} of lipase PS-D in the presence of molecular sieves (4 Å). [d] Reaction temperature 4 °C. [e] Reaction temperature 48 °C. [f] Reaction time 2 d. [g] *E* given only with clearly excellent enantioselectivity.

With this data available, the preparative-scale kinetic resolution of *rac*-**3a** was performed with ethyl methoxyacetate (6 vol.-%) in toluene in the presence of lipase PS-D (50 mg mL^{-1}) and molecular sieves (4 Å) at 48 °C (Entry 1, Table 3) to afford (*R*)-**4a** and (*S*)-**3a**. The outcome was slightly less satisfactory with $E = 98$ than what was expected on the basis of a small-scale reaction (Entry 18, Table 2). For that reason, the kinetic resolutions of *rac*-**3a**–**c** were next performed in isopropyl acetate in the presence of lipase PS-D (50 mg mL^{-1}) and molecular sieves (4 Å) at room temperature (Entries 2–4, Table 3). While the kinetic resolution of *rac*-**3c** gave the resolution products (*S*)-**3c** and (*R*)-**5c** with excellent enantiopurities after 4 d at 49% conversion, the reactions with substrates **3a** and **3b** slowed down beyond about 30–40% of conversion. For instance, the resolution of *rac*-**3a** was at 46% conversion after 3 d, but 6 more days were required to reach 49% conversion. Lipase PS-D, CAL-B and CAL-A were all unable to acylate *rac*-**3d** and *rac*-**3e** in neat isopropyl acetate. On the other hand, when the acyl donor was changed to ethyl methoxyacetate (20 vol.-% was required) in toluene, acylation of **3d** slowly proceeded in the presence of CAL-B, and after 7 d (*R*)-**4d** was obtained enantiopure (*ee* > 99%) at 31% conversion (Entry 5). *Rac*-**3e** stayed unreacted. The enantiomerically enriched unreacted (*S*)-**3a** (*ee* = 84%), (*S*)-**3b** (*ee* = 48%) and (*S*)-**3d** (*ee* = 44%) were further purified by subjecting them under the kinetic resolution conditions, yielding 99%, 95% and 72% *ee*, respectively. In general, the isolated yields for the unreacted (*S*)-amines stayed somewhat low and the need to further enantiomerically purify the products by repeating the enzymatic acylation lowered the yields. Our efforts to hydrolyze (*R*)-**4a** and (*R*)-**5a** gave also low yields for (*R*)-**3a** due to by-product formation (see Exp. Sect.).

According to the Kazlauskas rule, the (*R*)-enantio-preference was expected for the lipase PS-D in the present *N*-acylations.[17] This was confirmed when (*S*)-**3a** and (*S*)-**3c** were at our hands after the kinetic resolution allowing the sign of the $[\alpha]_D$ values to be compared to those given for the (*S*)-enantiomers in literature.[7c] In order to further support this suggestion, both enantiomers of **3a** were derivatized with (*S*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride [(*S*)-MTPA-Cl] giving a pair of diastereomeric amides that were characterized by ^{1}H NMR spectroscopy. The comparison of the $\Delta\delta$ values further corroborates the reacting stereoisomer of the amine to have the (*R*)-configuration.[18]

To extend the scope of the resolution, we then used ethyl and isopropyl acrylates and isopropyl 3-butenoate as functionalized acyl donors in the kinetic resolution of *rac*-**3a** in toluene (Table 4). We envisioned that the amides (*R*)-**6** and (*R*)-**7** could yield the corresponding enantiopure six- and seven-membered unsaturated lactams when used as substrates for ring-closing metathesis. The resolution with isopropyl acrylate was completely non-enantioselective (Entries 4–6) while excellent enantioselectivities were observed with ethyl acrylate (Entries 1–3) and with isopropyl 3-butenoate (Entries 7–9). The reactions with acrylate esters remained very slow, and it was not possible to affect reactivity by increasing the content of the acyl donor from 5 to 20 vol.-% (Entries 1–6). Finally, preparative-scale kinetic resolution produced (*R*)-**6** with 65% isolated yield (calculated from conversion) when 19% of the racemate had reacted (Scheme 3). The lipase-catalyzed Michael addition started to compete seriously with the *N*-acylation at this point.[19] Lacking Michael acceptor properties, isopropyl 3-butenoate (10 vol.-%) successfully afforded the amide (*R*)-**7** at 47% conversion with 85% isolated yield and *ee* > 99%.

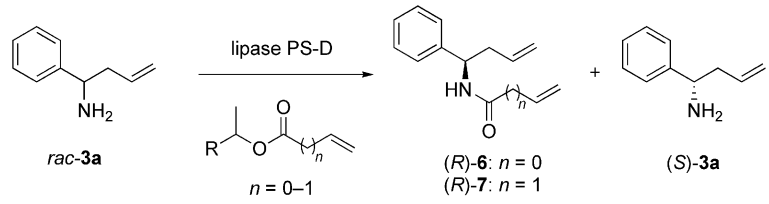
Table 3. Preparative-scale kinetic resolution of *rac*-**3a**–**e** (0.1 M) in isopropyl acetate (neat) at room temperature or with ethyl methoxyacetate in toluene in the presence of molecular sieves (4 Å).



Entry	Substrate	Time [d]	Conv. [%]	(*R*)-Amide Yield [%][a]	*ee* [%]	(*S*)-Amine Yield [%][a]	*ee* [%]
1	**3a**[b]	4	48	83	94	58	87
2	**3a**	3	46	92	99	66	84/99[e]
3	**3b**	4	33	75	>99	75	48/95[e]
4	**3c**	4	49	65	>99	93	94
5	**3d** [c]	7	31	quant.	>99	35	44/72[e]
6	**3e** [d]	–	–	–	–	–	–

[a] Isolated yields based on conversion. [b] Ethyl methoxyacetate (6 vol.-%) in toluene at 48 °C. [c] CAL-B (50 mg mL^{-1}) in the place of lipase PS-D and ethyl methoxyacetate (20 vol.-%) in toluene at room temp. [d] No reaction with any applied method. [e] *ee* after enantiomeric enrichments.

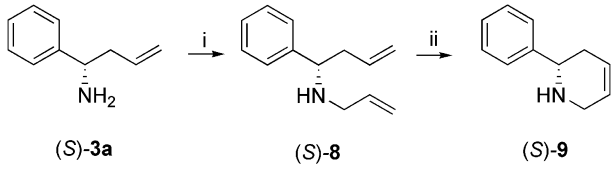
Table 4. Kinetic resolution of *rac*-**3a** (0.1 M) with ethyl and isopropyl acrylate and isopropyl 3-butenoate (toluene was used as cosolvent) in the presence of lipase PS-D (50 mg mL^{-1}) and molecular sieves (4 Å) at room temperature; reaction time 3 d.



Entry	R	*n*	Acyl donor [vol.-%]	Conv. [%]	$ee^{(R)\text{-amide}}$ [%]	$ee^{(S)\text{-}\mathbf{3a}}$ [%]	*E*
1	H	0	5	17	98	21	>100
2	H	0	10	16	98	19	>100
3	H	0	20	18	98	21	>100
4	CH_3	0	5	7	3	<1	1
5	CH_3	0	10	1	23	<1	2
6	CH_3	0	20	2	13	<1	1
7	CH_3	1	5	40	>99	67	>200
8	CH_3	1	10	45	>99	83	>200
9	CH_3	1	20	48	>99	91	>200

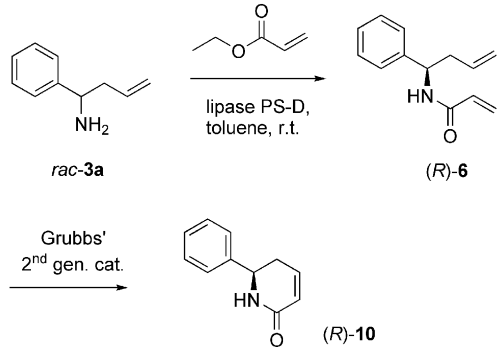
Synthesis of N-Containing Heterocycles

In our previous work, the protected crotylated amine was converted into the corresponding diallylic sulfamide that was then ring-closed using Grubbs' 2nd generation catalyst to yield a substituted dehydropiperidine in excellent overall yield.[5] Unfortunately, the removal of the *N*,*N*-dimethylsulfamoyl protective group from this tertiary amine proved unsuccessful. In the present work, having the enantiopure amine at hand, we were encouraged to redesign the synthesis strategy in order to prepare enantiopure dehydropiperidines in a similar fashion. Accordingly, the unprotected amine (*S*)-**3a** was converted into the corresponding diallylic amine (*S*)-**8** by deprotonation with KOH and subsequent reaction with one equivalent of allyl bromide in 67% yield. The diallylic amine obtained was then subjected to ring-closing metathesis. As known from the literature, free amines are detrimental to the Grubbs-type ruthenium catalysts.[20] When, however, the diallylic amine was converted into the corresponding salt by adding one equivalent of *p*-toluenesulfonic acid (*p*TsA) the ring-closure proceeded smoothly affording the enantiopure dehydropiperidine (*S*)-**9** in 70% isolated yield (Scheme 2).



Scheme 2. Synthesis of cyclic secondary amine (*S*)-**9**. i) allyl bromide (1 equiv.), KOH (3 equiv.), DMF. ii) Grubbs' 2nd generation cat. (10 mol-%), *p*TsA (1 equiv.), CH_2Cl_2, 40 °C.

Finally, the diallylic resolution products (*R*)-**6** and (*R*)-**7** were subjected to ring-closing metathesis using Grubbs' 2nd generation catalyst. A similar type of approach, although based on a longer synthetic route for preparation of the enantiopure diallyl precursors, has been described by Fiorelli and Savoia.[21] In their work, a number of substituted diallylic amides were successfully ring-closed to yield the corresponding α,β-unsaturated δ-lactams in good to excellent yields. In accordance with this published procedure,[21] the δ-lactam (*R*)-**10** was synthesized from (*R*)-**6** in 83% isolated yield (Scheme 3). In our hands, however, the corresponding seven-membered lactam (*R*)-**11** was formed in low yield only (22%) when starting from the diallylic amide (*R*)-**9**.



Scheme 3. Kinetic resolution of **3a** to yield amide (*R*)-**6** and the synthesis of the lactam (*R*)-**10**.

Nevertheless, this work has shown that a number of biologically relevant N-containing heterocycles could be produced by combining the elegancy of enzymatic and metal-catalyzed reactions. Currently, we are investigating the possibilities to extend the scope of this protocol to synthesis of some natural products and analogues.

Conclusions

We have shown that the indium-mediated allylation of *N*,*N*-dimethylsulfamoyl-protected aldimines and the subse-

quent deprotection by transamination is a reliable procedure for production of homoallylic amines with different electronic and steric properties. Moreover, our study has shown that the enzymatic kinetic resolution of the sterically more demanding benzyl homoallylamines (allyl as the medium-sized group) is possible by carefully adjusting the most critical reaction parameters. As the steric crowding is transferred closer to the reaction center, the resolution becomes more challenging. Furthermore, by utilizing acyl donors with a terminal double bond, the *N*-acylation has been used as a synthetic step, as the resolution product can be directly subjected to ring-closing metathesis yielding unsaturated lactam products as exemplified by the straightforward synthesis of an enantiopure α,β-unsaturated δ-lactam. Finally, an enantiopure amine has been transferred into its diallylic counterpart, which has been subjected to ring-closing metathesis to afford a substituted enantiopure dehydropiperidine product. The obtained N-containing heterocycles represent an attractive class of moieties found in a number of biologically and pharmaceutically relevant targets.

Experimental Section

Materials and Methods: The allylation and ring-closing reactions were performed under dry argon using anhydrous solvents. THF was distilled from Na/benzophenone and CH_2Cl_2 was distilled from CaH_2. The anhydrous solvents were then stored under argon. *N*,*N*-dimethylsulfamide was readily prepared from commercial dimethylsulfamoyl chloride and 30% aqueous ammonia. All other reagents were purchased and used as received. Solvents and acyl donors for enzymatic reactions were obtained from commercial sources and stored over molecular sieves unless stated otherwise. Isopropyl acrylate and isopropyl 3-butenoate were prepared according to literature procedures.[22] *Burcholderia cepacia* lipase (lipase PS-D) was acquired from Amano Europe, *Candida antarctica* lipase B (CAL-B, Novozym 435), *Thermomyces lanuginosus* lipase (Lipozyme TL IM) and *Rhizopus miehei* lipase (lipase RM IM) were purchased from Novozymes, *Candida antarctica* lipase A (CAL-A, immobilized) was from Biocatalytics, *Candida rugosa* lipase (CRL) and Protease (Subtilisin Carlsberg) were from Sigma and Acylase I (on Eupergit C) was from Fluka. Enantiomeric excesses of the amines **3a**–**e** as the corresponding acet-, propan- or butanamides (amines derivatized with the corresponding anhydride) were determined with a HP1090 gas chromatograph equipped with a Varian CP Chirasil-Dex CP chiral column. For retention times and temperature programs, see Table 5. NMR spectra were recorded with Bruker Avance 500 MHz or 600 MHz spectrometers. ^{1}H NMR spectra were analyzed by PERCH software with spin simulation/iteration techniques.[23] HRMS were measured in ESI$^+$ mode with Bruker micrOTOF-Q quadrupole-TOF or Fisons ZABSpec-oaTOF spectrometers. Melting points were recorded with a Gallenkamp apparatus and are uncorrected. Optical rotations were determined with a PerkinElmer 241 or 341 polarimeter, and $[a]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. Enzymatic reactions were performed at room temperature (23–24 °C) unless indicated otherwise. The determination of *E* was based on equation $E = \ln[(1 - c)(1 - ee_S)]/\ln[(1 - c)(1 + ee_S)]$ with $c = ee_S/(ee_S + ee_P)$ using linear regression (*E* as the slope of the line $\ln[(1 - c)(1 - ee_S)]$ vs. $\ln[(1 - c)(1 + ee_S)]$).[24] Flash chromatography was performed using silica gel (60 Å, Merck, 230–400 mesh, enriched with 0.1% Ca).

Table 5. Gas chromatographic analysis of the resolved compounds.

Amine	Amide derivative	Oven temp. [°C]	t_r[(*S*)/(*R*)] [min]
3a[a]	acetamide	130	37.7/39.3
3a[a]	acetamide	130	43.1/45.5
3a	butanamide	130	85.3/87.3
3a	methoxyacetamide	130	57.0/58.5
3a	acrylamide	160, then 130	27.2/28.3
3a	3-butenamide	160, then 130	36.4/37.2
3b	acetamide	130	53.0/54.4
3c	acetamide	130	147.1/147.4
3d	acetamide	130	54.1/56.3
3d	methoxyacetamide	130	84.6/89.7

[a] The acetamides were analyzed with two columns, the retention times depending on the column specifics.

Synthesis of *N*,*N*-(Dimethylsulfamoyl)benzaldimines 1a–c: Compounds **1a**–**c** were synthesized according to a literature procedure.[25] The corresponding benzaldehyde (20 mmol) and *N*,*N*-dimethylsulfamide (2.54 g, 20.5 mmol) were dissolved in toluene (80 mL) and water was azeotropically distilled for 16 h using a Dean–Stark apparatus. After removal of the solvent under reduced pressure, the residue was dissolved in CH_2Cl_2 and filtered. Solvents were evaporated under reduced pressure and the crude product was used as such in the allylation step.

Standard Procedure for the Synthesis of Homoallylic Amines (Table 1): In a Schlenk tube flushed with argon, substrate **1a**–**c** was dissolved in anhydrous THF (0.10–0.18 M solution). Indium (3 equiv.) and allylating agent (3 equiv.) were added and the resulting mixture was stirred overnight at room temperature. The reaction was quenched by adding 1 M HCl until pH ≈ 3 and extracted with diethyl ether. The combined organic phase was washed with saturated $NaHCO_3$ solution and brine, and dried with anhydrous Na_2SO_4. After evaporation of ether, the crude product was subjected to analysis and purified by flash chromatography (eluent: hexane/EtOAc, 4:1) affording **2a**–**e** as a white solid. Compound **2a**–**e** was then dissolved in 1,3-diaminopropane (24-fold molar excess), the mixture was heated to 140 °C and refluxed for 2 h. After cooling to room temperature, the mixture was diluted with CH_2Cl_2 and washed with water. The organic phase was dried with anhydrous Na_2SO_4 and concentrated to yield **3a**–**e**.

1-Phenylbut-3-en-1-amine (3a): Step 1: starting from **1a** (1.95 g, 9.18 mmol) to yield **2a** (1.67 g, 6.56 mmol, 71%). Step 2: starting from **2a** (2.14 g, 8.41 mmol) to yield **3a** (1.13 g, 7.68 mmol, 91%) as light yellow oil. ^{1}H NMR (600.13 MHz, $CDCl_3$, 25 °C): δ = 7.38–7.33 (m, 4 H, arom. H), 7.28–7.23 (m, 1 H, arom. H), 5.75 (dddd, $J_{CH=,CH2a}$ = 6.3, $J_{CH=,CH2b}$ = 8.0, $J_{CH=,CH2cis}$ = 10.2, $J_{CH=,CH2trans}$ = 17.1 Hz, 1 H, CH_2-C*H*=CH_2), 5.12 (dddd, $J_{CH2trans,CH2b}$ = –1.2, $J_{CH2trans,CH2a}$ = –1.6, $J_{CH2trans,CH2cis}$ = –2.0, $J_{CH2trans,CH}$ = 17.1 Hz, 1 H, CH_2-CH=C*H*$_{2trans}$), 5.08 (dddd, $J_{CH2cis,CH2b}$ = –0.8, $J_{CH2cis,CH2a}$ = –1.2, $J_{CH2cis,CH2trans}$ = –2.0, $J_{CHcis,CH}$ = 10.2 Hz, 1 H, CH_2-CH=C*H*$_{2cis}$), 3.99 (dd, $J_{CH,CH2a}$ = 5.2, $J_{CH,CH2b}$ = 8.2 Hz, 1 H, C*H*NH_2), 2.46 (ddddd, $J_{CH2a,CH2cis}$ = –1.2, $J_{CH2a,CH2trans}$ = –1.6, $J_{CH2a,CH}$ = 5.2, $J_{CH2a,CH}$ = 6.2, $J_{CH2a,CH2b}$ = –13.8 Hz, 1 H, C*H*$_{2a}$-CH=CH_2), 2.36 (ddddd, $J_{CH2b,CH2cis}$ = –0.8, $J_{CH2b,CH2trans}$ = –1.2, $J_{CH2b,CH}$ = 8.0, $J_{CH2b,CH}$ = 8.2, $J_{CH2b,CH2a}$ = –13.8 Hz, 1 H, C*H*$_{2b}$-CH=CH_2), 1.53 (br. s., 2 H, NH_2) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$, 25 °C): δ = 145.9 (arom. C), 135.5 (*C*H=CH_2), 128.4 (2 arom. C), 126.9 (arom. C), 126.4 (2 arom. C), 117.6 (CH=*C*H_2), 55.4 (*C*HNH_2), 44.1 (*C*H_2-

CH=CH_2) ppm. HRMS: calcd. for $C_{10}H_{13}N$ $[M]^+$ 147.1071; found 147.1048.

1-(4-Fluorophenyl)but-3-en-1-amine (3b): Step 1: starting from **1b** (1.59 g, 6.91 mmol) to yield **2b** (1.28 g, 4.69 mmol, 68%). Step 2: starting from **2b** (1.28 g, 4.69 mmol) to yield **3b** (0.53 g, 3.21 mmol, 68%) as yellow oil. ^{1}H NMR (600.13 MHz, $CDCl_3$, 25 °C): δ = 7.33–7.29 (m, 2 H, arom. H), 7.04–6.99 (m, 2 H, arom. H), 5.73 (dddd, $J_{CH=,CH2a}$ = 6.2, $J_{CH=,CH2b}$ = 8.0, $J_{CH=,CH2cis}$ = 10.1, $J_{CH=,CH2trans}$ = 17.1 Hz, 1 H, CH_2-C*H*=CH_2), 5.11 (dddd, $J_{CH2trans,CH2b}$ = –1.2, $J_{CH2trans,CH2a}$ = –1.6, $J_{CH2trans,CH2cis}$ = –2.0, $J_{CH2trans,CH}$ = 17.1 Hz, 1 H, CH_2-CH=CH_{2trans}), 5.08 (dddd, $J_{CH2cis,CH2b}$ = –0.9, $J_{CH2cis,CH2a}$ = –1.2, $J_{CH2cis,CH2trans}$ = –2.0, $J_{CHcis,CH2}$ = 10.1 Hz, 1 H, CH_2-CH=CH_{2cis}), 3.99 (dd, $J_{CH,CH2a}$ = 5.3, $J_{CH,CH2b}$ = 8.1 Hz, 1 H, C*H*NH_2), 2.42 (ddddd, $J_{CH2a,CH2cis}$ = –1.2, $J_{CH2a,CH2trans}$ = –1.6, $J_{CH2a,CH}$ = 5.3, $J_{CH2a,CH}$ = 6.2, $J_{CH2a,CH2b}$ = –13.8 Hz, 1 H, CH_{2a}-CH=CH_2), 2.33 (ddddd, $J_{CH2b,CH2cis}$ = –0.9, $J_{CH2b,CH2trans}$ = –1.2, $J_{CH2b,CH}$ = 8.0, $J_{CH2b,CH}$ = 8.1, $J_{CH2b,CH2a}$ = –13.8 Hz, 1 H, CH_{2b}-CH=CH_2), 1.47 (br. s, 2 H NH_2) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$, 25 °C): δ = 161.8 (d, $^1J_{C,F}$ = 244.7 Hz, arom. *C*-F), 141.5 (d, $^4J_{C,F}$ = 3.3 Hz, arom. C), 135.2 (*C*H=CH_2), 127.8 (d, $^3J_{C,F}$ = 7.7 Hz, 2 arom. C), 117.8 (CH=*C*H_2), 115.1 (d, $^2Jc,_F$ = 20.9 Hz, 2 arom. C), 54.7 (*C*HNH_2), 44.3 (*C*H_2-CH=CH_2) ppm. HRMS: calcd. for $C_{10}H_{12}NF$ $[M]^+$ 165.0954; found 165.0929.

1-(4-Methoxyphenyl)but-3-en-1-amine (3c): Step 1: starting from **1c** (0.93 g, 4.42 mmol) to yield **2c** (0.85 g, 3.00 mmol, 68%). Step 2: starting from **2c** (0.85 g, 3.00 mmol) to yield **3c** (0.48 g, 2.70 mmol, 90%) as colorless oil. ^{1}H NMR (600.13 MHz, $CDCl_3$, 25 °C): δ = 7.28–7.24 (m, 2 H, arom. H), 6.89–6.85 (m, 2 H, arom. H), 5.75 (dddd, $J_{CH=,CH2a}$ = 6.2, $J_{CH=,CH2b}$ = 8.0, $J_{CH=,CH2cis}$ = 10.2, $J_{CH=,CH2trans}$ = 17.1 Hz, 1 H, CH_2-C*H*=CH_2), 5.11 (dddd, $J_{CH2trans,CH2b}$ = –1.3, $J_{CH2trans,CH2a}$ = –1.6, $J_{CH2trans,CH2cis}$ = –2.1, $J_{CH2trans,CH}$ = 17.1 Hz, 1 H, CH_2-CH=CH_{2trans}), 5.07 (dddd, $J_{CH2cis,CH2b}$ = –0.9, $J_{CH2cis,CH2a}$ = –1.1, $J_{CH2cis,CH2trans}$ = –2.1, $J_{CH2cis,CH2}$ = 10.2 Hz, 1 H, CH_2-CH=CH_{2cis}), 3.95 (dd, $J_{CH,CH2a}$ = 5.3, $J_{CH,CH2b}$ = 8.1 Hz, 1 H, C*H*NH_2), 3.80 (s, 3 H, OCH_3), 2.43 (ddddd, $J_{CH2a,CH2cis}$ = –1.1, $J_{CH2a,CH2trans}$ = –1.6, $J_{CH2a,CH}$ = 5.3, $J_{CH2a,CH}$ = 6.2, $J_{CH2a,CH2b}$ = –13.8 Hz, 1 H, CH_{2a}-CH=CH_2), 2.34 (ddddd, $J_{CH2b,CH2cis}$ = –0.9, $J_{CH2b,CH2trans}$ = –1.2, $J_{CH2b,CH}$ = 8.0, $J_{CH2b,CH}$ = 8.1, $J_{CH2b,CH2a}$ = –13.8 Hz, 1 H, CH_{2b}-CH=CH_2), 1.46 (br. s, 2 H NH_2) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$, 25 °C): δ = 158.5 (arom. C), 138.0 (arom. C), 135.6 (*C*H=CH_2), 127.3 (2 arom. C), 117.5 (CH=*C*H_2), 113.7 (2 arom. C), 55.3 (O*C*H_3), 54.8 (*C*HNH_2), 44.3 (*C*H_2-CH=CH_2) ppm. HRMS: calcd. for $C_{11}H_{15}NO$ $[M]^+$ 177.1154; found 177.1112.

2-Methyl-1-phenylbut-3-en-1-amine (3d): Step 1: starting from **1a** (2.42 g, 11.4 mmol) to yield **2d** (1.92 g, 7.15 mmol, 65%). Step 2: starting from **2d** (1.60 g, 5.86 mmol) to yield **3d** (0.72 g, 4.44 mmol, 76%) as light yellow oil. ^{1}H NMR (600.13 MHz, $CDCl_3$, 25 °C): δ = 7.38–7.35 (m, 2 H, arom. H), 7.35–7.31 (m, 2 H, arom. H), 7.26–7.22 (m, 1 H, arom. H), 4.85 [ddq, $J_{CHtrans,CHa}$ = –0.5, $J_{CH2trans,CH3}$ = 1.5, $J_{CHtrans,CHcis}$ = –2.2 Hz, 1 H, CH_2-C(CH_3)=CH_{2trans}], 4.80 [dddq, $J_{CH2cis,CH3}$ = 0.9, $J_{CHcis,CHb}$ = –0.9, $J_{CHcis,CHa}$ = –1.4, $J_{CHcis,CHtrans}$ = –2.2 Hz, 1 H, CH_2-C(CH_3)=CH_{2cis}], 4.10 (dd, $J_{CH,CH2a}$ = 4.5, $J_{CH,CH2b}$ = 9.5 Hz, 1 H, C*H*NH_2), 2.36 (dddd, $J_{CH2a,CH2trans}$ = –0.5, $J_{CH2a,CH2cis}$ = –1.4, $J_{H2a,CH}$ = 4.5, $J_{CH2a,CH2b}$ = –13.6 Hz, 1 H, CH_{2a}-CH=CH_2), 2.31 (ddd, $J_{CH2b,CH2cis}$ = –0.9, $J_{H2b,CH}$ = 9.5, $J_{CH2a,CH2b}$ = –13.7 Hz, 1 H, CH_{2b}-CH=CH_2), 1.76 (dd, $J_{CH3,CH2cis}$ = 0.9, $J_{CH3,CH2trans}$ = 1.5 Hz, 3 H, CH_3), 1.48 (br. s, 2 H NH_2) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$, 25 °C): δ = 146.2 (arom. C), 142.9 [*C*(CH_3)=CH_2], 128.4 (2 arom. C), 126.9 (arom. C), 126.3 (2 arom. C), 113.3 [CH(CH_3)=*C*H_2], 53.4 (*C*HNH_2), 48.6 [*C*H_2-C(CH_3)=CH_2], 22.2 (*C*H_3) ppm. HRMS: calcd. for $C_{11}H_{15}N$ $[M]^+$ 161.1205; found 161.1223.

2,2-Dimethyl-1-phenylbut-3-en-1-amine (3e): Step 1: starting from **1a** (2.12 g, 9.99 mmol) to yield **2e** (0.76 g, 2.69 mmol, 27%) after repeated purification by column chromatography. Step 2: starting from **2e** (1.25 g, 4.42 mmol) to yield **3e** (0.64 g, 3.67 mmol, 83%) as yellow oil. ^{1}H NMR (600.13 MHz, $CDCl_3$, 25 °C): δ = 7.30–7.27 (m, 4 H, arom. H), 7.25–7.22 (m, 1 H arom. H), 5.87 (dd, $J_{CH=,CH2cis}$ = 10.8, $J_{CH=,CH2trans}$ = 17.5 Hz, 1 H, C*H*=CH_2), 5.09 (dd, $J_{CH2cis,CH2trans}$ = –1.4, $J_{CHcis,CH=}$ = 10.8 Hz, 1 H, CH=CH_{2cis}), 5.03 (dd, $J_{CH2trans,CH2cis}$ = –1.4, $J_{CH2trans,CH}$ = 17.5 Hz, 1 H, CH=CH_{2trans}), 3.75 (s, 1 H, C*H*NH_2), 1.43 (br. s, 2 H, NH_2), 0.99 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$, 25 °C): δ = 145.8 (*C*H=CH_2), 142.9 (arom. C), 128.5 (2 arom. C), 127.5 (2 arom. C), 126.9 (arom. C), 113.0 (CH=*C*H_2), 64.1 (*C*HNH_2), 41.5 [*C*(CH_3)$_2$], 25.5 (*C*H_3), 21.7 (*C*H_3) ppm. HRMS: calcd. for $C_{12}H_{17}N$ $[M]^+$ 175.1361; found 175.1311.

Standard Procedure for the Small-Scale Enzymatic Kinetic Resolution: Lipase PS-D and molecular sieves (4 Å) were weighed in a reaction vial before *rac*-**3a** (0.1 M, 1.0 mL) in dry isopropyl acetate (or an acyl donor in an organic solvent) was added. Reactions proceeded under shaking at 170 rpm. The progress was followed by taking samples (100 μL) at intervals, filtering off the enzyme and analyzing the samples (diluted with hexane after derivatization of the amine with an appropriate acid anhydride) by GC.

Procedures for the Preparative-Scale Enzymatic Kinetic Resolutions

1-Phenylbut-3-en-1-amine (3a) with Ethyl Methoxyacetate: Lipase PS-D (0.93 g, 50 mg mL^{-1}) and molecular sieves (4 Å, 0.93 g) were weighed in the reaction vessel before *rac*-**3a** (273 mg, 1.85 mmol) in toluene (17 mL) containing ethyl methoxyacetate [6% (v/v)] was added. After 4 d at +48 °C the reaction was stopped at 48% conversion. The enzyme was filtered, washed with CH_2Cl_2 and the combined organic phases were concentrated in vacuo. The crude product was purified by silica gel chromatography (5% Et_3N in EtOAc) to yield (*S*)-**3a** as a pale yellow oil [82 mg, 0.56 mmol, 58%, *ee* = 87%, $[a]_D^{25}$ = –30 (*c* = 1.0, $CHCl_3$)] and (*R*)-**4a** as a white solid [162 mg, 0.74 mmol, 83%, *ee* = 94%, $[a]_D^{25}$ = +43 (*c* = 1.0, $CHCl_3$), m.p. 60 ± 1 °C]. (*R*)-**4a**: ^{1}H NMR ($CDCl_3$, 600.13 MHz, 25 °C): δ = 7.36–7.23 (m, 5 H, arom. H), 6.85 (d, $J_{NH,CH}$ = 8.6 Hz, 1 H, NH), 5.70 (dddd, $J_{CH=,CH2a}$ = 7.0, $J_{CH=,CH2b}$ = 7.0, $J_{CH=,CH2cis}$ = 10.2, $J_{CH=,CH2trans}$ = 17.1 Hz, 1 H, CH_2-C*H*=CH_2), 5.13 (ddd, $J_{CH,CH2a}$ = 5.8, $J_{CH,CH2b}$ = 8.0, $J_{CH,NH}$ = 8.6 Hz, 1 H, C*H*NH), 5.12 (dddd, $J_{CH2trans,CHa}$ = –1.4, $J_{CH2trans,CH2b}$ = –1.5, $J_{CH2trans,CH2cis}$ = –1.9, $J_{CH2trans,CH}$ = 17.1 Hz, 1 H, CH_2-CH=CH_{2trans}), 5.08 (dddd, $J_{CH2cis,CHa}$ = –1.0, $J_{CH2cis,CH2b}$ = –1.1, $J_{CH2cis,CH2trans}$ = –1.9, $J_{CH2cis,CH}$ = 10.2 Hz, 1 H, CH_2-CH=CH_{2cis}), 3.91 (d, $J_{CH2c,CH2d}$ = –15.1 Hz, 1 H, CH_{2c}OCH_3), 3.88 (d, $J_{CH2d,CH2c}$ = –15.1 Hz, 1 H, CH_{2d}OCH_3), 3.41 (s, 3 H, CH_2OCH_3), 2.59 (ddddd, $J_{CH2a,CH2cis}$ = –1.0, $J_{CH2a,CH2trans}$ = –1.4, $J_{CH2a,CH}$ = 5.8, $J_{CH2a,CH}$ = 7.0, $J_{CH2a,CH2b}$ = –14.0 Hz, 1 H, CH_{2a}-CH=CH_2), 2.59 (ddddd, $J_{CH2b,CH2cis}$ = –1.1, $J_{CH2b,CH2trans}$ = –1.5, $J_{CH2b,CH}$ = 7.0, $J_{CH2b,CH}$ = 8.0,, $J_{CH2b,CH2a}$ = –14.0 Hz, 1 H, CH_{2b}-CH=CH_2) ppm. ^{13}C NMR ($CDCl_3$,150.9 MHz, 25 °C): δ = 168.8 (*C*O), 141.4 (arom. C), 133.8 (*C*H=CH_2), 128.6 (2 arom. C), 127.4 (arom. C), 126.5 (2 arom. C), 118.3 (CH=*C*H_2), 72.0 (*C*H_2OCH_3), 59.2 (CH_2O*C*H_3), 51.8 (*C*HNH), 40.6 (*C*H_2-CH=CH_2) ppm. HRMS: calcd. for $C_{13}H_{17}NO_2Na$ [M + Na]$^+$ 242.1152; found 242.1171.

1-Phenylbut-3-en-1-amine (3a) with Isopropyl Acetate: Lipase PS-D (1.00 g, 50 mg mL^{-1}) and molecular sieves (4 Å, 1.00 g) were weighed in the reaction vessel before *rac*-**3a** (300 mg, 2.04 mmol) in neat isopropyl acetate (20 mL) was added. After 3 d the reaction was stopped at 46% conversion. The crude product was purified

by silica gel chromatography (EtOAc) to yield (*S*)-**3a** as a colorless oil (108 mg, 0.73 mmol, 66%, *ee* = 84%) and (*R*)-**5a** as white solid [163 mg, 0.86 mmol, 92%, *ee* = 99%, $[a]_D^{25}$ = +115 (*c* = 1.0, $CHCl_3$), m.p. 74 ± 1 °C]. A fraction of the enantiomerically enriched (*S*)-**3a** (86 mg, 0.59 mmol) was purified under kinetic resolution conditions, yielding (*S*)-**3a** as a colorless oil [38 mg, 0.26 mmol, 44%, *ee* = 99%, $[a]_D^{25}$ = –51 (*c* = 1.0, $CHCl_3$), $[a]_D^{25}$ (lit.) = –50.0 (*c* = 1.13, $CHCl_3$, *ee* = 96%)[7c]]. (*R*)-**5a**: ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ = 7.39–7.23 (m, 5 H, arom. H), 5.99 (d, $J_{NH,CH}$ = 8.2 Hz, 1 H, NH), 5.68 (dddd, $J_{CH=,CH2b}$ = 6.7, $J_{CH=,CH2a}$ = 7.3, $J_{CH=,CH2cis}$ = 10.1, $J_{CH=,CH2trans}$ = 17.2 Hz, 1 H, CH_2-C*H*=CH_2), 5.10 (dddd, $J_{CH2trans,CHa}$ = –1.4, $J_{CH2trans,CH2b}$ = –1.4, $J_{CH2trans,CH2cis}$ = –1.9, $J_{CH2trans,CH=}$ = 17.2 Hz, 1 H, CH_2-CH=CH_{2trans}), 5.07 (dddd, $J_{CH2cis,CHa}$ = –1.1, $J_{CH2cis,CH2b}$ = –1.1, $J_{CH2cis,CH2trans}$ = –1.9, $J_{CH2cis,CH}$ = 10.1 Hz, 1 H, CH_2-CH=CH_{2cis}), 5.07 (ddd, $J_{CH,CH2b}$ = 5.9, $J_{CH,CH2a}$ = 7.9, $J_{CH,NH}$ = 8.2 Hz, 1 H, C*H*NH), 2.57 (ddddd, $J_{CH2a,CH2cis}$ = –1.1, $J_{CH2a,CH2trans}$ = –1.4, $J_{CH2a,CH}$ = 7.3, $J_{CH2a,CH}$ = 7.9, $J_{CH2a,CH2b}$ = –13.8 Hz, 1 H, CH_{2a}-CH=CH_2), 2.56 (ddddd, $J_{CH2b,CH2cis}$ = –1.1, $J_{CH2b,CH2trans}$ = –1.4, $J_{CH2b,CH}$ = 5.9, $J_{CH2b,CH}$ = 6.7, $J_{CH2b,CH2a}$ = –13.8 Hz, 1 H, CH_{2b}-CH=CH_2), 1.99 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 125.8 MHz, 25 °C): δ = 169.3 (*C*O), 141.6 (arom. C), 134.0 (*C*H=CH_2), 128.6 (2 arom. C), 127.4 (arom. C), 126.5 (2 arom. C), 125.9 (C_{arom}), 118.2 (CH=*C*H_2), 52.5 (*C*HNH), 40.5 (*C*H_2-CH=CH_2), 23.4 (CO*C*H_3) ppm. HRMS:: calcd. for $C_{12}H_{15}NONa$ [M + Na]$^+$ 212.1046; found 212.1039.

1-Phenylbut-3-en-1-amine (3a) with Ethyl Acrylate: *rac*-**3a** (296 mg, 2.01 mmol) in 1:9 (v/v) mixture of ethyl acrylate in toluene was added on lipase PS-D (1.00 g, 50 mg mL^{-1}) and molecular sieves (4 Å, 1.00 g). After 5 d the reaction was stopped at 19% conversion. The crude product was dissolved in H_2O (5 mL) and the solution was acidified with 2 M HCl (5 mL) and extracted with EtOAc (3 × 10 mL). The organic phases were combined, dried with Na_2SO_4, concentrated and purified by silica pad filtration (EtOAc) to yield (*R*)-**6** as a white solid [50 mg, 0.25 mmol, 65%, *ee* = 95%, $[a]_D^{25}$ = +133 (*c* = 1.0, $CHCl_3$), m.p. 83 ± 1 °C]. ^{1}H NMR ($CDCl_3$, 600.13 MHz, 25 °C): δ = 7.36–7.24 (m, 5 H, arom. H), 6.28 (dd, $J_{CH2trans',CH2cis'}$ = –1.5, $J_{CH2trans',CH='}$ = 17.0 Hz, 1 H, CO-CH=CH_{2trans}), 6.11 (dd, $J_{CH=',CH2cis'}$ = 10.4, $J_{CH=',CH2trans'}$ = 17.0 Hz, 1 H, CO-C*H*=CH_2), 5.87 (d, $J_{NH,CH}$ = 8.1 Hz, 1 H, NH), 5.70 (dddd, $J_{CH=,CH2b}$ = 6.9, $J_{CH=,CH2a}$ = 7.1, $J_{CH=,CH2cis}$ = 10.2, $J_{CH=,CH2trans}$ = 17.1 Hz, 1 H, CH_2-C*H*=CH_2), 5.64 (dd, $J_{CH2cis',CH2trans'}$ = –1.5, $J_{CH2cis',CH}$ = 10.4 Hz, 1 H, CO-CH=CH_{2cis}), 5.17 (dd, $J_{CH,CH2b}$ = 6.4, $J_{CH,CH2a}$ = 7.3 Hz, 1 H, C*H*NH), 5.12 (dddd, $J_{CH2trans,CH2a}$ = –1.4, $J_{CH2trans,CH2b}$ = –1.5, $J_{CH2trans,CH2cis}$ = –1.9, $J_{CH2trans,CH}$ = 17.1 Hz, 1 H, CH_2-CH=CH_{2trans}), 5.09 (dddd, $J_{CH2cis,CH2a}$ = –1.0, $J_{CH2cis,CH2b}$ = –1.2, $J_{CH2cis,CH2trans}$ = –1.9, $J_{CH2cis,CH}$ = 10.2 Hz, 1 H, CH_2-CH=CH_{2cis}), 2.62 (ddddd, $J_{CH2a,CH2cis}$ = –1.0, $J_{CH2a,CH2trans}$ = –1.4, $J_{CH2a,CH}$ = 7.1, $J_{CH2a,CH}$ = 7.3, $J_{CH2a,CH2b}$ = –13.7 Hz, 1 H, CH_{2a}-CH=CH_2), 2.61 (ddddd, $J_{CH2b,CH2cis}$ = –1.2, $J_{CH2b,CH2trans}$ = –1.5, $J_{CH2b,CH}$ = 6.4, $J_{CH2b,CH}$ = 6.9, $J_{CH2b,CH2a}$ = –13.7 Hz, 1 H, CH_{2b}-CH=CH_2) ppm. ^{13}C NMR ($CDCl_3$, 150.9 MHz, 25 °C): δ = 164.7 (*C*O), 141.4 (arom. C), 133.9 (*C*H=CH_2), 130.7 (CO-*C*H=CH_2), 128.7 (2 arom. C), 127.4 (arom. C), 126.8 (CO-CH=*C*H_2), 126.5 (2 arom. C), 118.3 (CH=*C*H_2), 52.5 (*C*HNH), 40.4 (*C*H_2-CH=CH_2) ppm. HRMS: calcd. for $C_{13}H_{15}NONa$ [M + Na]$^+$ 224.1046; found 224.1144.

1-Phenylbut-3-en-1-amine (3a) with Isopropyl 3-Butenoate: *rac*-**3a** (693 mg, 4.71 mmol) in the 1:9 (v/v) mixture of isopropyl 3-butenoate in toluene was added on lipase PS-D (2.36 g, 50 mg mL^{-1}) and molecular sieves (4 Å, 2.40 g). After 5 d the reaction was stopped at 47% conversion. The crude product was dissolved in H_2O (10 mL) and the solution was acidified with 4 M HCl (4 mL) and extracted with EtOAc (3 × 20 mL). Purification as above yielded (*R*)-**7** as a white solid [504 mg, 1.88 mmol, 85%, *ee* > 99%, $[a]_D^{25}$ = +63 (*c* = 1.0, $CHCl_3$), m.p. 55 ± 1 °C]. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ = 7.35–7.31 (m, 2 H, arom. H), 7.27–7.23 (m, 3 H, arom. H), 5.94 (dddd, $J_{CH=',CH2a'}$ = 7.1, $J_{CH=',CH2b'}$ = 7.2, $J_{CH=',CH2cis'}$ = 10.1, $J_{CH=',CH2trans'}$ = 17.1 Hz, 1 H, CO-CH_2'-C*H*′=CH_2'), 5.92 (d, $J_{NH,CH}$ = 8.2 Hz, 1 H, NH), 5.67 ($J_{CH=,CH2a}$ = 6.9, $J_{CH=,CH2b}$ = 7.3, $J_{CH=,CH2cis}$ = 10.1, $J_{CH=,CH2trans}$ = 17.1 Hz, 1 H, CH_2-C*H*=CH_2), 5.25 (dddd, $J_{CH2cis',CH2b'}$ = –1.0, $J_{CH2cis',CH2a'}$ = –1.1, $J_{CH2cis',CH2trans'}$ = –1.6, $J_{CH2cis',CH='}$ = 10.1 Hz, 1 H, CO-CH_2'-CH′=CH_{2cis}'), 5.23 (dddd, $J_{CH2trans',CH2b'}$ = –1.4, $J_{CH2trans',CH2a'}$ = –1.4, $J_{CH2trans',CH2cis'}$ = –1.6, $J_{CH2trans',CH='}$ = 17.1 Hz, 1 H, CO-CH_2'-CH′=CH_{2trans}'), 5.10 (dddd, $J_{CH2trans,CH2b}$ = –1.4, $J_{CH2trans,CH2a}$ = –1.4, $J_{CH2trans,CH2cis}$ = –1.9, $J_{CH2trans,CH}$ = 17.1 Hz, 1 H, CH_2-CH=CH_{2trans}), 5.09 (ddd, $J_{CH,CH2a}$ = 5.9, $J_{CH,CH2b}$ = 7.6, $J_{CH,NH}$ = 8.2 Hz, 1 H, C*H*NH), 5.08 (dddd, $J_{CH2cis,CH2b}$ = –0.9, $J_{CH2cis,CH2a}$ = –1.2, $J_{CH2cis,CH2trans}$ = –1.9, $J_{CH2cis',CH='}$ = 10.1 Hz, 1 H, CH_2-CH=CH_{2cis}), 3.03 (dddd, $J_{CH2a',CH2cis'}$ = –1.1, $J_{CH2a',CH2trans'}$ = –1.4, $J_{CH2a',CH='}$ = 7.1, $J_{CH2a',CH2b'}$ = –14.1 Hz, 1 H, CO-CH_{2a}'-CH′=CH_2'), 3.02 (dddd, $J_{CH2b',CH2cis'}$ = –1.0, $J_{CH2b',CH2trans'}$ = –1.4, $J_{CH2b',CH='}$ = 7.2, $J_{CH2b,CH2a'}$ = –14.1 Hz, 1 H, CO-CH_{2b}'-CH′=CH_2'), 2.56 (ddddd, $J_{CH2a,CH2cis}$ = –1.2, $J_{CH2a,CH2trans}$ = –1.4, $J_{CH2a,CH}$ = 5.9, $J_{CH2a,CH}$ = 6.9, $J_{CH2a,CH2b}$ = –14.2 Hz, 1 H, CH_{2a}-CH=CH_2), 2.55 (ddddd, $J_{CH2b,CH2cis}$ = –0.9, $J_{CH2b,CH2trans}$ = –1.4, $J_{CH2b,CH}$ = 7.3, $J_{CH2b,CH}$ = 7.6, $J_{CH2b,CH2a}$ = –14.2 Hz, 1 H, CH_{2b}-CH=CH_2) ppm. ^{13}C NMR ($CDCl_3$, 125.8 MHz, 25 °C): δ = 169.6 (CO), 141.5 (arom. C), 133.9 (*C*H=CH_2), 131.3 (*C*′H=C′H_2), 128.6 (2 arom. C), 127.4 (arom. C), 126.4 (2 arom. C), 120.0 (C′H=*C*′H_2), 118.3 (CH=CH_2), 52.2 (*C*HNH), 41.7 (*C*′H_2-C′H=C′H_2), 40.5 (CH_2-CH=CH_2) ppm. HRMS: calcd. for $C_{14}H_{17}NONa$ [M + Na]$^+$ 238.1202; found 238.1187.

1-(4-Fluorophenyl)but-3-en-1-amine (3b) with Isopropyl Acetate: *rac*-**3b** (429 mg, 2.60 mmol) was resolved as above. After 4 d the reaction was stopped at 33% conversion. The work-up gave (*S*)-**3b** as a pale yellow oil (216 mg, 1.31 mmol, 75%, *ee* = 48%). The enzymatic purification gave (*S*)-**3b** as a pale yellow oil [71 mg, 0.43 mmol, 33%, *ee* = 95%, $[a]_D^{25}$ = –35 (*c* = 1.0, $CHCl_3$)]. (*R*)-**5b** was a white solid [133 mg, 0.64 mmol, 75%, *ee* > 99%, $[a]_D^{25}$ = +109.0 (*c* = 1.0, $CHCl_3$), m.p. 120 ± 1 °C]. (*R*)-**5b**: ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ = 7.26–7.22 (m, 2 H, arom. H), 7.04–6.99 (m, 2 H, arom. H), 5.75 (d, $J_{NH,CH}$ = 8.0 Hz, 1 H, NH), 5.66 (dddd, $J_{CH=,CH2b}$ = 6.8, $J_{CH=,CH2a}$ = 7.2, $J_{CH=,CH2cis}$ = 10.1, $J_{CH=,CH2trans}$ = 17.2 Hz, 1 H, CH_2-C*H*=CH_2), 5.11 (dddd, $J_{CH2trans,CHa}$ = –1.4, $J_{CH2trans,CH2b}$ = –1.5, $J_{CH2trans,CH2cis}$ = –1.9, $J_{CH2trans,CH=}$ = 17.2 Hz, 1 H, CH_2-CH=CH_{2trans}), 5.09 (dddd, $J_{CH2cis,CHa}$ = –1.1, $J_{CH2cis,CH2b}$ = –1.1, $J_{CH2cis,CH2trans}$ = –1.9, $J_{CH2cis,CH=}$ = 10.1 Hz, 1 H, CH_2-CH=CH_{2cis}), 5.05 (ddd, $J_{CH,CH2b}$ = 6.6, $J_{CH,CH2a}$ = 7.2, $J_{CH,NH}$ = 8.0 Hz, 1 H, C*H*NH), 2.54 (ddddd, $J_{CH2a,CH2cis}$ = –1.1, $J_{CH2a,CH2trans}$ = –1.4, $J_{CH2a,CH}$ = 7.2, $J_{CH2a,CH}$ = 7.2, $J_{CH2a,CH2b}$ = –13.9 Hz, 1 H, CH_{2a}-CH=CH_2), 2.54 (ddddd, $J_{CH2b,CH2cis}$ = –1.1, $J_{CH2b,CH2trans}$ = –1.5, $J_{CH2b,CH}$ = 6.6, $J_{CH2b,CH}$ = 6.8, $J_{CH2b,CH2a}$ = –13.9 Hz, 1 H, CH_{2b}-CH=CH_2), 1.99 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 125.8 MHz, 25 °C): δ = 169.3 (*C*O), 162.0 (d, $^1J_{C,F}$ = 245.8 Hz, arom. C), 137.5 (d, $^4J_{C,F}$ = 2.8 Hz, arom. C), 133.7 (*C*H=CH_2), 128.0 (d, $^3J_{C,F}$ = 8.3 Hz, 2 arom. C), 118.5 (CH=*C*H_2), 115.4 (d, $^2J_{C,F}$ = 21.1 Hz, 2 arom. C), 51.9 (*C*HNH), 40.5 (*C*H_2-CH=CH_2), 23.4 (CO*C*H_3) ppm. HRMS: calcd. for $C_{12}H_{14}FNONa$ [M + Na]$^+$ 230.0952; found 230.0949.

1-(4-Methoxyphenyl)but-3-en-1-amine (3c) with Isopropyl Acetate: *rac*-**3c** (227 mg, 1.28 mmol) was resolved as above. After 4 d the reaction was stopped at 49% conversion. The work-up gave (*S*)-**3c**

as a colorless oil [0.108 mg, 0.61 mmol, 93%, *ee* = 94%, $[\alpha]_D^{25}$ = –34 (*c* = 1.0, $CHCl_3$), $[\alpha]_D^{25}$ (lit.) = –42.3 (*c* = 0.81, $CHCl_3$, *ee* = 97%)[7c]] and (*R*)-**5c** as a white solid [91 mg, 0.41 mmol, 65%, *ee* >99%, $[\alpha]_D^{25}$ = +110 (*c* = 1.0, $CHCl_3$), m.p. 122 ± 1 °C]. (*R*)-**5c**: ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ = 7.22–7.18 (m, 2 H, arom. H), 6.88–6.84 (m, 2 H, arom. H), 5.84 (d, $J_{NH,CH}$ = 8.1 Hz, 1 H, NH), 5.68 (dddd, $J_{CH=,CH2b}$ = 6.9, $J_{CH=,CH2a}$ = 7.1, $J_{CH=,CH2cis}$ = 10.2, $J_{CH=,CH2trans}$ = 17.2 Hz, 1 H, CH_2-C*H*=CH_2), 5.09 (dddd, $J_{CH2trans,CHa}$ = –1.4, $J_{CH2trans,CH2b}$ = –1.5, $J_{CH2trans,CH2cis}$ = –1.9, $J_{CH2trans,CH}$ = 17.2 Hz, 1 H, CH_2-CH=CH_{2trans}), 5.06 (dddd, $J_{CH2cis,CHa}$ = –1.1, $J_{CH2cis,CH2b}$ = –1.1, $J_{CH2cis,CH2trans}$ = –1.9, $J_{CH2cis,CH}$ = 10.2 Hz, 1 H, CH_2-CH=CH_{2cis}), 5.03 (ddd, $J_{CH,CH2b}$ = 6.7, $J_{CH,CH2a}$ = 7.3, $J_{CH,NH}$ = 8.1 Hz, 1 H, C*H*NH), 2.56 (ddddd, $J_{CH2a,CH2cis}$ = –1.1, $J_{CH2a,CH2trans}$ = –1.4, $J_{CH2a,CH}$ = 7.1, $J_{CH2a,CH}$ = 7.3, $J_{CH2a,CH2b}$ = –14.2 Hz, 1 H, CH_{2a}-CH=CH_2), 2.53 (ddddd, $J_{CH2b,CH2cis}$ = –1.1, $J_{CH2b,CH2trans}$ = –1.5, $J_{CH2b,CH}$ = 6.7, $J_{CH2b,CH}$ = 6.9, $J_{CH2b,CH2a}$ = –14.2 Hz, 1 H, CH_{2b}-CH=CH_2), 1.97 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 125.8 MHz, 25 °C): δ = 169.2 (*C*O), 158.8 (arom. C), 134.2 (*C*H=CH_2), 133.7 (arom. C), 127.7 (2 arom. C), 118.0 (CH=*C*H_2), 114.0 (2 arom. C), 55.3 (O*C*H_3), 52.0 (*C*HNH), 40.4 (*C*H_2-CH=CH_2), 23.4 (CO*C*H_3) ppm. HRMS: calcd. for $C_{13}H_{17}NO_2Na$ $[M + Na]^+$ 242,1152; found 242,1257.

3-Methyl-1-phenylbut-3-en-1-amine (3d) with Ethyl Methoxyacetate: *rac*-**3d** (380 mg, 2.36 mmol) was resolved as above except that CAL-B (Novozym 435, 1.22 g, 50 mg mL^{-1}) was used in the place of lipase PS-D. After 7 d the reaction was stopped at 31% conversion. The crude product was dissolved in H_2O (10 mL) and the solution was acidified with 4 M HCl (4 mL) and extracted with EtOAc (3 × 20 mL). The aqueous phase was alkalized with 4 M NaOH (4 mL) and extracted with EtOAc (3 × 20 mL). The organic phases were combined, dried with Na_2SO_4 and concentrated to yield (*S*)-**3d** as a colorless oil (93 mg, 0.57 mmol, 35%, *ee* = 44%). The enantiomerically enriched (*S*)-**3d** was purified under kinetic resolution conditions, yielding (*S*)-**3d** as a colorless oil [20 mg, 0.12 mmol, 21%, *ee* = 72%, $[\alpha]_D^{25}$ = –31 (*c* = 1.0, $CHCl_3$)]. The combined organic phases containing (*R*)-**4d** was treated in the same way and purified by silica pad filtration (EtOAc) to yield (*R*)-**4d** as a white solid [184 mg, 0.79 mmol, quant. yield, *ee* > 99%, $[\alpha]_D^{25}$ = +45 (*c* = 1.0, $CHCl_3$), m.p. 53 ± 1 °C]. (*R*)-**4d**: ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ = 7.35–7.23 (m, 5 H, arom. H), 6.78 (d, $J_{NH,CH}$ = 8.4 Hz, 1 H, NH), 5.20 (ddd, $J_{CH,CH2a}$ = 5.8, $J_{CH,NH}$ = 8.4, $J_{CH,CH2b}$ = 9.4 Hz, 1 H, C*H*NH), 4.82 (ddq, $J_{CH2trans,CHa}$ = –0.6, $J_{CH2trans,CH3}$ = 1.4, $J_{CH2trans,CH2cis}$ = –2.0 Hz, 1 H, CH_2-CH=CH_{2trans}), 4.74 (dddq, $J_{CH2cis,CH3}$ = 0.9, $J_{CH2cis,CH2b}$ = –1.0, $J_{CH2cis,CHa}$ = –1.3, $J_{CH2cis,CH2trans}$ = –2.0 Hz, 1 H, CH_2-CH=CH_{2cis}), 3.88 (s, 2 H, CH_2OCH_3), 3.40 (s, 3 H, CH_2OCH_3), 2.54 (dddd, $J_{CH2a,CH2trans}$ = –0.6, $J_{CH2a,CH2cis}$ = –1.3, $J_{CH2a,CH}$ = 5.8, $J_{CH2a,CH2b}$ = –14.2 Hz, 1 H, CH_{2a}-CH=CH_2), 2.50 (ddd, $J_{CH2b,CH2cis}$ = –1.0, $J_{CH2b,CH}$ = 9.4, $J_{CH2b,CH2a}$ = –14.1 Hz, 1 H, CH_{2b}-CH=CH_2), 1.74 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 125.8 MHz, 25 °C): δ = 168.8 (*C*O), 142.1 (arom. C), 141.8 [*C*(CH_3)=CH_2], 128.6 (2 arom. C), 127.3 (arom. C), 126.3 (2 arom. C), 113.8 [C(CH_3)=*C*H_2], 72.0 (*C*H_2OCH_3), 59.3 (CH_2O*C*H_3), 50.5 (*C*HNH), 45.1 [*C*H_2-C(CH_3)=CH_2], 22.1 (*C*H_3) ppm. HRMS: calcd. for $C_{14}H_{19}NO_2Na$ $[M + Na]^+$ 256.1308; found 256.1396.

Procedure for the Hydrolysis of (*R*)-5a and (*R*)-4a: (*R*)-**5a** (169 mg, 0.89 mmol, *ee* = 97%) was refluxed in 4 M HCl for 19 h, and thereafter the solution was cooled to room temperature, alkalized with 4 M NaOH and extracted with EtOAc (3 × 25 mL). The combined organic layer was concentrated in vacuo and the residue purified through column chromatography (EtOAc) to yield (*R*)-**3a** (24 mg, 0.16 mmol, 18%, *ee* = 97%.). (*R*)-**4a** (74 mg, 0.34 mmol, *ee* = 94%) was refluxed in 6 M HCl for one hour, and thereafter handled identical to above except that the system was alkalized with 6 M NaOH and extracted with EtOAc (4 × 20 mL). Purification yielded (*R*)-**3a** (11 mg, 0.07 mmol, 21%, *ee* = 91%).

Synthesis of (1*S*)-1-Phenyl-*N*-(prop-2-en-1-yl)but-3-en-1-amine [(*S*)-8]: In a Schlenk tube flushed with argon, (*S*)-**3a** (60 mg, 0.41 mmol, *ee* 99%) was dissolved in anhydrous DMF (1.5 mL). KOH (70.2 mg, 1.25 mmol, 3 equiv.) was added and the mixture was stirred for 15 min. Allyl bromide (35 μL, 0.40 mmol, 1 equiv.) was added and the mixture was stirred at room temperature for 3 h. The reaction was quenched by adding H_2O (5 mL) and extracted with Et_2O (3 × 5 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and concentrated to yield the crude product that was purified by flash chromatography (eluent hexane/EtOAc, 1:1 + 1% Et_3N; silica enriched with ca. 0.1% Ca) yielding of (1*S*)-1-phenyl-*N*-(prop-2-en-1-yl)but-3-en-1-amine (51.5 mg, 0.27 mmol, 67%) as a colorless oil. $[\alpha]_D^{20}$ = –27 (*c* = 0.01, $CHCl_3$). R_f = 0.65 (hexane/EtOAc, 1:1). ^{1}H NMR (600.13 MHz, $CDCl_3$, 25 °C): δ = 7.35–7.29 (m, 4 H, arom. H), 7.26–7.22 (m, 1 H, arom. H), 5.86 (dddd, $J_{CH=',CH2a'}$ = 5.4, $J_{CH=',CH2b'}$ = 6.7, $J_{CH=',CH2cis'}$ = 10.2, $J_{CH=',CH2trans'}$ = 17.2 Hz, 1 H, CH_2'-C*H*′=CH_2'), 5.72 (dddd, $J_{CH=,CH2a}$ = 5.9, $J_{CH=,CH2b}$ = 8.3, $J_{CH=,CH2cis}$ = 10.1, $J_{CH=,CH2trans}$ = 17.1 Hz, 1 H, CH_2-C*H*=CH_2), 5.10 (dddd, $J_{CH2trans',CH2b'}$ = –1.4, $J_{CH2trans',CH2a'}$ = –1.7, $J_{CH2trans',CH2cis'}$ = –1.9, $J_{CH2trans',CH='}$ = 17.2 Hz, 1 H, CH_2'-CH′=C$H_{2trans'}$), 5.09 (dddd, $J_{CH2trans,CH2b}$ = –1.2, $J_{CH2trans,CH2a}$ = –1.7, $J_{CH2trans,CH2cis}$ = –2.0, $J_{CH2trans,CH}$ = 17.1 Hz, 1 H, CH_2-CH=CH_{2trans}), 5.06 (dddd, $J_{CH2cis',CH2b'}$ = –1.2, $J_{CH2cis',CH2a'}$ = –1.4, $J_{CH2cis',CH2trans'}$ = –1.9, $J_{CH2cis',CH='}$ = 10.2 Hz, 1 H, CH_2'-CH′=C$H_{2cis'}$), 5.05 (dddd, $J_{CH2cis,CH2b}$ = –0.9, $J_{CH2cis,CH2a}$ = –1.3, $J_{CH2cis,CH2trans}$ = –2.0, $J_{CH2cis,CH=}$ = 10.1 Hz, 1 H, CH_2-CH=CH_{2cis}), 3.70 (dd, $J_{CH,CH2a}$ = 5.8, $J_{CH,CH2b}$ = 7.9 Hz, 1 H, C*H*NH), 3.11 (dddd, $J_{CH2a',CH2cis'}$ = –1.4, $J_{CH2a',CH2trans'}$ = –1.7, $J_{CH2a',CH='}$ = 5.4, $J_{CH2a',CH2b'}$ = –14.2 Hz, 1 H, C*H*2a′-CH′=CH2′), 3.02 (dddd, $J_{CH2b',CH2cis'}$ = –1.2, $J_{CH2b',CH2trans'}$ = –1.4, $J_{CH2b',CH='}$ = 6.7, $J_{CH2b',CH2a'}$ = –14.2 Hz, 1 H, CH_{2b}′-CH′=CH_2'), 2.43 (ddddd, $J_{CH2a,CH2cis}$ = –1.3, $J_{CH2a,CH2trans}$ = –1.7, $J_{CH2a,CH}$ = 5.8, $J_{CH2a,CH}$ = 5.9, $J_{CH2a,CH2b}$ = –13.9 Hz, 1 H, CH_{2a}-CH=CH_2), 2.40 (ddddd, $J_{CH2b,CH2cis}$ = –0.9, $J_{CH2b,CH2trans}$ = –1.2, $J_{CH2b,CH}$ = 7.9, $J_{CH2a,CH=}$ = 8.3, $J_{CH2a,CH2b}$ = –13.9 Hz, 1 H, CH_{2a}-CH=CH_2) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$, 25 °C): δ = 143.7 (arom. C), 136.9 (*C*′H=C′H_2) 135.4 (*C*H=CH_2), 128.3 (2 arom. C) 127.2 (2 arom. C.), 127.0 (arom. C), 117.5 (CH=*C*H_2), 115.7 (CH′=*C*H_2'), 61.7 (*C*HNH), 50.0 (*C*′H_2-C′H=C′H_2), 43.0 (*C*H_2-CH=CH_2) ppm. HRMS: calcd. for $C_{13}H_{17}N$ $[M]^+$ 187.1361; found 187.1350.

Synthesis of (2*S*)-2-Phenyl-1,2,3,6-tetrahydropyridine [(*S*)-9]: In a Schlenk tube flushed with argon, (1*S*)-1-phenyl-*N*-(prop-2-en-1-yl) but-3-en-1-amine (*S*)-**8** (22.0 mg, 0.12 mmol) was dissolved in anhydrous CH_2Cl_2 (1.2 mL). *p*-toluenesulfonic acid monohydrate (23.4 mg, 0.12 mmol) of was added and the mixture was stirred for 10 min. Grubbs' second-generation catalyst (NHC)(PCy_3)-Cl_2Ru=CHR (10.2 mg, 0.012 mmol, 10 mol-%) was added and the resulting mixture was stirred at room temperature for 17 h. The solvent was evaporated and the residue dissolved in EtOAc (15 mL). The organic layer was extracted with 1 M HCl (4 × 5 mL). The combined aqueous layers were alkalized (pH = 14) by adding NaOH (s). The basic solution was extracted with EtOAc (3 × 10 mL). The organic layers were combined, dried with anhydrous Na_2SO_4, filtered and concentrated to yield the crude product that was purified by flash chromatography (eluent hexane/EtOAc, 1:1 + 1% Et_3N; silica enriched with ca. 0.1% Ca) yielding of (2*S*)-2-phenyl-1,2,3,6-tetrahydropyridine (13.4 mg, 0.084 mmol, 70%) as yellowish oil. $[\alpha]_D^{20}$ = –88 (*c* = 0.01, $CHCl_3$). R_f = 0.15 (hexane/EtOAc, 1:1). ^{1}H NMR (600.13 MHz, $CDCl_3$, 25 °C): δ = 7.40–7.37

(m, 2 H arom. H), 7.36–7.32 (m, 2 H, arom. H), 7.28–7.25 (m, 1 H, arom. H), 5.87 (ddddd, $J_{CH=,CH2a'}$ = –1.8, $J_{CH=,CH2a}$ = 1.8, $J_{CH=,CH2b}$ = 2.5, $J_{CH=,CH2b'}$ = –5.3, $J_{CH=,CH='}$ = 10.1 Hz, 1 H, C*H*′=CH′), 5.79 (ddddd, $J_{CH=',CH2b'}$ = 1.5, $J_{CH=',CH2b}$ = –1.9, $J_{CH=',CH2a'}$ = 2.7, $J_{CH=',CH2a}$ = –4.4, $J_{CH=',CH=}$ = 10.1 Hz, 1 H, CH′=C*H*′), 3.85 (dd, $J_{CH,CH2b'}$ = 3.8, $J_{CH,CH2a'}$ = 10.3 Hz, 1 H, C*H*), 3.62 (ddddd, $J_{CH2a,CH}$ = 1.8, $J_{CH2a,CH2a'}$ = –2.5, $J_{CH2a,CH2b'}$ = –3.4, $J_{CH2a,CH='}$ = –4.4, $J_{CH2a,CH2b}$ = –16.9 Hz, 1 H, C*H*2a-CH=CH′), 3.50 (ddddd, $J_{CH2b,CH2b'}$ = –0.9, $J_{CH2b,CH='}$ = –1.9, $J_{CH2b,CH}$ = 2.5, $J_{CH2b,CH2a'}$ = –4.7, $J_{CH2b,CH2a}$ = –16.9 Hz, 1 H, C*H*2b-CH=CH′), 2.29 (dddddd, $J_{CH2a',CH}$ = –1.8, $J_{CH2a',CH2a}$ = –2.5, $J_{CH2a',CH='}$ = 2.7, $J_{CH2a',CH2b}$ = –4.7, $J_{CH2a',CH}$ = 10.3, $J_{CH2a',CH2b'}$ = –17.3 Hz, 1 H, C*H*2a′-CH′=CH′), 2.25 (dddddd, $J_{CH2b',CH2b}$ = –0.9, $J_{CH2b',CH='}$ = 1.5, $J_{CH2b',CH2a}$ = –3.4, $J_{CH2b',CH}$ = 3.8, $J_{CH2b',CH}$ = –5.3, $J_{CH2b',CH2a'}$ = –17.3 Hz, 1 H, C*H*2b′-CH′=CH′) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$, 25 °C): δ = 144.4 (arom. C), 128.6 (2 arom. C), 127.2 (arom. C), 126.6 (2 arom. C) 125.9 (CH=*C*H′), 125.6 (*C*H=CH′), 57.7 (*C*H), 46.1 (CH_2), 34.1 (CH_2′) ppm. HRMS: calcd. for $C_{11}H_{13}N$ $[M]^+$ 159.1048; found 159.1046.

Synthesis of (6*R*)-6-Phenyl-5,6-dihydropyridin-2(1*H*)-one [(*R*)-10]: In a Schlenk tube flushed with argon, *(R)-N*-(1-phenylbut-3-enyl) acrylamide (*R*)-**6** (20.2 mg, 0.10 mmol, *ee* 95%) was dissolved in anhydrous CH_2Cl_2 (1.5 mL). Grubbs' second-generation catalyst (NHC)$(PCy_3)Cl_2$Ru=CHR (3.6 mg, 0.0042 mmol) dissolved in anhydrous CH_2Cl_2 (0.5 mL) was added and the resulting mixture was stirred at room temperature for 30 min and then refluxed (+40 °C) for 4 h after which Grubbs' second-generation catalyst (3.9 mg, 0.0046 mmol) dissolved in anhydrous CH_2Cl_2 (0.5 mL) was added and stirring at reflux was continued for 18.5 h. The crude product was purified by flash chromatography (eluent hexane/EtOAc, 1:1 + 1% Et_3N; silica enriched with ca. 0.1% Ca) yielding (6*R*)-6-phenyl-5,6-dihydropyridin-2(1*H*)-one (14.4 mg, 0.083 mmol, 83%) as a off-white solid. $[\alpha]_D^{20}$ = +210 (*c* = 0.01, $CHCl_3$). R_f = 0.09 (hexane/EtOAc, 1:1). ^{1}H NMR (600.13 MHz, $CDCl_3$, 25 °C): δ = 7.41–7.33 (m, 5 H, arom. H), 6.65 (ddd, $J_{CH=,CH2b}$ = –2.8, $J_{CH=,CH2a}$ = –5.5, $J_{CH=,CH='}$ = 10.0 Hz, 1 H, CO-C*H*=CH), 6.03 (dddd, $J_{CH=',CH}$ = –1.1, $J_{CH=',CH2a}$ = 1.4, $J_{CH=',CH2b}$ = 2.6, $J_{CH=',CH}$ = 10.0 Hz, 1 H, CO-CH=C*H*), 5.58 (br. s., 1 H, N*H*), 4.75 (dd, $J_{CH,CH2a}$ = 5.5, $J_{CH,CH2b}$ = 11.8 Hz, 1 H, C*H*), 2.59 (dddd, $J_{CH2a,CH='}$ = 1.4, $J_{CH2a,CH}$ = 5.5, $J_{CH2a,CH}$ = –5.5, $J_{CH2a,CH2b}$ = –17.8 Hz, 1 H, CH_{2a}), 2.52 (dddd, $J_{CH2b,CH='}$ = 2.6, $J_{CH2b,CH}$ = –2.8, $J_{CH2b,CH}$ = 11.8, $J_{CH2b,CH2b}$ = –17.8 Hz, 1 H, CH_{2b}) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$, 25 °C): δ = 166.5 (CO), 141.0 (arom. C), 140.3 (CO-*C*H=CH′), 129.0 (2 arom. C), 128.4 (arom. C), 126.4 (2 arom. C), 124.5 (CO-CH=*C*H′), 56.0 (*C*H), 33.1 (CH_2) ppm. HRMS: calcd. for $C_{11}H_{11}NONa$ $[M + Na]^+$ 196.0738; found 196.0750.

Synthesis (7*R*)-7-Phenyl-1,3,6,7-tetrahydro-2*H*-azepin-2-one [(*R*)-11]: Procedure as above starting from (*R*)-**7** (16.6 mg, 0.08 mmol, *ee* > 99%). Yield (3.2 mg, 0.017 mmol, 22%). The amount of purified material was not sufficient for reliable measurement of the optical rotation. R_f = 0.15 (hexane/EtOAc, 1:1), ^{1}H NMR (600.13 MHz, $CDCl_3$, 25 °C): δ = 7.42–7.38 (m, 2 H, arom. H), 7.37–7.33 (m, 3 H, arom. H), 5.76 (dd, $J_{NH=,CH2b'}$ = –2.3, $J_{NH=,CH}$ = 5.8 Hz, 1 H, N*H*), 5.74 (dddd, $J_{CH=,CH2a'}$ = 2.9, $J_{CH=,CH2a}$ = 3.1, $J_{CH=,CH2b'}$ = 5.1, $J_{CH=,CH='}$ = 11.6 Hz, 1 H, $COCH_2$C*H*=CH′), 5.66 (ddddd, $J_{CH=',CH2b'}$ = 1.8, $J_{CH=',CH2a'}$ = 2.4, $J_{CH=',CH2a}$ = 2.8, $J_{CH=',CH2b}$ = 8.6, $J_{CH=',CH}$ = 11.6 Hz, 1 H, $COCH_2$CH=C*H*′), 4.95 (ddd, $J_{CH,CH2b'}$ = 2.4, $J_{CH,NH}$ = 5.8, $J_{CH,CH2a'}$ = 12.1 Hz, 1 H, C*H*), 3.66 (ddddd, $J_{CH2a,CH='}$ = 2.8, $J_{CH2a,CH}$ = 3.1, $J_{CH2a,CH2b'}$ = –3.6, $J_{CH2a,CH2a'}$ = –4.3, $J_{CH2a,CH2b}$ = –16.7 Hz, 1 H, CO-CH_{2a}), 2.92 (dddd, $J_{CH2b,CH2a'}$ = –1.0, $J_{CH2b,CH2b'}$ = –1.9, $J_{CH2b,CH='}$ = 8.6, $J_{CH2b,CH2a}$ = –16.7 Hz, 1 H, CO-CH_{2b}), 2.71 (ddddd, $J_{CH2a',CH2b}$ = –1.0, $J_{CH2a',CH='}$ = 2.4, $J_{CH2a',CH}$ = 2.9, $J_{CH2a',CH2a}$ = –4.3, $J_{CH2a',CH}$ = 12.1, $J_{CH2a',CH2b'}$ = –18.2 Hz, 1 H, CH-CH_{2a}′), 2.48 (ddddddd, $J_{CH2b',CH='}$ = 1.8, $J_{CH2b',CH2b}$ = –1.9, $J_{CH2b',NH}$ = –2.3, $J_{CH2b',CH}$ = 2.4, $J_{CH2b',CH2a}$ = –3.6, $J_{CH2b',CH}$ = 5.1, $J_{CH2b',CH2a'}$ = –18.2 Hz) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$, 25 °C): δ = 174.2 (CO), 140.4 (arom. C), 129.2 (2 arom. C), 128.7 (*C*H=CH′), 128.4 (arom. C), 126.3 (2 arom. C), 120.3 (CH=*C*H′), 55.0 (*C*H), 37.1 (CH_2′), 35.4 (CH_2) ppm. HRMS: calcd. for $C_{12}H_{13}NO$ $[M]^+$ 187.0997; found 187.0993.

Supporting Information (see also the footnote on the first page of this article): Gas chromatograms of the resolved compounds and ^{1}H and ^{13}C NMR spectra of the prepared compounds.

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