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Indium-Mediated Asymmetric Barbier-Type Allylation of Aldimines in Alcoholic Solvents: Synthesis of Optically Active Homoallylic Amines

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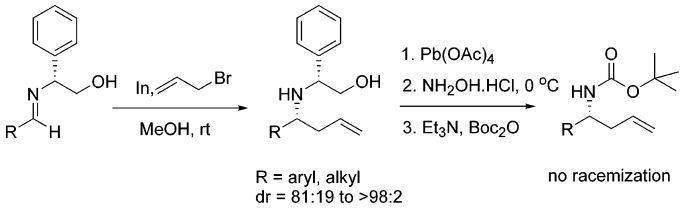

Chiral aldimines derived from phenylglycinol were diastereoselectively allylated with indium powder/allyl bromide in alcoholic solvents. Both aliphatic and aromatic aldimines provided good yield of the desired products with high diastereoselectivity. A racemization-free protocol for removal of the phenylglycinol auxiliary was also developed. The stereochemical assignment of the homoallylic amine was made by NMR spectroscopy and a transition state model was proposed to explain the selectivity.

Carbon−carbon bond formation by nucleophilic addition of carbon nucleophiles to imines is an important tool in organic synthesis.[1] Allylation of imines provides homoallyic amines, which are important intermediates for a wide range of pharmaceutical substances and biologically active compounds.[2] Extensive efforts have been made toward development of an effective chiral auxiliary or an asymmetric catalyst to induce high enantio- and diastereoselectivities. Although a number of excellent chiral reagents-based[3] and chiral catalysts-based[4] methods for allylation of imines have recently been developed, the range of substrates is still quite limited. At present, very few of such methods are applicable to enolizable aldimines derived from aliphatic aldehydes. On the other hand, auxiliary-based methods generally display better substrate tolerance and often provide better stereoselectivity.[5−7] Most of the synthetic

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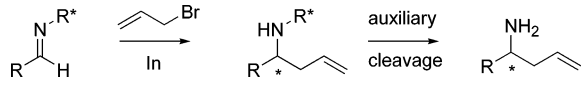
SCHEME 1

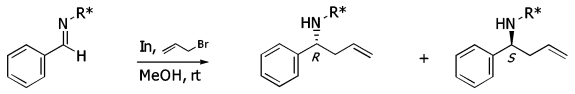


methods along this line commenced with imines bearing an electron-withdrawing group or an aryl group to stabilize the resulting amide anion to accelerate the reaction. These features extremely limit the applicability of the chiral auxiliary to be used for asymmetric allylation of imines. To overcome the limitation, we have recently developed a Barbier-type allylation of *N*-alkylimines using allyl bromide−indium in alcoholic solvents.[8−10] In this paper we wish to further investigate the scope of the reaction with emphasis on diastereoselective allylation of aldimines bearing a chiral auxiliary and subsequent removal of the chiral auxiliary to produce optically active homoallylic amines (Scheme 1).

(*S*)-Valine methyl ester has generally been used as a chiral auxiliary for asymmetric alkylation of aldimines. Recently Loh has reported a highly diastereoselective allylation and Mannich-type reaction of imines derived from (*S*)-valine methyl ester.[11] Unfortunately, cleavage of this auxiliary requires a multistep treatment.[12] Chiral 1,2-amino alcohols and their derivatives have also been successfully employed as chiral auxiliaries.[13] Recent works revealed that (*S*)-valinol and (*S*)-phenylglycinol are very effective chiral auxiliaries for allylation of aldimines in aprotic solvents.[5] Our preliminary results suggested that these amino alcohols similarly perform well as chiral auxiliaries in alcoholic solvents.

We initially screened a variety of amino acid-derived chiral amines as an auxiliary for asymmetric allylation of benzaldimines (Table 1**)**. Allylation of the chiral aldimines (**1a**−**f**) derived from benzaldehyde and an appropriate chiral amine was chosen as a model reaction. The allylation reaction was carried out in the presence of 2 equiv of indium powder and 3 equiv of allyl bromide in absolute methanol as a solvent at room temperature.[14] (*R*)-Methylbenzylamine as well as (*S*)-phenylalanine methyl ester and (*S*)-phenylalaninol gave poor diastereoselectivity (entries 1−3). In contrast, (*S*)-valinol, with its more bulky substituent together with a chelating group, appeared to be a better auxiliary (entry 4). Among all chiral amines investigated, (*S*)- and (*R*)-phenylglycinols were found to give the most impressive results

TABLE 1. Addition of Allyl Indium Reagent to Chiral Aldimines



	1a-1f		2a-2f		3a-3f
entry	**substrate**	**product**	**R***	**yield (%)**	**dr**[a]
1	**1a**	**2a, 3a**		76	70:30
2	**1b**	**2b, 3b**		55	73:27
3	**1c**	**2c, 3c**		40	67:33
4	**1d**	**2d, 3d**		51	90:10
5	**1e**	**2e, 3e**		90	94:6[b]
6	**1f**	**2f, 3f**		92	98:2[c]

[a] Ratio of major and minor isomers as determined by ^{1}H NMR (400 or 600 MHz). [b] $[\alpha]^{23}_D$ +43.0 (*c* 1.01, $CHCl_3$). [c] $[\alpha]^{23}_D$ −42.0 (*c* 1.05, $CHCl_3$) [lit. $[\alpha]^{29}_D$ for **2f** −42.3 (*c* 4.00, $CHCl_3$)] (ref 5g).

whereby the desired allylation products were isolated in 90% and 92% yield, respectively (entries 5 and 6). The diastereomeric ratios as determined by ^{1}H NMR spectroscopy on a 600 MHz spectrometer were over 15:1. By comparison of the specific rotation with a literature value, the (*R*,*R*)-homoallylic amine **2f** was found to be the major product derived from the (*R*)-phenylglycinol auxiliary. The homoallylic amine derived from (*S*)-phenylglycinol possesses the opposite specific rotation value; the structure of the major isomer was therefore assigned to be **3e** with (*S*)-configuration at the new stereogenic center.

Having established the most suitable chiral auxiliary, we next investigated the allylation reaction of a variety of chiral aldimines derived from (*R*)-phenylglycinol (Table 2). We were pleased to find that the reaction is applicable to a wide range of substrates including those bearing a hydroxy group or heterocycles to give the products in good yields and excellent diastereoselectivity.

It is also interesting to observe that imines derived from aromatic aldehydes bearing ortho substituents (entries 2, 5, 7, and 12) consistently gave lower selectivity. It should be noted that indium-mediated allylation of imines derived from 5-formyluracil and chiral β-amino alcohols was reported to give high diastereoselectivity while the corresponding 2,4-dimethoxypyrimidine derivatives gave very poor diastereoselectivity.[15] The authors invoked the mutual chelation between the uracil C=O, C=N, and OH group to explain the difference and concluded that an additional coordinating element on the substrate is essential to give high diastereoselectivity. Under our conditions, however, it appeared that the presence of an additional chelating group is not required. Good yield and excellent diastereoselectivity were observed in reactions with imines derived from aliphatic aldehydes as well (Table 3). The successful allylation of

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(12) Ozone and ^{t}BuOCl have been used successfully to oxidatively cleave amino acid auxiliaries. See: Namba, K.; Kawasaki, M.; Takada, I.; Iwama, S.; Izumida, M.; Shinada, T.; Ohfune, Y. *Tetrahedron Lett.* **2001**, *42*, 3733−3736.

(13) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835−875.

(14) Decreasing the amounts of indium and/or allyl bromides resulted in poorer yield. Ethanol and 2-propanol were successfully used as solvents but the reaction rates were considerably slower than methanol while the diastereoselectivities were similar.

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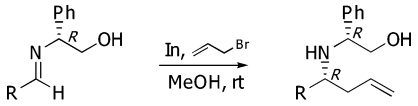
TABLE 2. Addition of Allyl Indium Reagent to Chiral Aldimines Derived from Aromatic Aldehydes and (*R*)-Phenylglycinol



1g-1r **2g-2r**

entry	substrate	product	R	yield (%)	dr[a]	$[\alpha]^{24}_D$, $CHCl_3$
1	**1g**	**2g**	4-MeC_6H_4-	94	93:7	−28.5 (*c* 1.02)
2	**1h**	**2h**	2-$MeOC_6H_4$-	82	87:13	−45.2 (*c* 1.04)
3	**1i**	**2i**	3-$MeOC_6H_4$-	84	91:9	−39.6 (*c* 1.11)
4	**1j**	**2j**	4-$MeOC_6H_4$-	93	92:8	−24.4 (*c* 1.20)
5	**1k**	**2k**	2-HOC_6H_4-	49	89:11	−63.6 (*c* 0.89)
6	**1*l***	**2*l***	3-HOC_6H_4-	88	92:8	−36.1 (*c* 0.97)
7	**1m**	**2m**	2-ClC_6H_4-	83	89:11	−36.2 (*c* 1.02)
8	**1n**	**2n**	3-ClC_6H_4-	87	97:3	−22.1 (*c* 1.13)
9	**1o**	**2o**	4-ClC_6H_4-	95	98:2	−18.3 (*c* 1.04)
10	**1p**	**2p**	2-pyridyl-	91	94:6	−15.2 (*c* 0.99)
11	**1q**	**2q**	2-furyl-	90	>98:2[b]	−5.7 (*c* 1.05)
12	**1r**	**2r**	1-naphthyl	81	81:19	−75.0 (*c* 1.00)

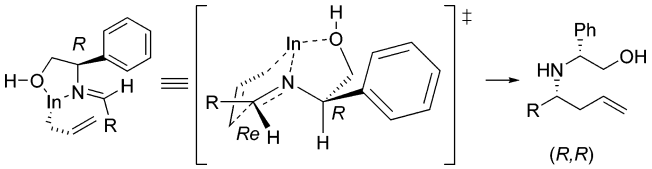
[a] Determined by ^1H NMR (400 MHz) integration. [b] Only one set of ^1H and ^{13}C signals was observed.

TABLE 3. Addition of Allyl Indium Reagent to Chiral Aldimines Derived from Aliphatic Aldehydes and (*R*)-Phenylglycinol

entry	substrate	product	R	yield (%)	dr[a]	$[\alpha]^{24}_D$, $CHCl_3$
1	**1s**	**2s**	^{i}Pr-	96	>98:2	−122.9 (*c* 0.98)
2	**1t**	**2t**	^{t}Bu-	84	>98:2	−135.7 (*c* 0.98)
4	**1u**	**2u**	Cy-	78	>98:2	−78.9 (*c* 1.07)
5	**1v**	**2v**	^{n}Pr-	80	>98:2	−91.4 (*c* 1.51)
6	**1w**	**2w**	^{n}Bu-	78	>98:2	−73.8 (*c* 0.66)
7	**1x**	**2x**	^{n}Hex-	73	>98:2	−61.6 (*c* 0.93)
8	**1y**	**2y**	cinnamyl-	90	96:4	+28.7 (*c* 1.03)
9	**1z**	**2z**	$PhCH_2CH_2$-	59	>98:2	−45.6 (*c* 1.02)

[a] Determined by ^1H NMR (400 MHz) integration. With the exception of **2y**, only one set of ^1H and ^{13}C signals was observed for each compound.

SCHEME 2



aliphatic imines bearing one or two α-hydrogens reflects the advantage of low basicity of organoindium reagents compared to other traditional organometallic reagents.

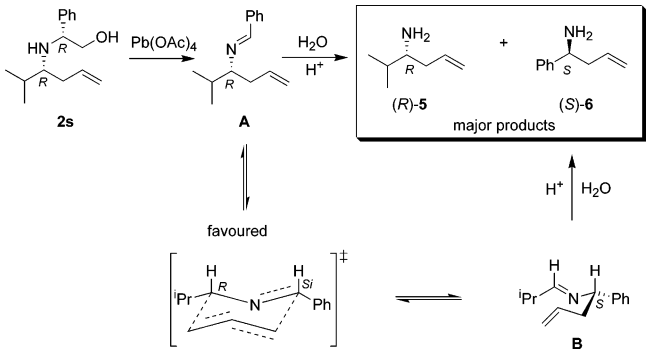
Several transition state models based on metal chelation have been proposed to explain the stereochemical outcome of the addition of imines derived from phenylglycinol.[16] It is well-known that the starting imines exist as an equilibrium mixture between the imine and oxazolidine forms. The effect of the equilibrium, which is dependent on several parameters including the solvent and the nature of the R group, on the stereoselectivity has not been well clarified. A simple transition model that is consistent with the results observed is shown in Scheme 2 whereby the imine assumes *E*-configuration and addition of the allyl group takes place from the opposite side of the phenyl group, which is the *Re* face for chiral imines derived from (*R*)-phenylglycinol. The high diastereoselectivity could be explained by formation of the rigid chelated transition state between indium and N/O atoms of the substrate.[17] A similar model has been previously proposed for indium-mediated allylation of imines bearing an L-valinol auxiliary.[5f] The high level of stereoselectivity and very fast reaction rate observed in protic solvents such as methanol are remarkable. It is possible that methanol is also able to coordinate to the indium metal center in the transition state besides the internal hydroxymethyl group itself. It can also immediately protonate the metal amide initially formed from allylation therefore preventing further side reactions. These features may play an important role in the stereochemical outcomes and rate acceleration of the present addition reaction.[18] The involvement of a discrete allylindium species was suggested by ^1H NMR experiments, although the radical pathway cannot be totally ruled out as a possibility. When a suspension of indium powder in CD_3OD was treated with allyl bromide (1.5 equiv), the indium was dissolved with some gas evolution. The ^1H NMR spectrum of the reaction mixture revealed two new allylic CH_2 signals at 1.92 and 1.68 ppm at a

(16) Alvaro, G.; Savoia, D. *Synlett* **2002**, 651−673.

(17) Investigating a CPK model of the transition state suggested that the rotating phenyl group carrying ortho substituents can hinder the approach of the allyl group from the *Re*-face in Scheme 2 to some extent, hence might be the cause of low diastereoselectivity.

(18) Rate enhancement of allylation of C=O and C=N in the presence of proton sources has previously been observed: (a) Cokley, T. M.; Harvey, P. J.; Marshall, R. L.; McCluskey, A.; Young, D. J. *J. Org. Chem.* **1997**, *62*, 1961−1964. (b) Yasuda, M.; Fujibayashi, T.; Baba, A. *J. Org. Chem.* **1998**, *63*, 6401−6404. (c) Tussa, L.; Lebreton, C.; Mosset, P. *Chem. Eur. J.* **1997**, *3*, 1064−1070.

SCHEME 3



ratio of about 5:1. Addition of *N*-benzylidenebenzylamine to this solution caused rapid disappearance of the signal at 1.92 ppm while a new signal due to allylic CH_2 of the homoallylic amine appeared at 2.80 and 2.95 ppm. The allylic species being responsible for the signal at 1.92 ppm is probably the same as allylindium(I) proposed by Chan as a possible intermediate in indium-mediated Barbier-type allylation of aldehydes in water.[19]

The chiral auxiliary was removed to give the free homoallylic amines. Among cleavage conditions tried, oxidative cleavage of the auxiliary by $Pb(OAc)_4$ was found to be the best condition.[20] It was disappointing, however, that the standard cleavage protocol involving $Pb(OAc)_4$ treatment followed by acid hydrolysis at room temperature[5a,21] gave a rather poor yield, and led to an unacceptable level of byproducts. When the amine **2s** (R = ^{i}Pr) was subjected to the above condition, 2-isopropyl-3-butenamine (**5**) and 2-phenyl-3-butenamine (**6**) were isolated (as their *N*-Boc derivatives) in 59% and 30% yield, respectively. To determine the optical purity, **5** and **6** were transformed into the corresponding Boc-(*R*)- and Boc-(*S*)-phenylglycine amide (BPG) derivatives that were analyzed by ^{1}H NMR.[22] Both **5** and **6** were found to have low optical purities. Interestingly, the major enantiomer of **6** was found to possess (*S*)-configuration, which is opposite to that of the major enantiomer of **5** and the starting amine **2s**.

The above results include two aspects on the generation of **6** and racemization of both **5** and **6**. A proposed reaction mechanism giving the byproduct **6** that involves a 2-aza-Cope rearrangement is illustrated in Scheme 3.[23] Cleavage of the chiral auxiliary from **2s** gave benzaldimine **A** that is in equilibrium with another imine **B** via the aza-Cope rearrangement. Hydrolysis of **A** and **B** would afford **5** and **6**, respectively. According to the product ratio **5**:**6** of ca. 2:1, the equilibrium would preferentially shift to **A**. When the rearrangement proceeds in a stable chair transition state whereby the ^{i}Pr and Ph groups occupy equatorial positions, the chirality transfer between the two should take place without loss of optical purity. The partial racemization observed in this experiment suggested that the diastereofacial discrimination during the rearrangement was incomplete. Possible causes for this include geometrical equilibrium of aldimines (*E*/*Z*), unfavorable transition states including an axial substituent in the chair transition states, or involvement of boat transition states.

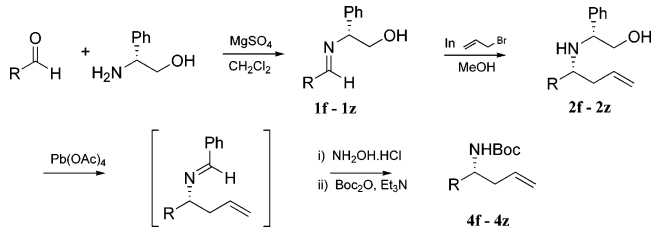
To overcome the problem of the aza-Cope rearrangement leading to both poor yield and racemization, the standard cleavage protocol was modified with the aim to avoid exposure of the intermediate Schiff base to high temperature, and to keep the lifetime of this intermediate the shortest. After several experiments, we were pleased to find that hydroxylamine hydrochloride is the reagent of choice to assist cleavage of the Schiff base at low tempearture.[6] According to the new protocol, the homoallylic amines **2** bearing the (*R*)-phenylglycinol auxiliary were treated with a slight excess of $Pb(OAc)_4$ in 1:1 CH_2Cl_2/MeOH at 0 °C for 30 min. An excess of a methanolic solution of hydroxylamine hydrochloride (10 equiv) was then added at 0 °C without isolation of the intermediate imine from the lead salts. After the solution was stirred for another 30 min, the organic solvents were removed in vacuo and the products were isolated as their *N*-Boc derivatives **4**. In this way, starting from 0.5 mmol of the imines **1f** and **1s** prepared in situ, the *N*-Boc homoallylic amines **4f** and **4s** were obtained in 75% and 55% overall yield, respectively, with only single chromatographic purification at the end of the reaction sequences. Furthermore, the chiral integrity of the products was almost completely preserved as the amides derived from coupling of *N*-Boc-deprotected **4f** and **4s** with (*R*)- and (*S*)-BPG[22] showed only one set of the ^{1}H NMR spectrum without a detectable level of the other diastereomer. A more quantitative analysis of enantiomeric ratio was performed by ^{1}H NMR and HPLC analysis of the corresponding (*R*)- and (*S*)-MTPA derivatives, which also showed no significant level of racemization. This auxiliary clevage condition therefore offered a significant improvement compared to the standard condition,[5a,21] which provided **4f** and **4s** in low optical purities (er = 70:30 and 80:20, respectively). The new cleavage method was tested with all remaining compounds **2**. In most cases, fair to good overall yield and enantiomeric purity of the *N*-Boc homoallylic amines **4** were obtained (Table 4). The only exceptions were hydroxyphenyl derivatives (**2k** and **2*l***), which gave complex mixtures containing none of the desired product after $Pb(OAc)_4$ cleavage.

The absolute configurations of the *N*-Boc homoallylic amines **4f**, **4p**, **4s**, **4u**, and **4y** were determined by ^{1}H NMR analysis of their BPG derivatives[22] to be (*R*). The absolute configuration of the *N*-Boc homoallylic amine **4e** derived from the (*S*)-phenylglycinol auxiliary was similarly determined, and was shown to be (*S*). The results indicated that the type of R group (aliphatic, aromatic) and substituents on the aromatic ring have virtually no effect on the selectivity of the reaction.

The present method offers significant advantages compared to the previously reported methods including the use of an inexpensive chiral auxiliary, fast reaction rates, simple reaction and workup conditions, good and predictable diastereoselectivity for a range of substrates, and the ease of removal of the auxiliary.

(19) Chan, T. H.; Yang, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3228−3229.
(20) Cleavage conditons attempted: H_5IO_6/$MeNH_2$, hydrogenolysis, *O*-tosylation or *N*-bromination followed by base-catalyzed elimination. In all cases the reactions were incomplete and several byproducts were formed.
(21) Spero, D. M.; Kapadia, S. R. *J. Org. Chem.* **1997**, *62*, 5537−5541.
(22) Seco, J. M.; Quinoa, E.; Riguera, R. *J. Org. Chem.* **1999**, *64*, 4669−4675.
(23) The aza-Cope rearrangement of similar substrates has been briefly mentioned in ref 6.

TABLE 4. Removal of the Auxiliary from the Homoallylic Amines



entry	substrate	product	R	yield (%)[a]	er[b]	$[\alpha]^{24}_D$, $CHCl_3$
1	**2f**	**4f**	Ph-	75	98:2	+45.0 (*c* 1.00)
2	**2g**	**4g**	4-MeC_6H_4-	71	94:6	+60.0 (*c* 1.00)
3	**2h**	**4h**	2-$MeOC_6H_4$-	68	88:12	+63.0 (*c* 1.00)
4	**2i**	**4i**	3-$MeOC_6H_4$-	63	91:9	+41.3 (*c* 0.80)
5	**2j**	**4j**	4-$MeOC_6H_4$-	71	93:7	+76.0 (*c* 1.00)
6	**2m**	**4m**	2-ClC_6H_4-	70	91:9	+49.0 (*c* 1.00)
7	**2n**	**4n**	3-ClC_6H_4-	69	93:7	+56.0 (*c* 1.00)
8	**2o**	**4o**	4-ClC_6H_4-	72	94:6	+58.0 (*c* 1.00)
9	**2p**	**4p**	2-pyridyl-	54	95:5	+15.3 (*c* 0.72)
10	**2q**	**4q**	2-furyl-	67	N.D.[c]	+93.0 (*c* 1.00)
11	**2r**	**4r**	1-naphthyl	60	82:18	+38.6 (*c* 0.70)
12	**2s**	**4s**	^{i}Pr-	55	96:4	−15.6 (*c* 0.90)
13	**2t**	**4t**	^{t}Bu-	52	97:3	−21.4 (*c* 0.70)
14	**2u**	**4u**	Cy-	63	>99:1	−16.0 (*c* 1.00)
15	**2v**	**4v**	^{n}Pr-	58	96:4	−18.9 (*c* 0.90)
16	**2w**	**4w**	^{n}Bu-	51	>99:1	−22.1 (*c* 0.68)
17	**2x**	**4x**	^{n}Hex-	60	95:5	−12.2 (*c* 0.90)
18	**2y**	**4y**	cinnamyl-	68	96:4	+43.0 (*c* 1.00)
19	**2z**	**4z**	$PhCH_2CH_2$-	51	99:1	−17.1 (*c* 0.70)

[a] Yield refers to isolated overall yield (5 steps) starting from aldehydes and (*R*)-phenylglycinol [b] Ratio of major:minor enantiomers as determined by HPLC or ^{1}H NMR (400 MHz) analyses of the crude products obtained from **4**, after removal of *N*-Boc group by TFA and derivatization with (*R*)- and (*S*)-MTPA. [c] The homoallylic amine **4q** decomposed on treatment with TFA before derivatization with MTPA.

In conclusion, we have demonstrated a highly diastereoselective allylation of chiral aldimines derived from optically active phenylglycinol mediated by indium metal in alcoholic solvents. We have also developed a racemization-free protocol for removal of the chiral auxiliary. The simplicity and compatibility to a variety of functional groups of the stereoselective indium-mediated allylation described herein should provide a convenient access to optically active homoallylic amines.

Experimental Section

General Procedure for the Allylation of Aldimines. To a mixture of the imine (1.0 mmol) and indium powder (288 mg, 2.0 mmol) in absolute methanol (5 mL) was added allyl bromide (3.0 mmol). The reaction was stirred vigorously at room temperature until all the metal had dissolved (30 min to 2 h), at which time TLC indicated complete reaction. The reaction mixture was diluted with 10% aqueous $NaHCO_3$ and extracted with ethyl acetate. The product was purified by flash column chromatography on silica gel, using hexanes−ethyl acetate as eluent.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(4″-methylphenyl)but-3′-enylamino]ethanol (2g). White solid (dr 93:7); mp 66−68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 2.57 (m, 2H), 3.62 (dd, J = 10.6, 6.9 Hz, 1H), 3.82 (m, 2H), 3.95 (m, 1H), 5.12 (m, 2H), 5.76 (m, 1H), 7.30 (m, 4H), 7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 41.3, 59.3, 61.2, 65.5, 117.3, 127.0, 127.2, 127.4, 128.6, 129.1, 135.1, 136.7, 140.6, 141.3; MS (ESI+) *m/z* 282.2 (100). Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 80.90; H, 8.41; N, 5.10.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(2″-methoxyphenyl)but-3′-enylamino]ethanol (2h). Yellow oil (dr 87:13); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (m, 2H), 2.90 (br s, 1H), 3.62 (dd, J = 10.4, 6.4 Hz, 1H), 3.74 (s, 3H), 3.82 (m, 2H), 4.18 (t, J = 7 Hz, 1H), 5.16 (m, 1H), 5.82 (m, 1H), 6.80 (d, J = 7 Hz, 1H), 6.96 (t, J = 7 Hz, 1H), 7.28 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.9, 55.0, 56.6, 61.7, 65.2, 110.5, 116.7, 120.4, 127.2, 127.3, 128.0, 128.3, 131.1, 136.0, 141.8, 157.1; MS (ESI+) *m/z* 298.1 (100). Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; N, 4.71. Found: C, 76.67; H, 7.65; N, 4.72.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(3″-methoxyphenyl)but-3′-enylamino]ethanol (2i). Yellow oil (dr 91:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.58 (m, 2H), 3.62 (dd, J = 11.7, 4.0 Hz, 1H), 3.79 (t, J = 7 Hz, 1H), 3.81 (s, 3H), 3.90 (dd, J = 7.0, 2.1 Hz, 2H), 5.15 (m, 1H), 5.78 (m, 1H), 6.82 (m, 3H), 7.32 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.3, 55.2, 60.0, 61.2, 65.7, 112.5, 112.8, 117.5, 119.6, 127.3, 127.5, 128.5, 129.4, 135.0, 141.3, 145.4, 159.6; HRMS(FAB+) Calcd for $C_{19}H_{23}NO_2{\cdot}H^+$ 298.1807, found 298.1800.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(4″-methoxyphenyl)but-3′-enylamino]ethanol (2j). Colorless solid (dr 92:8); mp 44−45 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.58 (m, 1H), 2.62 (m, 1H), 2.76 (br s, 1H), 3.62 (dd, J = 10.7, 7.1 Hz, 1H), 3.78 (dd, J = 10.8, 4.6 Hz, 2H), 3.82 (s, 3H), 3.94 (dd, J = 6.8, 4.4 Hz, 2H), 5.15 (m, 2H), 5.78 (m, 1H), 6.84 (d, J = 7.0 Hz, 2H), 7.21−7.40 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.2, 55.1, 59.0, 61.2, 65.5, 113.6, 117.1, 127.3, 127.5, 128.3, 128.6, 135.0, 135.6, 141.2, 158.5; HRMS(CI+) calcd for $C_{19}H_{23}NO_2{\cdot}H^+$ 298.1807, found 298.1817. Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.74; H, 7.80; N, 4.71. Found: C, 76.62; H, 7.82; N, 4.71.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(2″-hydroxyphenyl)but-3′-enylamino]ethanol (2k). Colorless oil (dr 89:11); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 (m, 2H), 3.81−4.00 (m, 4H), 5.24 (m, 2H), 5.82 (m, 1H), 6.78 (m, 2H), 6.96 (d, J = 7.5 Hz, 1H), 7.16 (t, J = 7 Hz, 1H), 7.26 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.1, 60.4, 61.2, 64.2, 116.9, 119.0, 125.5, 127.3, 127.7, 128.0, 128.4, 128.6, 128.9, 134.4, 139.3, 157.2; HRMS (ESI+) calcd for $C_{18}H_{21}NO_2{\cdot}H^+$ 284.1651, found 284.1638. Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.08; H, 7.45; N, 4.97.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(3″-hydroxyphenyl)but-3′-enylamino]ethanol (2*l*). Colorless oil (dr 92:8); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (m, 2H), 3.65 (m, 2H), 3.80 (m, 1H), 3.98 (m, 1H), 4.60 (br s, 1H), 5.06 (m, 2H), 5.66 (m, 1H), 6.78 (m, 3H), 7.17−7.38 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.7, 59.6, 61.2, 65.4, 114.3, 114.6, 117.6, 119.2, 127.3, 127.7, 128.6, 129.6, 134.8, 140.4, 144.9, 156.4; HRMS (ESI+) calcd for $C_{18}H_{21}NO_2{\cdot}H^+$ *m/z* 284.1651, found 284.1661.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(2″-chlorophenyl)but-3′-enylamino]ethanol (2m). White solid (dr 89:11); mp 67−68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.58 (m, 2H), 2.74 (br s, 1H), 3.62 (dd, J = 10.4, 6.1 Hz, 1H), 3.83 (m, 2H), 4.42 (t, J = 6.4 Hz, 1H), 5.16 (m, 2H), 5.82 (m, 1H), 7.16−7.42 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.5, 56.3, 62.0, 65.5, 117.9, 126.9, 127.3, 127.4, 128.4, 129.7, 133.2, 134.5, 140.9, 141.3; HRMS (ESI+) calcd for $C_{18}H_{20}ClNO{\cdot}H^+$ 302.1312, found 302.1311. Anal. Calcd for $C_{18}H_{20}ClNO$: C, 71.63; H, 6.68; N, 4.64. Found: C, 71.46; H, 6.88; N, 4.64.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(3″-chlorophenyl)but-3′-enylamino]ethanol (2n). White solid (dr 97:3); mp 67−68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (m, 2H), 3.62 (dd, J = 11.0, 7.1 Hz, 1H), 3.76 (m, 2H), 3.88 (dd, J = 2.4, 7.0 Hz, 1H), 5.09 (m, 2H), 5.71 (m, 1H), 7.10−7.40 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.2, 59.8, 62.1, 65.9, 118.0, 127.2, 127.6, 128.5, 128.6, 132.7, 134.4, 140.9, 145.9. Anal. Calcd for $C_{18}H_{20}ClNO$: C, 71.63; H, 6.68; N, 4.64. Found: C, 70.68; H, 6.54; N, 4.66.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(4″-chlorophenyl)but-3′-enylamino]ethanol (2o). White solid (dr 98:2); mp 68−70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (m, 2H), 3.60 (dd, J = 10.4, 6.8 Hz, 1H), 3.78 (m, 2H), 3.90 (m, 1H), 5.11 (m, 2H), 5.71 (m, 1H), 7.08−7.38 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.4, 59.4, 61.6, 65.8, 117.8, 127.1, 127.5, 128.4, 128.6, 132.7, 134.5, 140.9, 142.2; MS (ESI+) *m/z* 302.1 (100). Anal. Calcd for $C_{18}H_{20}ClNO$: C, 71.63; H, 6.68; N, 4.64. Found: C, 71.61; H, 6.70; N, 4.65.

(2*R*)-2-Phenyl-2-[(1′*R*)-1-(2″-pyridyl)but-3′-enylamino]ethanol (2p). Yellow oil (dr 94:6); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (m, 2H), 3.22 (br s, 1H), 3.54 (dd, J = 10.6, 7.6 Hz, 1H), 3.62 (m, 1H), 3.78 (m, 2H), 4.95 (m, 2H), 5.60 (m, 1H), 6.90−7.10 (m, 7H), 7.40 (t, J = 7.9 Hz, 1H), 8.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.5, 61.3, 62.8, 66.1, 117.6, 121.8, 122.3, 127.2, 127.4, 128.3, 134.8, 136.1, 141.0, 149.0, 162.4; HRMS (ESI+) calcd for $C_{17}H_{20}N_2O{\cdot}H^+$ 269.1654, found 269.1649. Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 74.83; H, 7.75; N, 10.36.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(2″-furyl)but-3′-enylamino]ethanol (2q). Yellow oil (dr > 98:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (m, 2H), 2.58 (br s, 1H), 3.43 (dd, J = 10.8, 7.4 Hz, 1H), 3.62 (dd, J = 10.8, 4.5 Hz, 1H), 3.76 (m, 2H), 4.98 (m, 2H), 5.58 (m, 1H), 5.98 (d, J = 3.1 Hz, 1H), 6.15 (m, 1H), 7.10−7.22 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 38.3, 53.7, 61.8, 66.0, 106.5, 109.9, 110.0, 117.7, 127.2, 127.5, 128.5, 134.5, 140.8, 141.5, 155.9; MS (ESI+) *m/z* 258.1 (100). Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.72; H, 7.43; N, 5.45.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-(1″-naphthyl)but-3′-enylamino]ethanol (2r). Colorless oil (dr 81:19); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.58 (br s, 1H), 2.80 (m, 2H), 3.62 (m, 1H), 3.86 (m, 1H), 4.02 (m, 1H), 4.77 (t, 1H), 5.16 (m, 2H), 5.82 (m, 1H), 7.25−8.08 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.6, 54.6, 61.5, 65.8, 117.6, 123.0, 124.0, 125.4, 125.5, 126.0, 127.3, 127.6, 127.8, 128.6, 129.1, 131.2, 134.0, 135.0, 139.2, 141.1; HRMS (CI+) calcd for $C_{22}H_{23}NO{\cdot}H^+$ 317.1780, found 317.1795. Anal. Calcd for $C_{22}H_{23}NO$: C, 83.24; H, 7.80; N, 4.41. Found: C, 82.90; H, 7.85; N, 4.72.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-*tert*-butylbut-3′-enylamino]ethanol (2t). Colorless oil (dr > 98:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.77 (s, 9H), 2.18 (m, 2H), 2.38 (m, 1H), 2.60 (br s, 1H), 3.60−3.65 (m, 2H), 3.98 (dd, J = 8.3, 4.6 Hz, 1H), 5.00 (d, J = 9.1 Hz, 1H), 5.02 (d, J = 16.0 Hz, 1H), 5.82 (m, 1H), 7.20−7.25 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.0, 35.1, 35.9, 62.4, 62.6, 66.9, 115.8, 127.7, 128.6, 129.7, 138.4, 141.0; HRMS (CI+) calcd for $C_{16}H_{25}NO{\cdot}H^+$ 248.2014, found 248.1999.

(2*R*)-2-Phenyl-2-[(1′*R*)-1′-cyclohexylbut-3′-enylamino]ethanol (2u). Colorless oil (dr > 98:2 determined by ^{1}H NMR); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90−1.84 (m, 11H), 2.23 (m, 2H), 2.38 (m, 1H), 3.54 (dd, J = 10.5, 8.5 Hz, 1H), 3.66 (dd, J = 10.5, 4.5 Hz, 1H), 3.92 (dd, J = 8.5, 4.5 Hz, 1H), 5.14 (m, 2H), 5.82 (m, 1H), 7.23−7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4, 28.8, 29.2, 34.8, 40.8, 58.7, 61.8, 66.8, 116.7, 127.4, 128.4, 136.0, 141.3; HRMS (CI+) calcd for $C_{18}H_{27}NO{\cdot}H^+$ 274.2171, found 274.2192.

(2*R*)-2-Phenyl-2-[(1′*S*)-1′-propylbut-3′-enylamino]ethanol (2v). Colorless oil (dr > 98:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (m, 3H), 1.22−1.38 (m, 4H), 2.22 (m, 2H), 2.57 (m, 1H), 3.56 (m, 1H), 3.67 (dd, J = 10.5, 4.5, 1H), 3.93 (dd, J = 8.6, 4.5 Hz, 1H), 5.15 (m, 2H), 5.82 (m, 1H), 7.30−7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 19.0, 37.0, 37.8, 53.5, 61.6, 65.8, 117.2, 127.2, 127.5, 128.6, 135.2, 141.3; MS (ESI+) *m/z* 234.2 (100). Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C, 77.51; H, 10.26; N, 5.71.

(2*R*)-2-Phenyl-2-[(1′*S*)-1′-butylbut-3′-enylamino]ethanol (2w). Colorless oil (dr > 98:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (m, 3H), 1.18−1.42 (m, 6H), 2.23 (m, 2H), 2.58 (m, 1H), 3.58 (m, 1H), 3.71 (dd, J = 10.6, 4.6, 1H), 3.92 (dd, J = 8.6, 4.5 Hz, 1H), 5.18 (m, 2H), 5.82 (m, 1H), 7.23−7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.7, 28.0, 34.4, 37.7, 53.7, 61.7, 66.8, 117.2, 127.2, 127.5, 128.6, 135.2, 141.2; MS (ESI+) *m/z* 248.2 (100). Anal. Calcd for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.51; H, 10.26; N, 5.72.

(2*R*)-2-Phenyl-2-[(1′*S*)-1′-hexylbut-3′-enylamino]ethanol (2x). Colorless oil (dr > 98:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.77 (t, J = 7 Hz, 3H), 1.08−1.42 (m, 10H), 2.22 (m, 2H), 2.38 (br s, 1H), 2.58 (m, 1H), 3.58 (dd, J = 10.7, 8.8 Hz, 1H), 3.74 (dd, J = 10.8, 4.6 Hz, 1H), 3.92 (dd, J = 8.6, 4.4 Hz, 1H), 5.15 (m, 2H), 5.82 (m, 1H), 7.28 and 7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.5, 25.7, 29.2, 31.7, 34.7, 37.8, 53.6, 61.6, 66.8, 117.1, 127.2, 127.4, 128.5, 135.2, 141.3; HRMS (CI+) calcd for $C_{18}H_{29}NO{\cdot}H^+$ 276.2328, found 276.2323.

(2*R*)-2-Phenyl-2-[(1′*S*)-1′-(2″-phenylethyl)but-3′-enylamino]ethanol (2z). Yellow oil (dr > 98:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.75 (m, 2H), 2.38 (m, 2H), 2.56 (m, 1H), 2.66 (m, 2H), 3.58 (dd, J = 9.8, 8.5 Hz, 1H), 3.76 (dd, J = 10.5, 4.4 Hz, 1H), 3.96 (dd, J = 8.8, 4.6 Hz, 1H), 5.16 (m, 2H), 5.82 (m, 1H), 7.05−7.40 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.1, 36.7, 37.8, 53.6, 61.8, 66.9, 117.4, 125.7, 127.3, 127.7, 128.4, 128.6, 134.9, 141.2, 142.2; HRMS (CI+) calcd for $C_{20}H_{25}NO{\cdot}H^+$ 296.2014, found 296.2007.

General Procedure for the Oxidative Cleavage of the Auxiliary and Boc-Protection. To a solution of the amino alcohol in CH_2Cl_2/MeOH (1:1) at 0 °C was added, in one portion, 1.2 equiv of lead tetraacetate [$Pb(OAc)_4$]. The reaction mixture was stirred for 30 min, at which time TLC indicated complete reaction. Then 10 equiv of hydroxylamine hydrochloride ($NH_2OH.HCl$) was added and the mixture was stirred for another 30 min. The residue remained after removal of the solvents was washed with hexanes and suspended in CH_2Cl_2 followed by filtration of the lead precipitates. To the CH_2Cl_2 solution of the amine salt was added Et_3N (2.0 equiv) and Boc_2O (1.2 equiv). The reaction was stirred for 2 h and then 3-morpholinopropylamine (1 equiv) was added as a scavenger for the excess Boc_2O and the stirring was continued for another 1 h. The solution was diluted with ethyl acetate and extracted with 5% HCl. The organic layer was dried with anhydrous Na_2SO_4 and evaporated. The crude product was purified by flash column chromatography on silica gel with hexanes−ethyl acetate as eluent.

General Procedure for Determination of Enantiomeric Purities of 4. Trifluoroacetic acid (0.2 mL) was added to the solution of the Boc-protected homoallylamine (**4**) in CH_2Cl_2 (5.0 mg in 0.2 mL). After standing at room temperature for 15 min, the solvents were removed by a gentle stream of nitrogen. The residual amine salt was dissolved in CH_2Cl_2 (1.0

mL) and then treated with Et_3N (10 μL) and (*R*)- or (*S*)-Mosher's acid chloride (5 μL). TLC indicated complete reaction after 30 min at room temperature. The crude product was purified by acid−base extraction and the (*R*)- and (*S*)-MTPA amides analyzed by normal phase HPLC (150 × 4.6 mm^2 silica gel column, 3 μm particle size) with hexanes−^{i}PrOH as eluants and UV detection at 254 nm. When the HPLC peaks were not well separated, the enantiomeric ratio was estimated by integration of ^{1}H NMR signals of the diastereomeric MTPA amides at 400 MHz.

***N-tert*-Butoxycarbonyl-(*R*)-1-phenylbut-3-enamine (4f).** White solid (er 98:2 determined by HPLC); mp 76−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 9H), 2.55 (m, 2H), 4.79 (br m, 1H), 5.10 (br m, 1H), 5.12 (dd, J = 10.0, 17.2 Hz, 3H), 5.72 (m, 1H), 7.27−7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 41.3, 54.1, 79.4, 118.1, 126.3, 127.1, 128.5, 134.1, 142.4, 155.2; HRMS (FAB+) calcd for $C_{15}H_{21}O_2N{\cdot}H^+$ *m/z* 248.1650, found 248.1649.

***N-tert*-Butoxycarbonyl-(*R*)-1-(4′-methylphenyl)but-3-enamine (4g).** White solid (er 94:6 determined by HPLC); mp 93−95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9H), 2.37 (s, 3H), 2.54 (m, 2H), 4.74 (br m, 1H), 4.96 (br m, 1H), 5.12 (m, 2H), 5.71 (m, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 28.4, 41.3, 53.8, 79.4, 118.1, 126.2, 129.2, 134.2, 136.7, 139.4, 155.2; HRMS (FAB+) calcd for $C_{16}H_{23}O_2N{\cdot}H^+$ *m/z* 262.1807, found 262.1794.

***N-tert*-Butoxycarbonyl-(*R*)-1-(2′-methoxyphenyl)but-3-enamine (4h).** White solid (er 88:12 determined by HPLC); mp 109−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 9H), 2.56 (m, 2H), 3.88 (s, 3H), 4.97 (br m, 1H), 4.98 (dd, J = 10.8, 18.4 Hz, 2H), 5.42 (br d, J = 8.0 Hz, 1H), 5.72 (m, 1H), 6.89−6.96 (m, 2H), 7.20 (d, J = 6.8 Hz, 1H), 7.27 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.5, 40.0, 51.9, 55.3, 79.1, 110.8, 117.3, 120.5, 128.1, 128.2, 129.9, 135.0, 155.2, 156.8; HRMS (FAB+) calcd for $C_{16}H_{23}O_3N{\cdot}H^+$ *m/z* 278.1756, found 278.1768.

***N-tert*-Butoxycarbonyl-(*R*)-1-(3′-methoxyphenyl)but-3-enamine (4i).** White solid (er 91:9 determined by ^{1}H NMR); mp 87−89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9H), 2.54 (m, 2H), 3.83 (s, 3H), 4.75 (br m, 1H), 4.93 (br m, 1H), 5.12 (m, 2H), 5.71 (m, 1H), 6.80−6.90 (m, 3H), 7.28 (t, J = 8.0 Hz 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 41.2, 54.0, 55.2, 79.5, 112.1, 112.3, 118.2, 118.5, 129.5, 134.0, 144.1, 155.2, 159.7; HRMS (FAB+) calcd for $C_{16}H_{23}O_3N{\cdot}H^+$ *m/z* 278.1756, found 278.1772.

***N-tert*-Butoxycarbonyl-(*R*)-1-(4′-methoxyphenyl)but-3-enamine (4j).** White solid (er 93:7 determined by ^{1}H NMR); mp 105−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 9H), 2.53 (m, 2H), 3.82 (s, 3H), 4.71 (br m, 1H), 4.90 (br m, 1H), 5.10 (dd, J = 10.0, 17.2 Hz, 2H), 5.70 (m, 1H), 6.88 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 41.2, 53.5, 55.2, 79.4, 113.8, 118.0, 127.4, 134.2, 155.2, 158.6; HRMS (FAB+) calcd for $C_{16}H_{23}O_3N{\cdot}H^+$ *m/z* 278.1756, found 278.1754.

***N-tert*-Butoxycarbonyl-(*R*)-1-(2′-chlorophenyl)but-3-enamine (4m).** White solid (er 91:9 determined by HPLC); mp 104−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 9H), 2.50 (m, 1H), 2.58 (m, 1H), 5.14 (m, 2H), 5.72 (m, 1H), 7.17−7.37 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 39.4, 51.4, 79.6, 118.5, 126.9, 127.2, 128.2, 129.9, 132.5, 133.7, 139.8, 155.0; HRMS (FAB+) calcd for $C_{15}H_{20}O_2NCl{\cdot}H^+$ *m/z* 282.1261, found 282.1266.

***N-tert*-Butoxycarbonyl-(*R*)-1-(3′-chlorophenyl)but-3-enamine (4n).** White solid (er 93:7 determined by HPLC); mp 72−74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (s, 9H), 2.49 (m, 2H), 4.72 (br m, 1H), 4.94 (br m, 1H), 5.14 (m, 2H), 5.67 (m, 1H), 7.16 (d, J = 7.6 Hz, 1H), 7.22−7.29 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 41.1, 53.6, 79.8, 118.8, 124.5, 126.4, 127.3, 129.8, 133.4, 134.4, 144.7, 155.2; HRMS (FAB+) calcd for $C_{15}H_{20}O_2NCl{\cdot}H^+$ *m/z* 282.1261, found 282.1268.

***N-tert*-Butoxycarbonyl-(*R*)-1-(4′-chlorophenyl)but-3-enamine (4o).** White solid (er 94:6 determined by HPLC); mp 89−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 9H), 2.50 (m, 2H), 4.73 (br m, 1H), 4.95 (br d, J = 6.8 Hz, 1H), 5.14 (m, 2H), 5.67 (m, 1H), 7.22 (d, J = 8.4, Hz, 2H), 7.32 (d, J = 8.4, Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 41.1, 53.4, 79.7, 118.6, 127.6, 128.6, 132.7, 133.5, 141.1, 155.1; HRMS (FAB+) calcd for $C_{15}H_{20}O_2NCl{\cdot}H^+$ *m/z* 282.1261, found 282.1258.

***N-tert*-Butoxycarbonyl-(*R*)-2-pyridylbut-3-enamine (4p).** Yellow oil (er 95:5 determined by ^{1}H NMR); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 9H), 2.61 (m, 2H), 4.83 (br m, 1H), 5.06 (m, 2H), 5.68 (m, 1H), 7.18−7.25 (m, 2H), 7.66 (m, 1H), 8.58 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 40.8, 55.0, 79.3, 118.1, 121.9, 122.2, 133.8, 136.5, 149.2, 155.4, 160.1; HRMS (FAB+) calcd for $C_{14}H_{20}O_2N_2{\cdot}H^+$ *m/z* 249.1603, found 249.1604.

***N-tert*-Butoxycarbonyl-(*R*)-2-furylbut-3-enamine (4q).** Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9H), 2.58 (m, 2H), 4.87 (br m, 1H), 4.93 (br m, 1H), 5.10 (m, 2H), 5.71 (m, 1H), 6.17 (d, J = 2.8 Hz, 1H), 6.31 (m, 1H), 7.35 (d, J = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 38.6, 48.2, 79.6, 105.9, 110.1, 118.2, 133.6, 141.7, 154.5, 155.1; HRMS (FAB+) calcd for $C_{13}H_{19}O_3N{\cdot}H^+$ *m/z* 238.1443, found 238.1437.

***N-tert*-Butoxycarbonyl-(*R*)-1-naphthylbut-3-enamine (4r).** White solid (er 82:18 determined by HPLC): mp 118−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (s, 9H), 2.65−2.86 (m, 2H), 5.07 (br m, 1H), 5.18 (2d, J = 10.0 and 16.8 Hz, 2H), 5.66 (br m, 1H), 5.79 (m, 1H), 7.48−7.61 (m, 4H), 7.83 (m, 1H), 7.91 (d, J = 7.6 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 40.3, 49.8, 79.6, 118.1, 122.6, 123.1, 125.2, 125.7, 126.3, 128.0, 128.9, 130.9, 134.0, 134.2, 137.9, 155.2; HRMS (FAB+) calcd for $C_{19}H_{23}O_2N{\cdot}H^+$ *m/z* 298.1807, found 298.1811.

***N-tert*-Butoxycarbonyl-(*R*)-1-isopropylbut-3-enamine (4s).** Colorless oil (er 96:4 determined by HPLC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H), 1.44 (s, 9H), 1.74 (m, 1H), 2.12 (m, 1H), 2.26 (m, 1H), 3.52 (br m, 1H), 4.37 (br d, J = 8.0 Hz, 1H), 5.07 (m, 2H), 5.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 17.7, 19.3, 28.4, 31.4, 37.0, 55.1, 78.8, 117.1, 135.0, 155.9; HRMS (CI+) calcd for $C_{12}H_{23}O_2N{\cdot}H^+$ *m/z* 214.1807, found 214.1795.

***N-tert*-Butoxycarbonyl-(*R*)-1-*tert*-butylbut-3-enamine (4t).** White solid (er 97:3 determined by HPLC); mp 66−68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (s, 9H), 1.44 (s, 9H), 1.85 (m, 1H), 2.42 (m, 1H), 3.45 (m, 1H), 4.28 (br d, J = 10.0 Hz, 1H), 5.05 (m, 2H), 5.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4, 28.4, 34.7, 35.3, 58.4, 78.8, 116.5, 136.1, 156.2; HRMS (CI+) calcd for $C_9H_{18}O_2N$ (M − ^{t}Bu + 2H) *m/z* 172.1337, found 172.1343.

***N-tert*-Butoxycarbonyl-(*R*)-1-cyclohexylbut-3-enamine (4u).** White solid (er > 99:1 determined by HPLC); mp 87−89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91−1.28 (m, 7H), 1.44 (s, 9H), 1.63−1.76 (m, 4H), 2.12 (m, 1H), 2.25 (m, 1H), 3.50 (br m, 1H), 4.36 (br d, J = 8.4 Hz, 1H), 5.07 (m, 2H), 5.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 26.3, 26.4, 28.3, 28.4, 29.7, 36.8, 41.5, 54.5, 78.9, 117.2, 135.1, 155.9; HRMS (FAB+) calcd for $C_{15}H_{27}O_2N{\cdot}H^+$ *m/z* 254.2120, found 254.2116.

***N-tert*-Butoxycarbonyl-(*S*)-1-propylbut-3-enamine (4v).** Colorless oil (er 96:4 determined by HPLC); δ 0.93 (t, J = 7.2 Hz, 3H), 1.24−1.36 (m, 4H), 1.44 (s, 9H), 2.22 (m, 2H), 3.66 (br m, 1H), 4.37 (br d, J = 7.2 Hz, 1H), 5.09 (m, 2H), 5.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 19.2, 28.4, 36.9, 39.6, 49.8, 78.9, 117.5, 134.6, 155.6; HRMS (CI+) calcd for $C_{12}H_{23}O_2N{\cdot}H^+$ *m/z* 214.1807, found 214.1822.

***N-tert*-Butoxycarbonyl-(*S*)-1-butylbut-3-enamine (4w).** Colorless oil (er > 99:1 determined by HPLC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 6.8 Hz, 3H), 1.33−1.40 (m, 6H), 1.46 (s, 9H), 2.14−2.30 (m, 2H), 3.63 (br m, 1H), 4.36 (br m, 1H), 5.10 (m, 2H), 5.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 28.1, 28.4, 34.4, 39.6, 50.1, 78.9, 117.6, 134.6, 155.6; HRMS (FAB+) calcd for $C_{13}H_{25}O_2N{\cdot}H^+$ *m/z* 228.1964, found 228.1981.

***N-tert*-Butoxycarbonyl-(*S*)-1-hexylbut-3-enamine (4x).** Colorless oil (er 95:5 determined by HPLC); ^{1}H NMR (400

MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3H), 1.22−1.36 (m, 10H), 1.45 (s, 9H), 2.13−2.28 (m, 2H), 3.63 (br m, 1H), 4.34 (br m, 1H), 5.09 (m, 2H), 5.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 25.9, 28.4, 29.2, 31.8, 34.7, 39.6, 50.1, 78.9, 117.6, 134.6, 155.6; HRMS (FAB+) calcd for $C_{15}H_{29}O_2N{\cdot}H^+$ *m/z* 256.2277, found 256.2276.

***N-tert*-Butoxycarbonyl-(*R*)-1-(2′-phenylethenyl)but-3-enamine (4y).** Yellow solid (er 96:4 determined by HPLC); mp 73−75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 9H), 2.41 (m, 2H), 4.41 (br m, 1H), 4.66 (br m, 1H), 5.15 (m, 2H), 5.83 (m, 1H), 6.15 (dd, J = 5.6, 16.0 Hz, 1H), 6.53 (d, J = 16.0 Hz, 1H), 7.23−7.39 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 39.9, 51.7, 79.5, 118.3, 126.4, 127.5, 128.6, 129.9, 130.1, 133.8, 136.8, 155.3; HRMS (FAB+) calcd for $C_{17}H_{23}O_2N{\cdot}H^+$ *m/z* 274.1807, found 274.1815.

***N-tert*-Butoxycarbonyl-(*S*)-1-(2′-phenylethyl)but-3-enamine (4z).** White solid (dr 99:1 determined by HPLC); mp 56−58 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.62−1.92 (m, 2H), 2.22 (m, 2H), 2.70 (m, 2H), 3.76 (br m, 1H), 4.40 (br d, J = 7.2 Hz, 1H), 5.13 (m, 2H), 5.81 (m, 1H), 7.21−7.34 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 32.5, 36.7, 39.7, 50.0, 79.1, 117.8, 125.9, 128.4, 128.5, 134.3, 142.0, 155.6; HRMS (FAB+) calcd for $C_{17}H_{25}O_2N{\cdot}H^+$ *m/z* 276.1963, found 276.1978.

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Supporting Information Available: Characterization data for known compounds; ^{1}H NMR spectra of (*R*)- and (*S*)-BPG derivatives of **4e**, **4f**, and **4s**, ^{1}H NMR spectra of allyl bromide−indium in CD_3OD before and after addition of *N*-benzylidenebenzylamine, and ^{1}H and ^{13}C NMR spectra of **2e**−**z** and **4e**−**z**. This material is available free of charge via the Internet at http://pubs.acs.org.

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