Diastereoselective Barbier-Type and Palladium-Mediated Allylation of Optically Active Aldimine with Allylindium Reagents

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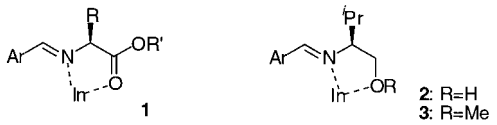
The first ionization potential of indium (In) (5.8 eV) is as low as that of Li and Na. Therefore, it is easy for indium to affect SET (single electron transfer) processes. In addition, indium is comparatively stable in air, and the toxicity observed in many metals is little known in In.[1] For these reasons, In is one of the most notable metals at present, and its usefulness in organic synthesis has been studied in terms of green chemistry.[2] Whereas numerous allylation reactions of carbonyl compounds with In have been reported,[3] there are few reports on the allylation reactions of imines with In due to their poor reactivity compared with the corresponding carbonyl compounds. Thus far, three allylation reactions of optically active imines such as **1** have been reported, and all of these utilized the chelation of iminoester **1** with In to attain moderate to good diastereoselectivities (50−90% de).[4] Here, we report that the Barbier-type allylation of the optically active imino alcohol-type aldimine **2** proceeded with high regio- and stereoselectivity by a more effective chelation control via **2** (method A). Furthermore, we have developed a novel one-pot allylation of **2** with an In/$Pd(PPh_3)_4$ bimetallic system (method B) (Scheme 1).

We have already reported the reductive allylation reaction of the optically active imines **3** with samarium(0) and allyl halides.[5] In this reaction, high diastereoselectivities were obtained when the optically active imines

Scheme 1



3 bearing a methoxy group were employed. Then we first examined the allylation reaction of imine **3** with In and allyl bromide under the typical Barbier-type conditions. But the result was not satisfactory, giving the desired product **4a** in low yield. Previously, Paquette et al. reported that indium-mediated allylations of carbonyl compounds possessing a hydroxy group proceeded with high diastereoselectivity.[2,6] We next investigated the allylation reaction of imine **2** in expectation of good results by improving several conditions. When the reaction was carried out in the presence of imine **2**, 1.5 equiv of In and 1.5 equiv of allyl halides in DMF at room temperature (method A), (*S*,*S*)-allylation product **4a**[7] was obtained in high yields and high diastereoselectivities (Table 1, runs 1 and 2). The allylation reaction did not proceed when allyl chloride was used (run 3). Similar allylation with various allylic bromides proceeded regioselectively by attack of the γ-carbon of the allylindium reagents to the imine **2** (runs 4−9). Also in our experiments, high diastereoselectivities to C1′ were obtained (runs 1−9). When the γ position had two substituents, the reaction did not proceed (run 10).

Next, a different allylation method (method B) was examined to extend the reaction to other allylic substrates. Recently, Araki et al. reported the umpolung of π-allylpalladium(II) complexes (electrophile) with InI.[8] Although we adapted this procedure to imine **2**, most of the starting material was recovered with a trace amount of an allylated compound. After many experiments with other palladium-mediated methods, we found that the use of In and I_2 in place of InI dramatically enhanced the allylation reaction via umpolung. The allylation of the optically active imine **2** gave compound **4a** in 95% yield as the sole product (run 11). It would be considered that similarly an allylindium species (nucleophile) was formed in situ via a π-allylpalladium(II) complex (electrophile) with In and I_2.[9] Our method is economical, because reagents such as cheap In and I_2 can be used instead of expensive InI. Although Tuck et al. had previously reported a convenient synthetic method of InI,[10] it took much time and labor to prepare the reagent.

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(8) (a) Araki et al. reported recently that umpolung of the π-allylpalladium(II) with indium(I) salts proceeded smoothly to provide allylindium(III) reagents. The ^{1}H NMR spectrum of allylindium(III) compound in DMF-d_7 revealed the allylic protons at δ 2.08 ppm (2H). Araki, S.; Kamei, T.; Hirashita, T.; Yamamura, H.; Kawai, M. *Org. Lett.* **2000**, *2*, 847−849. (b) Ohno, H.; Hamaguchi, H.; Tanaka, T. *Org. Lett.* **2000**, *2*, 2161−2163.

(9) In (1.5 equiv), I_2 (0.75 equiv), $Pd(PPh_3)_4$ (5 mol %) or In (2 equiv), I_2 (2 equiv), $Pd(PPh_3)_4$ (5 mol %) and imine **2** were used for the preparation of InI.

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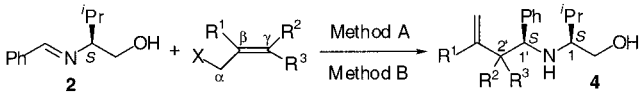
Table 1. Indium-Mediated Diastereoselective Allylation to Imine 2



2 **4**

run	method	R^1	R^2	R^3	X	reaction time (h)	product **4**	yield (%)	de (C1′, %)	dr (C2′)
1	A	H	H	H	Br	1	**4a**	95	>99	
2	A	H	H	H	I	1	**4a**	96	>99	
3	A	H	H	H	Cl	24	**4a**	trace		
4	A	Me	H	H	Br	1	**4b**	91	>99	
5	A	CO_2Me	H	H	Br	3	**4c**	48	94:6	
6	A	H	Me	H	Br	24	**4d**	79	>99	5:1[a]
7	A	H	Et	H	Br	24	**4e**	47	>99	5:1[a]
8	A	H	Ph	H	Br	24	**4f**	60	*b*	*b*
9	A	H	H	Et	Br	24	**4e**	21	>99	4:1[a]
10	A	H	Me	Me	Br	24		0		
11[c]	B	H	H	H	OAc	3	**4a**	95	>99	
12[c]	B	H	H	H	OCO_2Et	3	**4a**	92	>99	
13[d]	B	H	H	H	OPh	15	**4a**	81	>99	
14[d]	B	H	H	H	Cl	15	**4a**	52	95:5	
15[d]	B	H	H	H	OH	24	**4a**	24	89:11	

[a] Diastereomeric ratios (dr) of C2′ position were determined by ^{1}H NMR spectra. [b] Only this reaction, a mixture of four diastereoisomers was obtained. The ratio of the products by ^{1}H NMR is 82:6:4:8. The major isomer is thought to be the (*S*,*S*,*R*)- or (*S*,*S*,*S*)-isomer based on the allylation mechanism. [c] The reactions were carried out by using optically active imine (1 mmol), allyl halide (1.5 mmol), $Pd(PPh_3)_4$ (5 mol %), indium (1.5 mmol), and iodine (0.75 mmol) in DMF. [d] The reactions were carried out by using optically active imine (1 mmol), allyl halide (1.5 mmol), $Pd(PPh_3)_4$ (5 mol %), indium (2 mmol), and iodine (2 mmol) in DMF.

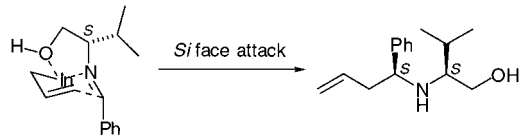


Figure 1. Plausible mechanism of indium-mediated diastereoselective allylation.

By using method B, allyl acetate, allyl carbamate, allyl phenyl ether, allyl chloride, and allyl alcohol could be used as the allylation reagent. The allylation products were obtained in good to moderate yield and in high diastereoselectivity, respectively (runs 11−14).

To clarify the difference in the above results, the ^{1}H NMR spectrum of the allylindium compounds was taken by methods A and B in $CDCl_3$. The experiments revealed the allylic proton signals at δ 1.7 (major) and 2.1 (minor) ppm after 30 min and 1 h of the reaction. These chemical shifts are in good accordance with the reported data of the allylindium(I) and allylindium(III) species, respectively.[8a,11] Because only the allylindium(III) species were obtained from Araki's method, it can be assumed that it is difficult to effect allylation of inactive imine **2**.

It is thought that the allylindium intermediate coordinates with both the hydroxy and nitrogen functions of imine **2** as Figure 1. Owing to this conformation, the bulky isopropyl group of the chiral auxiliary selectively shields the *re* face of the imine **2**, and hence, the allylic addition proceeds from the *si* face. This supported the high diastereoselectivity of these reactions.

In summary, we have developed the first regio- and stereoselective allylation of imine **2** bearing a hydroxy group on the chiral auxilialy under the Barbier-type conditions and revealed that the chelation between the nitrogen and hydroxy groups of the imine **2** with In is crucial for the high stereoselectivity. In addition, a new economical palladium-mediated allylation of imine **2** has been established. By removing the chiral auxiliary unit of these β-amino alcohol derivatives, it is possible to obtain the optically active homoallylamine in high yield.[5a,5b] In addition, the induction to optically active β-amino acid derivatives[5d,12] and γ- lactams,[13] etc., is also possible.

Experimental Section

All reactions were carried out under a positive pressure of argon or nitrogen. ^{1}H NMR spectra were recorded on a JEOL JNM-EX-270 or JEOL JNM-LA-500 spectrometer using tetramethylsilane (TMS) as an internal standard. ^{13}C NMR spectra were recorded on a JEOL JNM-EX-270 (67.8 MHz) spectrometer. Optical rotations were measured with a JASCO DIP-360 digital polarimeter. Nominal (LRMS) and exact mass (HRMS) spectra were recorded on a JEOL JMS−HX/HX-110A instrument. Metallic indium was purchased from Kojundo Chemical Laboratory Co., Ltd ($0.80−1.00 per gram). For flash chromatography, silica gel FL60D (Fuji Silysia Chemical Ltd.) was employed.

General Procedure for the Barbier-Type Allylation Reaction of Imine 2 (Method A). The mixture of imine **2** (1 mmol), In (1.5 mmol) and allyl bromide (1.5 mmol) in DMF (5 mL) was stirred for 1 h at room temperature under nitrogen. The reaction mixture was evaporated. AcOEt and 1 N aqueous HCl were added to the resulting suspension and stirred for 30 min. Aqueous NaOH (30%) was added to the resulting solution until neutral. The solution was stirred for 10 min. The mixture was extracted with AcOEt. The extract was washed with brine, dried over anhydrous potassium carbonate, and concentrated under reduced pressure. The mixture was purified by flash silica gel column chromatography with hexane/AcOEt = 8:1 to give the title compound **4a** (95% yield).

General Procedure for the Palladium-Mediated Allylation Reaction of Imine 2 (Method B). The mixture of imine **2** (1 mmol), $Pd(PPh_3)_4$ (5 mol %), In (1.5 mmol), I_2 (0.75 mmol), and allyl acetate (1.5 mmol) in DMF (5 mL) was stirred for 1 h at room temperature under nitrogen. The reaction mixture was evaporated. AcOEt and 1 N aqueous HCl were added to the resulting suspension and stirred for 30 min. Then 30% aqueous NaOH was added to the resulting solution until neutral. The

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solution was stirred for 10 min. The mixture was extracted with AcOEt. The extract was washed with brine, dried over anhydrous potassium carbonate, and concentrated under reduced pressure. The mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 9:1) to give the title compound **4a**[7] (95% yield).

3-Methyl-(2*S*)-[3-methyl-(1*S*)-phenylbut-3-enylamino]-butan-1-ol, 4b: colorless oil; R_f = 0.3, hexane/AcOEt = 3:1; $[\alpha]^{18}_D$ −46.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.80, 0.85 (d, *J* = 6.7 Hz, 6H, CH(C*H*$_3$)$_2$), 1.67 (dqq, *J* = 6.7, 6.7, 6.7 Hz, 1H, C*H*Me$_2$), 1.71 (s, 3H, C*H*$_3$), 2.22 (ddd, *J* = 4.2, 4.2, 6.7 Hz, 1H, C*H*^{i}Pr), 2.31 (dd, *J* = 6.1, 13.4 Hz, 1H, C*H*CN), 2.43 (dd, *J* = 7.9, 13.4 Hz, 1H, C*H*CN), 3.40, 3.61 (dd, *J* = 4.2, 10.7 Hz, 2H, C*H*$_2$OH), 3.82 (dd, *J* = 6.1, 7.9 Hz, 1H, PhC*H*), 4.70, 4.77 (d, *J* = 1.5 Hz, 2H, C*H*$_2$=), 7.22−7.33 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 19.0, 19.4, 22.4, 29.4, 47.2, 58.4, 59.9, 61.1, 113.2, 127.0, 127.1, 128.3, 142.8, 144.3. Anal. Calcd for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.80; H, 10.31; N, 5.48.

2-[[(1*S*)-Hydroxymethyl-2-methylpropylamino]-(3*S*)-2-phenylethyl]acrylic Acid Methyl Ester, 4c: colorless oil; R_f = 0.1, hexane/AcOEt = 3:1; ^{1}H NMR ($CDCl_3$) δ 0.81, 0.85 (d, *J* = 6.7 Hz, 6H, CH(C*H*$_3$)$_2$), 1.67 (dqq, *J* = 6.7, 6.7, 6.7 Hz, 1H, C*H*Me$_2$), 2.24 (ddd, *J* = 4.0, 4.0, 6.7 Hz, 1H, C*H*^{i}Pr), 2.57 (dd, *J* = 6.7, 13.7 Hz, 1H,allyl C*H*), 2.77 (dd, *J* = 7.9, 13.7 Hz, 1H, allyl C*H*), 3.36, 3.58 (dd, *J* = 4.0, 11.0 Hz, 2H, C*H*$_2$OH), 3.74 (s, 3H, CO_2CH_3), 3.85 (dd, *J* = 6.7, 7.6 Hz, 1H, PhCH), 5.43 (d, *J* = 1.2 Hz, 1H, C*H*=), 6.09 (d, *J* = 1.2 Hz, 1H, C*H*=), 7.24−7.33 (m, Ph, 5H); ^{13}C NMR ($CDCl_3$) δ 18.9, 19.5, 29.4, 41.0, 51.9, 59.8, 59.9, 61.0, 126.7, 127.0, 127.2, 128.4, 138.0, 143.5, 168.0; LRMS (FAB) *m*/*z*, 292 (M^+). Anal. Calcd for $C_{17}H_{25}NO_3$: C, 70.70; H, 8.65; N, 4.81. Found: C, 70.35; H, 8.72; N, 4.67.

3-Methyl-(2*S*)-[2-methyl-(1*S*)-phenylbut-3-enylamino]-butan-1-ol, 4d (major): colorless oil; R_f = 0.3, hexane/AcOEt = 3:1; $[\alpha]^{16}_D$ −84.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.77 (d, *J* = 6.7 Hz, 3H, CHC*H*$_3$), 0.81 (d, *J* = 6.7 Hz, 6H, CHC*H*$_3$, C*H*$_3$), 1.63 (dqq, *J* = 6.7, 6.7, 6.7 Hz, 1H, C*H*Me$_2$), 2.12 (brs, 2H, NH, OH), 2.12 (ddd, *J* = 3.7, 4.0, 7.0 Hz, 1H, C*H*^{i}Pr), 2.37 (ddq, *J* = 7.6, 7.6, 7.6 Hz, 1H, MeC*H*), 3.38 (d, *J* = 8.2 Hz, 1H, PhC*H*), 3.40 (dd, *J* = 3.7, 11.0 Hz, 1H, C*H*$_2$OH), 3.58 (dd, *J* = 4.3, 11.0 Hz, 1H, C*H*$_2$OH), 5.10 (dd, *J* = 1.2, 10.1 Hz, 1H, C*H*$_2$=), 5.11 (dd, *J* = 0.9, 17.1 Hz, 1H, C*H*$_2$=), 5.81 (ddd, *J* = 8.2, 10.4, 17.1 Hz, 1H, CH$_2$=C*H*), 7.21−7.33 (m, Ph, 5H); ^{13}C NMR ($CDCl_3$) δ 17.9, 19.1, 19.5, 29.2, 45.2, 59.5, 61.1, 64.8, 115.3, 127.1, 127.7, 128.2, 142.2, 142.9. Anal. Calcd for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.42; H, 10.23; N, 5.63.

3-Methyl-(2*S*)-[2-methyl-(1*S*)-phenylbut-3-enylamino]-butan-1-ol, 4d (minor): colorless oil; R_f = 0.3, hexane/AcOEt = 3:1; ^{1}H NMR ($CDCl_3$) δ 0.83, 0.88 (d, *J* = 7.0 Hz, 6H, CH-(C*H*$_3$)$_2$), 1.00 (d, *J* = 7.0 Hz, 3H, C*H*$_3$), 1.71 (dqq, *J* = 7.0, 7.0, 7.0 Hz, 1H, C*H*Me$_2$), 2.18−2.19 (m, 1H, C*H*^{i}Pr), 2.41 (brs, 2H, NH, OH), 2.51−2.55 (m, 1H, MeC*H*), 3.41 (dd, *J* = 3.4, 11.0 Hz, 1H, C*H*$_2$OH), 3.57−3.61 (m, *2*H, C*H*$_2$OH, PhC*H*), 5.00 (d, *J* = 9.3 Hz, 1H, C*H*$_2$=), 5.00 (d, *J* = 16.0 Hz, 1H, C*H*$_2$=), 5.61 (ddd, *J* = 7.9, 9.3, 17.0 Hz, 1H, CH$_2$=C*H*), 7.16−7.32 (m, Ph, 5H); ^{13}C NMR ($CDCl_3$) δ 16.9, 19.1, 19.6, 29.3, 43.8, 59.1, 60.6, 63.9, 115.4, 126.9, 127.9, 128.0, 140.6, 141.4. Anal. Calcd for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.73; H, 10.42; N, 5.42.

(2*S*)-[2-Ethyl-(1*S*)-phenylbut-3-enylamino]3-methylbutan-1-ol, 4e (major): colorless oil; R_f = 0.3, hexane/AcOEt = 3:1; $[\alpha]^{17}_D$ −79.7 (*c* 0.94, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 0.75 (t, *J* = 7.3 Hz, 3H, C*H*$_3$), 0.76, 0.79 (d, *J* = 6.7 Hz, 6H, CH(C*H*$_3$)$_2$), 1.01−1.11 (m, 1H, CH$_3$C*H*), 1.17−1.25 (m, 1H, CH$_3$C*H*), 1.62 (dqq, *J* = 6.7, 6.7, 6.7 Hz, 1H,Me$_2$C*H*), 2.10−2.16 (m, 2H, C*H*^{i}Pr, allyl CH), 2.58 (brs, 2H, NH, OH), 3.41 (dd, *J* = 3.7, 11.0 Hz, 1H, C*H*OH), 3.46 (d, *J* = 8.5 Hz, 1H, PhCH), 3.58 (dd, *J* = 4.3, 11.0 Hz, 1H, C*H*OH), 5.12 (dd, *J* = 1.8, 17.1 Hz, 1H, C*H*=), 5.20 (dd, *J* = 1.8, 10.4 Hz, 1H, C*H*=), 5.62 (ddd, *J* = 10.1, 10.1, 17.1 Hz, 1H, CH$_2$=C*H*), 7.23−7.33 (m, Ph, 5H); ^{13}C NMR ($CDCl_3$) δ 12.0, 19.4, 19.8, 24.6, 29.5, 53.6, 59.7, 61.3, 63.8, 117.5, 127.2, 128.1, 128.4, 140.7, 143.5. Anal. Calcd for $C_{17}H_{27}NO$: C, 78.11; H, 10.41; N, 5.36. Found: C, 78.13; H, 10.69; N, 5.18.

(2*S*)-[2-Ethyl-(1*S*)-phenylbut-3-enylamino]3-methylbutan-1-ol, 4e (minor): colorless oil; R_f = 0.3, hexane/AcOEt = 3:1; ^{1}H NMR ($CDCl_3$) δ 0.83, 0.88 (d, *J* = 7.0 Hz, 6H, CH(C*H*$_3$)$_2$), 0.84 (dd, *J* = 7.3, 7.3 Hz, 3H, C*H*$_3$), 1.02−1.26 (m, 2H, CH$_3$C*H*$_2$), 1.69−1.73 (m, 1H,Me$_2$C*H*), 2.16−2.19 (m, 1H, C*H*^{i}Pr), 2.23−2.30 (1H, m, allyl CH$_2$), 3.41 (dd, *J* = 3.7, 11.0 Hz, 1H, C*H*$_2$OH), 3.58 (dd, *J* = 4.3, 11.0 Hz, 1H, C*H*$_2$OH), 3.68 (d, *J* = 8.5 Hz, 1H, PhC*H*), 5.04−5.10 (m, 2H, C*H*$_2$=), 5.41 (ddd, *J* = 10.1, 10.1, 16.8 Hz, 1H, CH$_2$=C*H*), 7.05−7.47 (m, Ph, 5H). Anal. Calcd for $C_{17}H_{27}NO$: C, 78.11; H, 10.41; N, 5.36. Found: C, 77.85; H, 10.70; N, 5.30.

(2*S*)-[(1*S*)-2-Diphenylbut-3-enylamino]-3-methylbutan-1-ol, 4f (major): colorless oil; R_f = 0.3, hexane/AcOEt = 3:1; $[\alpha]^{18}_D$ +10.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.70, 0.73 (d, *J* = 6.7 Hz, 6H, 2 × C*H*$_3$), 1.52 (dqq, *J* = 6.7, 6.7, 6.7 Hz, 1H, Me$_2$C*H*), 2.10 (ddd, *J* = 3.7, 4.0, 6.7 Hz, 1H, C*H*^{i}Pr), 3.28, 3.46 (dd, *J* = 3.7, 10.1 Hz, 2H, C*H*$_2$OH), 3.53 (dd, *J* = 8.5, 8.2 Hz, 1H, allyl C*H*), 3.90 (d, *J* = 8.9 Hz, 1H, PhC*H*), 4.82 (dd, *J* = 1.2, 17.1 Hz, 1H, C*H*$_2$=CH), 4.91 (dd, *J* = 1.2, 10.1 Hz, 1H, C*H*$_2$=CH), 0.5.86 (ddd, *J* = 8.2, 10.1, 17.1 Hz, 1H, Ph, C*H*=), 7.22−7.33 (m, Ph, 10H); ^{13}C NMR ($CDCl_3$) δ 19.0, 19.5, 29.1, 57.5, 59.4, 61.1, 64.8, 116.6, 126.7, 127.2, 128.0, 128.1, 128.2, 128.6, 138.6, 142.0, 142.1; LRMS (CI) *m*/*z*, 310 (MH^+), 192; HRMS calcd for $C_{21}H_{28}NO$ (MH^+) 309.4452, found 310.2163. Anal. Calcd for $C_{21}H_{27}NO$: C, 81.51; H, 8.79; N, 4.53. Found: C, 81.35; H, 8.89; N, 4.38.

(2*S*)-[(1*S*)-2-Diphenylbut-3-enylamino]3-methyl-butan-1-ol, 4f (minor-1): colorless oil; R_f = 0.3, hexane/AcOEt = 3:1; ^{1}H NMR ($CDCl_3$) δ 0.43, 0.64 (d, *J* = 7.0 Hz, 6H, 2 × C*H*$_3$), 1.76 (m, 1H, Me$_2$C*H*), 2.23 (ddd, *J* = 4.3, 4.3, 8.5 Hz, 1H, C*H*^{i}Pr), 2.94−3.50 (m, 3H, C*H*$_2$OH, allyl C*H*), 3.96 (d, *J* = 10.1 Hz, 1H, PhC*H*), 4.65 (d, *J* = 16.8 Hz, 1H, C*H*$_2$=CH), 4.80 (d, *J* = 10.4 Hz, 1H, C*H*$_2$=CH), 5.73 (ddd, *J* = 7.6,10.6, 16.8 Hz, 1H, C*H*=), 6.94−7.47 (m, Ph, 10H); LRMS (CI) *m*/*z* 310 (MH^+), 192; HRMS calcd for $C_{21}H_{28}NO$ (MH^+) 309.4452, found 310.2180.

(2*S*)-[(1*S*)-2-Diphenylbut-3-enylamino]-3-methylbutan-1-ol, 4f (minor-2): colorless oil; R_f = 0.3, hexane/AcOEt = 3:1; ^{1}H NMR ($CDCl_3$) δ 0.78, 0.83 (d, *J* = 6.7 Hz, 6H, 2 × C*H*$_3$), 1.66 (m, 1H, Me$_2$C*H*), 2.15 (m, 1H, C*H*^{i}Pr), 2.94−3.50 (m, 2H, C*H*$_2$-OH, allyl C*H*), 3.60 (dd, *J* = 3.7, 10.7 Hz, 1H, C*H*$_2$OH), 3.89 (d, *J* = 8.5 Hz, 1H, PhC*H*), 5.17 (d, *J* = 17.7 Hz, 1H, C*H*$_2$=CH), 5.19 (d, *J* = 10.4 Hz, 1H, C*H*$_2$=CH), 0.6.15−6.25 (m, 1H, C*H*=), 6.94−7.47 (m,10H, Ph); LRMS (CI) *m*/*z* 310 (MH^+), 192; HRMS calcd for $C_{21}H_{28}NO$ (MH^+) 309.4452, found 310.2166.

(2*S*)-[(1*S*)-2-Diphenylbut-3-enylamino]-3-methylbutan-1-ol, 4f (minor-3). colorless oil; R_f = 0.3, hexane/AcOEt = 3:1; ^{1}H NMR ($CDCl_3$) δ 0.85, 0.89 (d, *J* = 7.0 Hz, 6H, 2 × C*H*$_3$), 1.96 (m, 1H, Me$_2$C*H*), 2.34 (ddd, *J* = 4.3, 4.3, 8.5 Hz, 1H, C*H*^{i}Pr), 2.94−3.50 (m, 3H, C*H*$_2$OH, allyl C*H*), 3.93 (d, *J* = 9.5 Hz, 1H, PhC*H*), 5.26 (d, *J* = 10.1 Hz, 1H, C*H*$_2$=CH), 5.32 (d, *J* = 17.1 Hz, 1H, C*H*$_2$=CH), 0.6.19 (ddd, *J* = 10.1, 10.1, 17.1 Hz, 1H, Ph, C*H*=), 6.94−7.47 (m, Ph, 10H); LRMS (CI) *m*/*z* 310 (MH^+), 192; HRMS Calcd for $C_{21}H_{28}NO$ (MH^+) 309.4452, found 310.2180.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for new compounds **4** are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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