Rhodium-Catalyzed Asymmetric Amination of Allylic Trichloroacetimidates

Jeffrey S. Arnold, Hien M. Nguyen*

Department of Chemistry, University of Iowa, Iowa City, IA 52242, USA
E-mail: hien-nguyen@uiowa.edu

Received: 22.02.2013; Accepted after revision: 20.03.2013

Abstract: A summary is presented of dynamic kinetic asymmetric transformations of racemic allylic trichloroacetimidates in the presence of chiral diene-ligated rhodium catalysts. The reaction is applicable to a wide variety of secondary and tertiary trichloroacetimidates containing aniline or benzylamine nucleophiles, affording nitrogen-containing tertiary and quaternary centers in good yields and with high levels of regio- and enantioselectivity. This catalytic method addresses many of the limitations previously associated with syntheses of these compounds.

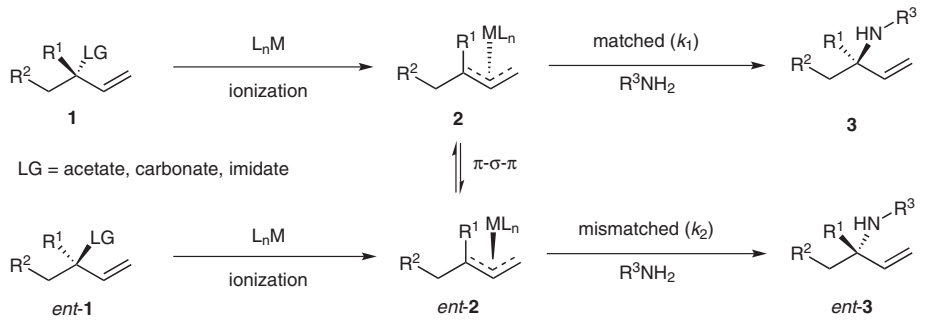
Key words: asymmetric catalysis, aminations, rhodium, catalysis, imidates

Chiral amine functional groups are widely distributed in the architecture of the natural world, and they have been embedded into many materials, catalysts, pharmaceuticals, and agrochemicals to impart a range of desirable structural, physical, and chemical properties.[1] As a result, the development of new strategies for introducing nitrogen into organic molecules in a highly selective manner continues to be a focus of investigation.[2] One major area that continues to evolve is the utilization of transition metals (such as palladium,[3] iridium,[4] or rhodium[5]) to catalyze asymmetric aminations in allylic systems. These methods produce allylic amine moieties that are valuable precursors for subsequent transformations. In general, the reactions employ linear allylic acetates or carbonates, providing secondary branched amines in good yields and with high regio- and enantioselectivities.

Alternatively, enantiomerically enriched amines can be prepared by transition-metal catalyzed dynamic kinetic asymmetric transformations (DYKATs)[6] of branched allylic electrophiles (Scheme 1). Besides their utility in resolution-type methods, these racemic substrates have the advantage of being easily prepared from allylic alcohols derived by vinylic addition reactions of a variety of aldehydes and ketones. Furthermore, they react more rapidly than their linear counterparts because of the lower degree of steric congestion at the olefin moiety.[7] At the start of our investigation, there were few reports of kinetic[8] or DYKAT-type[9] resolutions that gave enantiopure allylic amine products.

Following our successes with transition metal-catalyzed stereoselective transformations with glycal and glycosyl trichloroacetimidates,[10] we investigated amination reactions with allylic substrates bearing a branched trichloroacetimidate leaving group.[11] Taking our lead from the pioneering work of Evans and co-workers in developing rhodium-catalyzed enantiospecific amination reactions with secondary allylic carbonates,[12] we selected rhodium catalysts in combination with allylic trichloroacetimidates for our studies. In 2010, we reported a high-yielding regioselective preparation of α-substituted allylic aryl amines from secondary trichloroacetimidates and a wide range of anilines.[7a] In 2011, we described a new method for the preparation of α,α-disubstituted allylic aryl amines.[13] Our regioselective amination[7a,13] ultimately provided a path to the discovery of rhodium-catalyzed DYKAT with aniline nucleophiles.

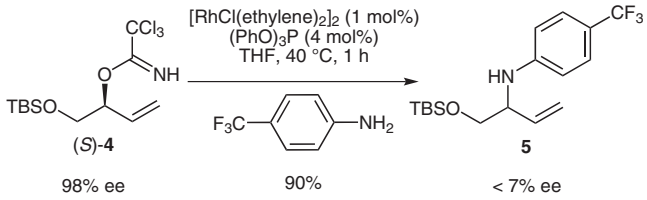
To clarify the stereochemical outcome of our allylic amination, we performed control experiments with enantiomerically enriched allylic trichloroacetimidate **4** (98% ee) (Scheme 2).[7a] The reaction was not enantiospecific, as evidenced by the significant degree of racemization of the amination product **5** (<7% ee). This result is in stark con-



Scheme 1 Transition metal-catalyzed asymmetric aminations of branched allylic electrophiles

SYNTHESIS 2013, 45, 2101–2108
Advanced online publication: 30.04.2013
DOI: 10.1055/s-0032-1316921; Art ID: SS-2013-C0145-ST

trast to other transition-metal-catalyzed allylic substitution reactions, which have been reported to provide products with net retention of stereochemistry.[12] The outcome of this experiment can be rationalized by comparing the rate of equilibration of diastereomeric organorhodium complexes (for example, **2** and *ent*-**2**) with that of nucleophilic attack by aniline (Scheme 1). We hypothesized that the rate of aniline substitution (k_1 and k_2) is slower than that of π–σ–π interconversion, resulting in racemization in the amine product **3**. On the basis of this study, we explored the possibility of rendering the process regio- and enantioselective. By employing a chiral ligand, a more sterically encumbered environment is established, which slows down the rate of substitution by aniline nucleophiles and increases the time allowed for the equilibration between the two diastereomeric complexes, **2** and *ent*-**2**. An unfavorable interaction between one of the two π-allylrhodium intermediates will determine which enantiomer of the amination product (**3** or *ent*-**3**) is formed preferentially.

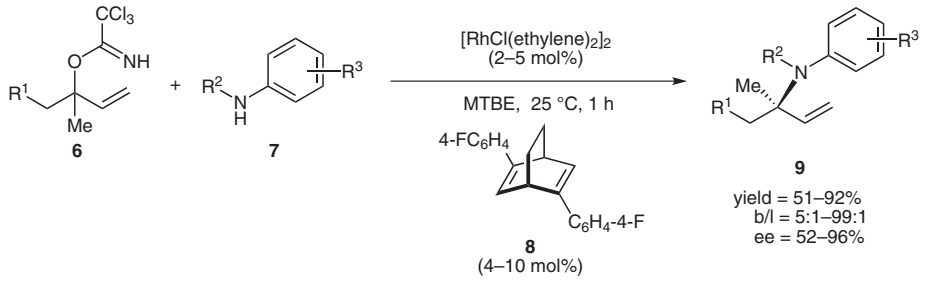


Scheme 2 Rhodium(I)-catalyzed amination of enantiomerically enriched trichloroacetimidate **4**

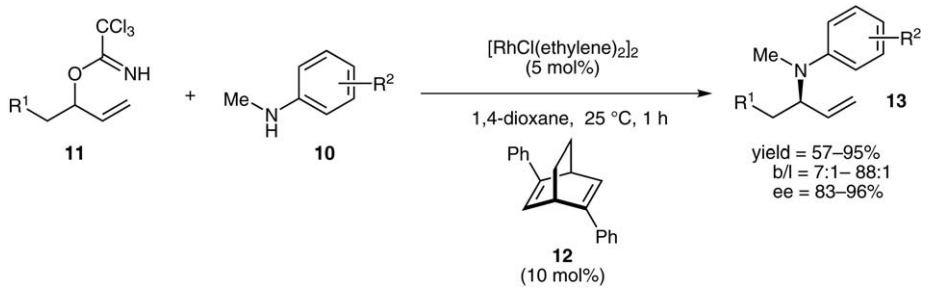
We commenced our studies on DYKAT reactions using tertiary allylic trichloroacetimidates. We surmised that these substrates might slow down the rate of nucleophilic attack by aniline.[14] To mimic the regioselective conditions that worked best with dichlorobis(norbornadiene)dirhodium as catalyst,[13] we investigated a number of chiral diene ligands.[7c,15] We found that Hiyashi's bicyclo[2.2.2]octadienes were the most effective.[15c,d] We continued our optimization studies by varying the electronic and steric properties of the aryl ring of the chiral diene and observing the effects on the DYKAT reaction. We found an optimal balance occurred in the case of the electron-withdrawing diene ligand **8** (Scheme 3), presumably as a result of increased back-donation and, therefore, binding affinity to the rhodium center.[14] For all substrates, the optimal yields and regio- and enantioselectivities were obtained by using 2 mol% of dichlorotetrakis(ethylene)dirhodium and 4 mol% of the chiral diene ligand **8** in methyl *tert*-butyl ether at 25 °C for one hour (Scheme 3). This DYKAT process could be applied to a number of tertiary allylic trichloroacetimidates **6** and aniline nucleophiles **7**, providing the corresponding α,α-disubstituted allylic *N*-arylamines **9** in moderate-to-high yields (51–92%) and good-to-excellent regioselectivities [branched/linear (b/l) = 5:1–99:1] and enantiomeric excesses (52–96% ee). A current limitation of the amination reaction with tertiary trichloroacetimidates is that only moderate regio- and enantioselectivities are achieved with substrates lacking a chelating functional group in the β-position.

In an effort to expand the capabilities of the DYKAT method, we pursued the development of a method for preparing enantiopure α-substituted allylic *N*-methylarylamines (Scheme 4) through regio- and enantioselective amination of secondary trichloroacetimidates. A number of challenges had to be addressed in developing such a DYKAT process. First, secondary allylic trichloroacetimidates are less sterically congested than their tertiary counterparts, and so nucleophilic attack by anilines[14] might be faster than the π–σ–π interconversion between the diastereomeric π-allylrhodium complexes. Secondly, low regioselectivity has been reported in iridium-catalyzed asymmetric aminations with *N*-methylanilines.[4e] Despite these potential difficulties, we chose to examine the rhodium-catalyzed DYKAT of a variety of racemic secondary trichloroacetimidates with *N*-methylanilines.[16] Gratifyingly, the reaction was most effective when we used the commercially available Hayashi chiral diene ligand **12** (Scheme 4). The highest yield, regio- and enantioselectivity were obtained with 5 mol% of dichlorotetrakis(ethylene)dirhodium and 10 mol% of the bicyclo[2.2.2]octadiene ligand **12** in 1,4-dioxane for one hour. The transformation can be applied to a number of *N*-methylanilines **10** with secondary allylic imidates **11** (Scheme 4). Allylic *N*-methyl arylamines **13** were obtained in good yields (57–95%) and high enantioselectivities (83–96% ee). High regioselectivity was also observed for all the substrates. The reaction shows a high tolerance to various functional groups, including allylic imidates lacking accessible oxygen atoms at the β-position.

To expand the range of substrates available for the DYKAT process, we examined the reactions of a variety



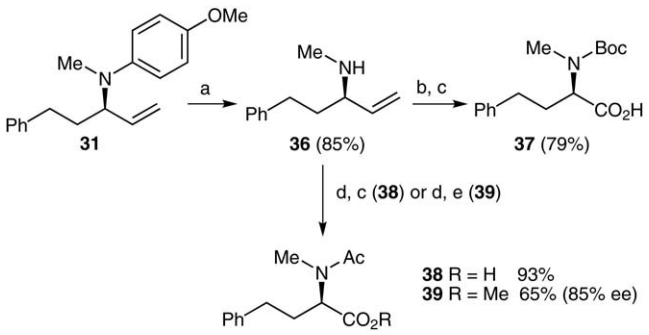
Scheme 3 Rhodium-catalyzed DYKAT of racemic tertiary allylic trichloroacetimidates with anilines



Scheme 4 Rhodium-catalyzed DYKAT of racemic secondary allylic trichloroacetimidates with *N*-methylanilines

of aniline and benzylamine nucleophiles **17a**–**f** with the secondary trichloroacetimidates **14**–**16** (Table 1). Trichloracetimidate **14** (Table 1, entry 1) possesses a β-oxygen substituent that can provide additional chelation control along the reaction coordinate, whereas the allylic imidates **15** and **16** lack such an ether oxygen. Substrate **16**, which contains the α-branching cyclohexyl group, has been reported to produce low regioselectivity in amination reactions.[12d] Although raising the temperature to 40 °C improved the yield and enantioselectivity with the secondary substrates **14**–**16**, the regioselectivity tended to be higher at room temperature. As shown in Table 1, the electron-deficient primary aniline **17a** (entry 1) and the electron-rich primary aniline **17b** (entry 2) gave the corresponding allylic amination products **18**–**23** in good yields (82–92%) and excellent regioselectivities (b/l = 20:1 to >99:1) and enantioselectivities (80– 95% ee). Even the *ortho*-methylated aniline **17c** (entry 3) gave the corresponding *N*-arylamines **24**–**26** in high regioselectivities and enantiomeric excesses, highlighting the efficacy of our rhodium-catalyzed method with sterically challenging nucleophiles. Entries 4 and 5 clearly illustrate the electronic effects of the *para*-substituents on the aryl rings in the *N*-methylanilines **17d** and **17e**. The benzyloxyimidate **14** reacted efficiently with the electron-deficient aniline **17d** to give the allylic amine **27** in 72% yield with a good regioselectivity (b/l = 30:1) and 93% ee (entry 4), whereas the reaction of imidate **15** with this nucleophile was low-yielding (42%) and showed poor selectivity (b/l = 2:1; 57% ee). No amination product was observed with the α-branching cyclohexyl substrate **16** (entry 4). A marked difference in reactivity was observed in the reaction of the electron-rich 4-methoxy-*N*-methylaniline (**17e**; entry 5) with imidate **14**. Although the product **30** was isolated in high yield, the enantioselectivity was much lower (56% ee) than that with electron-deficient aniline **17d** (93% ee, entry 4). This outcome can be rationalized in terms of competition between the rate of nucleophilic substitution and that of π–σ–π interconversion (Scheme 1). In contrast, when imidate **15** was treated with aniline **17e**, the amination product **31** was isolated in a higher yield (92%) and with greater selectivity (b/l = 19:1; 85% ee; entry 5) than when imidate **15** was paired with electron-withdrawing aniline **17d** (42%; 57% ee; b/l = 2:1) (entry 4). To our delight, we found that the DYKAT process could also be applied to alkyl amines (entry 6). For instance, the use of *N*-methylbenzylamine (**17f**) in the amination provided the allylic amines **33**–**35** in moderate yields, regioselectivities, and enantiomeric excesses.

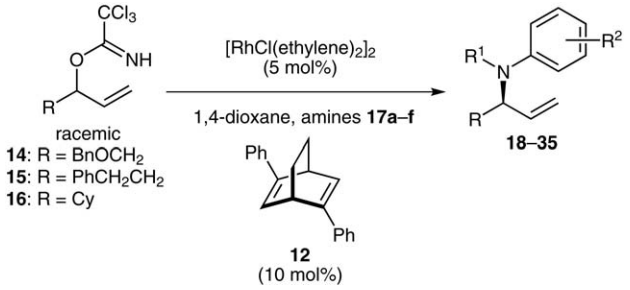
To illustrate the efficacy of our rhodium-catalyzed DYKAT method, we transformed the allylic *N*-methylanisidine **31** (Table 1, entry 5) into the corresponding *N*-methylhomophenylalanine derivatives **37**–**39**,[16] which are found in antillatoxin B, a potent activator of sodium-ion channels (Scheme 5).[17] This showed that anilines function not only as competent nucleophiles in our method, but can also serve as masking groups, ultimately providing the enantiomerically enriched *N*-methylamine **36**, a synthetically useful intermediate for bioactive targets.

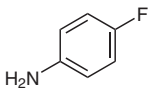
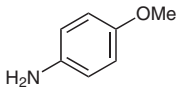
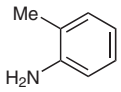
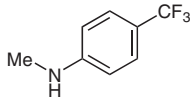
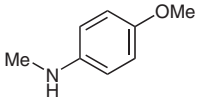
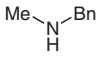


Scheme 5 Preparation of *N*-methylhomophenylalanine derivatives. *Reagents and conditions*: (a) CAN, MeCN–H_2O, 15 min; (b) Boc_2O, K_2CO_3, THF–H_2O (1:1); (c) $RuCl_3$, $NaIO_4$; (d) Ac_2O, py; (e) O_3, NaOH, MeOH.

In conclusion, we have developed a highly versatile rhodium-catalyzed DYKAT reaction of racemic secondary and tertiary trichloroacetimidates with a wide variety of anilines, *N*-methylanilines, and benzylamines. The reaction is operationally simple and displays broad functional-group tolerance, providing a number of nitrogen-containing tertiary and quaternary centers in high yields and high regio- and enantioselectivities. The utility of this reaction has been highlighted by a simple synthesis of *N*-methylhomophenylalanine derivatives. Additional studies of the substrate scope, mechanistic details of the DYKAT reaction, and applications of the DYKAT process to synthetic targets of interest, are currently under investigation and will be reported in due course.

Table 1 Regio- and Enantioselective Allylic Aminations with a Wide Range of Anilines and Benzylic Amines



Entry	Amine	Product	Temp (°C)	Time (h)	Yield[a] (%)	b/l[b]	ee[c]
1	 **17a**	**18**, R = CH_2OBn	40	1	90	>99:1	87
		19, R = $(CH_2)_2Ph$	40	1	92	>99:1	93
		20, R = Cy	25	1	82	20:1	90
2	 **17b**	**21**, R = CH_2OBn	40	1	86	28:1	80
		22, R = $(CH_2)_2Ph$	40	1	83	>99:1	89
		23, R = Cy	25	2	82	>99:1	95
3	 **17c**	**24**, R = CH_2OBn	40	1	75	>99:1	90
		25, R = $(CH_2)_2Ph$	40	1	81	90:1	96
		26, R = Cy	25	22	44	79:1	82
4	 **17d**	**27**, R = CH_2OBn	40	1	72	30:1	93[d]
		28, R = $(CH_2)_2Ph$	40	20	42	2:1	57
		29, R = Cy	25	22	0	-	-
5	 **17e**	**30**, R = CH_2OBn	40	1	88	52:1	56
		31, R = $(CH_2)_2Ph$	40	1	92	19:1	85[d]
		32, R = Cy	25	2	88	11:1	96[d]
6	 **17f**	**33**, R = CH_2OBn	40	22	51	8:1	34
		34, R = $(CH_2)_2Ph$	25	24	59	5:1	53
		35, R = Cy	25	22	67	18:1	66

[a] Isolated yield.
[b] Determined by GC.
[c] Determined by HPLC.
[d] Previously reported.

All reactions were performed under positive argon pressure in oven-dried Schlenk flasks fitted with glass stoppers. Organic solutions were concentrated by rotary evaporation below 40 °C at 25 Torr. Analytical TLC and GC were routinely used to monitor the progress of the reactions. TLC was performed using glass plates precoated with 230- to 400-mesh silica gel impregnated with a fluorescent indicator (250 nm). Visualization was accomplished using UV radiation, $KMnO_4$, or phosphomolybdic acid. Dry solvents were obtained from an SG Waters solvent-purification system containing activated alumina columns under argon pressure, or they were purchased from Sigma-Aldrich in Sure/Seal bottles. The Rh catalysts and chiral diene ligands were handled and transferred to Schlenk flasks under N_2 in a glove box. All chemicals and reagents were obtained from commercial vendors and used without further purification. Trichloroacetimidate substrates **14**, **15**, and **16** were prepared by following the procedures described in the literature.

Monitoring by GC was performed on an Agilent 6850 with an autosampler fitted with an HP-1 (30 m × 0.320 mm) column operated at a temperature gradient of 100–250 °C over 10 min. Flash chromatography was performed on a Teledyne Isco CombiFlash R_f system using normal-phase pre-column cartridges and gold high-performance columns. Values of the ee were determined on Agilent 1200-series HPLC equipment with a Diacel Chiralcel (4.6 × 250 mm) OD-H or a Diacel Chiralcel OJ-3 (4.6 × 150 mm) column fitted with a guard column. The flow rates and mobile phases were as indicated below. All ^1H NMR spectra were recorded on a Bruker Avance DRX 400 MHz spectrometer. All ^{13}C NMR spectra were recorded on the same instrument at 100 MHz. Chemical shifts expressed in ppm (δ scale) are referenced to residual $CHCl_3$ (^1H: δ = 7.24 ppm, ^{13}C: δ = 77.23 ppm) in the NMR solvent. IR spectra were recorded on a Jasco 4100 FT/IR spectrometer. Optical rotations were measured on a Jasco P-2000 polarimeter at r.t. High-resolution

time-of-flight mass spectrometry with electrospray ionization in positive mode was performed on a Waters QTOF Premier instrument.

Alkenylanilines 18–35; General Procedure

A 10 mL, oven-dried, Schlenk flask was charged with [RhCl(ethylene)$_2$]$_2$ (2.7 mg, 7.0 μmol, 5 mol%) and (1*S*,4*S*)-2,5-diphenylbicyclo[2.2.2]octa-2,5-diene (**12**; 3.6 mg, 14 μmol, 10 mol%) in a glove box. The flask was sealed and removed from the glove box, 1,4-dioxane (0.35 mL) was added, and the mixture was stirred for 15 min to give a bright-red soln. A separate 10 mL Schlenk flask was charged with appropriate allylic imidate **14**–**16** (1.0 equiv), 1,4-dioxane (0.35 mL), and aniline **17** (1.5 equiv). The Rh catalyst soln was then transferred by means of a purged syringe to the flask containing the soln of the imidate and **17**. The flask was immediately placed in an oil bath at r.t. or 40 °C and the mixture was stirred under argon at 40 °C or r.t. while the progress of the reaction was monitored (GC). The crude mixture was purified by direct adsorption onto a dry 5 g Teledyne Isco silica gel cartridge under vacuum followed by elution onto an equilibrated 24 g silica gel flash column (0–20% EtOAc–hexane).

***N*-{1-[(Benzyloxy)methyl]prop-2-en-1-yl}-4-fluoroaniline (18)**

Prepared by the general procedure from allylic imidate **14** (45 mg, 0.14 mmol, 1.0 equiv) and aniline **17a** (20 μL, 0.21 mmol, 1.5 equiv) at 40 °C for 1 h to give a light-brown oil; yield: 34 mg (90%; b/l >99:1); $[\alpha]_D^{25}$ –7.0 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane, 2 μL injection, 4.6 × 150 mm Chiralcel OJ-3, 1 mL/min, 2.5% *i*-PrOH in hexanes, 254 nm; major: 16.2 min, minor: 14.4 min: 87% ee.

IR (film): 3398, 2898, 2858, 1602, 1508, 1453, 1360, 1313, 1215, 1095, 1076, 1027, 992, 922, 819, 736, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.37–7.27 (m, 5 H), 6.84 (t, *J* = 6.7 Hz, 2 H), 6.57–6.52 (m, 2 H), 5.84–5.76 (m, 1 H), 5.30 (dt, *J* = 17.3, 1.3 Hz, 1 H), 5.19 (dt, *J* = 10.3, 1.2 Hz, 1 H), 4.55 (d, *J* = 12.1 Hz, 1 H), 4.54 (d, *J* = 12.1 Hz, 1 H), 4.07 (s, 1 H, NH), 3.97–3.93 (m, 1 H), 3.61 (dd, *J* = 9.6, 4.3 Hz, 1 H), 3.51 (dd, *J* = 9.6, 6.5 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 156.1 (d, J_{CF} = 234 Hz), 144.1, 138.0, 137.4, 128.7, 128.1, 128.0, 117.1, 115.8, 115.6, 115.0, 114.9, 73.4, 72.7.

(4-Fluorophenyl)[1-(2-phenylethyl)prop-2-en-1-yl]amine (19)

Prepared by the general procedure from allylic imidate **15** (43 mg, 0.14 mmol, 1.0 equiv) and aniline **17a** (20 μL, 0.21 mmol, 1.5 equiv) at 40 °C for 1 h to give a light-brown oil; yield: 33 mg (92%; b/l >99:1); $[\alpha]_D^{25}$ +0.33 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane, 2 μL injection, 4.6 × 250 mm Chiralcel OD-H, 1 mL/min, 2.5% *i*-PrOH in hexanes, 254 nm; major: 16.1 min, minor: 11.2 min: 93% ee.

IR (film): 3412, 3083, 3061, 3026, 3003, 2977, 2922, 2857, 1507, 1454, 1313, 1218, 992, 920, 817, 778, 749, 699 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.29–7.24 (m, 2 H), 7.21–7.16 (m, 3 H), 6.83 (t, *J* = 8.8 Hz, 2 H), 6.46 (dd, *J* = 9.0, 4.4 Hz, 2 H), 5.78–5.69 (m, 1 H), 5.18 (dt, *J* = 17.2, 1.3 Hz, 1 H), 5.14 (dt, *J* = 10.3, 1.2 Hz, 1 H), 3.74 (q, *J* = 6.1 Hz, 1 H), 3.50 (s, 1 H, NH), 2.73 (t, *J* = 6.9 Hz, 2 H), 1.92–1.87 (m, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.9 (d, J_{CF} = 233 Hz), 143.9, 141.8, 139.9, 128.7, 126.2, 115.8, 115.6, 114.5, 114.4, 56.2, 37.4, 32.4.

***N*-(1-Cyclohexylprop-2-en-1-yl)-4-fluoroaniline (20)**

Prepared by the general procedure from allylic imidate **16** (40 mg, 0.14 mmol, 1.0 equiv) and aniline **17a** (20 μL, 0.21 mmol, 1.5 equiv) at r.t. for 1 h to give a dark-brown oil; yield: 27 mg (82%; b/l 20:1); $[\alpha]_D^{25}$ –3.3 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane, 2 μL injection, 4.6 × 150 mm Chiralcel OJ-3, 1 mL/min, 2.5% *i*-PrOH in hexanes, 254 nm; major: 4.2 min, minor: 4.5 min: 90% ee.

IR (film): 3422, 2923, 2851, 1507, 1449, 1315, 1289, 993, 917, 816 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.82 (t, *J* = 8.8 Hz, 2 H), 6.49 (dd, *J* = 9.1, 4.4 Hz, 2 H), 5.75–5.62 (m, 1 H), 5.14 (d, *J* = 2.0 Hz, 1 H), 5.11 (dd, *J* = 3.8, 1.5 Hz, 1 H), 3.53 (br s, 2 H), 1.84–1.62 (m, 5 H), 1.48–1.44 (m, 1 H), 1.25–1.03 (m, 5 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.7, (d, J_{CF} = 234 Hz), 144.5, 138.5, 116.1, 115.8, 115.5, 114.3, 114.2, 62.0, 42.9, 29.7, 29.5, 26.7, 26.5, 26.4.

***N*-{1-[(Benzyloxy)methyl]prop-2-en-1-yl}-4-methoxyaniline (21)**

Prepared by the general procedure from allylic imidate **14** (45 mg, 0.14 mmol, 1.0 equiv) and aniline **17b** (26 mg, 0.21 mmol, 1.5 equiv) at 40 °C for 1 h to give a brown oil; yield: 27 mg (86%; b/l 28:1); $[\alpha]_D^{25}$ –11.2 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane, 2 μL injection, 4.6 × 250 mm Chiralcel OD-H, 1 mL/min, 5% *i*-PrOH in hexanes, 254 nm; major: 9.3 min, minor: 9.8 min: 80% ee.

IR (film): 3387, 2931, 2902, 2857, 2832, 1601, 1509, 1463, 1453, 1233, 1178, 1097, 1036, 992, 818, 736, 697 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.36–7.27 (m, 5 H), 6.74 (d, *J* = 9.0 Hz, 2 H), 6.60 (d, *J* = 9.0 Hz, 2 H), 5.87–5.79 (m, 1 H), 5.31 (dt, *J* = 17.3, 1.3 Hz, 1 H), 5.18 (dt, *J* = 10.3, 1.2 Hz, 1 H), 4.56 (d, *J* = 12.0 Hz, 1 H), 4.52 (d, *J* = 12.0 Hz, 1 H), 3.98–3.94 (m, 1 H), 3.72 (s, 3 H), 3.60 (dd, *J* = 9.5, 4.5 Hz, 1 H), 3.53 (dd, *J* = 9.5, 6.4 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 152.7, 141.8, 138.2, 137.9, 128.6, 128.0, 127.9, 116.9, 115.7, 115.0, 73.4, 72.8, 57.2, 56.0.

(4-Methoxyphenyl)[1-(2-phenylethyl)prop-2-en-1-yl]amine (22)

Prepared by the general procedure from allylic imidate **15** (43 mg, 0.14 mmol, 1.0 equiv) and aniline **17b** (26 mg, 0.21 mmol, 1.5 equiv) at 40 °C for 1 h to give a dark-brown oil; yield: 31 mg (83%; b/l >99:1); $[\alpha]_D^{25}$ +1.5 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane, 2 μL injection, 4.6 × 250 mm Chiralcel OD-H, 0.6 mL/min, 2.5% *i*-PrOH in hexanes, 254 nm; major: 28.0 min, minor: 27.2 min: 89% ee.

IR (film): 3395, 3081, 3061, 3025, 2998, 2932, 2856, 2830, 1602, 1508, 1463, 1453, 1441, 1231, 1178, 1036, 992, 817, 816, 747, 699 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.29–7.25 (m, 2 H), 7.20–7.16 (m, 3 H), 6.73 (d, *J* = 8.8 Hz, 2 H), 6.51 (d, *J* = 8.8 Hz, 2 H), 5.78–5.69 (m, 1 H), 5.20 (d, *J* = 17.2 Hz, 1 H), 5.13 (d, *J* = 10.3 Hz, 1 H), 3.75 (q, *J* = 6.7 Hz, 1 H), 3.73 (s, 3 H), 3.36 (br s, 1 H, NH), 2.73 (t, *J* = 7.7 Hz, 2 H), 1.91–1.85 (m, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 152.2, 142.0, 141.7, 140.3, 128.7, 128.6, 126.1, 115.7, 115.0, 114.9, 56.5, 55.9, 37.5, 32.3.

***N*-(1-Cyclohexylprop-2-en-1-yl)-4-methoxyaniline (23)**

Prepared by the general procedure from allylic imidate **16** (40 mg, 0.14 mmol, 1.0 equiv) and aniline **17b** (26 mg, 0.21 mmol, 1.5 equiv) at r.t. for 2 h to give a light-brown oil; yield: 28 mg (82%; b/l >99:1); $[\alpha]_D^{25}$ –10.7 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane, 2 μL injection, 4.6 × 150 mm Chiralcel OJ-3, 1 mL/min, 2.5% *i*-PrOH in hexanes, 254 nm; major: 9.3 min, minor: 8.7 min: 95% ee.

IR (film): 3405, 2922, 2850, 2831, 1509, 1481, 1463, 1448, 1232, 1178, 1038, 994, 915, 815 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.73 (d, *J* = 8.8 Hz, 2 H), 6.53 (d, *J* = 8.8 Hz, 2 H), 5.72–5.63, (m, 1 H), 5.13 (dt, *J* = 9.4, 1.2 Hz, 1 H),

5.11 (dt, J = 18.3, 0.96 Hz, 1 H), 3.71 (s, 3 H), 3.53 (t, J = 6.5 Hz, 1 H), 3.41 (s, 1 H, NH), 1.85–1.64 (m, 5 H), 1.51–1.44 (m, 1 H), 1.28–1.00 (m, 5 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 151.9, 142.4, 138.9, 115.9, 115.0, 114.8, 62.3, 56.0, 42.9, 29.7, 29.5, 26.8, 26.6, 26.5.

_N_-{1-[(Benzyloxy)methyl]prop-2-en-1-yl}-2-methylaniline (24)
Prepared by the general procedure from allylic imidate **14** (45 mg, 0.14 mmol, 1.0 equiv) and aniline **17c** (23 μL, 0.21 mmol, 1.5 equiv) at 40 °C for 1 h to give a light-brown oil; yield: 28 mg (75%; b/l >99:1); $[\alpha]_D^{25}$ –11.3 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane, 2 μL injection, 4.6 × 150 mm Chiralcel OJ-3, 0.6 mL/min, 1% *i*-PrOH in hexanes, 254 nm; major: 22.5 min, minor: 24.4 min: 90% ee.

IR (film): 3405, 2895, 2857, 1605, 1586, 1508, 1477, 1448, 1359, 1313, 1262, 1102, 1050, 1026, 989, 920, 744, 715, 697 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.34–7.30 (m, 5 H), 7.05–7.03 (m, 2 H), 6.66–6.59 (m, 2 H), 5.89–5.81 (m, 1 H), 5.32 (d, J = 17.3 Hz, 1 H), 5.21 (d, J = 10.4 Hz, 1 H), 4.56 (d, J = 12.0 Hz, 1 H), 4.55 (d, J = 12.0 Hz, 1 H), 4.11–4.08 (m, 1 H, NH), 3.66–3.57 (m, 2 H), 2.15 (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 145.7, 138.2, 137.7, 130.2, 128.7, 128.0, 127.8, 127.1, 122.6, 117.4, 116.8, 111.3, 73.2, 72.7, 55.9, 17.7.

[1-(2-Phenylethyl)prop-2-en-1-yl](2-tolyl)amine (25)
Prepared by the general procedure from allylic imidate **15** (43 mg, 0.14 mmol, 1.0 equiv) and aniline **17c** (23 μL, 0.21 mmol, 1.5 equiv) at 40 °C for 1 h to give a light-brown oil; yield: 29 mg (81%; b/l 90:1); $[\alpha]_D^{25}$ –8.1 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane, 2 μL injection, 4.6 × 250 mm Chiralcel OD-H, 1 mL/min, 2.5% *i*-PrOH in hexanes, 254 nm; major: 7.9 min, minor: 6.4 min: 96% ee.

IR (film): 3434, 3025, 2920, 2854, 1605, 1586, 1509, 1497, 1478, 1447, 1314, 1257, 990, 916, 744, 698, 682 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.30–7.26 (m, 2 H), 7.21–7.17 (m, 3 H), 7.08–7.03 (m, 2 H), 6.62 (t, J = 7.4 Hz, 1 H), 6.51 (d, J = 7.9 Hz, 1 H), 5.83–5.75 (m, 1 H), 5.21 (dt, J = 17.2, 1.4 Hz, 1 H), 5.13 (dt, J = 10.3, 1.2 Hz, 1 H), 3.90 (q, J = 6.5 Hz, 1 H), 3.47 (s, 1 H, NH), 2.73 (t, J = 7.5 Hz, 2 H), 2.1 (s, 3 H), 1.98–1.94 (m, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 145.4, 141.9, 140.0, 130.3, 128.7, 127.1, 126.1, 121.8, 116.9, 115.5, 110.9, 55.4, 37.6, 32.5, 17.7.

_N_-(1-Cyclohexylprop-2-en-1-yl)-2-methylaniline (26)
Prepared by the general procedure from allylic imidate **16** (40 mg, 0.14 mmol, 1.0 equiv) and aniline **17c** (23 μL, 0.21 mmol, 1.5 equiv) at r.t. for 22 h to give a light-brown oil; yield: 14 mg (44%; b/l 79:1); $[\alpha]_D^{25}$ +1.2 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane 1 μL injection, 4.6 × 250 mm Chiralcel OD-H, 0.6 mL/min, 1% *i*-PrOH in hexanes, 254 nm; major: 8.1 min, minor: 7.8 min: 82% ee.

IR (film): 3442, 2922, 1605, 1586, 1509, 1477, 1447, 1315, 1302, 1288, 1254, 1051, 984, 916, 794, 743, 713 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.08–7.01 (m, 2 H), 6.61–6.54 (m, 2 H), 5.77–5.68 (m, 1 H), 5.16 (dt, J = 9.2, 1.4 Hz, 1 H), 5.14 (dt, J = 18.4, 1.2 Hz, 1 H), 3.70–3.69 (m, 1 H), 3.56 (br s, 1 H, NH) 2.15 (s, 3 H), 1.88–1.74 (m, 5 H), 1.69–1.55 (m, 1 H), 1.27–1.05 (m, 5 H).

^{13}C NMR ($CDCl_3$, 100 MHz): Matches literature values.[7a]

_N_-{1-[(Benzyloxy)methyl]prop-2-en-1-yl}-_N_-methyl-4-(trifluoromethyl)aniline (27)
Prepared by the general procedure from allylic imidate **14** (45 mg, 0.14 mmol, 1.0 equiv) and aniline **17d** (30 μL, 0.21 mmol, 1.5 equiv) at 40 °C for 1 h to give a brown oil; yield: 34 mg (72%; b/l 30:1). Spectral and analytical data were previously reported.[16]

_N_-Methyl-_N_-[1-(2-phenylethyl)prop-2-en-1-yl]-4-(trifluoromethyl)aniline (28)
Prepared by the general procedure from allylic imidate **15** (43 mg, 0.14 mmol, 1.0 equiv) and aniline **17d** (30 μL, 0.21 mmol, 1.5 equiv) at 40 °C for 20 h to give a light-brown oil; yield: 19 mg (42%; b/l 2:1); $[\alpha]_D^{25}$ +9.0 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane, 2 μL injection, 4.6 × 250 mm Chiralcel OD-H, 0.6 mL/min, 1% *i*-PrOH in hexanes, 254 nm; major: 10.2 min, minor: 10.7 min: 57% ee.

IR (film): 3085, 3063, 3027, 2943, 2858, 1616, 1529, 1496, 1478, 1454, 1385, 1329, 1200, 1164, 1111, 1071, 989, 925, 818, 748, 700 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ (branched) = 7.41 (d, J = 8.8 Hz, 2 H), 7.25–7.22 (m, 2 H), 7.19–7.15 (m, 1 H), 7.11–7.07 (m, 2 H), 6.68 (d, J = 8.9 Hz, 2 H), 5.82–5.74 (m, 1 H), 5.16 (dt, J = 10.6, 1.5 Hz, 1 H), 5.09 (dt, J = 17.3, 1.4 Hz, 1 H), 4.33–4.28 (m, 1 H), 2.82 (s, 3 H), 2.58–2.51 (m, 1 H), 2.33 (q, J = 7.7 Hz, 1 H), 2.04–1.97 (m, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 152.7, 141.4, 136.6, 128.7, 128.6, 126.6, 126.5, 126.3, 116.3, 111.9, 111.4, 59.0, 33.9, 32.9, 31.7.

HRMS (ESI): *m/z* $[M + H]^+$calcd for $C_{19}H_{21}NF_3$: 320.1626; found: 320.1609.

_N_-(1-(Benzyloxy)but-3-en-2-yl)-4-methoxy-_N_-methylaniline (30)
Prepared by the general procedure from allylic imidate **14** (45 mg, 0.14 mmol, 1.0 equiv) and aniline **17e** (29 mg, 0.21 mmol, 1.5 equiv) at 40 °C for 1 h to give a brown oil; yield: 37 mg (88%; b/l 52:1); $[\alpha]_D^{25}$ +2.4 (*c* 2.00, $CHCl_3$).

HPLC: 2.5 mg/mL in 50:50 *i*-PrOH–hexane, 2 μL injection, 4.6 × 250 mm Chiralcel OD-H, 0.6 mL/min, 1% *i*-PrOH in hexanes, 254 nm; major: 19.9 min, minor: 18.7 min: 56% ee.

IR (film): 3083, 3062, 3030, 2989, 2896, 2861, 2833, 1716, 1640, 1510, 1464, 1454, 1244, 1181, 1105, 1038, 993, 925, 816, 737, 699 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.33–7.25 (m, 5 H), 6.81 (d, J = 9.0 Hz, 2 H), 6.79 (d, J = 9.2 Hz, 2 H), 5.88–5.80 (m, 1 H), 5.20 (dt, J = 9.8, 1.4 Hz, 1 H), 5.19 (dt, J = 18.7, 1.6 Hz, 1 H), 4.50 (s, 2 H), 4.39–4.35 (m, 1 H), 3.75 (s, 3 H), 3.67 (dd, J = 9.8, 6.9 Hz, 1 H), 3.61 (dd, J = 9.8, 6.4 Hz, 1 H), 2.74, (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 152.3, 145.1, 138.4, 135.2, 128.5, 127.9, 127.8, 117.2, 116.2, 114.7, 73.3, 70.4, 62.0, 56.0, 33.6.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{24}NO_2$: 298.1807; found: 298.1791.

(4-Methoxyphenyl)methyl[1-(2-phenylethyl)prop-2-en-1-yl]amine (31)
Prepared by the general procedure from allylic imidate **15** (43 mg, 0.14 mmol, 1.0 equiv) and aniline **17e** (29 mg, 0.21 mmol, 1.5 equiv) at 40 °C for 1 h to give a light brown oil; yield: 36 mg (92%; b/l 19:1). Spectral and analytical data were previously reported.[16]

_N_-(1-Cyclohexylprop-2-en-1-yl)-4-methoxy-_N_-methylaniline (32)
Prepared by the general procedure from allylic imidate **16** (40 mg, 0.14 mmol, 1 equiv) and aniline **17e** (29 mg, 0.21 mmol, 1.5 equiv) at 40 °C for 1 h to give a dark brown oil; yield: 32 mg (88%; b/l 11:1). Spectral and analytical data were previously reported.[16]

_N_-Benzyl-1-(benzyloxy)-_N_-methylbut-3-en-2-amine (33)
Prepared by the general procedure from allylic imidate **14** (45 mg, 0.14 mmol, 1.0 equiv) and *N*-methylbenzylamine (**17f**; 27 μL, 0.21 mmol, 1.5 equiv) at 40 °C for 22 h to give a light-yellow oil; yield: 20 mg (51%; b/l 8:1); $[\alpha]_D^{25}$ –4.4 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane 1 μL injection, 4.6 × 250 mm Chiralcel OD-H, 0.15 mL/min, 1% *i*-PrOH in hexanes, 254 nm; major: 41.9 min, minor: 40.5 min: 34% ee.

IR (film): 3085, 3063, 3028, 2975, 2944, 2850, 2791, 1954, 1870, 1811, 1663, 1639, 1605, 1586, 1510, 1494, 1453, 1419, 1363, 1314, 1259, 1207, 1103, 1076, 1038, 1027, 994, 923 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.32–7.21 (m, 10 H), 5.90–5.80 (m, 1 H), 5.26 (d, *J* = 10.4 Hz, 1 H), 5.20 (d, *J* = 17.3 Hz, 1 H), 4.53 (s, 2 H), 3.71–3.65 (m, 2 H), 3.57–3.48 (m, 2 H), 3.34–3.29 (q, *J* = 7.3 Hz, 1 H), 2.21 (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 135.3, 129.0, 128.5, 128.4, 127.9, 127.7, 127.0, 118.5, 73.3, 71.4, 65.2, 58.7, 38.5.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{24}NO$: 282.1858; found: 282.1846.

***N*-Benzyl-*N*-methyl-5-phenylpent-1-en-3-amine (34)**
Prepared by the general procedure from allylic imidate **15** (43 mg, 0.14 mmol, 1.0 equiv) and *N*-methylbenzylamine (**17f**; 27 μL, 0.21 mmol, 1.5 equiv) at r.t. for 24 h to give a clear oil; yield: 22 mg (59%; b/l 5:1); $[\alpha]_D^{25}$ –3.2 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane 1 μL injection, 4.6 × 150 mm Chiralcel OJ-3, 0.6 mL/min, 1% *i*-PrOH in hexanes, 254 nm; major: 8.6 min, minor: 7.5 min: 53% ee.

IR (film): 3083, 3062, 3026, 2939, 2851, 2790, 1945, 1869, 1803, 1718, 1636, 1603, 1495, 1454, 1418, 1367, 1316, 1259, 1214, 1155, 1125, 1076, 1028, 998, 921, 740, 698 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.33–7.13 (m, 10 H), 5.86–5.77 (m, 1 H), 5.24 (dd, *J* = 10.3, 1.8 Hz, 1 H), 5.08 (dd, *J* = 17.2, 1.3 Hz, 1 H), 3.64 (d, *J* = 13.3 Hz, 1 H), 3.39 (d, *J* = 13.2 Hz, 1 H), 2.99 (q, *J* = 7.6 Hz, 1 H), 2.69–2.64 (m, 1 H), 2.15 (s, 3 H), 2.03–1.94 (m, 1 H), 1.81–1.72 (m, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 142.8, 140.2, 136.7, 129.0, 128.7, 128.5, 128.4, 126.9, 125.9, 117.9, 65.8, 58.2, 37.6, 34.4, 32.9.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{24}N$: 266.1909; found: 266.1885.

***N*-Benzyl-1-cyclohexyl-*N*-methylprop-2-en-1-amine (35)**
Prepared by the general procedure from allylic imidate **16** (40 mg, 0.14 mmol, 1.0 equiv) and *N*-methylbenzylamine (**17f**; 27 μL, 0.21 mmol, 1.5 equiv) at r.t. for 22 h to give a clear semi-solid; yield: 23 mg (67%; b/l 18:1); $[\alpha]_D^{25}$ –35.8 (*c* 2.00, $CHCl_3$).

HPLC: 2 mg/mL in 50:50 *i*-PrOH–hexane 1 μL injection, 4.6 × 150 mm Chiralcel OJ-3, 0.6 mL/min, 1% *i*-PrOH in hexanes, 254 nm; major: 8.6 min, minor: 7.5 min: 53% ee.

IR (film): 3083, 3064, 3027, 2973, 2922, 2849, 2791, 1723, 1494, 1450, 1417, 1366, 1261, 1230, 1125, 1021, 977, 919, 833, 740, 699 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.32–7.18 (m, 5 H), 5.64 (dt, *J* = 17.1, 9.9 Hz, 1 H), 5.23 (dd, *J* = 9.8, 2.0 Hz, 1 H), 4.96 (dd, *J* = 17.2, 2.0 Hz, 1 H), 3.60 (d, *J* = 13.5 Hz, 1 H), 3.33 (d, *J* = 13.5 Hz, 1 H), 2.51 (t, *J* = 9.6 Hz, 1 H), 2.16 (d, *J* = 13.2 Hz, 1 H), 2.09 (s, 3 H), 1.75–1.64 (m, 4 H), 1.52–1.44 (m, 1 H), 1.23–1.12 (m, 3 H), 0.94–0.87 (m, 1 H), 0.85–0.74 (m, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 140.7, 135.5, 128.9, 128.3, 126.7, 118.4, 72.1, 58.4, 38.8, 37.5, 30.9, 30.7, 27.1, 26.6.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{26}N$: 244.2065; found: 244.2048.

***N*-Methyl-5-phenylpent-1-en-3-amine (36)**
Preparation and analytical and spectral data as previously reported.[16]

***N*-Methylhomophenylalanine Derivatives 37–39**
Preparation and analytical and spectral data as previously reported.[16]

Acknowledgment

The authors are grateful for financial support from the University of Iowa. J.S.A. thanks the Graduate College for a Summer Research Fellowship.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

References

(1) (a) *Chiral Amine Synthesis: Methods, Developments and Applications*; Nugent, T., Ed.; Wiley-VCH: Weinheim, **2010**. (b) Xu, L.; Luo, J.; Lu, Y. *Chem. Commun. (Cambridge)* **2009**, 1807. (c) Chen, Y. *Synlett* **2008**, 1919.

(2) (a) Nugent, T. C.; El-Shazly, M. *Adv. Synth. Catal.* **2010**, *352*, 753. (b) Nugent, T. C. In *Process Chemistry in the Pharmaceutical Industry*; Vol. 2; Gadamasetti, K.; Braish, T., Eds.; CRC Press: Boca Raton, **2008**, 137. (c) Johannsen, M.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689. (d) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921.

(3) (a) Uozumi, Y.; Tanaka, H.; Shibatomi, K. *Org. Lett.* **2004**, *6*, 281. (b) Faller, J. W.; Wilt, J. C. *Org. Lett.* **2005**, *7*, 633. (c) Fischer, D. F.; Xin, Z.; Peters, R. *Angew. Chem. Int. Ed.* **2007**, *46*, 7704. (d) Lei, A.; Lu, X. *Org. Lett.* **2000**, *2*, 2357. (e) Hayashi, T.; Yamamoto, A.; Ito, Y.; Nishioka, E.; Miura, H.; Yanagi, K. *J. Am. Chem. Soc.* **1989**, *111*, 6301. (f) Nemoto, T.; Tamura, S.; Sakamoto, T.; Hamada, Y. *Tetrahedron: Asymmetry* **2008**, *19*, 1751. (g) Sudo, A.; Saigo, K. *J. Org. Chem.* **1997**, *62*, 5508.

(4) (a) Gärtner, M.; Jäkel, M.; Achatz, M.; Sonnenschein, C.; Tverskoy, O.; Helmchen, G. *Org. Lett.* **2011**, *13*, 2810. (b) He, H.; Liu, W.; Dai, L.; You, S. *Angew. Chem. Int. Ed.* **2010**, *49*, 1496. (c) Leitner, A.; Shekhar, S.; Pouy, M. J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 15506. (d) Ohmura, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 15164. (e) Shu, C.; Leitner, A.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2004**, *43*, 4797. (f) Pouy, M. J.; Leitner, A.; Weix, D. J.; Ueno, S.; Hartwig, J. F. *Org. Lett.* **2007**, *9*, 3949. (g) Singh, O. V.; Han, H. *J. Am. Chem. Soc.* **2007**, *129*, 774. (h) Stanley, L. M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 8971. (i) Yamashita, Y.; Gopalarathnam, A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 7508. (j) Ye, K.; He, H.; Liu, W.; Dai, L.; Helmchen, G.; You, S. *J. Am. Chem. Soc.* **2011**, *133*, 19006.

(5) (a) Cooke, M. L.; Xu, K.; Breit, B. *Angew. Chem. Int. Ed.* **2012**, *51*, 10876. (b) Lebel, H.; Spitz, C.; Leogane, O.; Trudel, C.; Parmentier, M. *Org. Lett.* **2011**, *13*, 5460. (c) Cochet, T.; Bellosta, V.; Roche, D.; Ortholand, J.-Y.; Greiner, A.; Cossy, J. *Chem. Commun (Cambridge)* **2012**, *48*, 10745.

(6) (a) Trost, B. M.; Bunt, R. C.; Lemoine, R. C.; Calkins, T. L. *J. Am. Chem. Soc.* **2000**, *122*, 5968. (b) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2003**, *125*, 3090. (c) Trost, B.; Fandrick, D.; Brodmann, T.; Stiles, D. *Angew. Chem. Int. Ed.* **2007**, *46*, 6123. (d) Trost, B. M.; Fandrick, D. R. *Aldrichimica Acta* **2007**, *40*, 59. (e) Trost, B. M.; Osipov, M.; Dong, G. *J. Am. Chem. Soc.* **2010**, *132*, 15800.

(7) (a) Arnold, J. S.; Stone, R. F.; Nguyen, H. M. *Org. Lett.* **2010**, *12*, 4580. (b) Bartels, B.; García-Yebra, C.; Rominger, F.; Helmchen, G. *Eur. J. Inorg. Chem.* **2002**, 2569. (c) Fischer, C.; Defieber, C.; Suzuki, T.; Carreira, E. M. *J. Am. Chem. Soc.* **2004**, *126*, 1628.

(8) (a) Vrieze, D. C.; Hoge, G. S.; Hoerter, P. Z.; Van Haitsma, J. T.; Samas, B. M. *Org. Lett.* **2009**, *11*, 3140. (b) Stanley, L.

M.; Bai, C.; Ueda, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 8918.
(9) (a) You, S.; Zhu, X.; Luo, Y.; Hou, X.; Dai, L. *J. Am. Chem. Soc.* **2001**, *123*, 7471. (b) Lafrance, M.; Roggen, M.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2012**, *51*, 3470. (c) Defieber, C.; Ariger, M. A.; Moriel, P.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 3139. (d) Roggen, M.; Carreira, E. M. *J. Am. Chem. Soc.* **2010**, *132*, 11917.
(10) (a) Mercer, G. J.; Yang, J.; McKay, M. J.; Nguyen, H. M. *J. Am. Chem. Soc.* **2008**, *130*, 11210. (b) Mensah, E. A.; Nguyen, H. M. *J. Am. Chem. Soc.* **2009**, *131*, 8778. (c) Mensah, E. A.; Yu, F.; Nguyen, H. M. *J. Am. Chem. Soc.* **2010**, *132*, 14288. (d) Yu, F.; Nguyen, H. M. *J. Org. Chem.* **2012**, *77*, 7330.
(11) (a) Overman, L. E. *J. Am. Chem. Soc.* **1974**, *96*, 597. (b) Overman, L. E.; Carpenter, N. E. *Org. React. (N. Y.)* **2005**, *66*, 1. (c) Kirsch, S. F.; Overman, L. E. *J. Am. Chem. Soc.* **2005**, *127*, 2866. (d) Cannon, J. S.; Kirsch, S. F.; Overman, L. E. *J. Am. Chem. Soc.* **2010**, *132*, 15185. (e) Cannon, J. S.; Kirsch, S. F.; Overman, L. E.; Sneddon, H. F. *J. Am. Chem. Soc.* **2010**, *132*, 15192.
(12) (a) Evans, P. A.; Nelson, J. D. *J. Am. Chem. Soc.* **1998**, *120*, 5581. (b) Evans, P. A.; Nelson, J. D. *Tetrahedron Lett.* **1998**, *39*, 1725. (c) Evans, P. A.; Robinson, J. E.; Nelson, J. D. *J. Am. Chem. Soc.* **1999**, *121*, 6761. (d) Evans, P. A.; Robinson, J. E.; Moffett, K. K. *Org. Lett.* **2001**, *3*, 3269.
(13) Arnold, J. S.; Cizio, G. T.; Nguyen, H. M. *Org. Lett.* **2011**, *13*, 5576.
(14) Arnold, J. S.; Nguyen, H. M. *J. Am. Chem. Soc.* **2012**, *134*, 8380.
(15) (a) Wang, Z.-Q.; Feng, C.-G.; Xu, M.-H.; Lin, G.-Q. *J. Am. Chem. Soc.* **2007**, *129*, 5336. (b) Okamoto, K.; Hayashi, T.; Rawal, V. H. *Org. Lett.* **2008**, *10*, 4387. (c) Otomaru, T.; Okamoto, K.; Shintani, T.; Hayashi, T. *J. Org. Chem.* **2005**, *70*, 2503. (d) Tokunaga, N.; Otomaru, Y.; Okamoto, K.; Ueyama, K.; Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2004**, *126*, 13584.
(16) Arnold, J. S.; Cizio, G. T.; Heitz, D. R.; Nguyen, H. M. *Chem. Commun. (Cambridge)* **2012**, *48*, 11531.
(17) Nogle, L. M.; Okino, T.; Gerwick, W. H. *J. Nat. Prod.* **2001**, *64*, 983.

