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Catalyst Control in Sequential Asymmetric Allylic Substitution: Stereodivergent Access to *N,N*-Diprotected Unnatural Amino Acids

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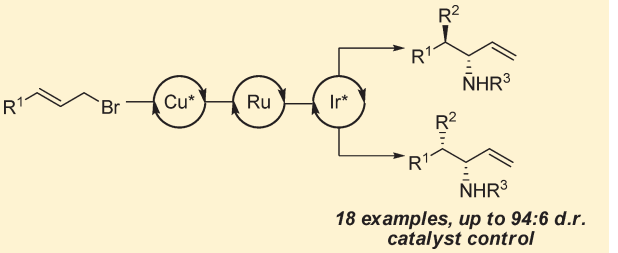
Supporting Information

ABSTRACT: The sequential use of Cu-catalyzed asymmetric allylic alkylation, olefin cross-metathesis, and Ir-catalyzed asymmetric allylic amination allows the concise, stereodivergent synthesis of complex chiral amines with complete regiocontrol and good diastereoselectivity, exemplified by the synthesis of a pair of diastereoisomeric unnatural branched amino acid derivatives.



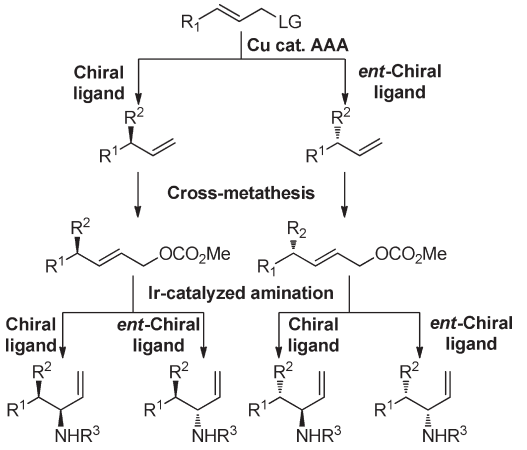
Within the field of asymmetric synthesis, methods that allow the sequential introduction of multiple contiguous stereocenters of any possible configuration are of great interest. The catalyst-controlled generation of new stereocenters is especially challenging, where asymmetric reactions have to be carried out selectively and independently of the pre-existing chirality in the substrate in order to control the relative configuration of the final products.[1]

As part of our program in diversity-oriented array synthesis,[2] we were interested in the synthesis of arrays of stereochemically diverse amines. Our strategy features an initial Cu-catalyzed asymmetric allylic alkylation of Grignard reagents[3−7] followed by a cross-metathesis reaction[8,9] between the resulting terminal alkene and an appropriate partner to produce a chiral substrate for a final Ir-catalyzed allylic amination[10−13] (Scheme 1).

Such a strategy would allow us to create chiral building blocks containing contiguous stereocenters potentially of any desired configuration. Minnaard, Feringa, and co-workers have utilized a sequential substitution/metathesis/conjugate addition strategy for the synthesis of contiguous carbon-based stereocenters.[14] However, the influence of adjacent stereocenters on the regio- and stereochemical outcomes of Ir-catalyzed asymmetric allylic amination has not previously been systematically examined.[15−17] Herein we report the successful execution of our strategy, exemplified by the stereocomplementary asymmetric synthesis of diastereomeric unnatural amino acid derivatives.

In the first step, chiral terminal olefin building blocks were prepared by Cu-catalyzed asymmetric alkylation of allylic bromides using commercially available Taniaphos ligands.[18,19] As expected, the reactions proceeded smoothly to afford building blocks **3** with complete regiocontrol and high yield and enantioselectivity, especially when functionalized allylic bromides were employed as substrates. Two enantiomeric catalysts were used, generating three enantiomeric pairs of chiral terminal alkenes (Table 1).

Scheme 1. Proposed Iterative Protocol Featuring Cross-Metathesis and Asymmetric Allylic Substitutions



The enantioenriched terminal alkenes **3a**−**c** and ***ent*-3a**−**c** were then subjected to a cross-metathesis reaction with (*Z*)-butenyl-1,4-bis-carbonate **4** employing Grubbs' second-generation catalyst **5**. The metatheses worked efficiently, affording carbonates **6a**−**c** and ***ent*-6a**−**c** with good stereoselectivity in favor of the *E*-configured products (Table 1).

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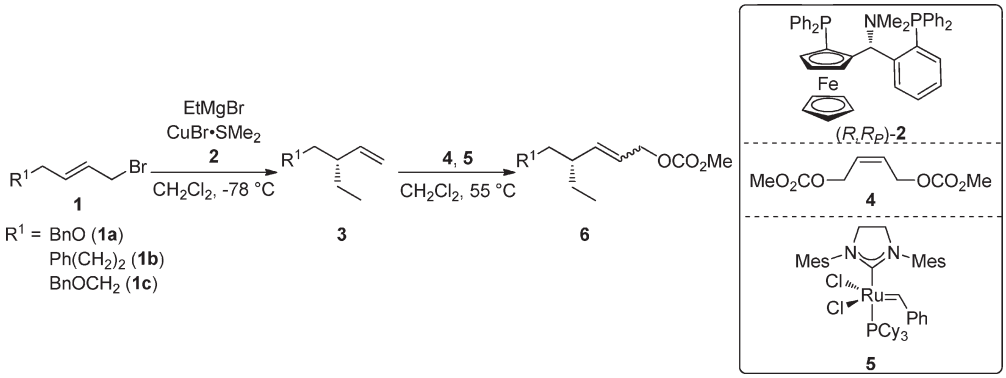
Table 1. Synthesis of Chiral Allylic Carbonates by Sequential Cu-Catalyzed Allylic Alkylation and Cross-Metathesis with 4[a]



	Cu-catalyzed AAA					cross-metathesis		
entry	R^1 (**1**)	ligand	yield[b] (%)	ee[c] (%)	**3**	yield (%)	*E*/*Z* ratio[d]	**6**
1	BnO (**1a**)	**2**	92	96 (*S*)	**3a**	65	90:10	**6a**
2	$Ph(CH_2)_2$ (**1b**)	**2**	87	92 (*R*)	**3b**	63	87:13	**6b**
3	$BnOCH_2$ (**1c**)	**2**	93	86 (*R*)	**3c**	69	90:10	**6c**
4	BnO (**1a**)	***ent*-2**	89	94 (*R*)	***ent*-3a**	65	90:10	***ent*-6a**
5	$Ph(CH_2)_2$ (**1b**)	***ent*-2**	90	93 (*S*)	***ent*-3b**	61	87:13	***ent*-6b**
6	$BnOCH_2$ (**1c**)	***ent*-2**	88	90 (*S*)	***ent*-3c**	67	90:10	***ent*-6c**

[a] Conditions: for Cu-catalyzed AAA: EtMgBr (1.2 equiv), CuBr·SMe_2 (1.0 mol %), **2** or ***ent*-2** (1.5 mol %), 4−6 h; for cross-metathesis: **4** (2.0 equiv), **5** (3.0 mol %), 20 h. [b] Isolated yield of S_N2' product; no trace of linear S_N2 byproduct observed by ^{1}H NMR analysis of the crude reaction mixture. [c] Determined by chiral HPLC analysis. [d] Determined by ^{1}H NMR analysis of the purified products.

With both enantiomers of substrates **6a**−**c** in hand, we next examined the use of Ir-catalyzed allylic amination as the final step of our synthetic sequence. A goal of our work was to develop reactions capable of ready use in parallel synthesis formats without a protective atmosphere, and so we chose to use the air- and moisture-stable catalyst species derived from $[Ir(dbcot)Cl]_2$ precatalyst (dbcot = dibenzo[a,e]cyclooctatetraene) and commercially available chiral phosphoramidite **8**.[20,21] Our first attempt involved reaction of **6a** with aniline **7a** as the nucleophile (Table 2). To our surprise, the reaction was very slow and did not go to completion even after 48 h using the standard conditions shown; the use of higher temperatures (up to 75 °C in a sealed tube) or catalyst loading (up to 10 mol % of $[Ir(dbcot)Cl]_2$) did not improve the outcome. Nevertheless, this initial result showed promising potential, affording product **9a** with excellent diastereoselectivity (entry 1, Table 2).

After some experimentation we found that the poor performance of the allylic substitution reaction was due to the presence of residual impurities (presumably ruthenium-based) from the previous cross-metathesis reaction. In fact, when allylic carbonate **6a** was carefully purified with the aid of a metal scavenger resin (commercially available Quadrapure TU), the outcome of the Ir-catalyzed amination was drastically improved (cf. entries 1 and 2, Table 2).

Table 2 shows the results obtained using three different primary amines as nucleophiles for the asymmetric amination of carbonates **6** and ***ent*-6**. The reactions were conveniently carried out using a Radleys GreenHouse synthesizer without the need for a protective nitrogen atmosphere, affording products **9a**−**i** and ***ent*-10a**−**i** as single regioisomers in all cases (as judged by examination of the crude ^{1}H NMR spectra). This is noteworthy, since related iridium-catalyzed substitutions on (*Z*)-alkenes have been shown to give rise to linear products.[22] Good diastereoselectivities were observed for the same catalyst with both enantiomeric series of starting materials, demonstrating that the stereochemical outcome of the reactions are under strong catalyst control. Slightly higher diastereoselectivities were observed in the *anti*-series (entries 2−10; 94:6 to 86:14 dr) as compared to the *syn*-series (entries 11−19; 91:9 to 74:26 dr), indicative of a slight mismatched substrate/catalyst pairing in the latter case. It should be noted that, since the starting materials are highly enantioenriched but not enantiopure, the observed diastereoselectivities are lower than the intrinsic diastereoselectivities (since the minor enantiomer will give rise predominantly to the opposite diastereomer cf. the major enantiomer). Additionally, it has previously been observed that the presence of minor (*Z*)-isomers in allylic alkylation substrates leads to a small but perceptible erosion in stereoselectivity.[16] However, in terms of the current sequential substitution/metathesis/substitution approach to stereochemically diverse amines, the yields and selectivities obtained over the three steps in both series are still synthetically useful and hence asymmetric allylic amination using the catalyst derived from ligand **8** can be regarded as a very powerful tool in catalyst-controlled stereoselective synthesis.

As an exemplification of the utility of this methodology, we envisaged that the oxidation of the resulting olefin in products **9** or **10** would give access to interesting unnatural α-amino acids bearing two vicinal stereocenters. Therefore, allylic amines **9b** and ***ent*-10b** were protected as trichloroacetamides and subsequently subjected to a two-step, one-pot alkene oxidation involving ozonolysis and subsequent Pinnick oxidation[23] of the resulting crude aldehyde, giving the desired *N*,*N*-diprotected

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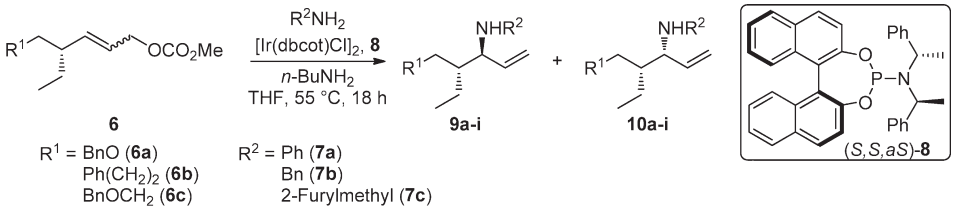
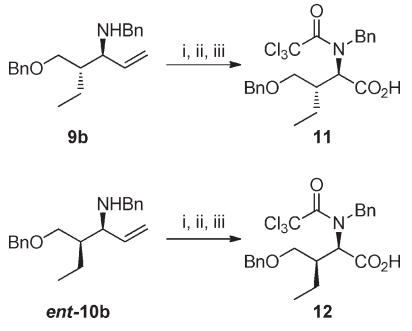
Table 2. Scope of the Ir-Catalyzed Asymmetric Allylic Amination[a]



entry	R^1 (6)	R^2 (7)	yield[b] (%)	dr (9:10)[c]	major product
1	BnO (**6a**)	Ph (**7a**)	41[d]	94:6	**9a**
2	BnO (**6a**)	Ph (**7a**)	73	94:6	**9a**
3	BnO (**6a**)	Bn (**7b**)	70	90:10	**9b**
4	BnO (**6a**)	2-furylmethyl (**7c**)	71	90:10	**9c**
5	$Ph(CH_2)_2$ (**6b**)	Ph (**7a**)	83	90:10	**9d**
6	$Ph(CH_2)_2$ (**6b**)	Bn (**7b**)	69	86:14	**9e**
7	$Ph(CH_2)_2$ (**6b**)	2-furylmethyl (**7c**)	73	88:12	**9f**
8	$BnOCH_2$ (**6c**)	Ph (**7a**)	92	93:7	**9g**
9	$BnOCH_2$ (**6c**)	Bn (**7b**)	73	90:10	**9h**
10	$BnOCH_2$ (**6c**)	2-furylmethyl (**7c**)	71	90:10	**9i**
11	BnO (***ent*-6a**)	Ph (**7a**)	69	9:91	***ent*-10a**
12	BnO (***ent*-6a**)	Bn (**7b**)	63	16:84	***ent*-10b**
13	BnO (***ent*-6a**)	2-furylmethyl (**7c**)	71	11:89	***ent*-10c**
14	$Ph(CH_2)_2$ (***ent*-6b**)	Ph (**7a**)	63	11:89	***ent*-10d**
15	$Ph(CH_2)_2$ (***ent*-6b**)	Bn (**7b**)	57	12:88	***ent*-10e**
16	$Ph(CH_2)_2$ (***ent*-6b**)	2-furylmethyl (**7c**)	64	14:86	***ent*-10f**
17	$BnOCH_2$ (***ent*-6c**)	Ph (**7a**)	65	24:76	***ent*-10g**
18	$BnOCH_2$ (***ent*-6c**)	Bn (**7b**)	69	26:74	***ent*-10 h**
19	$BnOCH_2$ (***ent*-6c**)	2-furylmethyl (**7c**)	62	22:78	***ent*-10i**

[a] Conditions: **7** (1.3 equiv), $[Ir(dbcot)Cl]_2$ (2.0 mol %), **8** (4.0 mol %), *n*-$BuNH_2$ (4.0 mol %). [b] Isolated yield of S_N2' product; no linear byproduct observed by ^1H NMR analysis of the crude reaction mixture. [c] Determined by 400 MHz ^1H NMR analysis of the purified product; in cases where the crude dr's could be determined, they agreed with the isolated values within experimental error (±2%). [d] Using **6a** not purified with Quadrapure TU resin.

Scheme 2. Conversion of 9b and *ent*-10b into the Corresponding *N,N*-Diprotected α-Amino Acids[a]



[a] Reagents and conditions: (i) $ClCOCCl_3$, Hünig's base, CH_2Cl_2, rt, 16 h, 92−95%; (ii) O_3, CH_2Cl_2, −78 °C, 10 min then Me_2S, −78 °C to rt; (iii) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, tBuOH/H_2O, rt, 16 h, 78−82% (two steps in one pot).

amino acids **11** and **12** in good yields as single diastereoisomers after purification by flash-chromatography (Scheme 2). The relative and absolute configuration of **12** was established by X-ray crystallographic analysis,[24] and confirms that both the Cu and Ir catalyzed allylic substitutions have proceeded with the sense of asymmetric induction expected based upon literature precedent.[12,16−19,25−28]

In summary, we have optimized an iterative synthetic strategy for the highly diastereoselective preparation of chiral, functionalized complex amine building blocks with excellent catalyst control of stereochemistry, with only minor matched/mismatched effects being observed. The allylic substitution reactions were conveniently performed using parallel synthesizers without the requirement for a protective atmosphere using commercially available chiral ligands. The general strategy has been applied to the synthesis of a diastereoisomeric pair of unnatural α-amino acids and further applications are the subject of current study.

EXPERIMENTAL SECTION

General Methods. Reactions were performed under N_2 atmosphere unless otherwise stated. Unless otherwise stated, all reagents and solvents were obtained from commercial sources and used without further purifications. Flash chromatography purifications were carried

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out using Fisher Matrix silica gel 60. Petroleum ether (40−60 °C) is referred as petrol. NMR spectra were recorded in $CDCl_3$ at 400 MHz (^1H) and 100 MHz (^{13}C); coupling constants (J) are expressed in hertz (Hz).

Dibenzo[*a*,*e*]cyclooctatraene (dbcot),[29] $[Ir(dbcot)Cl]_2$,[30] **1a**,[31] **1b**,[32,33] and **4**[34] were prepared following literature procedures.

(3*E*)-5-Bromo-3-penten-1-yl phenylmethyl ether, 1c. To a solution of **5** (327 mg, 0.385 mmol) in CH_2Cl_2 (125 mL) were added 3-buten-1-ylphenylmethyl ether[35] (2.08 g, 12.8 mmol) and (*Z*)-1,4-dibromo-2-butene[36] (5.48 g, 25.6 mmol). The resulting mixture was refluxed for 20 h, allowed to reach rt, concentrated in vacuo and purified by flash chromatography (100:0 to 95:5, cyclohexane−Et_2O) to give a brownish oil that was dissolved in CH_2Cl_2 (25 mL) and stirred with Quadrapure TU (1.5 g) at rt for 20 h to afford **1c** as a colorless oil (2.22 g, 68%): δ_H 7.39−7.26 (5H, m), 5.86−5.72 (2H, m), 4.51 (2H, s), 3.95 (2H, d, J = 6.5), 3.52 (2H, t, J = 6.5), 2.39 (2H, q, J = 6.5); δ_C 138.2, 132.7, 128.4, 128.1, 127.6, 127.5, 72.9, 69.1, 33.1, 32.5; ν_{max}/cm^{-1} 3030, 2856, 1453, 1360, 1203, 1100, 963; HRMS (ES+) $[M + Na]^+$ 277.0204, $C_{12}H_{15}OBrNa$ requires 277.0198.

General Procedure A. To a −78 °C solution of $CuBr\cdot SMe_2$ (0.01 equiv) and Taniaphos ligand **2** or ***ent*-2** (0.015 equiv) in CH_2Cl_2 was added dropwise EtMgBr (3 M in Et_2O, 1.2 equiv). The allylic bromide was added as a solution in CH_2Cl_2 over 2 min (final concentration of allylic bromide ≈ 0.4 M). The reaction was stirred at −78 °C for 4−6 h. Excess Grignard reagent was quenched by addition of MeOH (typically 1.0 mL), and the mixture allowed to reach rt. NH_4Cl (aq 1 M, 5 mL) and Et_2O (5 mL) were added and the layers separated; the aqueous phase was extracted with Et_2O (3 × 2 mL), dried over $MgSO_4$, and concentrated in vacuo to afford a yellow oil that was purified by flash chromatography.

(+)-(2*S*)-2-Ethyl-3-buten-1-yl phenylmethyl ether, 3a:[18] colorless oil; $[\alpha]^{20}_D$ +22 (*c* 1.1, $CHCl_3$) [lit. (94% ee), $[\alpha]^{20}_D$ + 19 (*c* 1.1, $CHCl_3$)[18]]; ee 96% by chiral HPLC: Chiracel OD-H 0.46 × 25 cm, 99.75:0.25 *n*-heptane−*i*-PrOH, 0.5 mL/min, 215 nm, 40 °C, t_R (min) 9.4 (minor), 10.3 (major). ^1H and ^{13}C NMR spectra correspond with the data reported.[18]

(+)-[(4*R*)-4-Ethyl-5-hexen-1-yl]benzene, 3b: colorless oil; $[\alpha]^{21}_D$ +16.2 (*c* 1.0, $CHCl_3$); δ_H 7.39−7.33 (2H, m), 7.29−7.23 (3H, m), 5.60 (1H, ddd, J = 17.1, 10.3, 8.8), 5.09−5.00 (2H, m), 2.75−2.60 (2H, m), 2.03−1.92 (1H, m), 1.80−1.58 (2H, m) 1.58−1.43 (2H, m), 1.43−1.27 (2H, m), 0.94 (3H, t, J = 7.3); δ_C 143.0, 142.8, 128.4, 128.2, 125.6, 114.3, 45.8, 36.1, 34.3, 29.2, 27.7, 11.7; ν_{max}/cm^{-1} 3065, 3027, 2961, 2929, 2856, 1495, 1454, 995; HRMS (EI+) $[M]^+$ 188.1569, $C_{14}H_{20}$ requires 188.1565; ee 92% determined on the corresponding alcohol **3b-OH**.

(+)-(3*R*)-3-Ethyl-6-phenyl-1-hexanol, 3b-OH. 9-BBN dimer (53 mg, 0.22 mmol) was added to a 0 °C solution of **3b** (64 mg, 0.34 mmol) in THF (3.0 mL) and the mixture stirred for 5 h at 0 °C. EtOH (2 mL), NaOH (aq 1 M, 2 mL) and H_2O_2 (aq 30%, 1.5 mL, 14.7 mmol) were sequentially added, and the mixture was stirred for 20 h at rt. $Na_2S_2O_3$ (aq 10%, 5 mL) was added, the layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with brine (3 mL), dried over $MgSO_4$, and concentrated in vacuo to give a colorless oil that was purified by flash chromatography (10:0 to 7:3, cyclohexane−EtOAc) to afford **3b-OH** as a colorless oil (50 mg, 71%): $[\alpha]^{21}_D$ +1.39 (*c* 1.1, $CHCl_3$); δ_H 7.31−7.23 (2H, m), 7.20−7.13 (3H, m), 3.63 (2H, t, J = 6.8), 2.62−2.56 (2H, m), 1.74−1.25 (10H, m), 0.84 (3H, t, J = 7.3); δ_C 142.7, 128.3, 128.2, 125.6, 61.2, 36.4, 36.3, 35.5, 32.8, 28.5, 25.9, 10.7; ν_{max}/cm^{-1} 3328, 2927, 2858, 1495, 1454, 1056; HRMS (ES+) $[M + Na]^+$ 229.1560, $C_{14}H_{22}ONa$ requires 229.1563; ee 92% by chiral HPLC Chiralpak AD-H 0.46 × 25 cm, 99:1 *n*-heptane−EtOH, 1 mL/min, 215 nm, rt, t_R (min) 19.8 (major), 22.4 (minor).

(−)-(3*R*)-3-Ethyl-4-penten-1-yl phenylmethyl ether, 3c: colorless oil; $[\alpha]_D^{20}$ −33.2 (*c* 1.1, $CHCl_3$); δ_H 7.38−7.22 (5H, m), 5.51 (1H, ddd, J = 16.9, 10.3, 9.1 Hz), 5.01−4.91 (2H, m), 4.49 (1H, d, J = 12.1 Hz), 4.46 (1H, d, J = 12.1 Hz), 3.53−3.40 (2H, m), 2.11−1.99 (1H, m), 1.79−1.68 (1H, m), 1.57−1.36 (2H, m), 1.33−1.19 (1H, m), 0.85 (3H, t, J = 7.3); δ_C 142.4, 138.7, 128.3, 127.6, 127.4, 114.7, 72.9, 68.5, 42.5, 34.5, 27.8, 11.5; ν_{max}/cm^{-1} 3068, 3031, 2961, 2927, 2856, 1454, 1363, 1100, 996, 911; HRMS (ES+) $[M + H]^+$ 205.1595, $C_{14}H_{21}O$ requires 205.1587; ee 86% determined on the corresponding alcohol **3c-OH**.

(+)-(3*S*)-3-Ethyl-5-[(phenylmethyl)oxy]-1-pentanol, 3c-OH. Prepared according to the procedure for **3b-OH**: colorless oil; $[\alpha]^{22}_D$ +3.1 (*c* 1.1, $CHCl_3$); δ_H 7.39−7.25 (5H, m), 4.50 (2H, s), 3.72−3.60 (2H, m), 3.57−3.45 (2H, m), 1.75 (1H, br s), 1.67−1.44 (5H, m), 1.33 (2H, qd, J = 7.4, 5.0), 0.87 (3H, t, J = 7.3); δ_C 138.4, 128.3, 127.6, 127.5, 73.0, 68.7, 61.0, 36.4, 33.1, 33.0, 26.6, 10.7; ν_{max}/cm^{-1} 3389, 2959, 2928, 2862, 1454, 1363, 1094, 1073, 1027; HRMS (ES+) $[M + H]^+$ 223.1700, $C_{14}H_{23}O_2$ requires 223.1698; ee 86% by chiral HPLC: Chiracel OD-H 0.46 × 25 cm, 99:1 *n*-heptane−EtOH, 1 mL/min, 215 nm, rt, t_R (min) 21.2 (minor), 23.6 (major).

General Procedure B. To a solution of **5** (0.03 equiv) in CH_2Cl_2 were added the relevant olefin **3a**−**c** or ***ent*-3a**−**c** (1.0 equiv) and **4** (2.0 equiv) (final concentration of olefin ≈ 0.15 M). The reaction mixture was refluxed for 20 h, allowed to reach rt, and concentrated in vacuo. The crude mixture was purified by flash-chromatography to give a brownish oil that was dissolved in CH_2Cl_2 (25 mL) and stirred with Quadrapure TU (1.5 g) at rt for 20 h to give the desired products **6a**−**c** or ***ent*-6a**−**c**.

(+)-Methyl (2*E*,4*S*)-4-[[(phenylmethyl)oxy]methyl]-2-hexen-1-yl carbonate, 6a: pale pink oil; $[\alpha]^{20}_D$ +21.9 (*c* 1.3, $CHCl_3$); δ_H 7.37−7.25 (5H, m), 5.73−5.61 (2H, m), 4.61 (2H, d, J = 5.0), 4.50 (2H, s), 3.77 (3H, s), 3.40 (2H, d, 6.0), 2.35−2.25 (1H, m), 1.65−1.53 (1H, m), 1.38−1.24 (1H, m), 0.88 (3H, t, J = 7.6); δ_C 155.6, 138.5, 137.9, 128.2, 127.5, 127.4, 124.4, 73.2, 72.9, 68.5, 54.6, 44.2, 24.1, 11.4; ν_{max}/cm^{-1} 2959, 2859, 1746, 1443, 1254, 1097, 941; HRMS (ES+) $[M + Na]^+$ 301.1409, $C_{16}H_{22}O_4Na$ requires 301.1410.

(+)-(2*E*,4*R*)-4-Ethyl-7-phenyl-2-hepten-1-yl methyl carbonate, 6b: colorless oil; $[\alpha]^{20}_D$ +59.2 (*c* 1.1, $CHCl_3$); δ_H 7.29−7.23 (2H, m), 7.19−7.13 (3H, m), 5.58−5.49 (2H, m), 4.58 (2H, d, J = 5.0), 3.76 (3H, s), 2.64−2.47 (2H, m), 1.98−1.86 (1H, m), 1.70−1.48 (2H, m), 1.47−1.34 (2H, m), 1.33−1.14 (2H, m), 0.82 (3H, t, J = 7.6); δ_C 155.7, 142.6, 141.2, 128.4, 128.2, 125.6, 123.4, 68.6, 54.6, 44.1, 36.0, 34.2, 29.0, 27.6, 11.6; ν_{max}/cm^{-1} 3026, 2957, 2931, 2857, 1746, 1443, 1254, 941; HRMS (ES+) $[M + Na]^+$ 299.1617, $C_{17}H_{24}O_3Na$ requires 299.1618.

(−)-(2*E*,4*R*)-4-Ethyl-6-[(phenylmethyl)oxy]-2-hexen-1-yl methyl carbonate, 6c: colorless oil; $[\alpha]^{22}_D$ −30.6 (*c* 1.0, $CHCl_3$); δ_H 7.39−7.26 (5H, m), 5.60−5.49 (2H, m), 4.58 (2H, d, J = 5.0), 4.50 (1H, d, J = 12.1), 4.46 (1H, d, J = 12.1), 3.79 (3H, s), 3.51−3.38 (2H, m), 2.19−2.07 (1H, m), 1.82−1.70 (1H, m), 1.58−1.38 (2H, m), 1.35−1.17 (1H, m), 0.85 (3H, t, J = 7.3); δ_C 155.6, 140.4, 138.6, 128.3, 127.7, 127.5, 123.8, 72.9, 68.5, 68.3, 54.6, 41.0, 34.4, 27.7, 11.5; ν_{max}/cm^{-1} 2958, 2930, 2857, 1746, 1443, 1225, 1101, 941; HRMS (ES+) $[M + Na]^+$ 315.1553, $C_{17}H_{24}O_4Na$ requires 315.1567.

General Procedure C. A stock solution of iridium catalyst was prepared by adding *n*-butylamine (9 μL, 9 × 10 μmol) to a THF solution (4.5 mL) of $[Ir(dbcot)Cl]_2$ (39 mg, 9 × 5.0 μmol) and phosphoramidite **8** (49 mg, 9 × 10.0 μmol) under a N_2 atmosphere. The resulting mixture was stirred for 30 min at 55 °C in a sealed vessel, allowed to reach rt, and used directly. Carbonates **6a**−**c** or ***ent*-6a**−**c** (0.25 mmol) and amines **7a**−**c** (0.33 mmol) were weighed into GreenHouse vessels to provide all nine combinations included in Table 2, and 0.5 mL of the stock solution prepared above was added to each vessel under air. The reaction mixtures were placed in a Radleys GreenHouse equipped with a condenser and stirred without a protective atmosphere at 55 °C for 18 h. The solvent was evaporated by applying low vacuum to the GreenHouse, the conversion/regioselectivity determined by ^1H NMR, and the product purified by flash chromatography.

***N*-[(1*S*)-1-((1*S*)-1-[[(Phenylmethyl)oxy]methyl]propyl)-2-propen-1-yl]aniline, 9a:** yellow oil; δ_H 7.38−7.25 (5H, m), 7.13−7.07 (2H, m), 6.60 (1H, tt, *J* = 7.3, 1.3), 6.50 (2H, d, *J* = 7.6), 5.74 (1H, ddd, *J* = 16.1, 10.6, 5.5), 5.20 (1H, dt, *J* = 17.1, 1.5), 5.13 (1H, dt, *J* = 11.5, 1.5), 4.74 (1H, br s), 4.50 (1H, d, *J* = 11.6), 4.47 (1H, d, *J* = 11.6), 4.00 (1H, br s), 3.69 (1H, dd, *J* = 9.3, 2.8), 3.50 (1H, dd, *J* = 9.3, 4.8), 1.72−1.46 (3H, m), 0.92 (3H, t, *J* = 7.6); δ_C 148.1, 138.7, 138.3, 129.0, 128.4, 127.6, 127.5, 116.3, 115.7, 112.7, 73.4, 70.3, 57.7, 44.7, 21.7, 12.0; ν_{max}/cm^{-1} 3403, 2962, 2873, 1600, 1505, 1317, 1091, 1061, 992; HRMS (ES+) $[M + H]^+$ 296.2005, $C_{20}H_{26}ON$ requires 296.2014.

(3*S*,4*S*)-*N*-(Phenylmethyl)-4-[[(phenylmethyl)oxy]methyl]-1-hexen-3-amine, 9b: yellow oil; δ_H 7.36−7.17 (10H, m), 5.65 (1H, ddd, *J* = 17.5, 9.3, 8.9), 5.17 (1H, dd, *J* = 9.6, 2.0), 5.08 (1H, ddd, *J* = 17.5, 2.0, 1.0), 4.49 (1H, d, *J* = 11.9), 4.45 (1H, d, *J* = 11.9), 3.82 (1H, d, *J* = 13.1), 3.60 (1H, d, *J* = 13.1), 3.55 (1H, dd, *J* = 9.1, 4.5), 3.46 (1H, dd, *J* = 9.1, 6.5), 3.17 (1H, dd, *J* = 8.6, 6.0), 1.70−1.48 (3H, m), 1.34−1.14 (1H, m) 0.87 (3H, t, *J* = 7.6); δ_C 141.0, 139.5, 138.6, 128.3, 128.2, 128.1, 127.5, 127.4, 126.6, 116.6, 73.1, 70.9, 62.1, 51.4, 44.9, 20.8, 12.0; ν_{max}/cm^{-1} 3064, 3028, 2961, 2872, 1725, 1494, 1453, 1363, 1095, 1027, 996; HRMS (ES+) $[M + H]^+$ 310.2158, $C_{21}H_{28}ON$ requires 310.2171.

(3*S*,4*S*)-*N*-(2-Furanylmethyl)-4-[[(phenylmethyl)oxy]methyl]-1-hexen-3-amine, 9c: yellow oil; δ_H 7.35−7.24 (6H, m), 6.28 (1H, dd, *J* = 3.3, 2.8), 6.11 (1H, dd, *J* = 3.0, 1.0), 5.62 (1H, ddd, *J* = 17.1, 10.1, 8.6), 5.16 (1H, dd, *J* = 10.1, 2.0), 5.09 (1H, ddd, *J* = 17.1, 2.0, 1.0), 4.49 (1H, d, *J* = 12.1), 4.44 (1H, d, *J* = 12.1), 3.79 (1H, d, *J* = 14.6), 3.61 (1H, d, *J* = 14.6), 3.52 (1H, dd, *J* = 9.6, 4.5), 3.42 (1H, dd, *J* = 8.6, 5.5), 3.15 (1H, dd, *J* = 8.6, 5.5), 1.74 (1H, br s), 1.68−1.59 (1H, m), 1.57−1.47 (1H, m), 1.28−1.16 (1H, m), 0.86 (3H, t, *J* = 7.6); δ_C 154.4, 141.5, 139.0, 138.6, 128.2, 127.5, 127.4, 117.1, 110.0, 106.6, 73.0, 70.9, 62.4, 44.7, 43.8, 20.8, 11.9; ν_{max}/cm^{-1} 3067, 3030, 2962, 2873, 1725, 1498, 1454, 1361, 1147, 1094, 1075, 1004; HRMS (ES+) $[M + H]^+$ 300.1953, $C_{19}H_{26}O_2N$ requires 300.1964.

***N*-[(1*S*)-1-[(1*R*)-1-Ethyl-4-phenylbutyl]-2-propen-1-yl]aniline, 9d:** yellow oil; δ_H 7.30−7.23 (2H, m), 7.20−7.09 (5H, m), 6.65 (1H, t, *J* = 7.6), 6.56 (2H, d, *J* = 7.6), 5.71 (1H, ddd, *J* = 17.0, 10.7, 6.0), 5.19−5.10 (2H, m), 3.89 (1H, br s), 3.61 (1H, br s), 2.60 (2H, t, *J* = 7.6), 1.79−1.58 (2H, m), 1.55−1.41 (3H, m), 1.40−1.26 (2H, m), 0.89 (3H, t, *J* = 7.1); δ_C 147.8, 142.4, 138.3, 129.1, 128.4, 128.3, 125.7, 117.0, 115.7, 113.2, 57.6, 44.3, 36.2, 29.4, 29.2, 23.0, 11.9; ν_{max}/cm^{-1} 3420, 3054, 3024, 2930, 2860, 1600, 1501, 1454, 1429, 1313, 1253, 992; HRMS (ES+) $[M + H]^+$ 294.2221, $C_{21}H_{28}N$ requires 294.2222.

(3*S*,4*R*)-4-Ethyl-7-phenyl-*N*-(phenylmethyl)-1-hepten-3-amine, 9e: yellow oil; δ_H 7.35−7.13 (10H, m), 5.62 (1H, ddd, *J* = 17.1, 10.6, 8.6), 5.15 (1H, dd, *J* = 10.6, 2.0), 5.05 (1H, ddd, *J* = 17.1, 2.0, 1.0), 3.82 (1H, d, *J* = 13.1), 3.59 (1H, d, *J* = 13.1), 2.98 (1H, dd, *J* = 8.1, 5.0), 2.58 (1H, d, *J* = 7.5), 2.56 (1H, d, *J* = 7.5), 1.66−1.11 (8H, m), 0.82 (3H, t, *J* = 7.6); δ_C 142.7, 141.0, 139.4, 128.3 (× 2), 128.2 (× 2), 126.7, 125.6, 116.3, 63.0, 51.4, 44.3, 36.3, 29.3, 29.0, 22.5, 11.8; ν_{max}/cm^{-1} 3063, 3026, 2929, 2857, 1723, 1494, 1453, 1224, 1101, 1053, 996; HRMS (ES+) $[M + H]^+$ 308.2369, $C_{22}H_{30}N$ requires 308.2378.

(3*S*,4*R*)-4-Ethyl-*N*-(2-furanylmethyl)-7-phenyl-1-hepten-3-amine, 9f: yellow oil; δ_H 7.32 (1H, d, *J* = 2.5), 7.28−7.22 (2H, m), 7.18−7.12 (3H, m), 6.30−6.26 (1H, m), 6.11 (1H, d, *J* = 4.0), 5.59 (1H, ddd, *J* = 17.1, 10.1, 8.1), 5.14 (1H, dd, *J* = 9.6, 2.0), 5.04 (1H, ddd, *J* = 17.1, 2.0, 1.0), 3.79 (1H, d, *J* = 14.6), 3.60 (1H, d, *J* = 14.6), 2.98 (1H, dd, *J* = 8.1, 4.5), 2.58 (1H, d, *J* = 7.5), 2.54 (1H, d, *J* = 7.6), 1.61−1.28 (7H, m), 1.21−1.08 (1H, m) 0.82 (3H, t, *J* = 7.6); δ_C 154.3, 142.6, 141.5, 138.9, 128.3, 128.2, 125.6, 116.8, 110.0, 106.7, 62.5, 44.2, 43.8, 36.2, 29.3, 28.9, 22.4, 11.8; ν_{max}/cm^{-1} 3064, 3026, 2930, 2861, 1723, 1602, 1496, 1455, 1147, 1097, 1076, 1006; HRMS (ES+) $[M + H]^+$ 298.2159, $C_{20}H_{28}NO$ requires 298.2171.

***N*-((1*S*)-1-[(1*R*)-1-Ethyl-3-[(phenylmethyl)oxy]propyl]-2-propen-1-yl)aniline, 9g:** yellow oil; δ_H 7.38−7.24 (5H, m), 7.11−7.05 (2H, m), 6.62 (1H, tt, *J* = 7.3, 1.3), 6.51 (2H, dd, *J* = 8.8, 1.3), 5.73 (1H, ddd, *J* = 16.9, 10.6, 5.8), 5.23−5.11 (2H, m), 4.52 (2H, s), 3.97 (1H, br s), 3.85 (1H, t, *J* = 5.3), 3.63−3.56 (1H, m), 3.55−3.44 (1H, m), 1.86−1.74 (1H, m), 1.70−1.43 (3H, m), 1.41−1.27 (1H, m), 0.91 (3H, t, *J* = 7.4); δ_C 148.0, 138.5, 138.4, 129.1, 128.4, 127.7, 127.6, 116.8, 115.9, 113.1, 73.1, 69.0, 57.9, 41.6, 29.9, 23.5, 11.7; ν_{max}/cm^{-1} 3364, 3027, 2960, 2929, 2869, 1600, 1501, 1454, 1431, 1315, 1094, 1028, 992; HRMS (ES+) $[M + H]^+$ 310.2164, $C_{21}H_{28}ON$ requires 310.2171.

(3*S*,4*R*)-4-Ethyl-*N*-(phenylmethyl)-6-[(phenylmethyl)oxy]-1-hexen-3-amine, 9h: yellow oil; δ_H 7.36−7.17 (10H, m), 5.63 (1H, ddd, *J* = 17.1, 10.6, 8.6), 5.16 (1H, dd, *J* = 10.6, 2.0), 5.07 (1H, dd, *J* = 17.1, 2.0), 4.46 (2H, s), 3.81 (1H, d, *J* = 13.6), 3.57 (1H, d, *J* = 13.1), 3.51−3.45 (2H, m), 2.98 (1H, dd, *J* = 8.3, 5.3), 1.79−1.68 (1H, m), 1.67−1.39 (3H, m), 1.28−1.11 (2H, m), 0.84 (3H, t, *J* = 7.3); δ_C 141.0, 139.3, 138.7, 128.3, 128.2, 128.1, 127.5, 127.4, 126.7, 116.4, 72.8, 69.0, 63.2, 51.4, 41.6, 30.0, 22.8, 11.7; ν_{max}/cm^{-1} 3064, 3028, 2959, 2929, 2870, 1724, 1495, 1453, 1362, 1246, 1097, 1027, 997; HRMS (ES+) $[M + H]^+$ 324.2313, $C_{22}H_{30}ON$ requires 324.2327.

(3*S*,4*R*)-4-Ethyl-*N*-(2-furanylmethyl)-6-[(phenylmethyl)oxy]-1-hexen-3-amine, 9i: yellow oil; δ_H 7.39−7.23 (6H, m), 6.28 (1H, dd, *J* = 3.0, 2.0), 6.11 (1H, d, *J* = 2.5), 5.62 (1H, ddd, *J* = 17.1, 10.3, 8.3), 5.17 (1H, dd, *J* = 10.6, 1.8), 5.09 (1H, ddd, *J* = 17.1, 2.0, 1.0), 4.47 (2H, s), 3.79 (1H, d, *J* = 14.6), 3.61 (1H, d, *J* = 14.6), 3.48 (2H, td, *J* = 6.8, 1.0), 2.99 (1H, dd, *J* = 8.6, 5.0), 1.75−1.42 (5H, m), 1.26−1.11 (1H, m), 0.84 (3H, t, *J* = 7.3); δ_C 154.3, 141.5, 138.7, 138.6, 128.2, 127.5, 127.4, 116.9, 110.0, 106.6, 72.8, 68.8, 62.8, 43.8, 41.5, 29.9, 22.7, 11.7; ν_{max}/cm^{-1} 3067, 3030, 2959, 2930, 2870, 1725, 1498, 1454, 1361, 1203, 1147, 1096, 1027, 1005; HRMS (ES+) $[M + H]^+$ 314.2108, $C_{20}H_{28}O_2N$ requires 314.2120.

***N*-[(1*S*)-1-((1*R*)-1-[[(Phenylmethyl)oxy]methyl]propyl)-2-propen-1-yl]aniline, *ent*-10a:** yellow oil; δ_H 7.32−7.19 (5H, m), 7.05 (2H, t, *J* = 7.8), 6.56 (1H, t, *J* = 7.3), 6.45 (2H, d, *J* = 8.1), 5.67 (1H, ddd, *J* = 16.9, 10.3, 6.0), 5.18−5.06 (2H, m), 4.67 (1H, br s), 4.45 (1H, d, *J* = 12.1), 4.39 (1H, d, *J* = 12.1), 4.00 (1H, br s), 3.48−3.41 (2H, m), 1.94−1.76 (1H, m), 1.39−1.14 (2H, m), 0.91 (3H, t, *J* = 7.6); δ_C 147.8, 138.2, 136.7, 129.0, 128.4, 127.7, 127.6, 116.7, 116.6, 113.1, 73.4, 71.4, 57.6, 44.6, 21.1, 12.4; ν_{max}/cm^{-1} 3403, 2962, 2873, 1600, 1505, 1317, 1091, 1061, 992; HRMS (ES+) $[M + H]^+$ 296.2008, $C_{20}H_{26}ON$ requires 296.2014.

(3*S*,4*R*)-*N*-(Phenylmethyl)-4-[[(phenylmethyl)oxy]methyl]-1-hexen-3-amine, *ent*-10b: yellow oil; δ_H 7.34−7.17 (10H, m), 5.68 (1H, ddd, *J* = 17.1, 10.3, 8.3), 5.17 (1H, dd, *J* = 10.6, 2.0), 5.10 (1H, ddd, *J* = 17.1, 2.0, 1.0), 4.46 (1H, d, *J* = 11.6), 4.43 (1H, d, *J* = 11.6), 3.82 (1H, d, *J* = 13.1), 3.58 (1H, d, *J* = 13.6), 3.54 (1H, dd, *J* = 9.1, 6.5), 3.41 (1H, dd, *J* = 9.1, 5.0), 3.16 (1H, dd, *J* = 8.6, 4.5), 1.79−1.69 (1H, m), 1.65 (1H, s), 1.48−1.33 (2H, m), 0.89 (3H, t, *J* = 7.3); δ_C 140.9, 139.0, 138.6, 128.3, 128.2, 128.1, 127.5, 127.4, 126.6, 116.6, 73.1, 71.0, 62.5, 51.3, 44.8, 20.8, 12.0; ν_{max}/cm^{-1} 3064, 3028, 2961, 2872, 1725, 1494, 1453, 1363, 1095, 1027, 996; HRMS (ES+) $[M + H]^+$ 310.2162, $C_{21}H_{28}ON$ requires 310.2171.

(3*S*,4*R*)-*N*-(2-Furanylmethyl)-4-[[(phenylmethyl)oxy]methyl]-1-hexen-3-amine, *ent*-10c: yellow oil; δ_H 7.37−7.25 (6H, m), 6.29 (1H, dd, *J* = 3.0, 2.0), 6.12 (1H, d, *J* = 3.0), 5.66 (1H, ddd, *J* = 17.1, 10.1, 8.6), 5.18 (1H, dd, *J* = 10.1, 2.0), 5.08 (1H, ddd, *J* = 17.1, 2.0, 1.0), 4.46 (2H, s), 3.81 (1H, d, *J* = 14.6), 3.61 (1H, d, *J* = 14.1), 3.53 (1H, dd, *J* = 9.6, 6.5), 3.40 (1H, dd, *J* = 9.3, 5.3), 3.15 (1H, dd, *J* = 8.3, 4.3), 1.82 (1H, br s), 1.78−1.69 (1H, m), 1.43−1.34 (2H, m), 0.88 (3H, t, *J* = 7.1); δ_C 154.3, 141.5, 138.6, 138.5, 128.3, 127.5, 127.4, 117.0, 110.0, 106.6, 73.2, 70.9, 62.3, 44.7, 43.9, 20.8, 11.8; ν_{max}/cm^{-1} 3067, 3030, 2962, 2873, 1725, 1498, 1454, 1361, 1147, 1094, 1075, 1004; HRMS (ES+) $[M + H]^+$ 300.1952, $C_{19}H_{26}O_2N$ requires 300.1964.

***N*-[(1*S*)-1-[(1*S*)-1-Ethyl-4-phenylbutyl]-2-propen-1-yl]aniline, *ent*-10d:** yellow oil; δ_H 7.30−7.24 (2H, m), 7.21−7.10 (5H, m), 6.66 (1H, t, *J* = 7.3), 6.57 (2H, d, *J* = 7.6), 5.71 (1H, ddd, *J* = 17.0, 10.7, 6.0), 5.20−5.11 (2H, m), 3.90 (1H, t, *J* = 5.0), 3.63 (1H, br s), 2.59 (2H,

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t, J = 7.8), 1.75−1.56 (2H, m), 1.56−1.41 (3H, m), 1.40−1.27 (2H, m) 0.94 (3H, t, J = 7.6); δ_C 147.8, 142.4, 138.1, 129.1, 128.4, 128.3, 125.7, 117.0, 115.8, 113.2, 57.5, 44.2, 36.1, 29.4, 29.2, 22.6, 12.0; ν_{max}/cm^{-1} 3420, 3054, 3024, 2930, 2860, 1600, 1501, 1454, 1429, 1313, 1253, 992; HRMS (ES+) $[M + H]^+$ 294.2210, $C_{21}H_{28}N$ requires 294.2222.

(3*S*,4*S*)-4-Ethyl-7-phenyl-*N*-(phenylmethyl)-1-hepten-3-amine, *ent*-10e: yellow oil; δ_H 7.34−7.13 (10H, m), 5.63 (1H, ddd, J = 17.1, 10.1, 8.1), 5.16 (1H, dd, J = 10.6, 2.0), 5.08 (1H, ddd, J = 17.1, 2.0, 1.0), 3.83 (1H, d, J = 13.6), 3.59 (1H, d, J = 13.1), 3.00 (1H, dd, J = 8.6, 4.5), 2.58 (1H, d, J = 7.5), 2.55 (1H, d, J = 7.5), 1.69−1.10 (8H, m), 0.83 (3H, t, J = 7.6); δ_C 142.8, 141.0, 139.3, 128.4, 128.3 (× 2), 128.2, 126.7, 125.6, 116.4, 62.7, 51.4, 44.2, 36.3, 29.5, 29.2, 22.6, 11.5; ν_{max}/cm^{-1} 3063, 3026, 2929, 2857, 1723, 1494, 1453, 1224, 1101, 1053, 996; HRMS (ES+) $[M + H]^+$ 308.2370, $C_{22}H_{30}N$ requires 308.2378.

(3*S*,4*S*)-4-Ethyl-*N*-(2-furanylmethyl)-7-phenyl-1-hepten-3-amine, *ent*-10f: yellow oil; δ_H 7.34 (1H, d, J = 2.5), 7.29−7.24 (2H, m), 7.20−7.12 (3H, m), 6.29 (1H, dd, J = 3.3, 1.8), 6.12 (1H, d, J = 4.0), 5.60 (1H, ddd, J = 17.1, 10.1, 8.6), 5.16 (1H, dd, J = 10.1, 2.0), 5.09 (1H, ddd, J = 17.1, 2.0, 1.0), 3.80 (1H, d, J = 14.6), 3.62 (1H, d, J = 14.6), 2.99 (1H, dd, J = 8.1, 4.5), 2.61−2.52 (2H, m), 1.67−1.07 (8H, m), 0.82 (3H, t, J = 7.3); δ_C 154.3, 142.8, 141.6, 138.8, 128.3, 128.2, 125.6, 117.0, 110.0, 106.8, 62.3, 44.1, 43.7, 36.4, 29.5, 29.3, 22.6, 11.4; ν_{max}/cm^{-1} 3064, 3026, 2930, 2861, 1723, 1602, 1496, 1455, 1147, 1097, 1076, 1006; HRMS (ES+) $[M + H]^+$ 298.2170, $C_{20}H_{28}NO$ requires 298.2171.

***N*-((1*S*)-1-[(1*S*)-1-Ethyl-3-[(phenylmethyl)oxy]propyl]-2-propen-1-yl)aniline, *ent*-10g:** yellow oil; δ_H 7.32−7.18 (5H, m), 7.06−6.98 (2H, m), 6.55 (1H, t, J = 7.3), 6.38 (2H, d, J = 7.8), 5.66 (1H, ddd, J = 16.9, 10.6, 5.8), 5.17−5.03 (2H, m), 4.44 (2H, s), 4.04 (1H, br s), 3.84−3.76 (1H, m), 3.57−3.35 (2H, m), 1.77−1.20 (5H, m), 0.89 (3H, t, J = 7.4); δ_C 147.9, 138.3, 137.3, 129.0, 128.4, 127.7, 127.6, 116.7, 116.2, 113.0, 73.0, 69.1, 57.6, 41.8, 30.1, 24.3, 12.0; ν_{max}/cm^{-1} 3366, 3028, 2960, 2929, 2861, 1601, 1502, 1455, 1432, 1361, 1316, 1257, 1095, 1028, 993; HRMS (ES+) $[M + H]^+$ 310.2162, $C_{21}H_{28}ON$ requires 310.2171.

(3*S*,4*S*)-4-Ethyl-*N*-(phenylmethyl)-6-[(phenylmethyl)oxy]-1-hexen-3-amine, *ent*-10h: yellow oil; δ_H 7.30−7.12 (10H, m), 5.58 (1H, ddd, J = 17.2, 10.2, 8.3), 5.11 (1H, dd, J = 10.3, 2.0), 5.02 (1H, dd, J = 17.4, 2.0), 4.39 (2H, s), 3.74 (1H, d, J = 13.3), 3.52 (1H, d, J = 13.1), 3.45−3.35 (2H, m), 2.96 (1H, dd, J = 8.1, 4.8), 1.84−1.09 (6H, m), 0.78 (3H, t, J = 7.3); δ_C 140.9, 139.2, 138.8, 128.3, 128.2, 128.1, 127.6, 127.4, 126.7, 116.7, 72.8, 69.2, 62.7, 51.4, 41.2, 29.7, 23.3, 11.5; ν_{max}/cm^{-1} 3064, 3029, 2959, 2929, 2860, 1494, 1454, 1363, 1204, 1097, 1028, 997; HRMS (ES+) $[M + H]^+$ 324.2315, $C_{22}H_{30}ON$ requires 324.2327.

(3*S*,4*S*)-4-Ethyl-*N*-(2-furanylmethyl)-6-[(phenylmethyl)oxy]-1-hexen-3-amine, *ent*-10i: yellow oil; δ_H 7.29−7.16 (6H, m), 6.21 (1H, dd, J = 3.1, 1.6), 6.04 (1H, d, J = 3.0), 5.55 (1H, ddd, J = 17.2, 10.1, 8.4), 5.11 (1H, dd, J = 10.2, 1.9), 5.03 (1H, dd, J = 17.2, 1.4), 4.40 (2H, s), 3.72 (1H, d, J = 14.4), 3.55 (1H, d, J = 14.4), 3.45−3.36 (2H, m), 2.95 (1H, dd, J = 8.6, 5.0), 1.81−1.06 (6H, m), 0.77 (3H, t, J = 7.4); δ_C 154.2, 141.5, 138.6, 138.3, 128.3, 127.5, 127.4, 117.2, 110.0, 106.8, 72.8, 69.1, 62.3, 43.7, 41.0, 29.6, 23.3, 11.4; ν_{max}/cm^{-1} 3066, 3030, 2959, 2929, 2861, 1640, 1496, 1454, 1363, 1205, 1147, 1097, 1027, 1005; HRMS (ES+) $[M + H]^+$ 314.2119, $C_{20}H_{28}O_2N$ requires 314.2120.

***N*-Benzyl-*N*-((3*S*,4*S*)-4-((benzyloxy)methyl)hex-1-en-3-yl)-2,2,2-trichloroacetamide, 9b-TAc.** To a 0 °C solution of ***anti*-10** (65 mg, 0.21 mmol) and Hünig's base (110 μL, 0.63 mmol) in CH_2Cl_2 (2.0 mL) was slowly added trichloroacetyl chloride (47 μL, 0.42 mmol). The mixture was allowed to reach rt and stirred for 16 h and sequentially washed with HCl (aq 1 M, 3 mL), $NaHCO_3$ (aq. sat., 3 mL) and brine (3 mL). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* to give a brown oil that was purified by flash-chromatography (100:0 to 90:10 petrol−Et_2O) to afford **9b-TAc** as a yellow oil (91 mg, 95%); δ_H 7.37−7.09 (10H, m), 6.14 (1H, dt, J = 17.2, 9.5), 5.35 (1H, d, J = 15.8), 4.86 (1H, d, J = 10.5), 4.49 (1H, d, J = 11.7), 4.45 (1H, d, J = 11.1), 4.35 (1H, d, J = 15.5), 4.23 (1H, d, J = 17.2), 3.46 (2H, d, J = 2.6), 3.40 (1H, t, J = 9.8), 2.35 (1H, br s), 1.29−1.13 (2H, m), 0.77 (3H, t, J = 7.3); δ_C 159.5, 138.1, 135.1, 135.0, 129.0, 128.4, 128.1, 128.0, 127.9, 127.8, 119.5, 94.0, 73.3, 67.5, 66.8, 55.6, 39.7, 21.2, 11.6; ν_{max}/cm^{-1} 3066, 3031, 2964, 2933, 2900, 2875, 1679, 1497, 1483, 1455, 1434, 1413, 1361, 1338, 1266, 1225, 1203, 1176, 1144, 1121, 1077, 1029, 998; HRMS (ES+) $[M + Na]^+$ 476.0934, $C_{23}H_{26}NO_2Cl_3Na$ requires 476.0921.

***N*-Benzyl-*N*-((3*S*,4*R*)-4-((benzyloxy)methyl)hex-1-en-3-yl)-2,2,2-trichloroacetamide, *ent*-10b-TAc.** Prepared according to the procedure for **9b-TAc** (0.17 mmol scale, 71 mg, 92%): yellow oil; δ_H 7.32−7.01 (10H, m), 6.07 (1H, dt, J = 17.0, 9.4), 5.20 (1H, d, J = 15.8), 4.88 (1H, d, J = 9.6), 4.52 (1H, d, J = 15.8), 4.42 (1H, d, J = 16.9), 4.28 (1H, d, J = 12.0), 4.22 (1H, d, J = 12.0), 3.70 (1H, t, J = 9.2), 3.41 (1H, d, J = 7.6), 3.18 (1H, d, J = 8.5), 2.29 (1H, br s), 1.48−1.30 (2H, m), 0.83 (3H, t, J = 7.3); δ_C 159.9, 138.7, 135.1, 134.5, 128.9, 128.3 (× 2), 128.2, 128.0, 127.3, 119.4, 94.0, 72.8, 67.1, 67.0, 55.9, 41.2, 19.8, 11.6; ν_{max}/cm^{-1} 3066, 3031, 2964, 2933, 2900, 2875, 1681, 1497, 1483, 1455, 1434, 1413, 1361, 1338, 1266, 1225, 1203, 1176, 1144, 1121, 1077, 1029, 998; HRMS (ES+) $[M + H]^+$ 454.1105, $C_{23}H_{27}NO_2Cl_3$ requires 454.1102.

(2*R*,3*S*)-2-(*N*-Benzyl-2,2,2-trichloroacetamido)-3-((benzyloxy)methyl)pentanoic Acid, 11. Ozone was bubbled through a −78 °C solution of **9b-TAc** (73 mg, 0.16 mmol) in CH_2Cl_2 (5 mL) for 5 min, when the solution turned blue. The reaction mixture was purged with N_2 for 10 min, turning colorless again. Dimethyl sulfide (200 μL) was then added at −78 °C and the mixture stirred for 20 min, allowed to reach rt, concentrated in vacuo, and redissolved in *t*BuOH (2 mL). 2-Methyl-2-butene (380 μL, 3.5 mmol) was added followed by a solution of $NaH_2PO_4 \cdot 2H_2O$ (76 mg, 0.49 mmol) and $NaClO_2$ (45 mg, 0.49 mmol) in water (2 mL). The resulting mixture was stirred at rt for 16 h, concentrated in vacuo to ∼3 mL, diluted with water (10 mL), acidified to pH ∼2 with HCl (aq 1 M), saturated with NaCl, and extracted with EtOAc (5 × 10 mL). The combined organic phases were dried over $MgSO_4$ and concentrated in vacuo to give a colorless oil that was purified by flash-chromatography (80:20 to 60:40, petrol−EtOAc) to afford **11** as a white solid (59 mg, 78%): mp 93−94 °C; δ_H 9.26 (1H, br s), 7.49−7.00 (10H, m), 5.39 (1H, d, J = 15.1), 4.56 (1H, d, J = 15.4), 4.46 (1H, d, J = 11.6), 4.42 (1H, d, J = 11.8), 3.54 (1H, d, J = 8.6), 3.45 (1H, dd, J = 10.1, 3.5), 3.34 (1H, dd, J = 10.3, 2.5), 2.44 (1H, br s), 1.62−1.38 (2H, m), 0.80 (3H, t, J = 7.3); δ_C 173.8, 160.9, 137.8, 134.0, 129.1, 128.5, 128.4, 128.3, 128.0, 127.9, 92.8, 73.4, 67.0, 63.3, 55.1, 39.5, 22.2, 11.6; ν_{max}/cm^{-1} 3031, 2923, 2893, 2588, 1738, 1732, 1682, 1496, 1462, 1455, 1434, 1368, 1353, 1328, 1316, 1226, 1207, 1151, 1122, 1092, 970; HRMS (ES+) $[M + H]^+$ 472.0852, $C_{22}H_{25}NO_4Cl_3$ requires 472.0844.

(2*R*,3*R*)-2-(*N*-Benzyl-2,2,2-trichloroacetamido)-3-((benzyloxy)methyl)pentanoic Acid, 12. Prepared according to the procedure for **11** (0.12 mmol scale, 47 mg, 82%): white solid (crystals for X-ray analysis obtained by slow diffusion of petrol into CH_2Cl_2); mp 106−107 °C; δ_H 7.36−7.04 (11H, m), 5.34 (1H, d, J = 15.1), 4.53 (1H, d, J = 15.4), 4.29 (2H, s), 3.90 (1H, d, J = 7.8), 3.51 (1H, dd, J = 10.1, 3.5), 3.46 (1H, dd, J = 10.1, 2.5), 2.48 (1H, br s), 1.46−1.21 (2H, m), 0.81 (3H, t, J = 6.8); δ_C 174.7, 160.9, 138.2, 133.8, 129.3, 128.5, 128.4, 128.2, 127.6, 127.5, 92.7, 73.1, 68.0, 61.0, 56.0, 40.6, 19.4, 11.7; ν_{max}/cm^{-1} 3032, 2923, 2586, 1738, 1732, 1673, 1497, 1455, 1434, 1368, 1352, 1328, 1316, 1226, 1207, 1151, 1122, 1092, 970; HRMS (ES+) $[M + H]^+$ 472.0845, $C_{22}H_{25}NO_4Cl_3$ requires 472.0844.

■ ASSOCIATED CONTENT

Supporting Information. ^1H and ^{13}C NMR spectra for all new compounds, chiral HPLC traces, and X-ray data for compound **12** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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