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Palladium-Catalyzed Regio-, Diastereo-, and Enantioselective Allylation of Nitroalkanes with Monosubstituted Allylic Substrates

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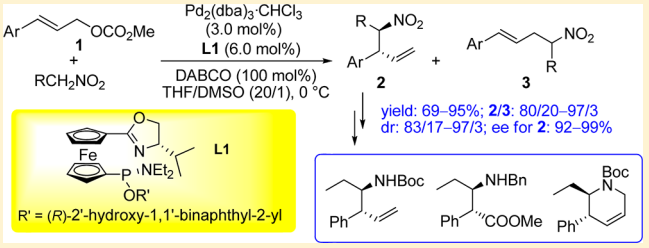
Supporting Information

ABSTRACT: Pd-catalyzed asymmetric allylic alkylation of nitroalkanes and monosubstituted allylic substrates was performed to afford products with two adjacent chiral centers and with excellent regio-, diastereo-, and enantioselectivities. The usefulness of the protocol in organic synthesis was demonstrated by transformation of the product to an optically active homoallylamine, a 2,3-disubstituted tetrahydropyridine, and an α,β-disubstituted amino acid derivative.



INTRODUCTION

Nitroalkanes are important in organic synthesis because they are readily available, and nitro groups can be easily transformed into other various functionalities.[1] To date, many strategies have been documented for the synthesis of chiral nitro compounds with one or two chiral centers,[2] but there is still a need to develop protocols for the synthesis of chiral nitro compounds with different functional groups. Pd-catalyzed asymmetric allylic alkylation (AAA) is one of the most important reactions in asymmetric catalysis because one or two chiral centers can be easily installed in products, with high-functionality tolerance.[3] This reaction has also been used for the reaction of nitroalkanes with allylic substrates.[4,5a] However, these reactions have some limitations: symmetrically 1,3-disubstituted and cyclic allylic substrates are usually used in the reactions,[4b−h] and there have been few reports of the use of monosubstituted allylic substrates; there have been even fewer reports of the successful construction of two chiral centers in the products, with control of diastereoselectivity.[4d] Regio-, diastereo-, and enantioselective transition-metal-catalyzed allylic alkylations of nitroalkanes with monosubstituted allylic substrates therefore remain to be explored. Recently, we achieved regio- and enantioselective Pd-catalyzed allylic alkylation of nitromethane in the presence of a ferrocene-based chiral ligand, SIOCPhox.[6h] On the basis of this and other results that we have obtained,[6] we describe here Pd-catalyzed enantioselective allylic alkylation of nitroalkanes with monosubstituted allylic substrates, furnishing the desired nitro compounds containing two vicinal stereogenic centers with high regio-, diastereo-, and enantioselectivities. The usefulness of the protocol in organic synthesis is also revealed by transformation of the product to homoallylamine, β-amino acid, and disubstituted tetrahydropyridine derivatives with two chiral centers.

RESULTS AND DISCUSSION

Our initial studies focused on the reaction of nitroethane with cinnamyl carbonate. Using DABCO as the base and (S_c,R_{phos},R_a)-**L1** as the ligand, the reaction in dichloromethane after 8 h gave branched and linear products in a ratio of 95:5. Although the diastereomeric ratio (dr) of **2a** was low, namely 75:25, the enantioselectivity was excellent. Encouraged by this result, an investigation of the impact of various parameters on the reaction was conducted (Table 1). The dr changed from 75:25 to 81:19, whereas the enantioselectivity was unchanged when the reaction was run in THF (entry 2). The dr value increased further to 91:9 when the reaction temperature was decreased from rt to 0 °C (entry 3). The reaction hardly proceeded at −20 °C (entry 4). The reaction was accelerated significantly by addition of a small amount of a polar solvent, DMSO (0.1 mL). The reaction was complete in 10 h and provided the products in high yields with excellent regio-, diastereo-, and enantioselectivities [94% yield, **2a**/**3a** ratio 93/7, dr 94/6 with 98% enantiomeric excess (ee) for **2a**; entry 5]. Other organic bases, such as diisopropylethylamine (DIPEA), triethylamine (TEA), and DMAP, were screened in a mixed solvent, THF/DMSO, but gave inferior results (entries 6−8). Other SIOCPhox ligands, shown in Figure 1, were tested. The reaction with the ligand (R_{phos},R_a)-**L2** resulted in a lower dr than that obtained with (S_c,R_{phos},R_a)-**L1**, suggesting an important role of the central chirality on the oxazoline ring in controlling the diastereoselectivity (entry 9 vs entry 5). The

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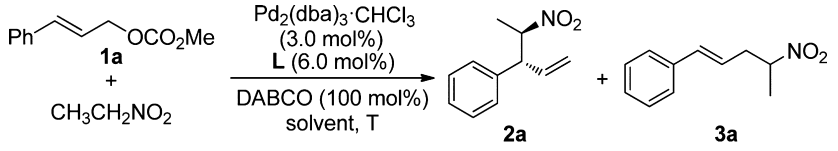
Table 1. Impact of Reaction Parameters on Pd-Catalyzed Reactions of Cinnamyl Methyl Carbonate (1a) with Nitroethane[a]



entry	ligand	T	base	solvent	2a/3a[c]	dr[c]	yield (%)[d]	ee (%)[e]
1	**L1**	rt	DABCO	DCM	95/5	75/25	80	98
2	**L1**	rt	DABCO	THF	91/9	81/19	68	98
3	**L1**	0 °C	DABCO	THF	93/7	91/9	51	98
4	**L1**	−20 °C	DABCO	THF			<10	
5	**L1**	0 °C	DABCO	THF/DMSO[b]	93/7	94/6	94	98
6	**L1**	0 °C	DIPEA	THF/DMSO[b]	86/14	90/10	91	98
7	**L1**	0 °C	TEA	THF/DMSO[b]	90/10	86/14	89	
8	**L1**	0 °C	DMAP	THF/DMSO[b]	91/9	88/12	84	96
9	**L2**	0 °C	DABCO	THF/DMSO[b]	95/5	78/22	78	98
10	**L3**	0 °C	DABCO	THF/DMSO[b]	93/7	49/51	71	−58[f]
11	**L4**	0 °C	DABCO	THF/DMSO[b]	91/9	80/20	54	−98[f]

[a]Conditions: molar ratio **1a**/DABCO/$Pd_2(dba)_3{\cdot}CHCl_3$/**L** = 100/100/2.5/5.0, 0.4 mL of $CH_3CH_2NO_2$, 2.0 mL of solvent. DCM: dichloromethane; THF: tetrahydrofuran; DMSO: dimethylsulfoxide; DABCO: 1,4-diazabicyclo[2.2.2]octane; DMAP: *N*,*N*-4-dimethylaminopyridine. [b]THF/DMSO = 20/1. [c]Determined by GC. [d]Isolated yield of products **2a** and **3a**. [e]Determined by chiral GC. [f]A minus sign means that the product has the opposite configuration.

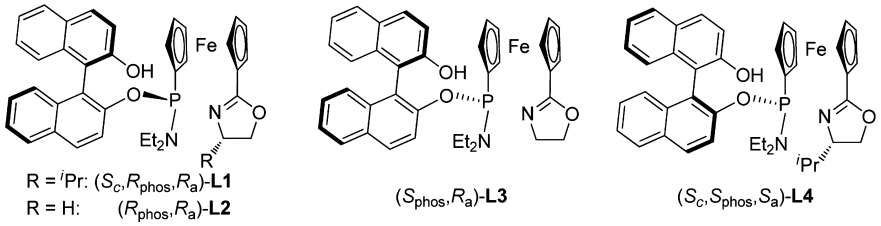


Figure 1. *P*,*N*-Ferrocene-based SIOCPhox ligands.

configuration at the phosphorus atom controls the configuration of the product because product **2a**, with the opposite configuration, was afforded when (S_{phos},R_a)-**L3** was used (entry 10 vs entry 9). Both the dr and ee are much lower with (S_{phos},R_a)-**L3** than with (R_{phos},R_a)-**L2**, indicating that the chiralities in **L2** are matched (entry 10 vs entry 9). The use of (S_c,S_{phos},S_a)-**L4** led to a lower dr and yield compared with (S_c,R_{phos},R_a)-**L1**, revealing that the chiralities in ligand **L4** are mismatched (entry 11 vs entry 5). It is interesting that **L4** still gave product **2a** with excellent enantioselectivity but the opposite configuration; this also supported the suggestion that the product's configuration was determined by that of the phosphorus atom of the ligand.[6b]

The substrate scope of the Pd-catalyzed AAA reaction of nitroalkanes was investigated under the optimized reaction conditions (Table 2). The reaction proceeded smoothly in all cases, affording alkylation products in high yields and with excellent regio-, diastereo-, and enantioselectivities; the **2**/**3** ratio was 80−97/20−3, dr was 83−97/17−3 for **2**, and the ee value was 96−99% for **2** (except for entry 10, see below). The nitroalkane structure exerted little influence on the regio-, diastereo-, and enantioselectivities of the reaction (entries 1−4). Nitromethylbenzene, with an acidic proton at the α-position of the NO_2 group and prone to epimerization under basic conditions, was a suitable nucleophile for affording products with good diastereoselectivity (entry 5). The reaction is tolerant of various substituents at the *para*, *meta*, or *ortho* positions of the phenyl group of allyl **1** (entries 6−17). The reaction also worked well for allylic substrates with two substituents on the phenyl ring, providing the corresponding products in excellent yields and with excellent regio-, diastereo-, and enantioselectivities (entries 15 and 16). Allyl **1**, with a furanyl substituent, was suitable for the reaction, affording the allyl product in high yield and with excellent selectivity (entry 17). The diastereoselectivity decreased slightly when allyl **1** with an electron-donating group was used (entries 11 and 13). A chlorine atom as a substituent at the *para* and *meta* positions and a fluorine atom at the *ortho* position of the phenyl ring have negative effects on the regioselectivity (entries 9, 12, and 14). The absolute configuration of the product **2j** was assigned as (*R*,*R*) by X-ray diffraction analysis of its derivative **4j** (see Supporting Information).

The α-H of nitroalkanes is acidic (the pK_a values for nitroalkanes are 16−17), and epimerization occurs easily, which may lead to the poor diastereoselectivity in transition-metal-catalyzed AAA reactions with nitroalkanes.[4g,5b] We observed that epimerization was suppressed when the reaction was performed at a lower temperature; however, the dr declined significantly if the reaction mixture was stirred at room temperature for a longer duration. It was also found that the dr of the branched product **2** could be maintained if the mixture was concentrated in vacuo below 10 °C during work up of the reaction product.

To demonstrate the utility of our methodology, the syntheses of optically active homoallylamine **4b**, 2,3-disubstituted tetrahydropyridine **6**, and α,β-disubstituted amino acid derivative **8** were undertaken from the common scaffold **2b** (Schemes 1 and 2). The allylic alkylation product **2b** was

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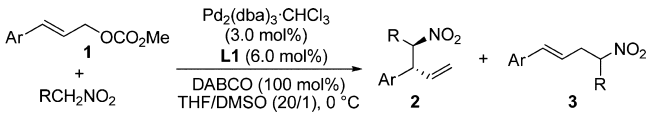
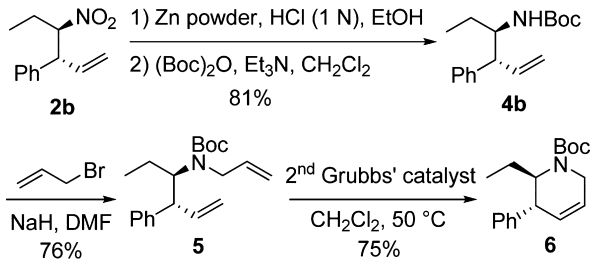
Table 2. Substrate Scope for Pd-Catalyzed Reactions of Allyl Methyl Carbonates 1 with Nitroalkanes[a]



entry	1, Ar	R	yield (%)[b]	2/3[c]	2, dr[c]	ee (%)[d]
1	Ph	Me	95	93/7	**2a**, 94/6	98
2	Ph	Et	91	91/9	**2b**, 96/4	99
3	Ph	*n*-Pr	93	96/4	**2c**, 97/3	99
4	Ph	*n*-Bu	86	96/4	**2d**, 95/5	99
5	Ph	Ph	69	93/7	**2e**, 83/17	99
6	*p*-$CH_3OC_6H_4$	Et	94	96/4	**2f**, 97/3	96
7	*p*-$CH_3C_6H_4$	Et	95	95/5	**2g**, 96/4	97
8	*p*-FC_6H_4	Et	89	93/7	**2h**, 96/4	98
9	*p*-ClC_6H_4	Et	88	88/12	**2i**, 93/7	99
10	*p*-BrC_6H_4	Et	92	91/9	**2j**, 94/6	92
11	*m*-$CH_3OC_6H_4$	Et	91	92/8	**2k**, 90/10	98
12	*m*-ClC_6H_4	Et	94	87/13	**2l**, 92/8	98
13	*o*-$CH_3OC_6H_4$	Et	90	92/8	**2m**, 88/12	97
14	*o*-FC_6H_4	Et	89	80/20	**2n**, 85/15	97
15	*m*-OCH_2O-*p*-C_6H_4	Et	95	96/4	**2o**, 95/5	99
16	*p*-OCH_3-*m*-$^cC_5H_9OC_6H_3$	Et	91	97/3	**2p**, 96/4	99
17	2-furanyl	Et	82	95/5	**2q**, 94/6	99

[a]Conditions: molar ratio **1a**/DABCO/$Pd_2(dba)_3$·$CHCl_3$/**L1** = 100/100/3/6, 0.6 mL of RCH_2NO_2, THF (2 mL)/DMSO (0.1 mL), 0 °C, overnight. [b]Isolated yield of products **2** and **3**. [c]Determined by GC. [d]Determined by chiral HPLC or GC.

Scheme 1. Synthesis of 2,3-Disubstituted Tetrahydropyridine 6 Using 2b



treated with activated zinc powder followed by protection of the resulting free amine with a Boc group to afford the protected homoallylamine **4b**. Allylation of amine **4b** and subsequent ring-closing metathesis, catalyzed by a second-generation Grubbs's catalyst, efficiently constructed tetrahydropyridine **6** in 46% overall yield in four steps (Scheme 1).

Ozonolysis of allylated **2b**, followed by a one-pot Pinnick oxidation and esterification, furnished ester **7** in 61% overall yield. Ester **7** was subjected to reduction with activated zinc powder, and the subsequent reductive amination gave the α,β-disubstituted amino acid derivative **8** in 44% overall yield in five steps (Scheme 2).

CONCLUSION

We achieved Pd-catalyzed AAA of nitroalkanes and monosubstituted allylic substrates, providing products with two chiral centers in high yields and with excellent regio-, diastereo-, and enantioselectivities. Epimerization of the products with two chiral centers was suppressed by running the reaction at a lower temperature, with DABCO as the base. The resulting products contain two adjacent stereogenic centers and two functional groups that can be easily elaborated to more complex products. Further studies investigating extension of the protocol to other nucleophiles and applications in organic synthesis are in progress.

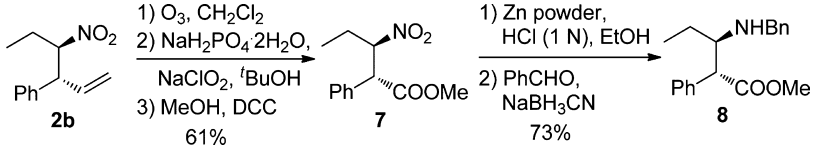
EXPERIMENTAL SECTION

General Methods. The reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were purified and dried prior to use using standard methods. Commercially available reagents were used without further purification. ^{1}H NMR spectra were recorded on an NMR instrument operated at 400 MHz. Chemical shifts are reported in parts per million (ppm) with the solvent resonance as the internal standard ($CDCl_3$ δ 7.26 ppm). ^{13}C NMR spectra were recorded on a NMR instrument operated at 100 MHz with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$ δ 77.1 ppm). Infrared spectra were recorded from thin films of pure samples. MS and HRMS were measured in EI or ESI mode, and the mass analyzer of the HRMS was TOF. Thin-layer chromatography was performed on precoated glassback plates and visualized with UV light at 254 nm. Flash-column chromatography was performed on silica gel. Enantiomer ratios were determined by chiral GC or HPLC analysis in comparison with authentic racemic materials.

General Experimental Procedure for Table 2. To a flame-dried Schlenk tube were added $Pd_2(dba)_3$·$CHCl_3$ (5.2 mg, 0.005 mmol), ligand (S,R_{phos},R)-SIOCPhox **L1** (6.8 mg, 0.010 mmol), freshly distilled anhydrous THF (1.0 mL), and DMSO (0.1 mL). The resulting mixture was allowed to stir for 30 min. The methyl carbonate **1** (0.15 mmol) and DABCO (0.15 mmol) were added subsequently, then distilled anhydrous THF (1.0 mL) and nitroalkane (0.6 mL) were added. The resulting reaction mixture was stirred at 0 °C overnight (TLC control). After the ratio of compounds **2** and **3** and diastereoselectivity of compound **2** were determined by GC, the volatiles were removed in vacuo. The resulting residue was purified by flash-column chromatography on silica gel with petroleum ether and EtOAc as eluents to give mixed products **2** and **3**. Pure product **2** was obtained by preparative TLC, and the enantioselectivity was determined by HPLC.

(3*R*,4*R*)-4-Nitropent-1-en-3-yl benzene (2a): Colorless oil, 95% yield (27.2 mg), **2a**/**3a** 93/7, dr 94/6, 98% ee; $[\alpha]_D^{20} = -93$ (c = 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (d, J = 6.8 Hz, 3H), 3.71 (t, J = 9.2 Hz, 1H), 4.85 (dq, J = 10.4, 6.8 Hz, 1H), 5.13 (d, J = 10.4 Hz, 1H), 5.15 (d, J = 17.2 Hz, 1H), 6.01 (ddd, J = 8.8, 10.4, 18.8 Hz, 1H), 7.18−7.20 (m, 2H), 7.25−7.38 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.8, 55.1, 87.5, 118.1, 127.7, 128.0, 129.2, 136.1, 138.1; MS

Scheme 2. Synthesis of α,β-Disubstituted Amino Acid Derivative 8 from 2b



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(EI) 65(11), 77 (12), 91 (53), 105 (13), 117 (100), 129 (67), 144 (82), 165 (1), 191 (M^+, 1.32); HRMS calcd for $C_{11}H_{13}NO_2$ 191.0946, found 191.0941; IR (film) 793, 866, 1018, 1089, 1260, 1452, 1549, 2917, 2962 cm^{-1}; chiral GC (CHIRALDEX G-BP column, 25 m × 0.25 mm × 0.12 μm, carrier gas nitrogen) (injector temperature 250 °C, split ratio 60, constant column flow 12 psi, column temperature 60 °C (2 min), 60−80 °C (1.0 °C/min), 80−160 °C (3 °C/min), FID detector temperature 250 °C, T_R = 38.4 min (major), 38.8 min (minor).

(3*R*,4*R*)-4-Nitrohex-1-en-3-yl benzene (2b): Colorless oil, 91% yield (27.9 mg), **2b**/**3b** 91/9, dr 96/4, 99% ee; $[\alpha]_D^{20}$ = −81 (*c* = 1.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.2 Hz, 3H), 1.41−1.55 (m, 1H), 1.75−1.89 (m, 1H), 3.71 (t, *J* = 9.6 Hz, 1H), 4.67 (td, *J* = 10.8, 3.0 Hz, 1H), 5.13 (d, *J* = 10.2 Hz, 1H), 5.15 (d, *J* = 17.1 Hz, 1H), 6.01 (ddd, *J* = 9.0, 9.9, 16.8 Hz, 1H), 7.18−7.20 (m, 2H), 7.25−7.38 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3, 25.3, 54.4, 94.5, 118.1, 127.6, 127.9, 129.2, 136.0, 138.3; MS (EI) 77 (7), 91 (47), 105 (8), 117 (100), 129 (23), 143 (24), 158 (43), 205 (M^+, 0.44); HRMS calcd for $C_{12}H_{15}NO_2$ 205.1103, found 205.1104; IR (film) 801, 1016, 1082, 1259, 1368, 1547, 2963 cm^{-1}; chiral GC (CHIRALDEX G-BP column, 25 m × 0.25 mm × 0.12 μm, carrier gas nitrogen) (injector temperature 250 °C, split ratio 60, constant column flow 10 psi, column temperature 50 °C (2 min), 50−80 °C (2.0 °C/min, 40 min), FID detector temperature 250 °C, T_R = 91.6 min (major), 92.1 min (minor).

(3*R*,4*R*)-4-Nitrohept-1-en-3-yl benzene (2c): Colorless oil, 93% yield (30.5 mg), **2c**/**3c** 96/4, dr 97/3, 99% ee; $[\alpha]_D^{20}$ = −50 (*c* = 0.45, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.81 (t, *J* = 7.2 Hz, 3H), 1.19−1.37 (m, 3H), 1.83−1.86 (m, 1H), 3.70 (t, *J* = 10 Hz, 1H), 4.67 (td, *J* = 10.8, 2.4 Hz, 1H), 5.13 (d, *J* = 9.2 Hz, 1H), 5.15 (d, *J* = 16.8 Hz, 1H), 6.01 (ddd, *J* = 8.8, 10, 16.8 Hz, 1H), 7.18−7.19 (m, 2H), 7.25−7.31 (m, 1H), 7.34−7.38 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.2, 19.1, 33.8, 54.6, 92.8, 118.1, 127.6, 127.9, 129.2, 136.1, 138.4; MS (EI) 51 (5), 65 (7), 77 (7), 91 (54), 117 (100), 129 (15), 143 (22), 172 (23), 219 (M^+, 0.44); HRMS calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1253; IR (film) 700, 796, 1082, 1361, 1493, 1549, 2924, 2962 cm^{-1}; chiral HPLC (Chiralcel PC-2, 0.46 cm × 250 mm, *n*-hexane/2-propanol 100/0.5, flow rate 0.5 mL/min, UV 214 nm), T_R = 15.8 min (major), 17.2 min (minor).

(3*R*,4*R*)-4-Nitrooct-1-en-3-yl benzene (2d): Colorless oil, 86% yield (30.1 mg), **2d**/**3d** 96/4, dr 95/5, 99% ee; $[\alpha]_D^{20}$ = −51 (*c* = 0.65, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.78 (t, *J* = 7.2 Hz, 3H), 1.15−1.26 (m, 4H), 1.37−1.58 (m, 1H), 1.82−1.86 (m, 1H), 3.69 (t, *J* = 9.6 Hz, 1H), 4.67 (td, *J* = 10.8, 2.4 Hz, 1H), 5.13 (d, *J* = 9.6 Hz, 1H), 5.15 (d, *J* = 16.4 Hz, 1H), 6.01 (ddd, *J* = 8.8, 10, 16.8 Hz, 1H), 7.17−7.19 (m, 2H), 7.25−7.30 (m, 1H), 7.34−7.38 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 21.8, 27.9, 31.5, 54.6, 93.0, 118.1, 127.6, 127.9, 129.2, 136.1, 138.4; MS (EI) 55 (7), 65 (5), 77 (5), 91 (50), 117 (100), 129 (14), 143 (20), 186 (18), 233 (M^+, 0.01); HRMS calcd for $C_{14}H_{19}NO_2$ 233.1416, found 233.1413; IR (film) 794, 1014, 1085, 1258, 1462, 1555, 2850, 2920, 2960 cm^{-1}; chiral HPLC (Chiralcel PC-2, 0.46 cm × 250 mm, *n*-hexane/2-propanol 98/2, flow rate 0.3 mL/min, UV 230 nm), T_R = 15.5 min (major), 17.5 min (minor).

(1*S*,2*R*)-1-Nitrobut-3-ene-1,2-diyl dibenzene (2e): White solid, mp 108−109 °C, 69% yield (21.3 mg), **2e**/**3e** 93/7, dr 83/17, 99% ee; $[\alpha]_D^{20}$ = −32 (*c* = 1.26, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.40 (dd, *J* = 11.2, 11.6 Hz, 1H), 5.22 (d, *J* = 10.8 Hz, 1H), 5.26 (d, *J* = 17.2 Hz, 1H), 5.76 (d, *J* = 11.6 Hz, 1H), 6.07−6.16 (m, 1H), 7.03−7.43 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 54.0, 95.2, 118.4, 127.2, 128.2, 128.4, 128.6, 128.7, 129.6, 132.4, 136.2, 137.3; MS (EI) 51 (11), 65 (8), 91 (87), 117 (100), 129 (67), 178 (9), 206 ($[M - HNO_2]^+$, 4); HRMS calcd for $C_{16}H_{14}$ 206.1096, found 206.1098; IR (film) 697, 725, 789, 1360, 1547; chiral HPLC (Chiralcel AD-H, 0.46 cm × 250 mm, *n*-hexane/2-propanol 98/2, flow rate 0.5 mL/min, UV 214 nm), T_R= 15.4 min (minor), 16.2 min (major).

1-Methoxy-4-[(3′*R*,4′*R*)-4′-nitrohex-1′-en-3′-yl]benzene (2f): Colorless oil, 94% yield (33.1 mg), **2f**/**3f** 96/4, dr 97/3, 96% ee; $[\alpha]_D^{20}$ = −69 (*c* = 0.65, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.6 Hz, 3H), 1.47−1.53 (m, 1H), 1.78−1.86 (m, 1H), 3.66 (t, *J* = 9.6 Hz, 1H), 3.80 (s, 3H), 4.62 (td, *J* = 10.8, 3.2 Hz), 5.13 (d, *J* = 10.4 Hz, 1H), 5.15 (d, *J* = 16.8 Hz, 1H), 6.01 (ddd, *J* = 8.8, 10.4, 16.8 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3, 25.3, 53.4, 55.2, 94.6, 114.5, 117.7, 128.9, 130.3, 136.3, 159.0; MS (EI) 55 (5), 65 (6), 77 (12), 91 (40), 147 (100), 159 (8), 188 (27), 235 (M^+, 1.4); HRMS calcd for $C_{13}H_{17}NO_3$ 235.1208, found 235.1213; IR (film) 805, 829, 1245, 1511, 1546, 1610, 2973 cm^{-1}; chiral HPLC (Chiralcel OJ-H, 0.46 cm × 250 mm, n-hexane/2-propanol 90/10, flow rate 0.3 mL/min, UV 230 nm), T_R = 32.8 min (major), 35.3 min (minor).

1-Methyl-4-[(3′*R*,4′*R*)-4′-nitrohex-1′-en-3′-yl]benzene (2g): Colorless oil, 95% yield (31.2 mg), **2g**/**3g** 95/5, dr 96/4, 97% ee; $[\alpha]_D^{20}$ = −77 (*c* = 0.76, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.2 Hz, 3H), 1.46−1.52 (m, 1H), 1.81−1.86 (m, 1H), 2.33 (s, 3H), 3.67 (t, *J* = 9.6 Hz, 1H), 4.64 (td, *J* = 10.8, 3.2 Hz, 1H), 5.08 (d, *J* = 10.4 Hz, 1H), 5.12 (d, *J* = 18.4 Hz, 1H), 5.98 (ddd, *J* = 8.4, 10, 18.8 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 21.0, 25.3, 54.0, 94.6, 117.8, 127.8, 129.8, 135.3, 136.2, 137.4; MS (EI) 41 (4), 53 (4), 65 (5), 77 (9), 91 (26), 115 (23), 131 (100), 143 (12), 157 (19), 172 (33), 219 (M^+, 0.99); HRMS calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1258; IR (film) 804, 815, 966, 1080, 1548, 2925, 2965 cm^{-1}; chiral HPLC (Chiralcel IC, 0.46 cm × 250 mm, *n*-hexane/2-propanol 95/5, flow rate 0.5 mL/min, UV 230 nm), T_R = 12.0 min (minor), 12.9 min (major).

1-Fluoro-4-[(3′*R*,4′*R*)-4′-nitrohex-1′-en-3′-yl]benzene (2h): Colorless oil, 89% yield (29.8 mg), **2h**/**3h** 93/7, dr 96/4, 98% ee; $[\alpha]_D^{20}$ = −42 (*c* = 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.6 Hz, 3H), 1.46−1.51 (m, 1H), 1.79−1.87 (m, 1H), 3.72 (t, *J* = 9.2 Hz, 1H), 4.63 (td, *J* = 10.8, 3.2 Hz, 1H), 5.13 (d, *J* = 10.8 Hz, 1H), 5.14 (d, *J* = 18.4 Hz, 1H), 5.97 (ddd, *J* = 9.2, 10, 18.8 Hz, 1H), 7.03−7.08 (m, 2H), 7.15−7.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 25.4, 53.4, 94.3, 116.1 (d, *J* = 21 Hz), 118.3, 129.4 (d, *J* = 8.1 Hz), 134.1 (d, *J* = 3.1 Hz), 135.8, 162.1 (d, *J* = 245.4 Hz); ^{19}F NMR (376 MHz) δ 114.5 (m); MS (EI) 55 (6), 65 (2), 77 (3), 83 (8), 109 (58), 115 (26), 135 (100), 147 (13), 161 (20), 176 (35), 223 (M^+, 0.24); HRMS calcd for $C_{12}H_{14}NO_2F$ 223.1009, found 223.1006; IR (film) 810, 833, 862, 1015, 1223, 1259, 1509, 1548, 2927, 2963 cm^{-1}; chiral GC (CHIRALDEX G-BP column, 25 m × 0.25 mm × 0.12 μm, carrier gas nitrogen) (injector temperature 250 °C, split ratio 60, constant column flow 12 psi, column temperature 60 °C (2 min), 60−80 °C (1.0 °C/min), 80−160 °C (3 °C/min, 30 min), FID detector temperature 250 °C, T_R = 42.8 min (major), 43.1 min (minor).

1-Chloro-4-[(3′*R*,4′*R*)-4′-nitrohex-1′-en-3′-yl]benzene (2i): Colorless oil, 88% yield (31.6 mg), **2i**/**3i** 88/12, dr 93/7, 99% ee; $[\alpha]_D^{20}$ = −78 (*c* = 1.42, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.6 Hz, 3H), 1.46−1.51 (m, 1H), 1.79−1.85 (m, 1H), 3.71 (t, *J* = 9.6 Hz, 1H), 4.63 (td, *J* = 10.8, 3.2 Hz, 1H), 5.13 (d, *J* = 10.8 Hz, 1H), 5.14 (d, *J* = 17.6 Hz, 1H), 5.95 (ddd, *J* = 8.4, 9.6, 17.2 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 25.3, 53.5, 94.1, 118.5, 129.3, 129.4, 133.5, 135.5, 136.8; MS (EI) 41 (11), 55 (12), 63 (10), 77 (13), 89 (16), 115 (100), 125 (57), 151 (91), 192 (40), 239 (M^+, 0.37); HRMS calcd for $C_{12}H_{14}NO_2Cl$ 239.0713, found 239.0710; IR (film) 802, 824, 1091, 1371, 1491, 1547, 2935, 2974 cm^{-1}; chiral GC (CHIRALDEX G-BP column, 25 m × 0.25 mm × 0.12 μm, carrier gas nitrogen) (injector temperature 250 °C, split ratio 60, constant column flow 10 psi, column temperature 60 °C (2 min), 60−150 °C (1.0 °C/min, 30 min), 150−180 °C (1 °C/min), FID detector temperature 250 °C, T_R = 88.4 min (major), 89.8 min (minor).

1-Bromo-4-[(3′*R*,4′*R*)-4′-nitrohex-1′-en-3′-yl]benzene (2j): Colorless oil, 92% yield (39.1 mg), **2j**/**3j** 91/9, dr 94/6, 92% ee; $[\alpha]_D^{20}$ = −83 (*c* = 1.46, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.6 Hz, 3H), 1.44−1.51 (m, 1H), 1.78−1.87 (m, 1H), 3.69 (t, *J* = 10 Hz, 1H), 4.63 (td, *J* = 10.8, 2.8 Hz, 1H), 5.13 (d, *J* = 10.4 Hz, 1H), 5.14 (d, *J* = 16.8 Hz, 1H), 5.95 (m, 1H), 7.06 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 25.3, 53.5, 94.1, 118.5, 129.3, 129.4, 133.5, 135.5, 136.8; MS (EI) 55 (9), 77 (7), 89 (9), 116 (100), 129 (35), 157 (44), 195 (17), 283 (M^+, 0.97); HRMS calcd for $C_{12}H_{14}NO_2Br$ 283.0208, found 283.0209; IR (film)

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801, 819, 1010, 1074, 1260, 1370, 1483, 1548, 2925 cm^{-1}; chiral HPLC (Chiralcel PC-2, 0.46 cm × 250 mm, *n*-hexane/2-propanol 200/1, flow rate 0.3 mL/min, UV 230 nm), T_R = 19.5 min (major), 21.3 min (minor).

1-Methoxy-3-[(3′*R*,4′*R*)-4′-nitrohex-1′-en-3′-yl]benzene (2k): Colorless oil, 91% yield (32.1 mg), **2k**/**3k** 92/8, dr 90/10, 98% ee; $[\alpha]_D^{20}$ = −93 (*c* = 1.35, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.2 Hz, 3H), 1.47−1.58 (m, 1H), 1.79−1.87 (m, 1H), 3.67 (t, *J* = 10 Hz, 1H), 3.81 (s, 3H), 4.65 (td, *J* = 10.8, 3.2 Hz, 1H), 5.09−5.16 (m, 2H), 5.96 (ddd, *J* = 8.8, 10.4, 17.2 Hz, 1H), 6.73 (s, 1H), 6.77−6.83 (m, 2H), 7.26−7.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 25.5, 54.4, 55.2, 94.4, 112.5, 114.0, 118.1, 120.1, 130.2, 135.9, 139.9, 160.1; MS (EI) 55 (14), 65 (16), 81 (30), 91 (80), 121 (62), 147 (100), 188 (21), 235 (M^+, 31); HRMS calcd for $C_{13}H_{17}NO_3$ 235.1208, found 235.1204; IR (film) 704, 810, 1042, 1261, 1547, 2969 cm^{-1}; chiral HPLC (Chiralcel OJ-H, 0.46 cm × 250 mm, *n*-hexane/2-propanol 95/5, flow rate 0.5 mL/min, UV 230 nm), T_R = 31.1 min (major), 35.9 min (minor).

1-Chloro-3-[(3′*R*,4′*R*)-4′-nitrohex-1′-en-3′-yl]benzene (2l): Colorless oil, 94% yield (33.7 mg), **2l**/**3l** 87/13, dr 92/8, 98% ee; $[\alpha]_D^{20}$ = −56 (*c* = 0.81, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.6 Hz, 3H), 1.45−1.52 (m, 1H), 1.80−1.88 (m, 1H), 3.70 (t, *J* = 9.6 Hz, 1H), 4.64 (td, *J* = 10.8, 3.2 Hz, 1H), 5.14 (d, *J* = 9.6 Hz, 1H), 5.15 (d, *J* = 18 Hz, 1H), 5.95 (ddd, *J* = 8.8, 10, 18.8 Hz, 1H), 7.07−7.09 (m, 1H), 7.19 (s, 1H), 7.29−7.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 25.4, 53.9, 94.0, 118.8, 126.1, 127.9, 128.1, 130.5, 135.0, 135.3, 140.4; MS (EI) 41 (13), 55 (18), 63 (10), 77 (14), 89 (17), 115 (100), 129 (34), 151 (78), 177 (9), 192 (32), 239 (M^+, 0.41); HRMS calcd for $C_{12}H_{14}NO_2Cl$ 239.0713, found 239.0718; IR (film) 700, 806, 928, 1081, 1370, 1548, 2974 cm^{-1}; chiral HPLC (Chiralcel PC-2, 0.46 cm × 250 mm, *n*-hexane/2-propanol 100/1, flow rate 0.3 mL/min, UV 230 nm), T_R = 21.3 min (major), 24.7 min (minor).

1-Methoxy-2-[(3′*R*,4′*R*)-4′-nitrohex-1′-en-3′-yl]benzene (2m): Colorless oil, 90% yield (31.7 mg), **2m**/**3m** 92/8, dr 88/12, 97% ee; $[\alpha]_D^{20}$ = −69 (*c* = 1.46, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.5 Hz, 3H), 1.41−1.49 (m, 1H), 1.78−1.89 (m, 1H), 3.85 (s, 3H), 4.05 (t, *J* = 9.6 Hz, 1H), 4.94 (td, *J* = 10.8, 2.7 Hz, 1H), 5.09 (d, *J* = 10.5 Hz, 1H), 5.13 (d, *J* = 17.1 Hz, 1H), 6.07−6.19 (m, 1H), 6.85−6.96 (m, 2H), 7.12 (d, *J* = 7.2 Hz, 1H), 7.26 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 25.3, 49.9, 55.3, 93.4, 111.1, 117.9, 121.1, 126.6, 128.7, 129.4, 135.4, 156.8; MS (EI) 51 (27), 65 (31), 77 (56), 91 (100), 115 (89), 147 (100), 173 (33), 188 (83), 235 (M^+, 36); HRMS calcd for $C_{13}H_{17}NO_3$ 235.1208, found 235.1211; IR (film) 798, 1022, 1090, 1258, 1547, 2963 cm^{-1}; chiral HPLC (Chiralcel PC-2, 0.46 cm × 250 mm, *n*-hexane/2-propanol 100/1, flow rate 0.5 mL/min, UV 230 nm); T_R = 12.1 min (major), 13.1 min (minor).

1-Fluoro-2-[(3′*R*,4′*R*)-4′-nitrohex-1′-en-3′-yl]benzene (2n): Colorless oil, 89% yield (29.8 mg), **2n**/**3n** 80/20, dr 85/15, 97% ee; $[\alpha]_D^{20}$ = −44 (*c* = 0.68, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.6 Hz, 3H), 1.46−1.53 (m, 1H), 1.83−1.92 (m, 1H), 4.02 (t, *J* = 9.6 Hz, 1H), 4.82 (td, *J* = 10.8, 3.2 Hz, 1H), 5.13 (d, *J* = 10.4 Hz, 1H), 5.19 (d, *J* = 16.8 Hz, 1H), 6.00−6.09 (m, 1H), 7.06−7.22 (m, 3H), 7.28−7.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.2, 25.4, 48.8, 93.2 (d, *J* = 3 Hz), 116.2 (d, *J* = 22.3 Hz), 119.0, 124.8 (d, *J* = 3.3 Hz), 125.3 (d, *J* = 14.5 Hz), 129.3 (d, *J* = 8.1 Hz), 129.6 (d, *J* = 4.5 Hz), 134.4, 160.3 (d, *J* = 244.7 Hz); ^{19}F NMR (376 MHz) δ −116.3 (m); MS (EI) 55 (14), 83 (10), 109 (75), 135 (100), 147 (10), 176 (25), 223 (M^+, 0.41); HRMS calcd for $C_{12}H_{14}NO_2F$ 223.1009, found 223.1008; IR (film) 756, 798, 1013, 1089, 1259, 1550, 2962 cm^{-1}; chiral HPLC (Chiralcel OJ-H, 0.46 cm × 250 mm, *n*-hexane/2-propanol 80/20, flow rate 0.5 mL/min, UV 230 nm), T_R = 14.7 min (major), 16.9 min (minor).

5-[(3′*R*,4′*R*)-4′-Nitrohex-1′-en-3′-yl]benzo[*d*][1,3]dioxole (2o): White solid, mp 58−59 °C, 95% yield (35.5 mg), **2o**/**3o** 96/4, dr 95/5, 99% ee; $[\alpha]_D^{20}$ = −68 (*c* = 1.76, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.2 Hz, 3H), 1.51−1.54 (m, 1H), 1.79−1.83 (m, 1H), 3.63 (t, *J* = 9.6 Hz, 1H), 4.58 (td, *J* = 10.8, 3.0 Hz, 1H), 5.08 (d, *J* = 9.9 Hz, 1H), 5.13 (d, *J* = 17.1 Hz, 1H), 5.88−6.00 (m, 3H), 6.64−6,67 (m, 2H), 6.79 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 25.3, 53.9, 94.5, 101.2, 107.9, 108.8, 117.9, 121.3, 131.9, 136.0, 146.9, 148.2; MS (EI) 51 (8), 63 (7), 77 (29), 103 (56), 115 (18), 131 (100), 161 (35), 202 (24), 249 (M^+, 23); HRMS calcd for $C_{13}H_{15}NO_4$ 249.1001, found 249.1005; IR (film) 796, 928, 1240, 1365, 1488, 1547, 2973 cm^{-1}; chiral HPLC (Chiralcel AD-H, 0.46 cm × 250 mm, *n*-hexane/2-propanol 98/2, flow rate 0.5 mL/min, UV 214 nm), T_R = 17.1 min (minor), 18.4 min (major).

2-(Cyclopentyloxy)-1-methoxy-4-[(3′*R*,4′*R*)-4′-nitrohex-1′-en-3′-yl]benzene (2p): Colorless oil, 91% yield (43.6 mg), **2p**/**3p** 97/3, dr 96/4, 99% ee; $[\alpha]_D^{20}$ = −53 (*c* = 2.33, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.2 Hz, 3H), 1.49−1.55 (m, 1H), 1.62−1.65 (m, 2H), 1.79−1.95 (m, 7H), 3.62 (t, *J* = 10 Hz, 1H), 3.83 (s, 3H), 4.61 (td, *J* = 10.4, 2.8 Hz, 1H), 4.75−4.79 (m, 1H), 5.08−5.15 (m, 2H), 5.97 (ddd, *J* = 8.8, 10.4, 16.8 Hz, 1H), 6.68−6.85 (m, 2H), 6.83 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.4, 23.9, 25.3, 32.6, 32.7, 53.7, 56.0, 80.5, 94.6, 112.3, 114.6, 117.7, 120.0, 130.5, 136.2, 147.9, 149.5; MS (EI) 55 (10), 69 (13), 91 (20), 103 (48), 131 (100), 163 (92), 204 (62), 319 (M^+, 26); HRMS calcd for $C_{18}H_{25}NO_4$ 319.1784, found 319.1787; IR (film) 745, 853, 994, 1136, 1511, 1547, 2873, 2961 cm^{-1}; chiral HPLC (Chiralcel IC, 0.46 cm × 250 mm, *n*-hexane/2-propanol 98/2, flow rate 0.5 mL/min, UV 230 nm), T_R = 18.6 min (major), 19.7 min(minor).

2-[(3′*S*,4′*R*)-4′-Nitrohex-1′-en-3′-yl]furan (2q): Yellow oil, 82% yield (23.9 mg), **2q**/**3q** 95/5, dr 94/6, 99% ee; $[\alpha]_D^{20}$ = −85 (*c* = 0.45, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.6 Hz, 3H), 1.55−1.62 (m, 1H), 1.85−1.92 (m, 1H), 3.89 (t, *J* = 9.2 Hz, 1H), 4.70 (td, *J* = 10.4, 3.2 Hz, 1H), 5.16 (d, *J* = 16.8 Hz, 1H), 5.17 (d, *J* = 11.2 Hz, 1H), 5.95 (ddd, *J* = 8.8, 10.0, 17.2 Hz, 1H), 6.17 (d, *J* = 3.2 Hz, 1H), 6.33 (q, *J* = 1.6 Hz, 1H), 7.38 (d, *J* = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.2, 25.3, 47.4, 92.5, 107.8, 110.5, 119.2, 132.9, 142.4, 151.0; MS (EI) 55 (32), 65 (17), 79 (100), 91 (40), 119 (14), 148 (50), 195 (M^+, 0.55); HRMS calcd for $C_{10}H_{13}NO_3$ 195.0895, found 195.0896; IR (film) 736, 796, 930, 1371, 1549, 2930 cm^{-1}; chiral GC (CHIRALDEX G-BP column, 25 m × 0.25 mm × 0.12 μm, carrier gas nitrogen) (injector temperature 250 °C, split ratio 60, constant column flow 10 psi, column temperature 60 °C (2 min), 60−150 °C (2 °C/min, 2 min), 150−180 °C (3 °C/min), FID detector temperature 250 °C, T_R = 26.5 min (major), 27.6 min (minor).

***tert*-Butyl [(3*R*,4*R*)-4-phenylhex-5-en-3-yl]carbamate (4b).** To an EtOH (1 mL) solution of the compound **2b** (31.5 mg, 0.15 mmol) was added an aqueous solution of HCl (1.5 mL, 1.0 N) and activated zinc powder (278 mg, 4.4 mmol). The resulting solution was allowed to stir overnight at room temperature. The reaction mixture was neutralized with saturated aqueous $NaHCO_3$ (pH = 9) before the aqueous phase was extracted with EtOAc (10 mL × 3). The combined organic phase was dried with anhydrous $MgSO_4$. After the solution was concentrated under reduced pressure, the residue was dissolved in MeOH (2.0 mL). NEt_3 (64 μL, 0.45 mmol) and $(Boc)_2O$ (98 mg, 0.45 mmol) were added to the solution, and the resulting mixtures were stirred for 1 h at room temperature. After the mixtures were concentrated in vacuo, the residue was purified by flash-column chromatography to give product **4b** as a white solid in 81% yield (33.4 mg): mp 78−79 °C; $[\alpha]_D^{20}$ = −44 (*c* = 3.33, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.2 Hz, 3H), 1.07−1.15 (m, 1H), 1.47−1.52 (m, 10H), 3.25 (t, *J* = 8.4 Hz, 1H), 3.84−3.86 (m, 1H), 4.34 (d, *J* = 8.8 Hz, 1H), 5.05 (d, *J* = 16.4 Hz, 1H), 5.07 (d, *J* = 10.8 Hz, 1H), 6.02−6.11 (m, 1H), 7.19−7.22 (m, 3H), 7.28−7.33 (m, 2H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 10.2, 25.6, 28.3, 55.7, 55.8, 78.9, 116.2, 126.5, 128.1, 128.5, 139.1, 141.7, 155.9; MS (ESI) 298 (M + Na)$^+$; HRMS (ESI) calcd for $C_{17}H_{25}NO_2$ 275.1885, found 275.1873; IR (film) 700, 1173, 1537, 1698, 2976, 3315 cm^{-1}.

***tert*-Butyl (3*R*,4*R*)-4-(4-bromophenyl)hex-5-en-3-ylcarbamate (4j).** Compound **4j**, a white solid (38.6 mg), was prepared with the same procedure for compound **4b**: mp 81−82 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.6 Hz, 3H), 1.12−1.13 (m, 1H), 1.43−1.51 (m, 10H), 3.25 (t, *J* = 8.0 Hz, 1H), 3.74−3,85 (m, 1H), 4.27−4.30 (m, 1H), 5.06 (d, *J* = 17.6 Hz, 1H), 5.09 (d, *J* = 10.8 Hz, 1H), 6.01 (ddd, *J* = 8.8, 10.4, 17.2 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.2, 25.6,

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28.4, 55.1, 55.6, 79.1, 116.9, 120.4, 129.8, 131.6, 138.3, 140.7, 155.8; MS (ESI) 376.0886 (M + Na)$^+$; HRMS (ESI) calcd for $C_{17}H_{24}BrNNaO_2$ 376.0883, found 376.0886.

***tert*-Butyl *N*-allyl [(3*R*,4*R*)-4-phenylhex-5-en-3-yl]carbamate (5).** To a stirred solution of **4b** (66.6 mg, 0.24 mmol) in DMF (2.0 mL) was added NaH (60% in mineral oil, 57.6 mg, 1.44 mmol) at 0 °C. After the mixture was stirred for 30 min at 0 °C, allyl bromide (62 μL, 0.72 mmol) was added. The resulting mixture was stirred for 1 h at room temperature before it was quenched with water. After the aqueous layer was extracted with ether (5 mL × 2), the combined organic layers were washed with water (1 mL × 2) and brine and then dried over Na_2SO_4. After the organic layers were concentrated in vacuo, the residue was purified by flash-column chromatography to afford product **5** as a colorless oil in 76% yield (57.5 mg). The ^{13}C NMR spectrum of compound **5** was unavailable due to conformational isomers: $[\alpha]_D^{20}$ = −55 (*c* = 0.75, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.74 (t, *J* = 7.2 Hz, 3H), 1.22−1.28 (m, 2H), 1.47−1.53 (m, 9H), 3.26−3.89 (m, 3H), 4.24−4.54 (m, 1H), 4.94−5.22 (m, 4H), 5.86−6.06 (m, 2H), 7.15−7.38 (m, 5H); MS (EI) 57 (100), 98 (94), 117 (24), 129 (11), 142 (95), 198 (25), 315 (M$^+$, 0.03); HRMS calcd for $C_{20}H_{29}NO_2$ 315.2198, found 315.2196; IR (film) 796, 1015, 1091, 1259, 1690, 2964 cm^{-1}.

(5*R*,6*R*)-*tert*-Butyl 6-ethyl-5-phenyl-5,6-dihydropyridine-1(2*H*)-carboxylate (6). A solution of CH_2Cl_2 (1 mL) of compound **5** (24 mg, 0.076 mmol) and the second-generation Grubbs catalyst (4.36 mg, 0.005 mmol, 6 mol %) was degassed using the freeze−pump−thaw cycle. The mixture was refluxed for 2 h under Ar atmosphere before it was concentrated under reduced pressure. The residue was purified by flash-column chromatography to provide product **6** as a colorless oil in 75% yield (16.6 mg): $[\alpha]_D^{20}$ = 202 (*c* = 0.83, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.2 Hz, 3H), 1.16 (s, 9H), 1.57−1.60 (m, 1H), 1.69−1.78 (m, 1H), 3.30 (m, 1H), 3.45−3.49 (m, 1H), 4.06−4.09 (m, 1H), 4.50−4.54 (m, 1H), 5.78−5.93 (m, 2H), 7.17−7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 25.4, 27.9, 38.9, 45.6, 58.3, 78.9, 124.9, 125.0, 126.3, 127.8, 128.2, 143.1, 155.2; MS (EI) 57 (58), 91 (15), 130 (100), 158 (5), 231 (6), 287 (M$^+$, 2); HRMS calcd for $C_{18}H_{25}NO_2$ 287.1885, found 287.1883; IR (film) 698, 1117, 1362, 1411, 1688, 2930 cm^{-1};

(2*R*,3*R*)-Methyl 3-nitro-2-phenylpentanoate (7). Dry ozone was bubbled through a solution of compound **2b** (61.5 mg, 0.3 mmol) in CH_2Cl_2 (3.0 mL) at −78 °C until complete consumption of **2b** (TLC control). A precooled (−78 °C) solution of dimethylsulfide (0.3 mL) in CH_2Cl_2 was then added. The solution was warmed to rt, and removal of the volatiles under reduced pressure gave the corresponding aldehyde. To this crude product were added successively $NaH_2PO_4{\cdot}2H_2O$ (102 mg, 0.65 mmol), 2-methyl-2-butene (0.73 mL), ^{t}BuOH (2.4 mL), and H_2O (0.75 mL). To the resulting mixture was added $NaClO_2$ (81 mg, 0.9 mmol) at 0 °C. After the reaction mixture was stirred for 2 h, the reaction was quenched by the addition of saturated aqueous NH_4Cl (0.5 mL), and the resulting mixture was stirred for another 10 min. After the solution was diluted with EtOAc (2 mL), the aqueous phase was extracted with EtOAc (2 mL). The combined organic phase was dried with anhydrous magnesium sulfate. The organic layer was filtered through Celite and was concentrated in vacuo. The residue was dissolved in MeOH (2 mL), and 4-dimethylaminopyridine (catalytic) and dicyclohexylcarbodiimide (74.1 mg, 0.36 mmol) at 0 °C were added. The resulting reaction mixture was stirred at room temperature until the disappearance of acid (TLC control). The reaction mixture was concentrated in vacuo. The residue was purified by silica gel to afford **7** as a colorless oil in 61% yield (43.1 mg): $[\alpha]_D^{20}$ = 135.7 (*c* = 1.75, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.2 Hz, 3H), 1.57−1.68 (m, 1H), 1.70−1.76 (m, 1H), 3.65 (s, 3H), 4.27 (d, *J* = 11.2 Hz, 1H), 5.05−5.12 (m, 1H), 7.27−7.41 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.1, 24.5, 52.6, 53.3, 89.2, 128.3, 128.7, 129.4, 133.2, 171.3; MS (ESI) 255.1342 (M + NH_4)$^+$; HRMS (ESI) calcd for $C_{12}H_{15}NO_4$ 237.1001, found 237.1004; IR (film) 700, 806, 1258, 1548, 1733, 2960 cm^{-1}.

(2*R*,3*R*)-Methyl 3-(benzylamino)-2-phenylpentanoate (8). To an EtOH (1 mL) solution of the compound **7** (34 mg, 0.11 mmol) was added an aqueous solution of HCl (1.5 mL, 1.0 N) and activated zinc powder (278 mg, 4.4 mmol). The resulting solution was allowed to stir overnight at room temperature. The reaction mixture was neutralized with saturated aqueous $NaHCO_3$ (pH = 9). The aqueous phase was extracted with EtOAc (10 mL × 3). The combined organic phase was dried with anhydrous $MgSO_4$. After it was concentrated under reduced pressure, the residue was dissolved in MeOH (2.0 mL), to which was added benzylaldehyde (13 μL, 0.14 mmol). After the resulting mixture was stirred for 0.5 h, $NaBH_3CN$ (29 mg, 0.48 mmol) was added at 0 °C, and the resulting mixture was stirred for 0.5 h. After the reaction was quenched by HCl (1.0 N), the mixture was extracted with CH_2Cl_2 (2 mL × 2). The combined organic layers were washed with $NaHCO_3$ (1 mL × 2) and brine and then dried over Na_2SO_4. After the residue was concentrated in vacuo, it was purified by flash-column chromatography to afford **8** as a white solid in 73% yield (23.8 mg): mp 41−42 °C; $[\alpha]_D^{20}$ = 1.8 (*c* = 0.57, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, *J* = 7.2 Hz, 3H), 1.10−1.21 (m, 1H), 1.43−1.48 (m, 1H), 3.29−3.34 (m, 1H), 3.63 (d, *J* = 10.4 Hz, 1H), 3.67 (s, 3H), 3.76 (d, *J* = 12.8 Hz, 1H), 3.86 (d, *J* = 12.8 Hz, 1H), 7.24−7.37 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.6, 22.6, 50.8, 51.8, 56.8, 60.6, 126.8, 127.4, 128.1, 128.3, 128.5, 128.7, 136.9, 140.7, 174.0; MS (ESI) 298.1801 (M + H)$^+$; HRMS (ESI) calcd for $C_{19}H_{24}NO_2$ 297.1729, found 297.1729; IR (film) 679, 793, 1025, 1732, 2959 cm^{-1}; Chiral HPLC (Chiralcel PA-2, 0.46 cm × 250 mm, *n*-hexane/2-propanol 98/2, flow rate 0.5 mL/min, UV 230 nm), T_R = 21.0 min (major), 19.1 min (minor).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectra of compounds **2a−2q**, **4−8**, and X-ray analysis data of **4j** in cif format. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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