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Asymmetric Organocatalytic Cascade Reaction of Aldehydes with 2-Amino-β-nitrostyrenes: Synthesis of Chiral Tetrahydroquinolines and Dihydroquinolines

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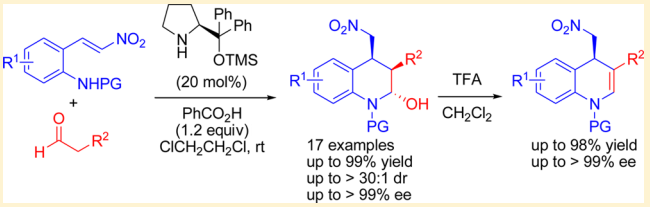
Supporting Information

ABSTRACT: An organocatalytic enantioselective Michael addition/aza-cyclization cascade reaction of aldehydes with 2-amino-β-nitrostyrenes has been developed for the construction of fully substituted chiral tetrahydroquinolines. The reaction, promoted by diphenylprolinol TMS ether as an organocatalyst, generated the chiral tetrahydroquinolines in good to high yield with excellent diastereo- and enantioselectivities (up to >30:1 dr, >99% ee). The method also provided an alternative access to chiral 1,4-dihydroquinolines, which are difficult to synthesize by other methodologies.



INTRODUCTION

Asymmetric cascade, domino, or tandem reactions, in which multiple bond-forming transformations occur under identical reaction conditions, have received wide acceptance as highly efficient and powerful methods for the synthesis of molecules with great structural complexity. These methods improve the efficiency of the overall process by reducing manual effort, and the quantities of chemicals and solvents used.[1] Asymmetric cascade reactions can be readily promoted by organocatalysts[2] that provide an efficient and environmentally friendly pathway to enantiomerically pure compounds for the synthesis of natural products, and biologically active compounds. Organocatalysts, as compared to metal-based catalysts, have several important advantages, as they are usually inexpensive, readily available, robust, and nontoxic. Implementation of asymmetric organocatalysis in a one-pot cascade process is, therefore, an important research area receiving a lot of interest.[3]

The hydroquinoline ring core occurs as an essential building block found in various natural products that possess a broad spectrum of biological activities. Accordingly, the hydroquinoline skeleton is of great importance in medicinal chemistry and is widely used in the pharmaceutical industry for the design of compounds with pharmacological properties.[4] In particular, chiral hydroquinolines are ubiquitously present as the structural core of many natural products and pharmaceuticals, which exhibit a broad range of biological activity, such as anti-HIV, antibacterial, antifungal, antimalarial, antitumor, and cardiovascular effects.[5] In view of their immense significance, numerous methods for the synthesis of chiral hydroquinolines with careful stereochemical control have been developed. In the past, in view of the biological importance, the main focus has been on the asymmetric synthesis of chiral tetrahydroquinolines.[6] However, although dihydroquinolines, including 1,2- and 1,4-dihydroquinoline, are important pharmaceutical scaffolds and synthetic intermediates in natural product synthesis,[4e,7] methods for the asymmetric synthesis of these compounds have been rarely disclosed.[8] Moreover, only one example is reported to date in the catalytic asymmetric synthesis of 1,4-dihydroquinolines.[9,10] Herein, we report a new synthetic strategy for the construction of chiral tetrahydroquinolines and 1,4-dihydroquinolines utilizing the organocatalytic enantioselective Michael addition/aza-cyclization cascade reaction of an aldehyde with 2-amino-β-nitrostyrene.

Recently, we reported the asymmetric synthesis of 4-substituted tetrahydroquinoline derivatives by an organocatalytic conjugate addition/cyclization domino reaction (Scheme 1, eq 1).[11] In this reaction, the methylene carbon of the dialkyl malonate attacks the β-carbon of the *o*-*N*-protected

Scheme 1. Organocatalytic Enantioselective Access to Chiral Tetrahydroquinolines

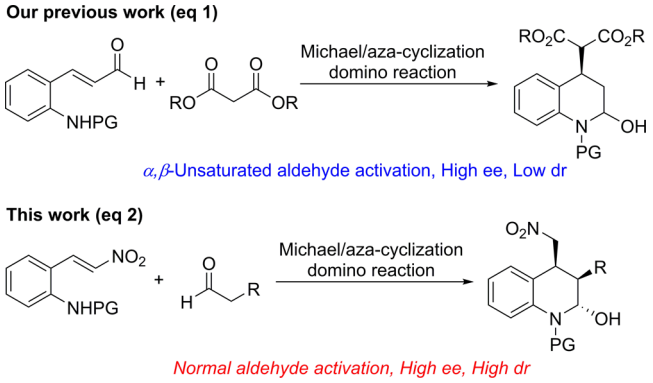


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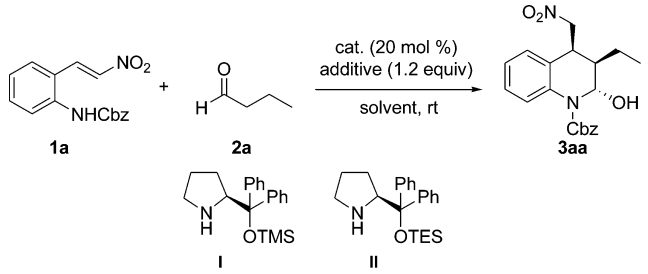
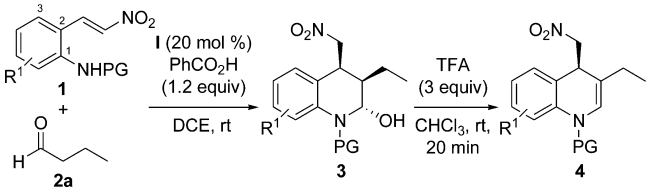
Table 1. Screening the Reaction Conditions[a]



entry	cat.	additive	solvent	time (h)	yield (%)[b]	.ee (%)[c]
1	**I**		CH_2Cl_2	72	[d]	nd
2	**I**	$PhCO_2H$	CH_2Cl_2	48	77	99
3	**I**	4-$NO_2C_6H_5CO_2H$	CH_2Cl_2	72	83	99
4	**I**	CH_3CO_2H	CH_2Cl_2	96	77	>99
5	**I**	NaOAc	CH_2Cl_2	72	trace	nd
6[e]	**I**	$PhCO_2H$	CH_2Cl_2	96	trace	nd
7[f]	**I**	$PhCO_2H$	CH_2Cl_2	96	40	>99
8	**II**	$PhCO_2H$	CH2Cl2	72	68	>99
9	**I**	$PhCO_2H$	toluene	72	74	>99
10	**I**	PhCO2H	MeOH	96	45	99
11	**I**	$PhCO_2H$	CH_3CN	96	76	99
12	**I**	$PhCO_2H$	DMF	96	trace	nd
13	**I**	PhCO2H	EtOAc	96	trace	nd
14	**I**	$PhCO_2H$	$CHCl_3$	72	74	99
15	**I**	$PhCO_2H$	$ClCH_2H_2Cl$	48	82	>99

[a]Unless otherwise specified, the reactions were carried out in solvent (0.2 M) with **1a** (0.25 mmol) and butyraldehyde (**2a**, 0.75 mmol) in the presence of 20 mol % catalyst at room temperature. [b]Isolated yield after chromatographic purification. [c]Determined by chiral-phase HPLC analysis after dehydration. [d]No reaction. [e]20 mol % $PhCO_2H$ was used. [f]10 mol % catalyst was used. nd = not determined

Table 2. Scope of Asymmetric Michael/Aza-cyclization Domino Reaction of *o*-*N*-Protected Amino-*β*-nitrostyrenes 1 to Butyraldehyde 2a[a,b]



entry	PG	R^1	time (h)	**3**/yield[c] (%)	**4**/yield[c] (%)	dr (**3**)[d]	ee (%)[e]
1	Cbz	H	48	**3aa**/82	**4aa**/93	28:1	>99
2	CO_2Et	H	48	**3ba**/78	**4ba**/90	>30:1	99
3	Boc	H	48	**3ca**/68	**4ca**/81	>30:1	99
4	Cbz	4-Me	60	**3da**/72	**4da**/93	>30:1	99
5	Cbz	6-Me	72	**3ea**/95	**4ea**/73	22:1	99
6	Cbz	4-Cl	36	**3fa**/73	**4fa**/88	>30:1	99
7	Cbz	5-Cl	36	**3ga**/66	**4ga**/98	16:1	99
8	Cbz	4-Br	36	**3ha**/65	**4ha**/68	>30:1	98

[a]All of the reactions were carried out in DCE (0.2 M) with **1** (0.25 mmol) and butyraldehyde (**2a**, 0.75 mmol) in the presence of catalyst **I** (20 mol %) at room temperature. [b]Reactions were carried out in $CHCl_3$ (0.1 M) with 1.0 equiv of tetrahydroquinolines **3** and 3.0 equiv of TFA at room temperature. [c]Isolated yield after chromatographic purification. [d]Diastereomeric ratio; major-(2*S*,3*R*,4*S*) vs minor-(2*R*,3*R*,4*S*) diastereomer determined by ^{1}H NMR analysis. [e]Determined by chiral-phase HPLC analysis.

aminocinnamaldehyde to afford the Michael adduct first, in which the organocatalyst activates the *o*-*N*-protected aminocinnamaldehyde and provides a chiral environment, followed by hemiacetalization. The cascade reaction achieved the desired tetrahydroquinoline derivatives in good yields with high enantioselectivities but relatively low diastereoselectivities. To achieve a high level of stereocontrol, including diastereoselectivity, we envisaged that tetrahydroquinoline derivatives could be accessed stereoselectively through a Michael addition/aza-cyclization cascade reaction of an aldehyde with 2-amino-*β*-nitrostyrene (eq 2). In this method, asymmetric Michael addition of an aldehyde to a nitroalkene[12,13] via an enamine intermediate was expected to give highly functionalized tetrahydroquinoline derivatives through subsequent aza-cyclization with high diastereoselectivities and excellent enantioselectivities.

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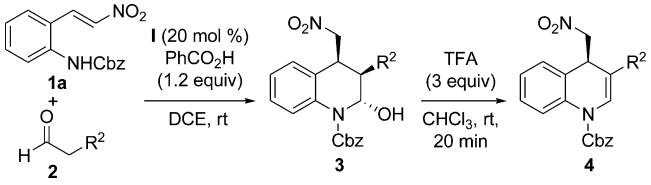
Table 3. Scope of Asymmetric Michael/Aza-cyclization Domino Reaction of *o*-*N*-Cbz-Amino-*β*-nitrostyrene 1a to Aldehydes 2[a,b]



entry	R^2	time (h)	**3**/yield[c] (%)	**4**/yield[c] (%)	dr (**3**)[d]	ee (%)[e]
1	Et	48	**3aa**/82	**4aa**/93	28:1	>99
2	Me	24	**3ab**/77	**4ab**/87	22:1	99
3	*n*-Pr	72	**3ac**/69	**4ac**/84	>30:1	99
4	*i*-Pr	72	**3ad**/62	**4ad**/97	>30:1	99
5	CH_2Ph	72	**3ae**/63	**4ae**/85	>30:1	>99
6	$(CH_2)_3CH{=}CH_2$	48	**3af**/81	**4af**/78	>30:1	>99
7	$(CH2)_6CH_3$	60	**3ag**/65	**4ag**/86	>30:1	99
8	$(CH_2)_3OCH_2Ph$	60	**3ah**/92	**4ah**/83	13:1	99
9	$(CH_2)_3OTBDPS$	96	**3ai**/60	**4ai**/65	18:1	98

[a]All of the reactions were carried out in DCE (0.2 M) with **1a** (0.25 mmol) and aldehydes **2a** (0.75 mmol) in the presence of catalyst **I** (20 mol %) at room temperature. [b]Reactions were carried out in $CHCl_3$ (0.1 M) with 1.0 equiv of tetrahydroquinolines **3** and 3.0 equiv of TFA at room temperature. [c]Isolated yield after chromatographic purification. [d]Diastereomeric ratio; major-(2*S*,3*R*,4*S*) vs minor-(2*R*,3*R*,4*S*) diastereomer determined by ^1H NMR analysis. [e]Determined by chiral-phase HPLC analysis.

RESULTS AND DISCUSSION

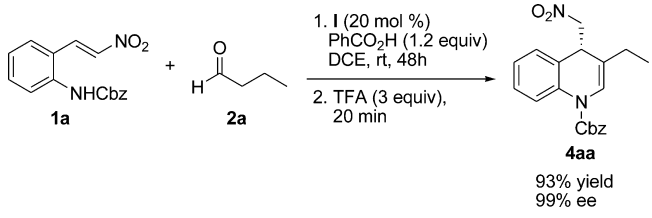
In our initial investigation, we began our studies on the domino reaction between *o*-*N*-Cbz-amino-*β*-nitrostyrene (**1a**) and butyraldehyde (**2a**) as the model substrates using diphenyl prolinol *O*-trimethylsilyl (*O*-TMS) ether **I** as the organocatalyst in CH_2Cl_2 at room temperature. Disappointingly, no reaction was observed in the absence of an acid or base additive (Table 1, entry 1). However, when 1.2 equiv of benzoic acid was used as additive, the reaction proceeded smoothly to afford the tetrahydroquinoline product **3aa** in good yield (77%) and with excellent enantioselectivity (99% ee, entry 2). Encouraged by these results, we screened a number of other additives. Benzoic acid emerged as the reagent of choice (entries 2−4), whereas bases were found to be unfavorable for the reaction (entry 5). Furthermore, the addition of a catalytic amount of acid additive and reducing the amount of organocatalyst to 10 mol % decreased the reaction activity (entries 6 and 7). Interchanging the *O*-TMS group in the organocatalyst to some bulkier ether group, for example, the *O*-triethylsilyl (*O*-TES) group, led to longer reaction times and similar enantioselectivity (entry 8). To further optimize the reaction efficiency, various solvents were then examined. The reaction medium was found to have a substantial impact on the conversion efficiency of the reaction. The best results (82% yield, >99% ee) were obtained with $ClCH_2CH_2Cl$ (entry15). In contrast, almost no reaction occurred in DMF or EtOAc (entries 12 and 13).

With optimized reaction conditions in hand (1 equiv of **1**, 3 equiv of **2**, 20 mol % catalyst **I**, and 1.2 equiv of $PhCO_2H$ in $ClCH_2CH_2Cl$), the substrate scope and generality of the reaction was investigated. First, we tested a variety of substrates **1** to examine the generality of the domino reaction to produce tetrahydroquinolines, which then undergo dehydration to yield dihydroquinoline derivatives (Table 2). It appeared that the carbamate protecting groups (such as Cbz, Boc, and CO_2Et groups) were tolerated, and the desired products were obtained in good yields (68−82%) with excellent diastereoselectivities (28:1 to >30:1 dr) and enantioselectivities (99 to >99% ee). Moreover, the electronic nature, bulkiness, and position of the substituent in the phenyl ring of the *N*-Cbz-2-amino-*β*-nitrostyrenes tested were found to have minimal impact on the reaction efficiency as well as diastereo- and enantioselectivity (entries 4−8).

Encouraged by the excellent results with various 2-amino-*β*-nitrostyrenes, we then investigated the domino reaction and the subsequent dehydration reaction with respect to aldehydes. As demonstrated in Table 3, the domino reaction products were obtained in good yields with excellent stereocontrol for a range of different aliphatic and functionalized aldehydes. Both linear and branched aliphatic aldehydes (entries 1−4) could be employed successfully as Michael donors to obtain the tetrahydroquinoline products **3aa**−**ad** in good yields (62−82%) with excellent diastereoselectivities (22:1 to >30:1 dr) and enantioselectivities (99 to >99% ee). The subsequent dehydration reaction generated the corresponding dihydroquinoline derivatives in high yields (84−97%). In addition, aldehydes bearing functional groups such as alkene, benzyloxy, and *t*-butyldiphenylsilyl were also tolerated as substrates (entries 6, 7, and 8).

Once the Michael addition/aza-cyclization cascade reaction to synthesize chiral tetrahydroquinolines and dihydroquinolines had been demonstrated, we then investigated a one-pot operation for the synthesis of dihydroquinolines from an aldehyde and 2-amino-*β*-nitrostyrene (Scheme 2). The cascade reaction between *o*-*N*-Cbz-amino-*β*-nitrostyrene (**1a**) and butyraldehyde (**2a**) was carried out in the presence of 20 mol

Scheme 2. One-Pot Asymmetric Synthesis of Dihydroquinoline



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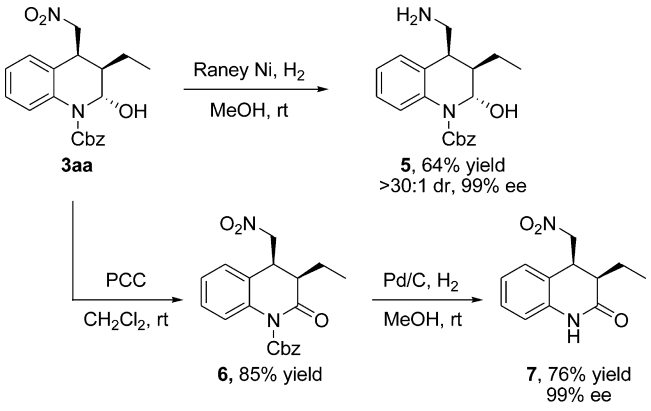
% of the catalyst for over 48 h under optimized reaction conditions. TFA (3 equiv) was then added in situ. The dihydroquinoline product **4aa** was obtained in high yield (93%) with excellent enantioselectivity (99% ee).

To further demonstrate the synthetic utility of this protocol, we have illustrated a representative procedure to convert the enantioenriched tetrahydroquinoline products into the corresponding amines **5** and 2-oxo-dihydroquinolines **6** and **7** (Scheme 3). Hydrogenation of **3aa** by Raney nickel catalyst

Scheme 3. Transformations of Tetrahydroquinoline 3aa



reduced the nitro group and produced compound **5** in high yield without affecting the diastereo- and enantioselectivity. In contrast, when **3aa** was treated with PCC, the 2-oxo compound **6** was obtained in good yield, which, after undergoing hydrogenation (H_2, Pd/C), produced Cbz-deprotected 2-oxo-dihydroquinoline **7** with complete retention of stereocontrol.

The relative stereochemistry of tetrahydroquinolines was established by NOESY. The absolute configurations of these tetrahydroquinoline and dihydroquinoline products were assigned based on previous studies. The reaction of aldehyde **2** with *β*-nitrostyrene or 2-hydroxynitrostyrene, catalyzed by the same organocatalyst **I**, has been reported to give Michael addition products of (2*R*,3*S*)-configuration.[12a,f,g,14] It is expected that the absolute configuration for the products of the present reaction can be assigned by analogy as being the same. On the basis of our experimental results, a plausible transition state for this asymmetric cascade reaction is shown in Figure 1. The *si*-face attack of *anti*-enamine to the *si*-face of

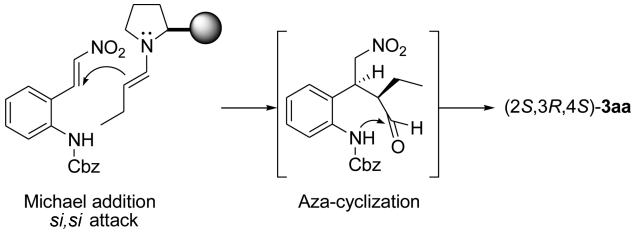


Figure 1. Plausible transition state.

nitroolefin led to the formation of the *R*,*S*-configurated intermediate, followed by aza-cyclization to give desired tetrahydroquinoline **3aa**.

CONCLUSION

In conclusion, we have developed an efficient organocatalytic Michael addition/aza-cyclization cascade reaction of an aldehyde with 2-amino-*β*-nitrostyrene to provide fully substituted chiral tetrahydroquinolines in good to high yields with excellent diastereo- and enantioselectivities. The method also provided access to an uncomplicated synthetic route to chiral 1,4-dihydroquinolines, which are difficult to synthesize by other methodologies.

EXPERIMENTAL SECTION

General Information. Organic solvents were distilled prior to use. Organic solutions were concentrated under reduced pressure using a rotary evaporator. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63. Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Developed chromatograms were visualized by fluorescence quenching and anisaldehyde stain. ^{1}H and ^{13}C NMR spectra were recorded on a 400 or 700 MHz instrument as noted and were internally referenced to residual protio solvent signals. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), and integration. Data for ^{13}C NMR are reported in terms of chemical shift. High-resolution mass data were measured on a Q-TOF-MS with ESI source. Enantiomeric excesses were determined on an HPLC instrument using Chiralpak columns as noted.

General Procedure for Preparation of 2-Amino-*β*-nitrostyrenes 1a−1h. To a solution of 2-*N*-protected benzaldehyde[15] (1.0 equiv) in $MeNO_2$ (1.0 M), water (1.0 M), and EtOH (1.0 M) was added NaOH in water (0.3 M solution, 1.0 equiv) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 24 h. Then, the reaction mixture was extracted with methylene chloride and washed successively with water and brine. The organic phase was separated and dried over $MgSO_4$. The solvent was evaporated under the reduced pressure, and the residue was purified using silica gel column chromatography using ethyl acetate and hexane as eluents to afford the corresponding nitroalcohol. To a solution of the obtained nitroalcohol (1.0 equiv) in Ac_2O (0.5 M) was added pyridine (2.5 equiv) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 12 h. Then, the reaction mixture was diluted with methylene chloride and washed successively with water and brine. The organic phase was separated and dried over $MgSO_4$. The solvent was evaporated under the reduced pressure, and the residue was purified using silica gel column chromatography using ethyl acetate and hexane as eluents to afford the corresponding 2-amino-*β*-nitrostyrenes **1a−1h**.

*Benzyl 2-((E)-2-Nitrovinyl)phenylcarbamate (**1a**).* White solid; 47% yield; mp 170−172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 13.6 Hz, 1H), 7.73 (d, J = 7.6 Hz, 1H), 7.48−7.57 (m, 3H), 7.36−7.47 (m, 5H), 7.26 (t, J = 8.0 Hz, 1H), 6.73 (brs, 1H), 5.25 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 138.8, 138.7, 136.9, 135.6, 133.0, 128.9, 128.62, 128.57, 128.54, 126.2, 125.9, 124.4, 66.7; IR (neat) 3270, 3107, 1700, 1525, 1509, 1339, 1256, 1238, 1054, 962, 753 cm^{-1}; HRMS (ESI): Calcd for $C_{16}H_{14}N_2O_4Na$ (M + Na)$^+$: 321.0851. Found: 321.0854.

*Ethyl 2-((E)-2-Nitrovinyl)phenylcarbamate (**1b**).* White solid; 43% yield; mp 166−168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 13.6 Hz, 1H), 7.73 (d, J = 7.6 Hz, 1H), 7.49−7.59 (m, 3H), 7.26 (t, J = 7.6 Hz, 1H), 6.63 (brs, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 138.3, 137.4, 134.3, 132.8, 127.9, 124.7, 124.6, 62.1, 14.5; IR (neat) 3291, 3106, 1694, 1524, 1503, 1334, 1237, 1060, 1012, 761 cm^{-1}; HRMS (ESI): Calcd for $C_{11}H_{12}N_2O_4Na$ (M + Na)$^+$: 259.0695. Found: 259.0693.

*tert-Butyl 2-((E)-2-Nitrovinyl)phenylcarbamate (**1c**).* White solid; 40% yield; mp 164−165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 13.6 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.47−7.55 (m, 3H), 7.23 (t, J = 7.6 Hz, 1H), 6.49 (brs, 1H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 138.0, 137.8, 134.6, 132.7, 127.8, 125.4, 124.5, 123.1, 81.7, 28.2; IR (neat) 3343, 3114, 1697, 1519, 1505, 1303, 1263, 1156, 964, 774 cm^{-1}; HRMS (ESI): Calcd for $C_{13}H_{16}N_2O_4Na$ (M + Na)$^+$: 287.1008. Found: 287.1011.

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*Benzyl 4-Methyl-2-((E)-2-nitrovinyl)phenylcarbamate (**1d**).* White solid; 56% yield; mp 151−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 13.6 Hz, 1H), 7.29−7.57 (m, 9H), 6.68 (brs, 1H), 5.23 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 138.0, 136.0, 135.6, 134.7, 134.3, 133.6, 128.7 (two peaks overlapping), 128.6, 128.5, 128.1, 125.3, 67.7, 20.9; IR (neat) 3268, 3112, 1697, 1520, 1508, 1257, 1117, 739 cm^{-1}; HRMS (ESI): Calcd for $C_{17}H_{16}N_2O_4Na$ (M + Na)$^+$: 335.1008. Found: 335.1008.

*Benzyl 2-Methyl-6-((E)-2-nitrovinyl)phenylcarbamate (**1e**).* White solid; 68% yield; mp 130−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 14.0 Hz, 1H), 7.27−7.58 (m, 9H), 6.33 (brs, 1H), 5.24 (s, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 138.1, 136.8, 135.8, 135.5, 135.3, 134.3, 128.7, 128.5, 128.3 (two peaks overlapping), 127.8, 125.6, 67.8, 18.2; IR (neat) 3282, 3104, 1694, 1518, 1507, 1345, 1235, 1112, 755 cm^{-1}; HRMS (ESI): Calcd for $C_{17}H_{16}N_2O_4Na$ (M + Na)$^+$: 335.1008. Found: 335.1004.

*Benzyl 4-Chloro-2-((E)-2-nitrovinyl)phenylcarbamate (**1f**).* White solid; 35% yield; mp 143−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 13.6 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.38−7.53 (m, 8H), 6.67 (s, 1H), 5.25 (s, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 153.8, 139.1, 135.7, 135.3, 132.8, 132.5, 128.8, 128.7, 128.6, 127.4, 68.0; IR (neat) 3278, 3110, 1688, 1524, 1506, 1246, 1107, 753 cm^{-1}; HRMS (ESI): Calcd for $C_{16}H_{13}ClN_2O_4Na$ (M + Na)$^+$: 355.0462. Found: 355.0465.

*Benzyl 5-Chloro-2-((E)-2-nitrovinyl)phenylcarbamate (**1g**).* White solid; 44% yield; mp 187−189 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 13.6 Hz, 1H), 7.38−7.56 (m, 6H), 7.09−7.25 (m, 3H), 6.68 (brs, 1H), 5.26 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d6) δ 154.6, 140.1, 139.1, 137.1, 136.7, 134.6, 130.2, 128.9, 128.7 (two peaks overlapping), 125.5, 125.0, 122.6, 66.9; IR (neat) 3264, 3110, 1694, 1508, 1328, 1245, 1234, 1060, 739 cm^{-1}; HRMS (ESI): Calcd for $C_{16}H_{13}ClN_2O_4Na$ (M + Na)$^+$: 355.0462. Found: 355.0463.

*Benzyl 4-Bromo-2-((E)-2-nitrovinyl)phenylcarbamate (**1h**).* White solid; 38% yield; mp 147−150 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.06 (d, J = 14.0 Hz, 1H), 7.61−7.68 (m, 2H), 7.59 (dd, J = 1.4, 8.4 Hz, 1H), 7.47 (d, J = 14.0 Hz, 1H), 7.37−7.44 (m, 5H), 6.88 (s, 1H), 5.23 (s, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 153.7, 139.1, 136.2, 135.4, 135.3, 132.7, 130.4, 128.8, 128.7, 128.6, 68.0; IR (neat) 3270, 3109, 1702, 1525, 1507, 1238, 1054, 748 cm^{-1}; HRMS (ESI): Calcd for $C_{16}H_{13}BrN_2O_4Na$ (M + Na)$^+$: 398.9956. Found: 398.9961.

General Procedure for Asymmetric Michael/Aza-cyclization Domino Reaction of 2-Amino-β-nitrostyrenes with Aldehydes. An amber 2-dram vial equipped with a magnetic stir bar, containing catalyst **I** (0.050 mmol, 20 mol %), 2-amino-β-nitrostyrene **1** (0.25 mmol, 1.0 equiv), and benzoic acid (0.30 mmol, 1.2 equiv), was charged with $ClCH_2CH_2Cl$ (1.2 mL) at room temperature. The solution was stirred for 5 min before the addition of aldehyde **2** (0.75 mmol, 3.0 equiv). The resulting mixture was stirred at constant temperature until complete consumption of 2-amino-β-nitrostyrene **1** was observed as determined by TLC. The resulting mixture was directly purified using silica gel column chromatography using ethyl acetate and hexane as eluents to afford the desired tetrahydroquinoline compound **3** as a colorless gum. Enantioselectivity was determined by HPLC analysis of the corresponding dihydroquinoline **4**.

*(2S,3R,4S)-Benzyl 3-Ethyl-3,4-dihydro-2-hydroxy-4-(nitromethyl)-quinoline-1(2H)-carboxylate (**3aa**).* Colorless gum; yield: 76 mg (82%); $[\alpha]_D^{26}$ = −33.2 (c = 1.2, $CHCl_3$); >99% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.4 Hz, 1H), 7.37−7.52 (m, 5H), 7.23 (dt, J = 1.6, 8.4 Hz, 1H), 6.99−7.09 (m, 2H), 5.73 (d, J = 3.2 Hz, 1H), 5.45 (d, J = 12.0 Hz, 1H), 5.30 (d, J = 12.0 Hz, 1H), 4.72−4.81 (m, 2H), 4.27 (brs, 1H), 3.66−3.72 (m, 1H), 1.91−1.99 (m, 1H), 1.62−1.89 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 135.4, 134.8, 129.0, 128.8, 128.7, 128.6, 128.3, 128.1, 123.7, 122.2, 79.3, 77.2, 68.4, 42.5, 38.8, 21.0, 11.7; IR (neat) 3503, 2964, 1679, 1546, 1492, 1284, 1257, 1080, 753 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{22}N_2O_5Na$ (M + Na)$^+$: 393.1426. Found: 393.1418.

*(2S,3R,4S)-Ethyl 3-Ethyl-3,4-dihydro-2-hydroxy-4-(nitromethyl)-quinoline-1(2H)-carboxylate (**3ba**).* Colorless gum; yield: 60 mg (78%); $[\alpha]_D^{25}$ = −58.1 (c = 1.1, $CHCl_3$); 99% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 1H), 7.23−7.29 (m, 1H), 6.98−7.08 (m, 2H), 5.70 (d, J = 2.8 Hz, 1H), 4.78 (d, J = 6.8 Hz, 2H), 4.31−4.46 (m, 3H), 3.68 (dd, J = 6.8, 10.8 Hz, 1H), 1.91−1.98 (m, 1H), 1.76−1.88 (m, 1H), 1.64−1.75 (m, 1H), 1.43 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 134.9, 129.0, 128.6, 128.1, 123.5, 122.2, 79.2, 77.2, 62.8, 42.6, 38.9, 21.0, 14.5, 11.8; IR (neat) 3495, 2966, 1673, 1549, 1406, 1316, 1240, 1047, 758 cm^{-1}; HRMS (ESI): Calcd for $C_{15}H_{20}N_2O_5Na$ (M + Na)$^+$: 331.1270. Found: 331.1274.

*(2S,3R,4S)-tert-Butyl 3-Ethyl-3,4-dihydro-2-hydroxy-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3ca**).* Colorless gum; yield: 57 mg (68%); $[\alpha]_D^{23}$ = −46.7 (c = 1.1, $CHCl_3$); 99% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.4 Hz, 1H), 7.23 (dt, J = 1.6, 8.4 Hz, 1H), 7.05 (dd, J = 1.2, 7.2 Hz, 1H), 6.98 (t, J = 7.2 Hz, 1H), 5.66 (t, J = 3.2 Hz, 1H), 4.78 (d, J = 7.2 Hz, 2H), 4.38 (s, 1H), 366 (dd, J = 6.4, 10.4 Hz, 1H), 1.29−1.44 (m, 2H), 1.60−1.71 (m, 1H), 1.62 (s, 9H), 1.10 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 135.3, 128.9, 128.5, 127.9, 123.2, 122.2, 83.2, 79.1, 77.2, 42.6, 39.0, 28.4, 21.0, 11.8; IR (neat) 3498, 2969, 1719, 1673, 1548, 1423, 1368, 1254, 1154, 1136, 753 cm^{-1}; HRMS (ESI): Calcd for $C_{17}H_{24}N_2O_5Na$ (M + Na)$^+$: 359.1583. Found: 359.1586.

*(2S,3R,4S)-Benzyl 3-Ethyl-3,4-dihydro-2-hydroxy-6-methyl-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3da**).* Colorless gum; yield: 69 mg (72%); $[\alpha]_D^{27}$ = −27.8 (c = 1.2, $CHCl_3$); 99% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 1H), 7.37−7.46 (m, 5H), 7.03 (dd, J = 1.6, 8.4 Hz, 1H), 6.86 (d, J = 1.6 Hz, 1H), 5.70 (ddd, J = 0.8, 3.6, 4.4 Hz, 1H), 5.43 (d, J = 12.4 Hz, 1H), 5.28 (d, J = 12.4 Hz, 1H), 4.70−4.80 (m, 2H), 4.30 (brs, 1H), 3.61−3.67 (m, 1H), 2.27 (s, 3H), 1.88−1.97 (m, 1H), 1.62−1.87 (m, 2H), 1.09 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 135.4, 133.3, 132.2, 129.0, 129.9, 129.8, 129.7, 129.6, 128.3, 122.1, 79.3, 77.2, 68.3, 42.7, 38.8, 21.1, 20.5, 11.8; IR (neat) 3492, 2964, 1676, 1547, 1500, 1380, 1284, 1260, 1145, 1013, 752 cm^{-1}; HRMS (ESI): Calcd for $C_{21}H_{24}N_2O_5Na$ (M + Na)$^+$: 407.1583. Found: 407.1577.

*(2S,3R,4S)-Benzyl 3-Ethyl-3,4-dihydro-2-hydroxy-8-methyl-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3ea**).* Colorless gum; yield: 91 mg (95%); $[\alpha]_D^{26}$ = −45.7 (c = 1.6, $CHCl_3$); 99% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13−7.48 (m, 6H), 7.10 (t, J = 7.6 Hz, 1H), 7.03 (d, J = 7.2 Hz, 1H), 5.53 (d, J = 7.2 Hz, 1H), 5.20−5.40 (m, 2H), 4.55 (d, J = 11.2 Hz, 1H), 4.41 (brs, 1H), 4.21 (t, J = 11.2 Hz, 1H), 3.56−3.63 (m, 1H), 2.07 (s, 3H), 1.80−1.93 (m, 2H), 1.42−1.51 (m, 1H), 1.02 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 135.6, 134.7, 133.6, 130.9, 128.6, 128.5, 128.4, 128.0, 126.4, 125.5, 83.0, 74.1, 68.2, 48.8, 39.1, 23.7, 17.9, 11.8; IR (neat) 3434, 2963, 1678, 1552, 1378, 1314, 1243, 1017, 750 cm^{-1}; HRMS (ESI): Calcd for $C_{21}H_{24}N_2O_5Na$ (M + Na)$^+$: 407.1583. Found: 407.1580.

*(2S,3R,4S)-Benzyl 6-Chloro-3-ethyl-3,4-dihydro-2-hydroxy-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3fa**).* Colorless gum; yield: 74 mg (73%); $[\alpha]_D^{25}$ = −14.9 (c = 1.1, $CHCl_3$); 99% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.8 Hz, 1H), 7.39−7.48 (m, 5H), 7.19 (dd, J = 2.4, 9.2 Hz, 1H), 7.08 (d, J = 2.8 Hz, 1H), 5.70 (t, J = 3.6 Hz, 1H), 5.44 (d, J = 12.4 Hz, 1H), 5.28 (d, J = 12.0 Hz, 1H), 4.71−4.79 (m, 2H), 4.21 (brs, 1H), 3.63−3.68 (m, 1H), 1.52−1.92 (m, 3H), 1.09 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 135.1, 133.5, 130.7, 128.9, 128.8, 128.7, 128.4, 128.3, 128.2, 123.5, 79.2, 76.7, 42.4, 38.5, 20.9, 11.7; IR (neat) 3495, 2968, 1672, 1550, 1504, 1380, 1284, 1248, 1145, 1052, 733 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{21}N_2O_5ClNa$ (M + Na)$^+$: 427.1037. Found: 427.1033.

*(2S,3R,4S)-Benzyl 7-Chloro-3-ethyl-3,4-dihydro-2-hydroxy-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3ga**).* Colorless gum; yield: 69 mg (66%); $[\alpha]_D^{23}$ = −56.7 (c = 1.4, $CHCl_3$); 99% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.39−7.49 (m, 5H), 6.99 (s, 2H), 5.71 (brs, 1H), 5.46 (d, J = 12.4 Hz, 1H), 5.30 (d, J = 12.4 Hz, 1H), 4.69−4.77 (m, 2H), 4.16 (brs, 1H), 3.63−3.71 (m, 1H), 1.89−1.97 (m, 1H), 1.62−1.87 (m, 2H), 1.09 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 135.8, 135.0, 133.8, 129.6, 128.9, 128.8, 128.4, 127.1, 123.6, 122.2, 79.1, 77.3, 68.7, 42.2, 38.2, 21.0, 11.7; IR (neat) 3516, 2968, 1722, 1548, 1381, 1254, 1215, 1081, 786 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{21}N_2O_5ClNa$ (M + Na)$^+$: 427.1037. Found: 427.1035.

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*(2S,3R,4S)-Benzyl 6-Bromo-3-ethyl-3,4-dihydro-2-hydroxy-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3ha**).* Colorless gum; yield: 73 mg (65%); $[\alpha]_D^{27}$ = −27.5 (*c* = 0.8, $CHCl_3$); 98% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.37−7.44 (m, 5H), 7.29 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.20 (d, *J* = 2.4 Hz, 1H), 5.67 (brs, 1H), 5.41 (d, *J* = 12.4 Hz, 1H), 5.26 (d, *J* = 12.4 Hz, 1H), 4.68−4.74 (m, 2H), 4.17 (brs, 1H), 3.61−3.67 (m, 1H), 1.58−1.90 (m, 3H), 1.06 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 135.2, 134.2, 131.4, 131.3, 129.0, 128.9, 128.6, 128.5, 124.0, 116.6, 76.4, 77.4, 68.8, 42.6, 38.6, 21.0, 11.8; IR (neat) 3504, 2960, 1698, 1558, 1384, 1254, 1213, 1078, 774 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{21}N_2O_5BrNa$ $(M + Na)^+$: 471.0532. Found: 471.0527.

*(2S,3R,4S)-Benzyl 3,4-Dihydro-2-hydroxy-3-methyl-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3ab**).* Colorless gum; yield: 73 mg (77%); $[\alpha]_D^{19}$ = −52.3 (*c* = 0.8, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.36−7.47 (m, 5H), 7.21−7.38 (m, 1H), 7.00−7.07 (m, 2H), 5.68 (d, *J* = 3.2 Hz, 1H), 5.41 (d, *J* = 12.0 Hz, 1H), 5.30 (d, *J* = 12.0 Hz, 1H), 4.75−4.87 (m, 2H), 4.14 (brs, 1H), 3.61 (dt, *J* = 4.0, 8.8 Hz, 1H), 2.27−2.35 (m, 1H), 1.23 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 154.8, 135.3, 134.8, 128.8, 128.7, 128.6, 128.4, 128.1, 127.5, 123.8, 122.6, 80.5, 76.9, 68.3, 40.1, 35.5, 12.6; IR (neat) 3487, 2967, 1683, 1547, 1380, 1277, 1217, 1011, 759 cm^{-1}; HRMS (ESI): Calcd for $C_{19}H_{20}N_2O_5Na$ $(M + Na)^+$: 379.1270. Found: 379.1268.

*(2S,3R,4S)-Benzyl 3,4-Dihydro-2-hydroxy-4-(nitromethyl)-3-propylquinoline-1(2H)-carboxylate (**3ac**).* Colorless gum; yield: 74 mg (77%); $[\alpha]_D^{23}$ = −26.8 (*c* = 1.1, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 1H), 7.38−7.49 (m, 5H), 7.23 (dt, *J* = 2.0, 8.8 Hz, 1H), 6.99−7.08 (m, 2H), 5.69 (brs, 1H), 5.45 (d, *J* = 12.0 Hz, 1H), 5.29 (d, *J* = 12.0 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 2H), 4.24 (brs, 1H), 3.65 (dd, *J* = 6.8, 10.8 Hz, 1H), 2.01−2.08 (m, 1H), 1.45−1.81 (m, 4H), 1.00 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 135.4, 134.8, 129.0, 128.8, 128.7, 128.6, 128.3, 128.1, 123.6, 122.2, 79.5, 77.3, 68.4, 40.5, 39.1, 30.0, 20.3, 14.1; IR (neat) 3502, 2958, 1678, 1547, 1492, 1285, 1238, 1020, 752 cm^{-1}; HRMS (ESI): Calcd for $C_{21}H_{24}N_2O_5Na$ $(M + Na)^+$: 407.1583. Found: 407.1577.

*(2S,3R,4S)-Benzyl 3,4-Dihydro-2-hydroxy-3-isopropyl-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3ad**).* Colorless gum; yield: 66 mg (69%); $[\alpha]_D^{20}$ = −26.7 (*c* = 1.0, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.6 Hz, 1H), 7.32−7.49 (m, 5H), 7.23 (dt, *J* = 1.6, 7.2 Hz, 1H), 7.06 (dd, *J* = 1.6, 7.2 Hz, 1H), 7.08 (dt, *J* = 0.8, 7.2 Hz, 1H), 5.84 (d, *J* = 2.8 Hz, 1H), 5.46 (d, *J* = 12.0 Hz, 1H), 5.29 (d, *J* = 12.0 Hz, 1H), 4.69−4.74 (m, 2H), 4.40 (brs, 1H), 3.85 (dd, *J* = 3.2, 7.6 Hz, 1H), 2.07−2.20 (m, 1H), 1.55−1.61 (m, 1H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 135.4, 134.7, 129.2, 128.8, 128.7, 128.6, 128.3, 128.2, 123.6, 122.1, 78.6, 68.4, 47.9, 37.4, 25.3, 22.4, 21.0, 20.6; IR (neat) 3449, 2960, 1673, 1550, 1494, 1400, 1282, 1240, 1008, 766 cm^{-1}; HRMS (ESI): Calcd for $C_{21}H_{24}N_2O_5Na$ $(M + Na)^+$: 407.1583. Found: 407.1581.

*(2S,3R,4S)-Benzyl 3-Benzyl-3,4-dihydro-2-hydroxy-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3ae**).* Colorless gum; yield: 68 mg (63%); $[\alpha]_D^{27}$ = −23.8 (*c* = 1.1, $CHCl_3$); >99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.4 Hz, 1H), 7.36−7.44 (m, 4H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.20−7.30 (m, 5H), 6.97−7.05 (m, 2H), 5.52−5.58 (m, 1H), 5.40 (d, *J* = 12.4 Hz, 1H), 5.25 (d, *J* = 12.4 Hz, 1H), 4.93 (dd, *J* = 3.2, 12.8 Hz, 1H), 4.84 (dd, *J* = 10.4, 13.2 Hz, 1H), 4.32 (brs, 1H), 3.62−3.69 (m, 1H), 3.10 (dd, *J* = 8.8, 13.6 Hz, 1H), 2.92 (dd, *J* = 6.8, 13.6 Hz, 1H), 2.29−2.37 (m, 1H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 154.7, 138.4, 135.3, 134.8, 129.0, 128.8, 128.7 (two peaks overlapping), 128.6, 128.3, 128.2 (two peaks overlapping), 126.8, 123.7, 122.2, 78.9, 77.2, 68.4, 43.1, 39.2, 34.3; IR (neat) 3490, 3029, 1680, 1547, 1492, 1259, 1216, 1053, 1016, 737 cm^{-1}; HRMS (ESI): Calcd for $C_{25}H_{24}N_2O_5Na$ $(M + Na)^+$: 455.1583. Found: 455.1582.

*(2S,3R,4S)-Benzyl 3,4-Dihydro-2-hydroxy-4-(nitromethyl)-3-(pent-4-enyl)quinoline-1(2H)-carboxylate (**3af**).* Colorless gum; yield: 83 mg (81%); $[\alpha]_D^{23}$ = −32.1 (*c* = 1.1, $CHCl_3$); >99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 1H), 7.36−7.47 (m, 5H), 7.24 (dt, *J* = 2.0, 8.8 Hz, 1H), 6.80−7.08 (m, 2H), 5.78−5.89 (m, 1H), 5.70 (t, *J* = 3.6 Hz, 1H), 5.45 (d, *J* = 12.4 Hz, 1H), 5.29 (d, *J* = 12.0 Hz, 1H), 4.88−5.10 (m, 2H), 4.76 (d, *J* = 6.8 Hz, 2H), 4.25 (brs, 1H), 3.65 (dd, *J* = 6.4, 10.4 Hz, 1H), 2.08−2.19 (m, 2H), 1.92−2.03 (m, 1H), 1.51−1.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 138.0, 135.4, 134.8, 128.9, 128.8, 128.7, 128.6, 128.3, 128.2, 123.7, 122.2, 115.2, 79.5, 77.2, 68.4, 40.8, 39.1, 33.6, 27.3, 26.4; IR (neat) 3491, 2928, 1678, 1547, 1492, 1381, 1262, 1216, 1012, 910, 754 cm^{-1}; HRMS (ESI): Calcd for $C_{23}H_{26}N_2O_5Na$ $(M + Na)^+$: 433.1739. Found: 433.1736.

*(2S,3R,4S)-Benzyl 3-Heptyl-3,4-dihydro-2-hydroxy-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3ag**).* Colorless gum; yield: 72 mg (65%); $[\alpha]_D^{19}$ = −28.1 (*c* = 1.1, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 1H), 7.39−7.49 (m, 5H), 7.24 (dd, *J* = 7.2, 8.4 Hz, 1H), 6.98−7.08 (m, 2H), 5.71 (s, 1H), 5.45 (d, *J* = 12.0 Hz, 1H), 5.29 (d, *J* = 12.0 Hz, 1H), 4.72−4.80 (m, 2H), 4.24 (brs, 1H), 3.62−3.69 (m, 1H), 1.99−2.08 (m, 1H), 1.58−1.81 (m, 2H), 1.26−1.51 (m, 10H), 0.92 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 135.4, 134.8, 129.0, 128.8, 128.7, 128.6, 128.3, 128.1, 123.6, 122.2, 79.6, 77.3, 68.4, 40.8, 39.1, 31.8, 29.6, 29.1, 27.9, 27.1, 22.6, 14.1; IR (neat) 3498, 2925, 1679, 1548, 1498, 1260, 1216, 1014, 754 cm^{-1}; HRMS (ESI): Calcd for $C_{25}H_{32}N_2O_5Na$ $(M + Na)^+$: 463.2209. Found: 463.2204.

*(2S,3R,4S)-Benzyl 3-(3-(Benzyloxy)propyl)-3,4-dihydro-2-hydroxy-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3ah**).* Colorless gum; yield: 113 mg (92%); $[\alpha]_D^{20}$ = −18.2 (*c* = 1.2, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.21−7.47 (m, 9H), 6.98−7.07 (m, 2H), 5.71 (d, *J* = 3.2 Hz, 1H), 5.45 (d, *J* = 12.0 Hz, 1H), 5.28 (d, *J* = 12.0 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 2H), 4.52 (s, 2H), 4.28 (brs, 1H), 3.66 (dd, *J* = 6.8, 10.8 Hz, 1H), 3.55 (t, *J* = 6.0 Hz, 1H), 2.01−2.09 (m, 1H), 1.63−1.92 (m, 4H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 154.8, 138.3, 135.5, 134.7, 133.7, 130.2, 128.9, 128.8, 128.7, 128.5, 128.4, 127.7, 127.6, 123.7, 122.2, 79.4, 77.2, 73.1, 69.8, 68.4, 40.6, 39.1, 27.3, 24.8; IR (neat) 3455, 2940, 1690, 1548, 1493, 1380, 1313, 1216, 1097, 1022, 737 cm^{-1}; HRMS (ESI): Calcd for $C_{28}H_{30}N_2O_6Na$ $(M + Na)^+$: 513.2002. Found: 513.1997.

*(2S,3R,4S)-Benzyl 3-(3-(tert-Butyldiphenylsilyloxy)propyl)-3,4-dihydro-2-hydroxy-4-(nitromethyl)quinoline-1(2H)-carboxylate (**3ai**).* Colorless gum; yield: 96 mg (60%); $[\alpha]_D^{20}$ = −4.0 (*c* = 1.1, $CHCl_3$); 98% ee; ^1H NMR (700 MHz, $CDCl_3$) δ 7.86 (d, *J* = 4.9 Hz, 1H), 7.63 (d, *J* = 7.0 Hz, 4H), 7.33−7.44 (m, 11H), 7.21 (t, *J* = 7.0 Hz, 1H), 6.96−7.03 (m, 2H), 5.62 (s, 1H), 5.45 (d, *J* = 11.9 Hz, 1H), 5.26 (d, *J* = 12.6 Hz, 1H), 4.67−4.76 (m, 2H), 4.17 (brs, 1H), 3.67−3.74 (m, 2H), 3.58 (d, *J* = 10.5 Hz, 1H), 1.98 (brs, 1H), 1.76−1.81 (m, 1H), 1.63−1.71 (m, 3H), 1.02 (s, 9H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 154.9, 135.6, 135.4, 134.8,134.7, 133.7, 129.7, 128.9, 128.7, 128.6, 128.4, 128.2, 127.7, 123.7, 122.2, 79.5, 77.1, 68.4, 63.5, 40.3, 39.1, 29.8, 26.9, 24.4, 19.2; IR (neat) 3349, 2929, 2856, 1676, 1551, 1470, 1427, 1109, 998, 818 cm^{-1}; HRMS (ESI): Calcd for $C_{37}H_{42}N_2O_6SiNa$ $(M + Na)^+$: 661.2710. Found: 661.2710.

General Procedure for Synthesis of Dihydroquinoline 4 from Tetrahydroquinoline 3. To a solution of tetrahydroquinoline compound **3** (0.15 mmol, 1.0 equiv) in chloroform (1.5 mL) was added trifluoroacetic acid (0.45 mmol, 3.0 equiv) at room temperature. After stirring for 20 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$, and the mixture was extracted with EtOAc. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude product was purified using silica gel column chromatography using ethyl acetate and hexane as eluents to afford the desired dihydroquinoline compound **4** as a colorless gum.

*(S)-Benzyl 3-Ethyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4aa**).* Colorless gum; yield: 49 mg (93%); $[\alpha]_D^{22}$ = −138.7 (*c* = 1.0, $CHCl_3$); >99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.30−7.51 (m, 6H), 7.12−7.20 (m, 2H), 6.97 (s, 1H), 5.34 (s, 2H), 4.39 (dd, *J* = 5.6, 12.0 Hz, 1H), 4.27 (dd, *J* = 8.8, 11.6 Hz, 1H), 4.12 (d, *J* = 5.6, 8.8 Hz, 1H), 2.14−2.34 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 136.4, 135.6, 128.7, 128.5, 128.2, 128.0, 127.8, 126.8, 125.4, 123.6, 123.0, 121.7, 78.3, 53.5, 41.4, 25.5, 12.3; IR (neat) 2959, 1715, 1549, 1489, 1377, 1317, 1234,

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1024, 756 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{20}N_2O_4Na$ $(M + Na)^+$: 375.1321. Found: 375.1320; Chiralpak AD-H column and AD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 220 nm); *major*-isomer t_r = 10.1 min and *minor*-isomer t_r = 11.8 min.

(S)-Ethyl 3-Ethyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ba**). Colorless gum; yield: 39 mg (90%); $[\alpha]_D^{24}$ = −154.9 (*c* = 1.0, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.27−7.35 (m, 1H), 7.12−7.18 (m, 2H), 6.95 (s, 1H), 4.36−4.42 (m, 3H), 4.27 (dd, *J* = 8.8, 11.6 Hz, 1H), 4.11 (d, *J* = 5.6, 8.8 Hz, 1H), 2.14−2.36 (m, 2H), 1.43 (t, *J* = 7.2 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 136.5, 128.0, 127.7, 126.7, 125.2, 123.7, 122.5, 121.6, 78.3, 62.8, 41.5, 25.5, 14.5, 12.3; IR (neat) 2970, 1714, 1548, 1489, 1372, 1316, 1233, 1039, 761 cm^{-1}; HRMS (ESI): Calcd for $C_{15}H_{18}N_2O_4Na$ $(M + Na)^+$: 313.1164. Found: 313.1161; Chiralpak AD-H column and AD-H guard column (1% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 19.4 min and *minor*-isomer t_r = 23.7 min.

(S)-tert-Butyl 3-Ethyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ca**). Colorless gum; yield: 39 mg (81%); $[\alpha]_D^{23}$ = −161.8 (*c* = 1.0, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 1H), 7.26−7.33 (m, 1H), 7.13 (dd, *J* = 1.2, 5.2 Hz, 2H), 6.91 (d, *J* = 0.8 Hz, 1H), 4.39 (dd, *J* = 5.2, 11.6 Hz, 1H), 4.27 (dd, *J* = 9.2, 12.0 Hz, 1H), 4.10 (d, *J* = 5.6, 8.8 Hz, 1H), 2.14−2.33 (m, 2H), 1.69 (s, 9H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 136.8, 128.0, 127.5, 126.7, 124.9, 124.0, 121.8, 121.6, 82.8, 78.3, 41.5, 28.3, 25.5, 12.3; IR (neat) 2971, 1711, 1549, 1488, 1349, 1305, 1238, 1144, 1020, 753 cm^{-1}; HRMS (ESI): Calcd for $C_{17}H_{22}N_2O_4Na$ $(M + Na)^+$: 341.1477. Found: 341.1476; Chiralpak OD-H column and OD-H guard column (1% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 11.0 min and *minor*-isomer t_r = 15.4 min.

(S)-Benzyl 3-Ethyl-6-methyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4da**). Colorless gum; yield: 51 mg (93%); $[\alpha]_D^{19}$ = −151.4 (*c* = 1.2, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 1H), 7.36−7.48 (m, 5H), 7.10 (dd, *J* = 1.2, 8.4 Hz, 1H), 6.95 (d, *J* = 4.0 Hz, 2H), 5.35 (s, 2H), 4.37 (dd, *J* = 5.6, 11.6 Hz, 1H), 4.26 (dd, *J* = 8.8, 11.6 Hz, 1H), 4.06 (dd, *J* = 5.6, 8.8 Hz, 1H), 2.32 (s, 3H), 2.12−2.31 (m, 2H), 1.14 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 135.7, 135.1, 133.9, 128.7, 128.5, 128.4, 128.3, 128.2, 126.7, 123.7, 123.0, 121.5, 78.4, 68.3, 41.4, 25.6, 20.7, 12.4; IR (neat) 2967, 1713, 1548, 1499, 1376, 1347, 1316, 1225, 1026, 753 cm^{-1}; HRMS (ESI): Calcd for $C_{21}H_{22}N_2O_4Na$ $(M + Na)^+$: 389.1477. Found: 389.1475; Chiralpak AD-H column and AD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 12.1 min and *minor*-isomer t_r = 27.9 min.

(S)-Benzyl 3-Ethyl-8-methyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ea**). Colorless gum; yield: 40 mg (73%); $[\alpha]_D^{19}$ = −231.2 (*c* = 1.0, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33−7.44 (m, 5H), 7.12−7.21 (m, 2H), 7.02 (d, *J* = 6.8 Hz, 1H), 6.85 (s, 1H), 5.35 (d, *J* = 12.4 Hz, 1H), 5.29 (d, *J* = 12.4 Hz, 1H), 4.32 (dd, *J* = 6.0, 12.0 Hz, 1H), 4.20 (dd, *J* = 8.8, 12.0 Hz, 1H), 4.03 (dd, *J* = 6.0, 8.8 Hz, 1H), 2.23 (s, 3H), 2.11−2.32 (m, 2H), 1.13 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 136.2, 135.9, 132.8, 131.2, 130.6, 129.3, 128.7, 128.4, 128.0, 126.3, 125.8, 125.4, 78.0, 68.0, 42.4, 25.4, 19.3, 12.1; IR (neat) 2966, 1713, 1540, 1467, 1375, 1339, 1309, 1271, 1219, 1171, 1047, 1023, 782 cm^{-1}; HRMS (ESI): Calcd for $C_{21}H_{22}N_2O_4Na$ $(M + Na)^+$: 389.1477. Found: 389.1471; Chiralpak AD-H column and AD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 8.8 min and *minor*-isomer t_r = 15.8 min.

(S)-Benzyl 7-Chloro-3-ethyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4fa**). Colorless gum; yield: 51 mg (88%); $[\alpha]_D^{20}$ = −112.2 (*c* = 1.3, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.38−7.49 (m, 5H), 7.14 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.94 (s, 1H), 5.37 (s, 2H), 4.37 (dd, *J* = 5.2, 12.0 Hz, 1H), 4.30 (dd, *J* = 9.2, 11.6 Hz, 1H), 4.08 (dd, *J* = 5.6, 9.2 Hz, 1H), 2.14−2.35 (m, 2H), 1.15 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 137.2, 135.3, 133.7, 129.0, 128.8, 128.7, 128.3, 125.5, 125.0, 123.4, 122.8, 121.9, 78.0, 68.6, 40.8, 25.4, 12.3; IR (neat) 2968, 1716, 1548, 1485, 1375, 1347, 1282, 1229, 1169, 1025, 749 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{19}N_2O_4ClNa$ $(M + Na)^+$: 409.0931. Found: 409.0927; Chiralpak AD-H column and AD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 15.7 min and *minor*-isomer t_r = 39.4 min.

(S)-Benzyl 6-Chloro-3-ethyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ga**). Colorless gum; yield: 57 mg (98%); $[\alpha]_D^{20}$ = −166.8 (*c* = 1.2, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 9.2 Hz, 1H), 7.38−7.48 (m, 5H), 7.27 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.14 (d, *J* = 2.0 Hz, 1H), 6.94 (s, 1H), 5.31−5.39 (m, 2H), 4.38 (dd, *J* = 5.2, 12.0 Hz, 1H), 4.27 (dd, *J* = 8.8, 12.0 Hz, 1H), 4.07 (dd, *J* = 5.6, 8.8 Hz, 1H), 2.12−2.33 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 135.4, 135.1, 130.5, 128.8, 128.6, 128.4, 128.3, 127.9, 127.7, 123.6, 122.9, 122.7, 77.9, 68.5, 40.9, 25.4, 12.3; IR (neat) 2968, 1718, 1548, 1485, 1376, 1300, 1229, 1170, 1039, 753 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{19}N_2O_4ClNa$ $(M + Na)^+$: 409.0931. Found: 409.0930; Chiralpak OD-H column and OD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 20.1 min and *minor*-isomer t_r = 24.8 min.

(S)-Benzyl 6-Bromo-3-ethyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ha**). Colorless gum; yield: 44 mg (68%); $[\alpha]_D^{19}$ = −126.2 (*c* = 1.0, $CHCl_3$); 98% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.8 Hz, 1H), 7.38−7.49 (m, 6H), 7.30 (d, *J* = 2.0 Hz, 1H), 6.94 (s, 1H), 5.31−5.39 (m, 2H), 4.37 (dd, *J* = 5.6, 12.0 Hz, 1H), 4.27 (dd, *J* = 8.8, 12.4 Hz, 1H), 4.07 (dd, *J* = 5.2, 8.8 Hz, 1H), 2.11−2.32 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 135.6, 135.4, 130.8, 130.7, 128.8 (two peaks overlapping), 128.6, 128.3, 123.5, 123.3, 122.8, 118.2, 77.9, 68.6, 40.9, 25.4, 12.3; IR (neat) 2967, 1716, 1547, 1455, 1375, 1347, 1295, 1229, 1025, 748 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{19}N_2O_4BrNa$ $(M + Na)^+$: 453.0426. Found: 453.0425; Chiralpak AD-H column and AD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 14.9 min and *minor*-isomer t_r = 41.4 min.

(S)-Benzyl 3-Methyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ab**). Colorless gum; yield: 44 mg (87%); $[\alpha]_D^{21}$ = −177.0 (*c* = 1.1, $CHCl_3$); 99% ee; ^1H NMR (700 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.23−7.50 (m, 6H), 7.10−7.20 (m, 2H), 6.95 (s, 1H), 5.28−5.39 (m, 2H), 4.39 (dd, *J* = 4.9, 11.2 Hz, 1H), 4.27 (d, *J* = 9.1 Hz, 1H), 4.04 (d, *J* = 4.9 Hz, 1H), 1.91 (s, 3H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 152.1, 136.1, 135.5, 128.7, 128.6, 128.5, 128.4, 128.3, 128.0, 127.8, 126.3, 125.4, 124.4, 121.6, 117.0, 78.1, 68.4, 42.7, 18.5; IR (neat) 2917, 1714, 1548, 1489, 1376, 1316, 1231, 1169, 1023, 750 cm^{-1}; HRMS (ESI): Calcd for $C_{19}H_{18}N_2O_4Na$ $(M + Na)^+$: 361.1164. Found: 361.1163; Chiralpak AD-H column and AD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 220 nm); *major*-isomer t_r = 17.3 min and *minor*-isomer t_r = 22.0 min.

(S)-Benzyl 4-(Nitromethyl)-3-propylquinoline-1(4H)-carboxylate (**4ac**). Colorless gum; yield: 46 mg (84%); $[\alpha]_D^{22}$ = −168.6 (*c* = 1.1, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.37−7.49 (m, 5H), 7.28−7.34 (m, 1H), 7.11−7.19 (m, 2H), 6.97 (s, 1H), 5.26 (s, 2H), 4.39 (dd, *J* = 5.6, 12.0 Hz, 1H), 4.26 (dd, *J* = 8.8, 12.0 Hz, 1H), 4.10 (dd, *J* = 5.6, 8.8 Hz, 1H), 2.19 (t, *J* = 7.6 Hz, 2H), 1.48−1.67 (m, 2H), 0.94 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 136.4, 135.6, 128.7, 128.5, 128.3, 128.0, 127.8, 126.8, 125.4, 124.3, 121.6, 121.4, 78.3, 68.3, 41.2, 34.3, 21.0, 13.7; IR (neat) 2965, 1713, 1547, 1488, 1376, 1348, 1315, 1230, 1168, 1025, 758 cm^{-1}; HRMS (ESI): Calcd for $C_{21}H_{22}N_2O_4Na$ $(M + Na)^+$: 389.1477. Found: 389.1477; Chiralpak AD-H column and AD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 220 nm); *major*-isomer t_r = 15.5 min and *minor*-isomer t_r = 19.2 min.

(S)-Benzyl 3-Isopropyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ad**). Colorless gum; yield: 53 mg (97%); $[\alpha]_D^{21}$ = −224.9 (*c* = 1.1, $CHCl_3$); 99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.4 Hz, 1H), 7.37−7.50 (m, 5H), 7.32 (dd, *J* = 4.0, 8.0 Hz, 1H), 7.16 (d, *J* = 4.0 Hz, 1H), 6.99 (s, 1H), 5.38 (s, 2H), 4.36 (dd, *J* = 4.4, 11.6 Hz, 1H), 4.24 (dd, *J* = 9.6, 11.2 Hz, 1H), 4.17 (dd, *J* = 4.4, 9.6 Hz, 1H), 2.50 (septet, *J* = 6.8 Hz, 1H), 1.19 (d, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 136.6, 135.7, 128.7, 128.5, 128.2, 127.8, 127.7, 127.5, 125.4, 123.2, 121.6 (two peaks overlapping), 78.4, 68.3, 40.2, 31.1, 22.1, 21.0; IR (neat) 2961, 1714, 1547, 1488, 1376, 1346, 1322, 1207, 1021, 758 cm^{-1}; HRMS (ESI): Calcd for $C_{21}H_{22}N_2O_4Na$ $(M + Na)^+$: 389.1477. Found: 389.1476;

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Chiralpak AD-H column and AD-H guard column (1% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 33.6 min and *minor*-isomer t_r = 38.9 min.

*(S)-Benzyl 3-Benzyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ae**).* Colorless gum; yield: 53 mg (85%); $[\alpha]_D^{21}$ = −170.2 (*c* = 1.1, $CHCl_3$); >99% ee; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.35−7.42 (m, 5H), 7.22−7.31 (m, 4H), 7.19 (d, *J* = 7.7 Hz, 2H), 7.10 (dt, *J* = 0.7, 7.7 Hz, 1H), 7.01 (dd, *J* = 0.7, 7.7 Hz, 1H), 6.99 (s, 1H), 5.30−5.35 (m, 2H), 4.13−4.21 (m, 2H), 4.04 (dd, *J* = 5.6, 8.4 Hz, 1H), 3.49 (dd, *J* = 15.4, 30.8 Hz, 2H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 152.1, 137.6, 136.2, 135.5, 128.9, 128.8, 128.7, 128.5, 128.1, 128.0, 127.8, 126.9, 126.4, 125.8, 125.5, 121.5, 120.6, 78.2, 68.4, 40.7, 38.9; IR (neat) 2915, 1717, 1547, 1488, 1377, 1317, 1230, 1161, 1025, 756 cm^{-1}; HRMS (ESI): Calcd for $C_{25}H_{22}N_2O_4Na$ (M + Na)$^+$: 437.1477. Found: 437.1474; Chiralpak OD-H column and OD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 43.6 min and *minor*-isomer t_r = 54.2 min.

*(S)-Benzyl 4-(Nitromethyl)-3-(pent-4-enyl)quinoline-1(4H)-carboxylate (**4af**).* Colorless gum; yield: 46 mg (78%); $[\alpha]_D^{21}$ = −168.5 (*c* = 1.1, $CHCl_3$); >99% ee; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.7 Hz, 1H), 7.35−7.45 (m, 5H), 7.28 (dt, *J* = 2.1, 8.4 Hz, 1H), 7.09−7.15 (m, 2H), 6.94 (s, 1H), 5.73−5.80 (m, 1H), 5.31−5.55 (m, 2H), 4.99 (dd, *J* = 1.4, 10.5 Hz, 1H), 4.97 (d, *J* = 9.8 Hz, 1H), 4.35 (dd, *J* = 4.9, 11.9 Hz, 1H), 4.23 (dd, *J* = 9.1, 11.9 Hz, 1H), 4.07 (dd, *J* = 5.6, 9.1 Hz, 1H), 2.13−2.24 (m, 2H), 2.01−2.11 (m, 2H), 1.51−1.68 (m, 2H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 152.2, 137.9, 136.3, 135.6, 128.7, 128.61, 128.58, 128.56, 128.51, 128.3, 128.0, 127.8, 126.7, 125.4, 124.4, 121.6, 121.1, 115.2, 78.2, 68.3, 41.2, 33.1, 31.6, 26.9; IR (neat) 2929, 1714, 1549, 1489, 1377, 1317, 1232, 1170, 1025, 910, 758 cm^{-1}; HRMS (ESI): Calcd for $C_{23}H_{24}N_2O_4Na$ (M + Na)$^+$: 415.1634. Found: 415.1633; Chiralpak AD-H column and AD-H guard column (1% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 220 nm); *major*-isomer t_r = 39.4 min and *minor*-isomer t_r = 43.1 min.

*(S)-Benzyl 3-Heptyl-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ag**).* Colorless gum; yield: 55 mg (86%); $[\alpha]_D^{22}$ = −88.1 (*c* = 1.1, $CHCl_3$); 99% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.4 Hz, 1H), 7.37−7.47 (m, 5H), 7.26−7.31 (m, 1H), 7.11 (dd, *J* = 7.6, 14.4 Hz, 2H), 6.93 (s, 1H), 5.33 (s, 2H), 4.35 (dd, *J* = 5.6, 11.6 Hz, 1H), 4.24 (dd, *J* = 9.2, 11.6 Hz, 1H), 4.07 (dd, *J* = 5.6, 8.8 Hz, 1H), 2.12−2.21 (m, 2H), 1.20−1.60 (m, 10H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 136.4, 135.6, 128.7(two peaks overlapping), 128.5, 128.3, 128.0, 127.8, 126.8, 125.4, 124.2, 121.6, 78.3, 68.3, 41.3, 32.3, 31.7, 29.2, 29.0, 27.8, 22.6, 14.1; IR (neat) 2926, 2855, 1716, 1552, 1489, 1378, 1319, 1234, 1170, 1026, 761 cm^{-1}; HRMS (ESI): Calcd for $C_{25}H_{30}N_2O_4Na$ (M + Na)$^+$: 445.2103. Found: 445.2100; Chiralpak OD-H column and OD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 13.5 min and *minor*-isomer t_r = 24.9 min.

*(S)-Benzyl 3-(3-(Benzyloxy)propyl)-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ah**).* Colorless gum; yield: 59 mg (83%); $[\alpha]_D^{22}$ = −156.5 (*c* = 1.0, $CHCl_3$); 99% ee; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.4 Hz, 1H), 7.43 (d, *J* = 7.0 Hz, 2H), 7.40 (t, *J* = 7.0 Hz, 2H), 7.34−7.38 (m, 1H), 7.25−7.33 (m, 6H), 7.12 (dt, *J* = 1.4, 7.7 Hz, 1H), 7.08 (dd, *J* = 1.4, 7.7 Hz, 1H), 6.94 (s, 1H), 5.33 (d, *J* = 11.9 Hz, 1H), 5.31 (d, *J* = 12.6 Hz, 1H), 4.45 (dd, *J* = 11.2, 18.9 Hz, 2H), 4.34 (dd, *J* = 5.6, 11.9 Hz, 1H), 4.21 (dd, *J* = 9.1, 11.9 Hz, 1H), 4.07 (dd, *J* = 5.6, 9.1 Hz, 1H), 3.44 (t, *J* = 7.7 Hz, 2H), 2.30−2.36 (m, 1H), 2.21−2.25 (m, 1H), 1.81−1.87 (m, 1H), 1.72−1.78 (m, 1H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 152.1, 138.3, 136.3, 135.5, 128.7, 128.5, 128.4, 128.3, 128.0, 127.8, 127.7, 127.6, 126.6, 125.4, 124.5, 121.6, 120.8, 78.1, 73.0, 69.1, 68.3, 41.2, 28.9, 27.9; IR (neat) 2921, 2854, 1717, 1547, 1488, 1377, 1318, 1231, 1170, 1100, 1025, 734 cm^{-1}; HRMS (ESI): Calcd for $C_{28}H_{28}N_2O_5Na$ (M + Na)$^+$: 495.1896. Found: 495.1890; Chiralpak AD-H column and AD-H guard column (5% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 24.8 min and *minor*-isomer t_r = 29.4 min.

*(S)-Benzyl 3-(3-(tert-Butyldiphenylsilyloxy)propyl)-4-(nitromethyl)quinoline-1(4H)-carboxylate (**4ai**).* Colorless gum; yield: 60 mg (65%); $[\alpha]_D^{23}$ = −89.8 (*c* = 1.0, $CHCl_3$); 98% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.4 Hz, 1H), 7.75 (dd, *J* = 2.0, 8.0 Hz, 3H), 7.62−7.69 (m, 4H), 7.36−7.49 (m, 8H), 7.33 (dt, *J* = 1.2, 7.6 Hz, 1H), 7.17 (dt, *J* = 1.2, 7.6 Hz, 1H), 7.10 (dd, *J* = 1.2, 7.6 Hz, 1H), 6.96 (s, 1H), 5.36 (d, *J* = 2.4 Hz, 2H), 4.35 (dd, *J* = 5.6, 12.0 Hz, 1H), 4.24 (dd, *J* = 5.2, 11.6 Hz, 1H), 4.09 (dd, *J* = 5.2, 8.8 Hz, 1H), 3.52−3.63 (m, 2H), 2.25−2.42 (m, 2H), 1.60−1.86 (m, 2H), 1.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 136.3, 135.6, 135.5, 135.2, 134.8, 133.7, 129.7, 128.7, 128.5, 128.3, 128.0, 127.81, 127.75, 127.69, 127.68, 126.7, 125.4, 124.5, 121.7, 120.9, 78.2, 68.4, 62.7, 41.2, 30.7, 28.5, 26.9, 26.6, 19.2, 19.0; IR (neat) 2929, 2856, 1720, 1550, 1488, 1427, 1348, 1318, 1107, 1026, 761, 736 cm^{-1}; HRMS (ESI): Calcd for $C_{37}H_{40}N_2O_5SiNa$ (M + Na)$^+$: 643.2604. Found: 643.2599; Chiralpak AD-H column and AD-H guard column (2% *i*-PrOH:hexanes, 1.0 mL/min flow, λ = 254 nm); *major*-isomer t_r = 12.2 min and *minor*-isomer t_r = 21.4 min.

*(2S,3R,4S)-Benzyl 4-(Aminomethyl)-3-ethyl-3,4-dihydro-2-hydroxyquinoline-1(2H)-carboxylate (**5**).* To a solution of compound **3aa** (37 mg, 0.10 mmol) in MeOH (1.0 mL) was added Raney-Ni (200 mg). Then, the reaction mixture was stirred under 1 atm of H_2 for 24 h at room temperature. The catalyst was filtered, and the filtrate was concentrated in vacuo and was purified using silica gel column chromatography (eluent: ethyl acetate/hexane, 7:3) to afford the title compound **5** (22 mg, 64% yield) as a colorless gum: $[\alpha]_D^{27}$ = −19.3 (*c* = 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.48 (m, 6H), 7.20−7.26 (m, 1H), 7.12 (dd, *J* = 1.2, 7.2 Hz, 1H), 7.06 (dd, *J* = 7.2, 7.6 Hz, 1H), 5.34 (d, *J* = 12.0 Hz, 1H), 5.24 (d, *J* = 12.4 Hz, 1H), 4.53 (dd, *J* = 4.4, 12.8 Hz, 1H), 4.32 (dd, *J* = 10.8, 12.4 Hz, 1H), 3.88 (brs, 1H), 3.63 (ddd, *J* = 4.0, 8.0, 14.8 Hz, 1H), 1.81−1.96 (m, 2H), 1.36−1.45 (m, 1H), 1.07 (d, *J* = 11.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 135.6, 134.9, 130.8, 128.8, 128.6, 128.4, 128.2, 127.9, 125.1, 124.8, 82.2, 74.1, 68.4, 46.6, 37.8, 23.2, 11.7; IR (neat) 3445, 2963, 1687, 1551, 1318, 1246, 1215, 1047, 1018, 748, 697 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{24}N_2O_3Na$ (M + Na)$^+$: 363.1685. Found: 363.1689.

*(3R,4S)-Benzyl 3-Ethyl-3,4-dihydro-4-(nitromethyl)-2-oxoquinoline-1(2H)-carboxylate (**6**).* To a solution of compound **3aa** (56 mg, 0.15 mmol) in CH_2Cl_2 (1.5 mL) was added PCC (65 mg, 3.0 mmol). Then, the reaction mixture was stirred for 24 h at room temperature, filtered through Celite, concentrated in vacuo. The residue was purified using silica gel column chromatography (eluent: ethyl acetate/hexane, 5:1) to afford the title compound **6** (47 mg, 85% yield) as a colorless gum: $[\alpha]_D^{28}$ = −45.8 (*c* = 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.48 (m, 5H), 7.23 (dt, *J* = 1.6, 7.6 Hz, 1H), 7.17 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.10 (dt, *J* = 1.2, 7.6 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 5.44 (d, *J* = 12.0 Hz, 1H), 5.39 (d, *J* = 12.0 Hz, 1H), 4.54 (ddd, *J* = 5.2, 7.2, 14.4 Hz, 1H), 2.01−2.12 (m, 1H), 1.41−1.53 (m, 1H), 1.10 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 153.0, 135.9, 134.3, 129.2, 129.1, 128.9, 128.8 (two peaks overlapping), 128.3, 126.0, 125.3, 119.1, 75.0, 70.4, 45.5, 38.8, 19.6, 12.1; IR (neat) 2967, 1772, 1698, 1553, 1375, 1201, 748, 697 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{20}N_2O_5Na$ (M + Na)$^+$: 391.1270. Found: 361.1271.

*(3R,4S)-3-Ethyl-3,4-dihydro-4-(nitromethyl)quinolin-2(1H)-one (**7**).* To a solution of compound **3aa** (37 mg, 0.10 mmol) in MeOH (1.0 mL) was added 10% Pd/C (5 mg). Then, the reaction mixture was stirred for 18 h at room temperature, diluted with CH_2Cl_2 (2 mL), filtered through Celite, concentrated in vacuo. The residue was purified using silica gel column chromatography (eluent: ethyl acetate/hexane, 4:1) to afford the title compound **7** (18 mg, 76% yield) as a colorless gum: $[\alpha]_D^{28}$ = −37.9 (*c* = 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.24−7.30 (m, 1H), 7.12 (d, *J* = 6.8 Hz, 1H), 7.01 (ddd, *J* = 0.8, 7.6, 8.4 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 4.56 (dd, *J* = 4.4, 12.0 Hz, 2H), 4.37 (dd, *J* = 10.8, 12.0 Hz, 1H), 3.86 (dd, *J* = 5.2, 10.4 Hz, 1H), 2.72 (dd, *J* = 6.8, 13.6 Hz, 1H), 2.09−2.20 (m, 1H), 1.42−1.52 (m, 1H), 1.15 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 136.3, 129.4, 128.2, 123.8, 123.3, 116.1, 75.1, 43.9, 38.6, 19.1, 12.3; IR (neat) 3211, 2965, 2922, 1674, 1549, 1375, 1258, 1036, 945, 753, 690 cm^{-1}; HRMS (ESI): Calcd for $C_{12}H_{14}N_2O_3Na$ (M + Na)$^+$: 257.0902. Found: 257.0898.

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■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H, ^{13}C NMR, and 2D NMR spectra and HPLC analysis. 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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