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Nickel-Catalyzed Decarboxylative Generation and Asymmetric Allylation of 2-Azaallyl Anions

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Nickel-Catalyzed Decarboxylative Generation and Asymmetric Allylation of 2-Azaallyl Anions

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Supporting Information Placeholder



ABSTRACT: The first nickel-catalyzed asymmetric decarboxylative allylation (DcA) of allyl 2,2-diarylglycinate imines is reported. This transformation utilizes a chiral ferrocenyl bidentate ligand and a Ni(o) pre-catalyst to mediate the decarboxylative generation and asymmetric allylation of 2-azaallyl anions, affording α -aryl homoallylic imines in modest-to-high yields and moderate-to-high enantiomeric ratios. The resulting Ni-catalyzed transformation proved to be less general in comparison to our previously reported analogous Pd-mediated protocol, but it still exhibited certain advantages in regard to the regio- and enantioselectivity of the C–C bond formation.

INTRODUCTION

Transition metal-catalyzed allylic alkylation (AA) has emerged as one of the most powerful methods for the construction of $C(sp^3)$ - $C(sp^3)$ bonds and considerable work has been done to realize and improve the asymmetric potential of this process.¹ In addition to Pd-catalysis, other transition metals, such as iridium² and nickel³ can be used to effect the enantioselecitve AA of C-centered nucleophiles. Decarboxylative allylation (DcA), which involves the concomitant decarboxylative generation and allylation of an anionic nucleophile by a transition metal catalyst, is an attractive offshoot from the traditional AA process.⁴ Asymmetric DcA reactions have primarily relied on Pd- and Ir-based catalytic systems and conformationally-constrained enolate nucleophilic intermediates.⁵ Despite being a more economical choice, there are only limited reports of Ni-catalyzed DcA reactions,⁶ and, to the best of our knowledge, there are no examples of Nicatalyzed asymmetric DcA reactions involving C-centered nucleophiles. For Ni-catalysis, alternate reaction pathways such as decarbonylative couplings are typically more common.⁷ Herein, inspired by our previous work with Pdcatalyzed asymmetric DcA reactions,^{8,9} we report the first Ni-catalyzed asymmetric DcA reaction involving a Ccentered nucleophile. Specifically, a combination of a Ni(o) pre-catalyst and the chiral bisphosphine ligand (S,S)-*f*-binaphane¹⁰ allowed for the decarboxylative generation and asymmetric allylation of semi-stabilized 2azaallyl anions¹¹ from allyl 2,2-diarylglycinate imines to afford α -aryl homoallylic imines in modest-to-high isolated yields and good-to-high enantiomeric ratios (Scheme 1). While the Ni-catalyzed transformation proved to be less general than our previously reported Pd-mediated reaction manifold,⁸ it still exhibited certain advantages in regard to the regio- and enantioselectivity of the C—C bond formation. The resulting enantioenriched homoallylic imine products are known to be valuable synthetic precursors to a large collection of biologically-relevant scaffolds.¹² Toward this end, we demonstrate that a convenient two-step Heck cyclization/Sharpless asymmetric dihydroxylation protocol can be employed to make new variants of an established small molecule α -helix mimetic scaffold.¹³

SCHEME 1. Ni-Catalyzed Decarboxylative Generation and Asymmetric Allylation of 2-Azaallyl Anions



RESULTS AND DISCUSSION

Preliminary studies focused on identifying appropriate conditions for the Ni-catalyzed DcA of allyl 2,2diphenylglycinate imines. Since it is established that elec-Environment

tron-withdrawing arylimines favor regioselective allylation of the less substituted carbon of the 2-azaallyl anion intermediate in the corresponding Pd-catalyzed transformation,⁸ the *p*-CO₂Me-substituted benzylaldimine 1a was chosen to initiate our studies with the hope that homoallylic imine 2a would be formed as the sole DcA product (Table 1). In all cases, Ni(cod), was employed as the Ni(o) source. To explore the general feasibility of the Ni-catalyzed DcA reaction, achiral ligands were initially employed (entries 1-3). We were pleased to discover that either monodentate (10 mol %, entry 1) or bidentate (5 mol %, entry 2) phosphine ligands, when combined with 5 mol % Ni(cod)₂ in THF (0.1 M) at 25 °C resulted in the essentially quantitative conversion of imino ester 1a into racemic 2a within 24 h. Nolan's group has shown success using N-heterocyclic carbene (NHC) ligands for the Nicatalyzed arylation of semi-stabilized 2-azaallyl anions,¹⁴

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TABLE 1. Determining Reaction Conditions for the Racemic and Asymmetric Ni-Catalyzed DcA of Imino Ester 1a.



2	dppf, THF (0.1 M)	>95 [°]	51:49
3	IPr, THF (0.1 M)	0	—
4	(S,S)-f-binaphane, THF (o.1 M)	90	89:11
5	(S,S)-f-binaphane, DMF (0.1 M)	90	94:6
6	(S,S)-f-binaphane, DMSO (0.1 M)	79	95:5
7	(S,S)-f-binaphane, THF (0.1 M), –20 ${}^\circ\!{\rm C}$	12	90:10
8	(S,S)-f-binaphane, THF (0.25 M)	98	89:11
9	Ni(cod) ₂ (2.5 mol %), (<i>S,S</i>)- <i>f</i> -binaphane (2.5 mol %), THF (0.25 M)	90	90:10
10	Ni(cod) ₂ (2.5 mol %), (<i>S,S</i>)- <i>f</i> -binaphane (2.5 mol %), DMSO (0.25 M)	79	95:5
11	Ni(cod)₂ (0.5 mol %), (<i>S,S</i>)- <i>f</i> -binaphane (0.5 mol %), THF (0.25 M)	7	90:10
12	NiCl ₂ (10 mol %), (<i>S</i> , <i>S</i>)- <i>f</i> -binaphane (10 mol %), Zn (40 mol %) DMSO (0.1 M)	15	92:8

^{*a*}Isolated yield after column chromatography. ^{*b*}Er determined by chiral HPLC analysis using a Chiralcel OD-H column. The ratios are listed corresponding to order of elution and, based on comparison to known compounds (ref. 8), are *S*:*R*. ^{*c*}Assay yield determined by ¹H NMR spectroscopic analysis versus 1,4-dimethoxybenzene as an internal standard.

but we were unable to effect the corresponding Nicatalyzed DcA reaction using an NHC ligand (entry 3). In previous studies, we determined that the ferrocenederived chiral bisphosphine ligand (S,S)-f-binaphane¹⁰ was uniquely suited for the Pd-catalyzed asymmetric DcA of allyl 2,2-diphenylglycinate imines.⁸ Gratifyingly, this ligand also allowed for the Ni-catalyzed asymmetric DcA of imino ester 1a (entries 4-11). When the reaction was conducted in THF (0.1 M), the desired homoallylic imine (S)-2a was isolated in 90% yield with an enantiomeric ratio (er) of 89:11 (entry 4). In accord with previous studies,⁸ increasing the polarity of the solvent resulted in a corresponding increase in the observed er values (entries 5,6), with DMSO providing the best result (er 95:5). It is worth noting that in all of the solvents explored, the Nicatalyzed asymmetric DcA of **1a** using (S,S)-*f*-binaphane provided 2a with higher er values than were obtained from the corresponding Pd-catalyzed transformations (er values for Pd: THF = 84.5:15.5, DMF = 89.5:10.5, DMSO = 94:6).^{8a} Cooling the reaction mixture down to -20 °C in THF resulted in less conversion without a noticeable increase in er (entry 7). Increasing the concentration of the reaction mixture, however, resulted in an improvement in yield (entry 8). Moreover, the amount of catalyst could be reduced to 2.5 mol % in either THF (entry 9) or DMSO (entry 10) without significant reductions in isolated yield or er. Further reduction in the amount of catalyst, however, negatively impacted the overall conversion (entry 11). In situ generation of the Ni(o) catalyst by reduction of an anhydrous Ni(II) source with zinc dust provided homoallylic imine 2a with drastically reduced conversion and a slightly lower er (entry 12). Oxophilic Lewis acids, such as Zn(II), are known to inhibit the critical decarboxylation of the free carboxylate to form the semi-stabilized 2-azaallyl anion intermediate,¹⁵ so this result was not surprising.

Having identified appropriate reaction conditions, we next explored the substrate scope for the Ni-catalyzed asymmetric DcA of allyl 2,2-diphenylglycinate arylimines 1 (Scheme 2). The observed trends closely matched those previously reported for the corresponding Pd-catalyzed transformation.⁸ For example, the isolated yields, regioisomeric ratios (rr; 2:3), and er values were all highest with electron-withdrawing substituents on the benzaldimine substituent (cf. 2a-c and 2g). In almost all cases, DMSO proved to be a superior solvent compared to THF; an added advantage of DMSO as a solvent is that the products (2 + 3), in most circumstances, simply can be extracted from the reaction mixture with hexane or petroleum ether without need for further purification. Nitro groups are notoriously incompatible with Ni(o)-catalysis,^{7C,16} so it came as no surprise that no-to-poor conversion was observed for *m*-nitrobenzaldimine **1h** in THF or DMSO. Remarkably, relatively high yield and outstanding er were observed for the formation of *p*-nitro-substituted **2g**, but only in THF as solvent. We currently do not have a satisfying explanation for this unique observation. For relatively electron-rich substrates (11-n), higher reaction temperatures (between 40-45 °C) were required to effect the transformation. In the case of the *N*-Boc-protected indole substrate \mathbf{in} , further heating to 60 $\,$ \mathbb{C} afforded the corre-

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sponding homoallylic imine **2n** in high yield (93%), with an understandable reduction in enantioselectivity (er 70:20). Aryl bromides (**2d** and **2e**) all survived the reaction conditions and *ortho*-substituents (**2e** and **2j**) could be tolerated with varying degrees of success. In all cases, the Ni-catalyzed DcA transformation achieved higher rr values and, except for *p*-bromo **2d** and *p*-methyl **2i**, higher er values when compared to the corresponding Pdcatalyzed process.⁸ This may be a result of the smaller ionic radius of the Ni(II) atom providing a more compact

SCHEME 2. Ni-Catalyzed Asymmetric DcA of Esters 1^a



^aRegioisomeric ratios (rr; **2**:3) were determined by ¹H NMR of concentrated reaction mixtures and, unless noted otherwise, were \geq 20:1. Er determined by chiral HPLC; see ref 8. Unless otherwise noted, all reported values (isolated combined yield, rr, and er) are an average of 2–4 runs. ^bIsolated yield and er after single recrystallization from hexane. ^cSingle result. ^d40 °C. ^e45 °C. ^f60 °C.

and more selective chiral steric environment around the catalyst. The Pd-mediated transformation, however, tended to afford higher isolated yields, especially for those benzaldimines with electron-donating substituents (e.g. 2i, 2j, and 2l). As has been noted elsewhere,⁸ the benzophenone Schiff base in homoallylic imines 2 facilitates enantiomeric enrichment via recrystallization in hexane. For example, the er of o-bromo-substituted (S)-**2e** could be increased from 85:15 to 99:1 after a single recrystallization. Importantly, the reaction could be conducted on gram-quantities of starting imino esters without deterioration of yield or enantioselectivity. For example, subjection of 1.25 g of imino ester 1c (2.95 mmol) to the standard reaction conditions outlined in Scheme 2 (DMSO) afforded the corresponding homoallylic imine 2c in 79% isolated yield with an er of 89:11 (see Experimental Section). It should be noted, however, that substitution on either alkenyl carbon of the allyl ester moiety in imino esters 1 was severely detrimental to the resulting conversion and er value (see Supporting Information).

A limitation to both the Ni-catalyzed transformation introduced herein and our previously reported Pd-catalyzed variation is the current inability to generate the requisite imine starting materials 1 in which the R group is an alkyl moiety.¹⁷ Attempts at imine condensation between allyl 2,2-diphenylglycinate and enolizable aliphatic aldehydes typically afford a complex mixture of products, presumably via imine-mediated aldol reactions. Conversely, attempts to condense the same highly hindered amino ester with bulky nonenolizable alkyl aldehydes, e.g. pivaldehyde, failed to afford any products. Similarly, ketones typically fail to condense with the sterically hindered amine group in allyl 2,2-diphenylglycinate. We were able, however, to generate the trifluoromethylated imine 10. Unfortunately, subjection of this imino ester to the Nicatalyzed reaction conditions resulted in low conversion (9-30%) and no production of the corresponding homoallylic imine 20. Instead, the corresponding gem-difluoro-2azadiene,¹⁸ which presumably formed via decarboxylative elimination of fluoride, was the only product observed in the concentrated reaction mixture (see Supporting Information).

Our group recently demonstrated that the observed rr values for the Pd-catalyzed decarboxylative formation and asymmetric allylation of 2-azaallyl anions could be improved by introducing both electron-donating substituents and steric elements into the aryl groups on the 2,2diarylglycine amino acid linchpins.^{8b} Specifically, exchanging the 2,2-diphenylglycine linchpin in 1 for 2,2di(2-methoxyphenyl)glycine (4) for the Pd-catalyzed asymmetric DcA process completely solved the regioselectivity issue, affording the corresponding homoallylic imines 5 exclusively with slight reductions in the observed er values. Surprisingly, this strategy was not as successful for the corresponding Ni-catalyzed process. As shown in Scheme 3, relatively electron-deficient arylimine substrates (4a, 4b, 4d) were converted to the corresponding homoallylic imines (5a, 5b, and 5d, respecitively) in high yield and without a reduction in er values. Indeed, pbromo-substituted 5d was obtained in higher yield and er

versus benzophenone imine 2d, even though the reaction had to be heated to 65 °C to achieve complete conversion. It should be noted, however, that the corresponding benzophenone imines 2a, 2b, and 2d were already all obtained as essentially single regioisomers (Scheme 2). The p-methyl-substituted product 2i, however, was obtained as a 4:1 mixture with the corresponding regioisomeric imine 3i in 53% combined yield (Scheme 2). The bis(2methoxyphenyl)methylene imine **5i** was obtained as a single regioisomer (determined by comparison of the concentrated reaction mixture to a known standard),^{8b} albeit with a significant relative reduction in isolated yield (21%), which potentially outweighs the improved regioselectivity. Addition of stronger electron-donating substituents onto the benzaldimine component of imino esters 4, e.g. p-methoxy, effectively inhibited the Ni-catalyzed transformation (see Supporting Information). This was not a limitation for the corresponding Pd-catalyzed process.^{8b}

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SCHEME 3. Ni-Catalyzed Asymmetric DcA of Esters 4



To highlight the usefulness of the Ni-catalyzed asymmetric DcA procedure, o-bromo-substituted homoallylic imine product (S)-2e was first converted to indene (S)-6 in 61% average yield via a Pd-catalyzed Heck cyclization (Scheme 4).¹⁹ Sharpless asymmetric dihydroxylation of exo-methylene 6 then afforded diols anti-7 and syn-8 in high yield but different ratios depending on the particular AD-mix combination employed.²⁰ The chirality of imine 6 appeared to be matched with AD-mix- α , preferentially forming anti-7 over syn-8 in at least a 17:1 ratio and 83% combined yield, and mismatched with AD-mix-B, which afforded only a slight preference for syn-8 over anti-7 (2:1, 90% combined yield). The relative stereochemistries for 7 and 8 were determined by extensive 2D-NMR spectroscopic analysis (see Supporting Information). Imino diols 7 and 8 are both unique variations of the venerable indane-based small molecule a-helix mimetic scaffold first introduced by Willems and co-workers.¹³ Our efforts to advance these imino diols into small molecule mimetics of the Bcl-2 homology domain 3 (BH3) α -helix of the proapoptotic regulator Bim²¹ will be reported elsewhere.

In conclusion, we have reported herein the first Nicatalyzed asymmetric DcA transformation involving a Ccentered nucleophilic intermediate. Specifically, a combination of Ni(cod)₂ and chiral bisphosphine (*S*,*S*)-*f*binaphane in either THF or DMSO allow for the catalytic decarboxylative generation and asymmetric allylation of

semi-stabilized 2-azaallyl anions from allyl 2,2-diarylglycinate arylimines. In regard to the regio- and enantioselectivity of the key C-C bond-forming event, this Nicatalyzed system proved superior to our previously reported Pd-mediated counterpart,⁸ with er values reaching up to 97:3. The corresponding Pd-catalyzed reaction manifold, however, possesses a broader substrate scope and higher associated yields, especially with electron-rich arvlimine moieties in the starting imino esters 1 and 4. The resulting enantiomerically-enriched homoallylic imine products are valuable precursors for the synthesis of important biologically-active organoamine constructs.¹² Attempts to extend these reaction conditions to other Nicatalyzed asymmetric decarboxylative alkylation transformations are on-going and will be reported in due course.

Scheme 4. Synthesis of Imino Diols 7 and 8



EXPERIMENTAL SECTION

General Methods. All non-aqueous reactions were performed in oven-dried flasks or vials under an atmosphere of dried and deoxygenated argon with dry solvents and magnetic stirring, unless stated otherwise. All non-aqueous reactions were carried out in oven or flame-dried glassware (prewashed with agua regia and distilled water) under an argon atmosphere with dry solvents and magnetic stirring, unless otherwise stated. All argon was purified by passage through an OXICLEARTM deoxygenation column. All solvents were made anhydrous by storing over activate 4Å molecular sieves for at least 48 h and sparged with Ar gas for at least 10 minutes.²² Anhydrous dichloromethane (CH₂Cl₂), benzene (PhH), dimethyl formamide (DMF) were used as received. The petroleum ether (PE) used in this project has a boiling point range of 60 - 90 °C. Triethylamine (Et₃N) was distilled and further dried over potassium hydroxide. (S,S)-f-Binaphane was purchased from Chiral Ouest and used as received. Other ligands were purchased from either Strem or Aldrich and used as received. Ni(cod)₂ was purchased from Strem and was stored and distributed in an inert atmosphere glove box. All other chemicals were used as received. Reaction progress was monitored by analytical TLC using 250 µm thick Partisil[®] K6F 60Å silica gel plates (Whatman). Developed TLC plates were visualized by UV light (254 nm) and/or ninhydrin or potassium permanganate (KMnO₄) stains. All chromatography was performed with indicated solvents and Purasil (Whatman) 60Å 230-400 mesh silica gel. All yields refer to chromatographically and spectroscopically pure compounds, unless otherwise indicated. Melting points determined with a Shanghai Shenguang WRS-18 digital melting point apparatus and are uncorrected. Infrared spectra were obtained from a NEXUS670FT-IR using a thin film deposited on freshly made KBr disks; only strong and functional groupspecific peaks are reported (in cm⁻¹, %T). All ¹H NMR and ¹³C{¹H} NMR taken on a Bruker Ascend 400 (101) at 300K, as

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indicated. Chemical shifts are reported in δ (ppm) units using residual solvent peak as a standard; CHCl₃: ¹H NMR δ 7.26 and ¹³C{¹H} NMR δ 77.16 ppm; d₆-DMSO: ¹H NMR δ 2.50 and ¹³C{¹H} NMR δ 39.52 ppm. No internal standard was used for ¹⁹F{¹H} NMR spectra. All product ratios and conversion determined from ¹H NMR analysis of the crude reaction mixture using 1,4-dimethoxybenzene as an internal standard. High resolution mass spectra obtained using an LCMS-IT-TOF at the Sichuan University Analytical Center. Enantiomeric ratios (er) were determined from samples separated on a Chiral Technologies Diacel OD-H or AD-H chiral column and comparison to a racemic standard. All known compounds matched literature reports.

General Procedure for Synthesis of Allyl 2,2-Diarylglycinates. To a flame-dried vial equipped with a magnetic spin vane was added allyl 2,2-diarylglycinate (1.00 equiv)⁸ and the corresponding substituted benzaldehyde (0.9 equiv). The resulting solvent-free mixture was stirred at $65 \ C$ at atmospheric pressure for 4h, the under reduced pressure using a standard laboratory oil pump for at least 2h to remove generated H₂O. After cooling to rt, the resulting mixture was purified by flash chromatography or recrystallization from hexanes or PE to afford the corresponding new allyl diarylglycinate imines 1j, 1m, 1n, and 4a (see below). Known allyl 2,2-diarylglycinate imines 1a-i, 1k, 1l, 4b, 4d, and 4i were obtained followed previously reported synthetic procedures.^{8,17,21}

Allyl 2-((2-methylbenzylidene)amino)-2,2-diphenylacetate (1j). Imine 1j was synthesized by condensation of allyl 2,2diphenylglycinate (0.50 g, 1.87 mmol) and 2-methylbenzaldehyde (0.20 g, 1.67 mmol) and was purified by flash chromatography (1% Et₃N in 20% EtOAc/PE), then recrystallized from hexane to afford a white solid (0.42 g, 1.09 mmol, 80%): mp 53..5-54.5 °C; R_f=0.65 (1% Et₂N in 20% EtOAc/hexane); IR (NaCl film) v 3050, 3024, 1732, 1599, 1491, 1447, 1212; ¹H NMR $(CDCl_3, 400 \text{ MHz}) \delta 8.21 \text{ (s, 1H)}, 8.02 \text{ (dd, J = 7.5, 1.6 Hz, 1H)},$ 7.44 - 7.38 (m, 4H), 7.38 - 7.28 (m, 8H), 7.15 (d, J = 6.9 Hz, 1H), 5.86 (ddt, J = 17.2, 10.7, 5.5 Hz, 1H), 5.23 - 5.12 (m, 2H), 4.70 (dt, J = 5.5, 1.5 Hz, 2H), 2.33 (s, 3H); ${}^{13}C{}^{1}H$ NMR (CDCl₂, 101 MHz) δ 171.9, 162.6, 142.5, 138.2, 134.4, 131.5, 130.8, 130.6, 129.3, 128.0, 127.6, 126.1, 118.3, 79.9, 66.2, 19.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{24}NO_2^+$ 370.1802; Found 370.1800.

Allyl 2-((3,4-dimethoxybenzylidene)amino)-2,2-diphenylacetate (1m). Imine 1m was synthesized by condensation of allyl 2,2-diphenylglycinate (0.98 g, 3.67 mmol) and 3,4dimethoxybenzaldehyde (0.68 g, 4.09 mmol) and was purified by recrystallization from hexane to afford a white solid (1.46 g, 3.51 mmol, 95%): mp 117.0-118.3 °C; R_f =0.38 (1% Et₃N in 20% EtOAc/hexane); IR (NaCl film) v 2925, 1735, 1688, 1506, 1459, 1268, 1024; ¹H NMR (CDCl₃, 400 MHz) δ 7.83 (s, 1H), 7.58 (s, 1H), 7.34 (ddd, J = 14.3, 13.9, 6.4 Hz, 10H), 7.18 (d, J = 8.2 Hz, 1H), 6.86 (d, J = 8.2 Hz, 1H), 5.86 (ddt, J = 16.1, 10.5,5.3 Hz, 1H), 5.16 (t, J = 14.7 Hz, 2H), 4.70 (d, J = 5.1 Hz, 2H), 3.97 (s, 3H), 3.92 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 101 MHz) δ 172.1, 162.9, 151.8, 149.3, 142.6, 131.6, 129.8, 129.3, 128.1, 127.6, 123.8, 118.2, 110.4, 109.4, 79.3, 66.1, 56.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{26}NO_4^+$ 416.1856; Found 416.1868.

tert-Butyl 2-(((2-(allyloxy)-2-oxo-1,1-diphenylethyl)imino)methyl)-1H-indole-1-carboxylate (1n). Imine 1n was synthesized by condensation of allyl 2,2-diphenylglycinate (1.03 g, 3.87 mmol) and 1-Boc-indole-2-carbaldehyde (1.02 g, 4.17 mmol) and was purified by flash chromatography (1% Et₃N in 10% EtOAc/PE) to afford a colorless oil (1.64 g, 3.31 mmol, 80%): R_f =0.45 (1% Et₃N in 5% EtOAc/hexane); IR (NaCl film) ν 2928, 1735, 1450, 1334, 1221, 1161, 1122; ¹H NMR (CDCl₃, 400 MHz) δ 8.49 (s, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.48 (s, 1H), 7.44 – 7.21 (m, 12H), 5.88 (ddd, *J* = 16.6, 10.7, 5.5 Hz, 1H), 5.29 – 5.09 (m, 2H), 4.71 (t, *J* = 9.4 Hz, 2H), 1.47 (s, 9H); ¹³C[¹H] NMR (CDCl₃, 101 MHz) δ 157.2, 142.3, 131.6, 129.3, 128.6, 128.0, 127.6, 125.8, 123.2, 121.7, 118.3, 115.7, 111.7, 84.6, 66.3, 28.1; HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₃₁H₃₁N₂O₄⁺ 495.2278; Found 495.2256.

Allyl 2.2-diphenyl-2-((2,2,2-trifluoroethylidene)amino)acetate (10). Imine 10 was synthesized by condensation of allyl 2,2-diphenylglycinate (0.94 g, 3.51 mmol) and 1-ethoxy-2,2,2trifluoroethan-1-ol (1.81 g, 12.62 mmol) and was purified by flash chromatography (1% Et₂N in 3% EtOAc/Pe) to afford 10 as a colorless liquid (0.43 g, 1.24 mmol, 35%). NOTE: The purified imine 10 is not stable and gradually decomposes in solution (e.g. CDCl₃), especially in the presence of water: $R_{f}=0.52$ (1% Et₂N in 5% EtOAc/PE); IR (NaCl film) v 2934, 1741, 1453, 1358, 1298, 1221, 1170; ¹H NMR (CDCl₃, 400 MHz, contains small amounts of decomposition products) δ 7.41 – 7.34 (m, 6H), 7.34 - 7.28 (m, 4H), 7.16 (q, J = 3.2 Hz, 1H), 5.86 (ddt, J = 17.3, 10.7, 5.5 Hz, 1H). 5.25 - 5.21 (m, 1H). 5.19 (t, J = 1.3 Hz, 1H), 4.71 (dt, J = 5.5, 1.3 Hz, 2H); ${}^{13}C{}^{1}H$ NMR (CDCl₂, 101 MHz, contains small amounts of decomposition products) δ 169.9, 152.2 (q, J_{C-F} = 38.6 Hz), 140.1, 131.1, 129.2, 128.5, 119.5 (q, $J_{C-F} = 275.4 \text{ Hz}$), 118.8, 79.7, 66.8; ¹⁹F{¹H} NMR (CDCl₃, 376 MHz, contains small amounts of decomposition products) δ -71.2; HRMS (ESI-TOF) m/z: [M + Na]⁺ Calcd for $C_{10}H_{16}F_3NNaO_2^+$ 370.1025; Found 370.1032.

Methvl 4-(((2-(allyloxy)-1,1-bis(2-methoxyphenyl)-2-oxoethyl)imino)methyl)benzoate (4a). Imine 4a was synthesized by condensation of allyl 2,2-di(2-methoxyphenyl)glycinate (0.37 g, 1.13 mmol)^{8b} and methyl 4-formylbenzoate (0.09 g, 0.55 mmol) and was purified by flash chromatography (1% Et₃N in 10% EtOAc/PE) to afford a white solid (0.25 g, 0.52 mmol, 95%): mp 181.8-182.9 °C; Rf=0.43 (1% Et₃N in 20% EtOAc/PE); IR (NaCl film) v 2952, 2842, 1729, 1590, 1488, 1435, 1277, 1247; ¹H NMR (CDCl₂, 400 MHz) δ 8.13 - 8.04 (m, 3H), 7.88 (d, J = 8.3 Hz, 2H), 7.35 - 7.23 (m, 4H), 6.99 - 6.84 (m, 4H), 5.93 - 5.80 (m, 1H), 5.22 - 5.07 (m, 2H), 4.68 (ddd, J = 11.9, 4.1, 1.3 Hz, 2H), 3.92 (s, 3H), 3.58 (s, 6H); ¹³C{¹H} NMR (CDCl_3, 101 MHz) δ 160.2, 157.3, 140.7, 132.1, 130.4, 129.7, 129.1, 128.5, 120.3, 117.6, 111.8, 65.8, 55.4, 52.2; HRMS (ESI-TOF) $m/z: [M + H]^{+}$ Calcd for $C_{28}H_{28}NO_{6}^{+}$ 474.1911; Found 474.1920.

General Procedure for the Ni-Catalyzed Asymmetric DcA of Allyl 2,2-Diphenylglycinate Imines 1. A flamedried screw-cap conical vial was charged with imine 1 (0.25 mmol) and a magnetic stir bar. The vial was capped with a rubber septum, the contents degassed with three consecutive vacuum/argon-fill cycles, and then transported into an inert environment glove box. Inside the glove box, Ni(cod)₂ (2.5 mol %) and (*S*,*S*)-*f*-binaphane (2.5 mol %) were added to the vial which was then recapped, brought out of the glove box, and placed under an Ar atmosphere. Solvent (THF or DMSO, 0.1 mL) was then added to the mixture via syringe and the resulting mixture was stirred 25 °C for 24 h. For reactions conducted in THF, the solvent was first removed by rotary evaporation and analyzed by ¹H NMR spectroscopy to determine the regioisomeric ratio (rr, 2:3) prior to chromatographic purification and determination of the isolated yields

and enantiomeric ratior (er) values for homoallylic imines 2. For reactions conducted in DMSO two different approaches were taken. To determine the rr (2:3) for reactions conducted in DMSO, the reaction mixture was extracted (x₃) with either hexanes or PE and the concentrated extract was analyzed by ¹H NMR spectroscopy. To determine the isolated yields and er for reactions conducted in DMSO, the reaction mixture was directly loaded onto a silica gel column and the homoallylic imine 2 was eluted with 1% Et₂N in either 3% or 10% EtOAc/PE. Unless otherwise specified, each reaction was repeated 2-4 times and the resulting er values, which were determined by HPLC separation on a chiral stationary phase, were averaged for the value reported in the main text (Scheme 2). Homoallylic imines (S)-2e, (S)-2j, (S)-2m, and (S)-2n are new compounds and were fully characterized (see below). All other homoallylic imines (S)-2 spectroscopically matched previous reports.

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Gram-Scale Procedures for the Ni-Catalyzed Asymmetric DcA of Allyl 2,2-Diphenylglycinate Imine 1c. The above general procedures were scaled up for the Ni-catalyzed DcA of imino ester 1c (1.25 g, 2.95 mmol) in DMSO without any other modifications to the reaction conditions. Purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine 2c (0.88 g, 2.33 mmol, 79%) as a colorless liquid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports^{8b} and chiral HPLC analysis (*vide infra*) demonstrated an er of 89:11, which is comparable with the smaller scale procedure (average er 88:12)

Methyl (S)-4-(1-((diphenylmethylene)amino)but-3-en-1-yl)benzoate (**2a**). Ni-catalyzed DcA of imino ester **1a** (0.10 g, 0.25 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine **2a** (0.07 g, 0.19 mmol, 79%) as a white solid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports.^{8a} The yields reported in Scheme **2** are an average of three runs, each providing **2a** in 79% isolated yield.

(*S*)-4-(1-((*diphenylmethylene*)*amino*)*but*-3-*en*-1-*y*])*benzonitrile* (*ab*). Ni-catalyzed DcA of imino ester **1b** (0.09 g, 0.25 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine *2b* (0.06 g, 0.19 mmol, 77%) as a colorless liquid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports.^{8a} The yields reported in Scheme 2 are an average of three runs, which provided *2b* in isolated yields of 70%, 77%, and 90%, respectively.

(S)-1,1-Diphenyl-N-(1-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)methanimine (**2c**). Ni-catalyzed DcA of imino ester **1c** (0.10 g, 0.25 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine **2c** (0.08 g, 0.21 mmol, 88%) as a colorless liquid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports.^{8b} The yields reported in Scheme 2 are an average of three runs, which provided **2c** in isolated yields of 65%, 87%, and 88%, respectively.

(*S*)-1,1-Diphenyl-*N*-(1-(4-bromophenyl)but-3-en-1-yl)methanimine (**2d**). Ni-catalyzed DcA of imino ester **1d** (0.11 g, 0.25 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine **2d** (0.08 g, 0.21 mmol, 85%) as a colorless liquid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports.^{8a} The yields reported in Scheme 2 are an average of three runs, which provided 2d in isolated yields of 71%, 75%, and 85%, respectively.

(S)-1,1-Diphenyl-N-(1-(2-bromophenyl)but-3-en-1-yl)methanimine (2e). Ni-catalyzed DcA of imino ester 1e (0.11 g, 0.25 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine 2e (0.09 g, 0.24 mmol, 98%) as an off-white solid: mp 79.8–80.3 °C; $R_f = 0.6$ (1% Et₃N in 10% EtOAc/hexane); IR (NaCl film) v 3065, 2925, 1622, 1468, 1444, 1316, 1027; $[\alpha]^{25.2}$ +97.6 (c 8.3 x 10⁻⁴ g/mL, CH₂Cl₂); ¹H NMR (CDCl₂, 400 MHz) δ 7.82 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.75 - 7.65 (m, 2H), 7.48 - 7.27 (m, 8H), 7.10 - 7.04 (m, 1H), 7.01 (dd, J = 6.2, 2.7 Hz, 2H), 5.71 (ddt, J = 17.2, 10.1, 7.1, 1H), 5.02 – 4.94 (m, 2H), 4.91 (dd, J = 7.2, 5.4 Hz, 1H), 2.64 – 2.51 (m, 2H); ¹³C{¹H} NMR (CDCl₃, 101 MHz) δ 167.9, 143.9, 140.0, 137.0, 135.4, 132.4, 130.0, 129.8, 128.7, 128.4, 128.3, 128.0, 127.9, 127.8, 127.5, 122.4, 116.9, 64.6, 43.0; HRMS (ESI-TOF) $m/z: [M + H]^{+}$ Calcd for $C_{23}H_{21}BrN^{+}$ 390.0852; Found 390.0855.HPLC conditions: Chiral Technologies Diacel OD-H chiral column, eluent: 1:1000 2-propanol/hexane, flow rate: 1 mL/min, average (S)-2e retention time = 5.625 min, average (*R*)-2e retention time = 6.524 min. The yields reported in Scheme 2 are an average of three runs, which provided 2e in isolated yields of 73%, 98%, and 99%, respectively.

(*S*)-1,1-Diphenyl-N-(1-phenylbut-3-en-1-yl)methanimine (*zf*). Ni-catalyzed DcA of imino ester **1f** (0.08 g, 0.25 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 3% EtOAc/PE) afforded homoallylic imine **2f** (0.05 g, 0.17 mmol, 66%) as a white solid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports.^{8a} The yields reported in Scheme **2** are an average of three runs, which provided **2f** in isolated yields of 66%, 70%, and 71%, respectively.

(*S*)-1,1-Diphenyl-N-(1-(4-nitrophenyl)but-3-en-1-yl)methanimine (**2g**). Ni-catalyzed DcA of imino ester **1g** (0.10 g, 0.25 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et_3N in 5% EtOAc/PE) afforded homoallylic imine **2g** (0.01 g, 0.03 mmol, 11%) as a colorless oil whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports.^{8a} The yields reported in Scheme 2 are an average of three runs, which provided **2g** in isolated yields of 10%, 11%, and 12%, respectively.

(*S*)-1,1-Diphenyl-N-(1-(3-nitrophenyl)but-3-en-1-yl)methanimine (**2h**). Ni-catalyzed DcA of imino ester **1h** (0.10 g, 0.25 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine **2h** (6.40 mg, 0.02 mmol, 7%) as a colorless oil whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports.^{8a} The yields reported in Scheme 2 are an average of three runs, which provided **2h** in isolated yields of 5%, 7%, and 9%, respectively.

(*S*)-1,1-Diphenyl-N-(1-(p-tolyl)but-3-en-1-yl)methanimine (*zi*). Ni-catalyzed DcA of imino ester *ii* (0.09 g, 0.25 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 3% EtOAc/PE) afforded homoallylic imine *zi* (52.3 mg, 0.16 mmol, 64%) as a white solid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports.^{8a} The yields reported in Scheme *z* are an average of three runs, which provided *zi* in isolated yields of 42%, 53%, and 64%, respectively.

(S)-1,1-Diphenyl-N-(1-(0-tolyl)but-3-en-1-yl)methanimine (**2j**). Ni-catalyzed DcA of imino ester **1j** (0.09 g, 0.26 mmol)

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in DMSO following the above general procedure and purification by flash chromatography (1% Et₂N in 3% EtOAc/PE) afforded homoallylic imine 2j (0.03 g, 0.11 mmol, 41%) as a white solid: mp 109.9–120.0 °C; $R_f = 0.5$ (1% Et₃N in 5% EtOAc/hexane); IR (NaCl film) v 3050, 3024, 2360, 1503, 1407, 1343, 1013; $[\alpha]_{D}^{23.2}$ +4.25 (c 4 x 10⁻³ g/mL, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) 8 7.74 - 7.65 (m, 3H), 7.44 - 7.29 (m, 6H), 7.19 (t, J = 7.2 Hz, 1H), 7.09 (td, J = 7.4, 1.4 Hz, 1H), 7.06 - 6.95 (m, 3H), 5.69 (ddt, J = 17.2, 10.1, 7.1 Hz, 1H), 5.04 - 4.90 (m, 2H), 4.63 (dd, J = 8.2, 4.9 Hz, 1H), 2.68 (ddd, J = 15.3, 8.2, 7.3) Hz, 1H), 2.56 – 2.45 (m, 1H), 2.33 (s, 1H), 1.90 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 101 MHz) & 166.8, 143.3, 140.0, 137.5, 136.0, 134.1, 129.9, 128.5, 128.2, 128.0, 127.6, 126.1, 116.5, 62.4, 43.5, 19.0; HRMS (ESI-TOF) m/z: $[M + H]^{+}$ Calcd for $C_{24}H_{24}N^{+}$ 326.1903; Found 326.1877. HPLC conditions: Chiral Technologies Diacel OD-H chiral column, eluent: 1:1000 2-propanol/hexane, flow rate: 1 mL/min, average (S)-2j retention time = 5.326min, average (R)-2i retention time = 6.699 min. The yields reported in Scheme 2 are an average of three runs, which provided 2j in isolated yields of 29%, 35%, and 41%, respectively.

(S)-N-(1-(3,5-dimethoxyphenyl)but-3-en-1-yl)-1,1-diphenylmethanimine (**2k**). Ni-catalyzed DcA of imino ester **1k** (0.10 g, 0.25 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine **2k** (0.06 g, 0.19 mmol, 76%) as a colorless liquid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports.^{8a} The yields reported in Scheme 2 are an average of three runs, which provided **2k** in isolated yields of 22%, 49%, and 76%, respectively.

(*S*)-1,1-Diphenyl-*N*-(1-(4-methoxyphenyl)but-3-en-1-yl)methanimine (*z***l**). Ni-catalyzed DcA of imino ester 1l (0.06 g, 0.16 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine *z*l (0.03 g, 0.08 mmol, 52%) as a colorless oil whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports.^{8b} The yields reported in Scheme 2 are an average of three runs, which provided *z*l in isolated yields of 50%, 52%, and 54%, respectively.

(S)-N-(1-(3,4-dimethoxyphenyl)but-3-en-1-yl)-1,1-diphenylmethanimine (2m). Ni-catalyzed DcA of imino ester 1m (0.21 g, 0.67 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 10% EtOAc/PE) afforded homoallylic imine 2m (0.08 g, 0.23 mmol, 45%) as a colorless oil: $R_{f=0.69}$ (1% Et₂N in 20%) EtOAc/hexane); IR (NaCl film) v 2934, 2836, 1599, 1524, 1447, 1268, 1027; $[\alpha]^{23,2}$ –7.36 (c1.4 x 10⁻² g/mL, CH₂Cl₂); ¹H NMR (CDCl₂, 400 MHz) 8 7.69 - 7.62 (m, 2H), 7.46 - 7.40 (m, 3H), 7.38 - 7.28 (m, 4H), 7.07 (dd, I = 6.5, 2.9 Hz, 2H), 6.90 (s, 1H), 6.79 (d, J = 0.8 Hz, 2H), 5.65 (ddt, J = 17.2, 10.2, 7.1 Hz, 1H),5.04 - 4.90 (m, 2H), 4.37 (dd, J = 7.8, 5.6 Hz, 1H), 3.87 (d, J = 5.0 Hz, 6H), 2.68 (dt, J = 15.0, 7.6 Hz, 1H), 2.57 (dt, J = 13.6, 6.2 Hz, 1H). ¹³C{¹H} NMR (CDCl₃, 101 MHz) δ 147.7, 137.1, 135.8, 130.1, 129.8, 128.5, 128.1, 126.6, 119.0, 116.6, 110.8, 110.3, 66.2, 55.8, 44.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for C₂₅H₂₆NO₂⁺ 372.1958; Found 372.1944. HPLC conditions: Chiral Technologies Diacel OD-H chiral column, eluent: 1:1000 2-propanol/hexane, flow rate: 1 mL/min, average (S)-2m retention time = 43.412 min, average (*R*)-2m retention time = 47.680 min. The yields reported in Scheme 2 are an average of three runs, which provided **2m** in isolated yields of 40%, 45%, and 50%, respectively.

tert-Butyl (S)-2-(1-((diphenylmethylene)amino)but-3-en-1-yl)-1H-indole-1-carboxylate (2n). Ni-catalyzed DcA of imino ester **in** (0.07 g, 0.15 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 3% EtOAc/PE) afforded homoallylic imine 2m (0.02 g, 0.05 mmol, 31%) as a colorless oil: $R_f=0.69$ (1% Et₃N in 5% EtOAc/PE); IR (NaCl film) v 2982, 1735, 1456, 1375, 1334, 1161, 1117; $[\alpha]^{23.3}$ +9.58 (c 2.4 x 10⁻³ g/mL, CH₂Cl₂); ¹H NMR (CDCl₃) 400 MHz) δ 8.21 (d, J = 8.3 Hz, 1H), 7.76 - 7.71 (m, 2H), 7.47 (d, J = 7.1 Hz, 1H), 7.43 - 7.35 (m, 7H), 7.24 - 7.17 (m, 2H),7.06 (dd, J = 6.6, 3.0 Hz, 2H), 6.80 (s, 1H), 5.78 (ddt, J = 17.0, 10.2, 7.1 Hz, 1H), 5.28 - 5.15 (m, 1H), 5.10 - 4.93 (m, 3H), 2.67 (t, J = 6.4 Hz, 2H), 1.39 (s, 9H).; ¹³C{¹H} NMR (CDCl₃, 101 MHz) & 168.3, 143.7, 139.9, 137.4, 137.0, 135.5, 130.1, 129.4, 128.7, 128.4, 128.1, 127.7, 123.5, 122.7, 120.2, 116.8, 115.6, 107.9, 83.7, 76.7, 60.5, 42.7, 27.9; HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for $C_{20}H_{21}N_{2}O_{2}^{+}$ 451.2380; Found 451.2343. HPLC conditions: Chiral Technologies Diacel OD-H chiral column, eluent: 1:1000 2-propanol/hexane, flow rate: 1 mL/min, average (S)-**2n** retention time = 7.546 min, average (*R*)-**2n** retention time = 8.594 min.General Procedure for the Ni-Catalyzed Asymmetric DcA of Allyl 2,2-Diarylglycinate Imines 4. A flame-dried screw-cap conical vial was charged with imine 4 (0.25 mmol) and a magnetic stir bar. The vial was capped with a rubber septum, the contents degassed with three consecutive vacuum/argon-fill cycles, and then transported into an inert environment glove box. Inside the glove box, Ni(cod)₂ (2.5 mol %) and (*S*,*S*)-*f*-binaphane (2.5 mol %) were added to the vial which was then recapped, brought out of the glove box, and placed under an Ar atmosphere. DMSO (0.1 mL) was then added to the mixture via syringe and the resulting mixture was stirred 25 °C (65 °C for 4d, 45 °C for 4i) for 24 h. The reaction mixture was directly purified by flash chromatography on SiO₂ eluting with 1% Et₂N in either 20% EtOAc/PE. For determination of the regioisomeric ratios, the products 5 were dissolved in MeOH, the imine was reduced with NaBH,CN over 6 d, and the resultant product mixture was analyzed by 'H NMR spectroscopy, as reported previously.8b In all cases, only a single product resulting from reduction on imines 5 was observed. Unless otherwise specified, each reaction was repeated 2-4 times and the resulting er values were averaged for the value reported in the main text (Scheme 2). Homoallylic imine (S)-5a is a new compound and was fully characterized (see below). All other homoallylic imines (*S*)-5 spectroscopically matched previous reports.⁸

Methyl (*S*)-*4*-(*1*-((*bis*(*2*-*methoxyphenyl*)*methylene*)*amino*but-3-en-1-yl)benzoate (5a). Ni-catalyzed DcA of imino ester **4a** (0.04 g, 0.09 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 10% EtOAc/PE) afforded homoallylic imine 5a (0.03 g, 0.08 mmol, 86%) as a white solid: mp 129.6-130.1 °C; R_f=0.46 (1% Et₂N in 20% EtOAc/PE); IR (NaCl film) v 2943, 2833, 1723, 1604, 1491, 1438, 1277,1241; [α]^{23.2}_D -99.31 (c 4.32 x 10^{-3} g/mL, CH₂Cl₂); poor peak resolution in ¹H and ¹³C{¹H} NMR due to hindered rotation about the aryl–C(imine) bond; ¹H NMR (CDCl₃, 400 MHz) δ 8.02 – 7.86 (m, 2H), 7.54 (dd, J = 7.6, 3.6 Hz, 1H), 7.45 - 7.36 (m, 1H), 7.33 - 7.27 (m, 2H), 7.09 (dd, J = 13.7, 5.9 Hz, 1H), 7.03 – 6.88 (m, 2H), 6.79 (t, J =16.8 Hz, 2H), 5.67 (s, 1H), 4.99 (d, J = 20.6 Hz, 2H), 4.40 (s, 1H), 3.90 (s, 2H), 3.83 (s, 1H), 3.57 (d, J = 2.1 Hz, 2H), 3.29 (s, 1H), 2.66 (t, J = 42.4 Hz, 2H); ¹³C{¹H} NMR (CDCl₂, 101 MHz) δ 157.3, 135.6, 130.1, 130.0, 129.3, 129.0, 125.6, 120.6, 117.8, 111.9, 66.2, 55.6, 52.0, 30.3; HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd

for $C_{27}H_{28}NO_4^+$ 430.2013; Found 430.1986. HPLC conditions: Chiral Technologies Diacel OD-H chiral column, eluent: 1:1000 2-propanol/hexane, flow rate: 1 mL/min, average (*S*)-**5a** retention time = 15.327 min, average (*R*)-**5a** retention time = 22.053 min.

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Due to hindered rotation about the aryl-imine bond, ¹H NMR and ¹³C NMR spectra were poorly resolved.^{8b} So as to fully confirm identity, imine 5a (0.02 g, 0.05 mmol) was dissolved in MeOH (0.25 mL) and reduced with one portion of NaBH₃CN (12.5 mg, 0.02 mmol, 4 equiv) under Ar over 6 d. The resulting reaction mixture was diluted with CH₂Cl₂ and washed with 1N aq NaOH (the aqueous layer was extracted with two more portions of CH₂Cl₂). The combined organic layers were dried (Na₂SO₄), filtered, and concentrated in vacuo. The resulting residue was passed through a short plug of silica gel to remove any unreduced imine (eluent: 10% EtOAc/PE) to afford the corresponding secondary amine as a white solid (23.5 mg, 0.05 mmol, 95%): Rf=0.60 (20% EtOAc/PE); ¹H NMR (CDCl₂, 400 MHz) δ 7.96 (d, J = 8.1 Hz, 2H), 7.38 – 7.30 (m, 3H), 7.23 – 7.16 (m, 2H), 7.12 (t, J = 7.7 Hz, 1H), 6.94 (t, J = 7.4 Hz, 1H), 6.81 (t, J = 8.7 Hz, 2H), 6.75 (d, J = 8.2 Hz, 1H), 5.74 - 5.60 (m, 1H), 5.14 (s, 1H), 5.10 - 5.01 (m, 2H), 4.11 (q, J = 7.2 Hz, 1H), 3.90 (s, 3H), 3.65 (s, 3H), 3.62 (s, 3H), 2.47 – 2.33 (m, 2H), 2.22 (d, J = 18.8 Hz, 1H); ${}^{13}C{}^{1}H$ NMR (CDCl₃, 101 MHz) & 167.2, 157.5, 156.8, 149.8, 135.4, 131.6, 130.3, 129.3, 129.0, 128.5, 127.6, 120.1, 117.5, 110.7, 60.3, 59.4, 55.1, 53.5, 51.9, 42.9, 14.1; HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for $C_{27}H_{30}NO_4^+$ 432.2169; Found 432.2195.

(*S*)-4-(1-((*bis*(2-*methoxyphenyl*)*methylene*)*amino*)*but*-3*en*-1-*yl*)*benzonitrile* (**5***b*). Ni-catalyzed DcA of imino ester **4b** (0.05 g, 0.12 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 10% EtOAc/PE) afforded homoallylic imine **5b** (0.04 g, 0.10 mmol, 84%) as a white solid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports (NOTE: due to hindered rotation about the aryl—imine bond, ¹H NMR and ¹³C NMR spectra were poorly resolved).^{8b}

(S)-N-(1-(4-bromophenyl)but-3-en-1-yl)-1,1-bis(2-methoxyphenyl)methanimine (5d). Ni-catalyzed DcA of imino ester 4d (0.06 g, 0.12 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine 5d (0.05 g, 0.10 mmol, 89%) as a white solid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports (NOTE: due to hindered rotation about the aryl—imine bond, ¹H NMR and ¹³C NMR spectra were poorly resolved).^{8b}

(S)-1,1-bis(2-methoxyphenyl)-N-(1-(p-tolyl)but-3-en-1-yl)methanimine (**5***i*). Ni-catalyzed DcA of imino ester **4***i* (0.06 g, 0.13 mmol) in DMSO following the above general procedure and purification by flash chromatography (1% Et₃N in 5% EtOAc/PE) afforded homoallylic imine **5***i* (0.01 g, 0.02 mmol, 21%) as a white solid whose ¹H NMR spectra (CDCl₃, 400 MHz) matched literature reports (NOTE: due to hindered rotation about the aryl—imine bond, ¹H NMR and ¹³C NMR spectra were poorly resolved).^{8b}

(S)-N-(3-methylene-2,3-dihydro-1H-inden-1-yl)-1,1-diphenylmethanimine (6). To a septum-capped flame-dried vial charged with Ph(PPh₃)₄ (75.7 mg, 10 mol %, distributed in a glove box) under an Ar atmosphere was added via syringe a solution of imine (S)-2e (255.7 mg, 1 equiv) in dry DMF (6.5 mL, 0.1M), followed by Et₃N (0.18 mL, 1 equiv). The resulting solution was stirred at 110 °C for 4 h. After cooling to room temperature, the reaction mixture was filtered through Celite

and concentrated azeotropically with toluene on a rotary evaporator. The resulting product was purified by flash chromatography (100% PE \rightarrow 1% Et₃N in 3% EtOAc/PE \rightarrow 1% Et₃N in 5% EtOAc/ PE) to obtain (S)-6 as an yellow-orange solid (167.1 mg, 61%) which was spectroscopically similar to previous reports for the racemic compound.¹⁶ Yellow-orange solid, mp 130.0–136.0 °C; R_f=0.53 (1% Et₃N in 5% EtOAc/PE); IR (NaCl film) v 3059, 1615, 1446, 1286; $\left[\alpha\right]^{23.1}$ D -35.25 (c 4.00 x 10⁻³ g/mL, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 7.69 - 7.64 (m, 2H), 7.55 – 7.27 (m, 10H), 7.24 (d, J = 4.4 Hz, 1H), 7.16 (dt, J = 3.8, 3.2 Hz, 1H), 5.46 (t, J = 2.4 Hz, 1H), 5.04 (t, J = 2.0 Hz, 1H), 4.97 (t, J = 6.9 Hz, 1H), 2.98 – 2.91 (m, 2H); ${}^{13}C{}^{1}H$ NMR (CDCl₃, 101 MHz) & 168.6, 147.9, 147.7, 140.6, 139.6, 136.9, 132.4, 132.0, 130.0, 128.8, 128.1, 127.9, 127.6, 124.9, 120.6, 103.0, 64.2, 41.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{20}N^+$ 310.1590; Found 310.1569.

Asymmetric Dihydroxylation of (S)-6 with AD-mix-α. In a glass vial was added tert-butanol (1 mL, 0.1 M) and H₂O (1 mL, 0.1 M), followed by commercially prepared AD-mix-α (0.28 g).²³ After stirring at room temperature for ~30 min, the resulting solution was cooled to \circ °C and alkene (S)-6 (35) mg, 0.1 mmol, 1 equiv) was added to the solution. The reaction mixture was stirred at 0 °C for a 4-6 h and then stored in a o °C freezer overnight. After the reaction was deemed complete by TLC, Na₂SO₃ (0.3 g, 24 equiv) was added to the reaction mixture at 0 °C, followed by stirring at rt for 30 min. The resulting mixture was then extracted with EtOAc (x₃), dried (Na₃SO₄), filtered, and concentrated in vacuo to afford a yellow liquid. This mixture was then purified by flash chromatography (1% Et₂N in 20% EtOAc/PE \rightarrow 1% Et₂N in 60% EtOAc/ PE) to obtain imino diol 7 (32.4 mg, 83%) The corresponding dr (7:8) value was determined to be $\geq 20:1$ by ¹H NMR. The relative stereochemistry of the major dihydroxvlation product was determined by extensive 2D-NMR analysis (see Supporting Information).

Asymmetric Dihydroxylation of (S)-6 with AD-mix-β. In a glass vial was added tert-butanol (1 mL, 0.1 M) and H₂O (1 mL, 0.1 M), followed by commercially prepared AD-mix-α (0.28 g).^{21a} After stirring at room temperature for ~30 min, the resulting solution was cooled to \circ °C and alkene (*S*)-6 (35) mg, 0.1 mmol, 1 equiv) was added to the solution. The reaction mixture was stirred at $o^{\circ}C$ for a 4-6 h and then stored in a o °C freezer overnight. After the reaction was deemed complete by TLC, Na₂SO₃ (0.3 g, 24 equiv) was added to the reaction mixture at 0 °C, followed by stirring at rt for 30 min. The resulting mixture was then extracted with EtOAc (x₃), dried (Na₂SO₄), filtered, and concentrated in vacuo to afford a yellow liquid. This mixture was then purified by flash chromatography (1% Et₃N in 20% EtOAc/PE \rightarrow 1% Et₃N in 60% EtOAc/ PE) to obtain imino diols 8 and 7 as an inseparable mixture (34.9 mg, 90%) The corresponding dr (8:7)value was determined to be 2:1 by ¹H NMR. The relative stereochemistry of the major dihydroxylation product was assumed to be the opposite syn-dihydroxylation product (versus 7). The relative stereochemistry of the major dihydroxylation product was determined by extensive 2D-NMR analysis (see Supporting Information).

(*iS*,3*S*)-3-((*Diphenylmethylene*)*amino*)-*i*-(*hydroxymethyl*)-2,3-*dihydro*-*iH*-*inden*-*i*-*ol* (7). Purified by flash chromatography (1% Et₃N in 60% EtOAc/PE). Yellow solid: mp 154.8– 155.6 °C; R_f=0.20 (1% Et₃N in 20% EtOAc/PE); IR (NaCl film) *v* 3407, 2920, 2854, 1730, 1617, 1382, 1278, 1039; $[\alpha]^{23.1}_{D}$ –152.33 (c 2.14 x 10⁻³ g/mL, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 7.58

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- 7.46 (m, 6H), 7.40 - 7.27 (m, 7H), 7.08 (d, J = 7.4 Hz, 1H), 5.13 - 5.06 (m, 1H), 4.27 (s, 1H), 4.07 (d, J = 10.3 Hz, 1H), 3.94 (d, J = 10.4 Hz, 1H), 2.46 - 2.39 (m, 2H), 2.20 (br s, 1H); ¹³C[¹H] NMR (CDCl₃, 101 MHz) δ 167.5, 145.3, 144.4, 139.0, 136.4, 130.4, 130.0, 129.1, 128.9, 128.5, 128.2, 127.9, 124.8, 123.4, 83.4, 69.6, 63.6, 47.8; HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₂₃H₂₂NO₂⁺ 344.1645; Found 344.1635.

(1R, 3S)-3-((Diphenylmethylene)amino)-1-(hydroxymethyl)-2,3-dihydro-1H-inden-1-ol (8). Purified by flash chromatography (1% Et₃N in 60% EtOAc/PE) to afford a 2:1 mixture with 7. White solid; $R_{f}=0.20$ (1% Et₃N in 20% EtOAc/PE); IR (NaCl film) v 3360, 2926, 2869, 2363, 1617, 1438, 1284, 1043; ¹H NMR (CDCl₃, 400 MHz, 2:1 mixture with 7 as minor component; only data for 8 provided) δ 7.59 - 7.45 (m, 6H), 7.41 - 7.27 (m, 7H), 7.13 – 7.10 (m, 1H), 4.87 (dd, J = 6.3, 4.7 Hz, 1H), 3.86 (d, J = 11.3 Hz, 1H), 3.66 (br s, 1H), 3.62 (d, J = 10.8 Hz, 1H), 2.58 (dd, J = 13.2, 6.4 Hz, 1H), 2.27 (dd, J = 13.0, 4.9 Hz, 1H, overlap), 2.27 (br s, 1H, overlap); ¹³C{¹H} NMR (CDCl₃, 101 MHz, 2:1 mixture with 7 as minor component; only data for 8 provided) & 176.6, 145.2, 144.8, 139.4, 136.6, 130.5, 130.2 129.2, 128.90, 128.88, 128.83, 128.78, 128.4, 125.1, 124.8, 123.7, 82.5, 68.1, 63.8, 46.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{22}NO_2^+$ 344.1645; Found 344.1635.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Detailed reaction conditions screens, NMR spectra for known and new compounds, chiral-phase HPLC traces (PDF).

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Notes

The authors declare no completing financial interest.

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