JOC The Journal of Organic Chemistry

ARTICLE

pubs.acs.org/joc

A General Strategy for the Synthesis of Cyclic *N*-Aryl Hydroxamic Acids via Partial Nitro Group Reduction

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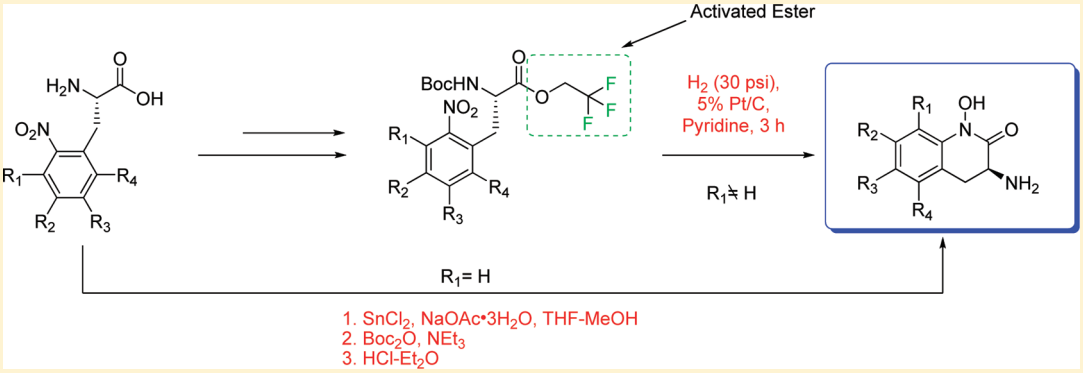
Supporting Information

ABSTRACT:



We describe a generalized approach to stereocontrolled synthesis of substituted cyclic hydroxamic acids (3-amino-1-hydroxy-3,4-dihydroquinolinones) by selective reduction of substituted 2-nitrophenylalanine substrates. Compounds in this series have antibacterial properties and have also recently been reported as KAT II inhibitors. The key nitrophenyl alanine intermediates are prepared enantioselectively in excellent yield by phase transfer catalyzed alkylation of the corresponding nitrobenzyl bromides. The scope and limitations of the reductive cyclization transformation have been explored with attention to the effects of substitution pattern and electronics on reaction efficiency and byproduct formation. In addition, a novel activated trifluoroethyl ester cyclization strategy has been developed as an alternate approach to the most sterically demanding systems in this series.

INTRODUCTION

The synthesis of *N*-hydroxy-3-amino-3,4-dihydroquinolinones as antibacterial agents was first reported by Davis and co-workers over thirty years ago (**1**, Figure 1).[1] More recently, these scaffolds have been identified as potent inhibitors of kynurenine aminotransferase II (KAT II), an enzyme currently being investigated as a therapeutic target for cognitive impairment associated with schizophrenia, among other disorders.[2,3] As part of our program to identify optimal KAT II inhibitors, we have extensively explored synthetic approaches to differentially substituted 3-amino-1-hydroxy-3,4-dihydroquinolinones. Herein we describe a generalized approach to synthesis of substituted cyclic hydroxamic acids **1** by selective reduction of substituted 2-nitrophenylalanine substrates. The scope and limitations of this transformation have been explored, with attention to the effects of substitution pattern and electronics on reaction efficiency. In addition, a novel activated ester cyclization strategy has provided synthetic access to the most sterically hindered and electronically disfavored systems in this series.

Several synthetic approaches to the hydroxamic acid core **1** were pursued (Figure 1). In one approach, cyclization of phenylalanine hydroxamic acids **2** is achieved using SET oxidizing reagents such as PIFA.[2,4] A significant limitation of this approach is that it is only applicable to electron-rich aromatic systems. In addition, unsymmetrical substitution patterns give rise to a mixture of regioisomeric products. Tomkinson and co-workers have reported Pd-catalyzed amination conditions for the addition of protected hydroxylamine derivatives onto aryl halides.[5] We attempted to use this approach in the context of our targets of interest, but it proved unsuccessful.

Reductive cyclization of the synthetically accessible 2-nitrophenylalanine derivatives **4** has offered the most flexible approach to the 3-amino-1-hydroxy-3,4-dihydroquinolinones. One challenge associated with reductive cyclization is the propensity of the nitro group to be over-reduced to the aniline product, resulting in formation of a lactam. To overcome this issue, we carried out hydrogenations using a sulfided platinum catalyst reported by the Davis group.[6] Although these conditions are suitable for some substitution patterns, the reductive cyclization reaction process is strongly influenced by the steric and electronic nature of the aryl

Received: March 14, 2011
Published: March 31, 2011

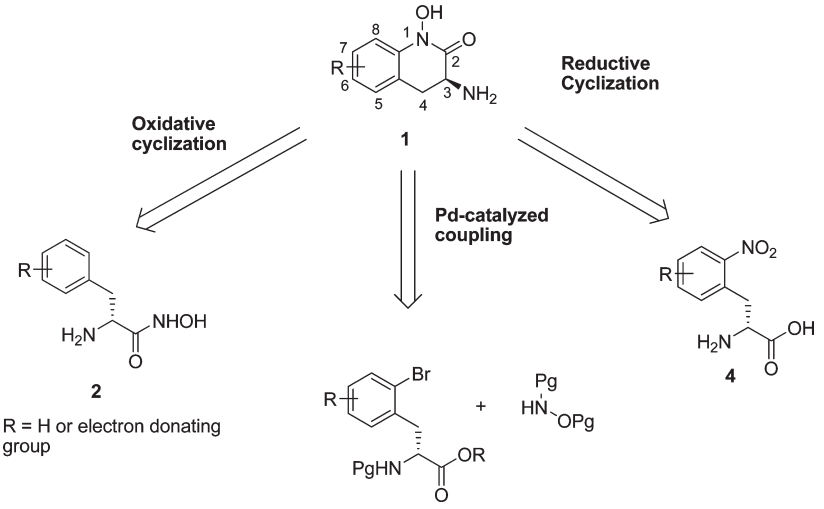
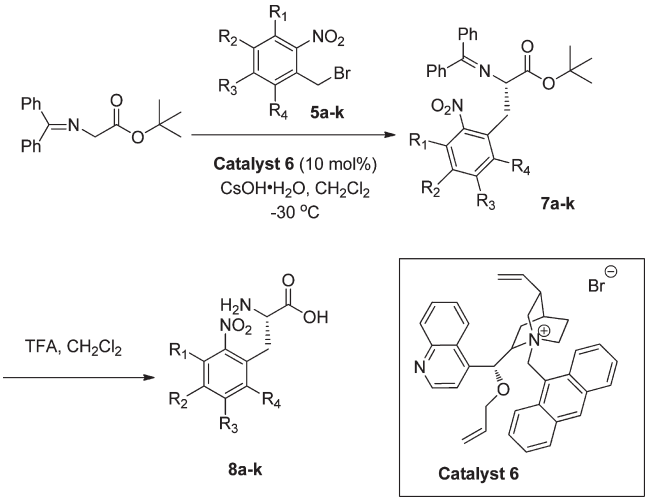


Figure 1. Strategies for the preparation of cyclic hydroxamic acids.

Scheme 1. Asymmetric Synthesis of Substituted 2-Nitrophenylalanines Using Phase Transfer Catalyzed Asymmetric Alkylation



ring. Specifically, electron-rich systems are readily over-reduced to generate the lactam product, while compounds substituted at C-8 do not undergo cyclization.

We report herein two new approaches toward the cyclization of 2-nitrophenylalanines to 3-amino-1-hydroxy-3,4-dihydroquinolinones **1**. First, the application of a $SnCl_2$/NaOAc reducing system has enabled the efficient, selective synthesis of cyclic hydroxamic acids without over-reduction to lactams. These conditions expanded the substrate scope to include C-5, C-6, and C-7 substituted hydroxamic acids of electron-rich, electron-poor, and neutral electronic character. Second, a method for synthesis of the problematic C-8 substituted hydroxamic acids has been identified. This subset of targets, especially those bearing electron-rich substituents, is particularly challenging due to steric hindrance around the nitro group slowing the reduction rate, which leads to undesired side reactions. To address this limitation, we employed a novel activated ester reductive cyclization approach that provides access to these compounds in excellent yields while suppressing the formation of byproduct.

Table 1. Asymmetric Alkylation of 2-Nitrobenzyl Bromides Using Cinchonidine Phase Transfer Catalyst

entry	bromide **5**	R_1	R_2	R_3	R_4	% yield[d] of **7a**−**k**	% ee[a]
1	**5a**	H	H	H	Me	72	91[b]
2	**5b**	H	H	H	F	79	89[b]
3	**5c**	H	H	Me	H	74	100[b]
4	**5d**	H	H	Cl	H	50	75[b]
5	**5e**	H	H	CF_3	H	72	90[c]
6	**5f**	H	H	OCF_3	H	60	86[b]
7	**5g**	H	OMe	H	H	89	94[b]
8	**5h**	H	Me	H	H	89	93[b]
9	**5i**	H	Cl	H	H	49	90[b]
10	**5j**	OCF_3	H	H	H	92	96[b]
11	**5k**	CF_3	H	H	H	82	96[c]

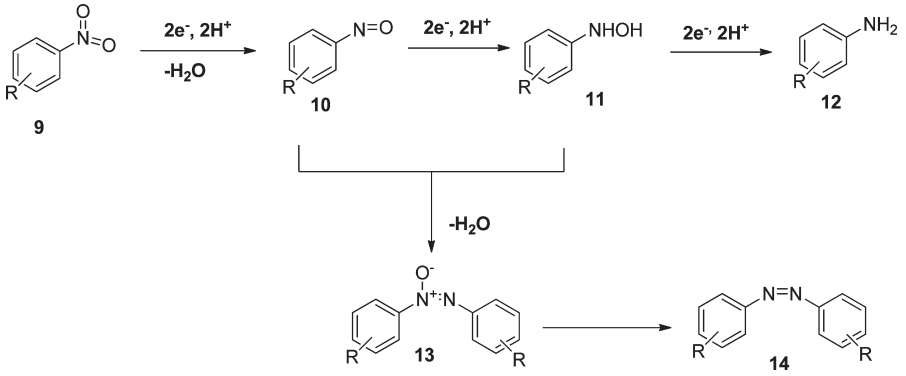
[a] Racemic versions of compounds **7a**−**k** were prepared from bromides **5a**−**k** using TBAF instead of chiral catalyst **6**. [b] ee values were determined using chiral supercritical fluid chromatography (SFC; Chiracel OD-H, 4.6 mm × 25 cm column, Mobile phase 95/5 CO_2/propanol). [c] ee determined using chiral HPLC (Chirobiotic V column, 4.6 mm × 25 cm; mobile phase 50/50 MeOH/MeCN) after conversion to **8e** (for **7e**) or **8k** (for **7k**). [d] Yields are reported for isolated material obtained after chromatographic purification.

RESULTS AND DISCUSSION

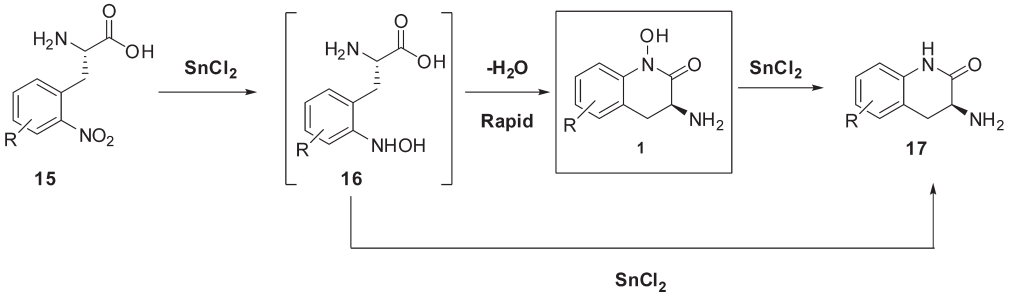
Asymmetric Synthesis of 2-Nitrophenylalanine Derivatives. Because our target compounds of interest contain a (3*S*)-amino group, an asymmetric synthesis of the 2-nitrophenylalanine substrates was required. Chiral phase transfer catalysis has been established as a robust methodology for the asymmetric synthesis of α-amino acids.[7] For example, the asymmetric alkylation of *tert*-butyl *N*-(diphenylmethylidene)glycinate with simple 2-nitrobenzyl bromides using the commercially available cinchonidine alkaloid **6**[8] as catalyst has been reported to give the protected amino acid of the desired configuration in excellent yield and enantiomeric excess.[9,10] In an extension of the scope of these alkylations, a wide variety of 2-nitrobenzyl bromides (**5a**−**k**) underwent asymmetric alkylation at −30 °C to afford the desired amino acids **7a**−**k** in respectable yields and excellent enantioselectivities (generally >90%) (Scheme 1); Table 1 provides representative examples. Higher ee values for this

dx.doi.org/10.1021/jo200530j |*J. Org. Chem.* 2011, 76, 3484–3497

Scheme 2. Process of Reduction of Nitroaromatics



Scheme 3. $SnCl_2$ Reduction of 2-Nitrophenylalanine Derivatives



step can be achieved by conducting the alkylation at −78 °C; however, the reaction proceeds significantly more slowly and in lower yields.

Discovery of a $SnCl_2$/NaOAc System for Selective Reduction to Cyclic Hydroxamic Acids. Many reagent systems have been reported, with varying efficiencies, to reduce nitroaryl groups to hydroxylamines. These include $SnCl_2$,[11] H_2−Pt/C,[12] Zn/NH_4Cl,[13] hydrazine with Pd/C,[14] and enzymatic reduction using Baker's yeast.[15] The main challenge in this transformation is achieving selective reduction to the hydroxylamine without over-reduction to the aniline or the formation of byproduct such as azoxy or diazo compounds. Scheme 2 depicts the mechanisms by which a range of products can be obtained upon reduction of a simple nitroaromatic.[16]

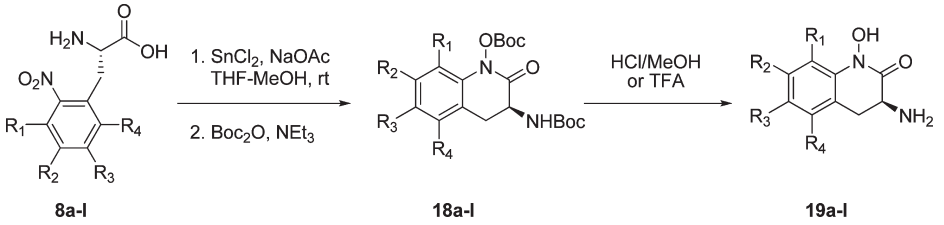
To achieve selective reduction and maximize yield it is often necessary to carefully control the reaction temperature, monitor reaction progress, and terminate prior to complete conversion, to minimize byproduct formation. In our system, identification of a reagent system that could be generally applied to all of our substrates proved challenging. Moderate product yields could be obtained by treating some substrates with $SnCl_2$ in ethanol at 60 °C (Scheme 3). However, the efficiency of the reduction/cyclization and the nature and quantity of the byproduct were highly dependent on the electronic and steric nature of the amino acid substrate. In some cases, reaction progress was monitored very closely and reactions were terminated as soon as over-reduction was observed (Scheme 3). This protocol led to mixtures of product **1**, starting material **15** and lactam **17** byproduct, which were difficult to separate chromatographically.

In a related method aimed at the synthesis of 7-hydroxyaminobenzodiazepines, Walser and co-workers[17] reported the reduction of a nitroaryl group to the hydroxylamine using $SnCl_2$ buffered with NaOAc trihydrate. The reaction proceeded at room temperature and did not result in aniline formation. Additionally, only minor quantities of azoxy compound impurities were observed. Application of these conditions has, however, been limited. Gratifyingly, when applied to our systems these conditions cleanly gave the desired hydroxamic acid product (Table 2). Crucially, no over-reduction to the lactam was observed over the time course necessary for complete consumption of starting material. Furthermore, these conditions effected reduction at room temperature for substrates **8a**−**i**, whereas the $SnCl_2$/EtOH system required a reaction temperature of 60 °C. This observation suggests that the $SnCl_2$/NaOAc conditions provide a more activated reducing system than the more conventional $SnCl_2$/EtOH system. As shown in Table 2, use of $SnCl_2$/NaOAc enabled the synthesis of a wide range of substituted cyclic hydroxamic acids bearing substituents at the R_2, R_3, and R_4 positions with varied electronic properties. For ease of isolation and purification, the crude amino hydroxamic acids were protected in situ as the di-Boc derivatives; after chromatographic purification, deprotection was carried out with acid. This reaction sequence furnished our desired products **19a**−**i** in high purity, without concomitant generation of byproduct.

Synthesis of C-8 Substituted Cyclic Hydroxamic Acids. In the cases of substrates **8k** and **8*l*** (Table 2, entries 11 and 12), which bear a substituent ortho to the nitro group, the mild $SnCl_2$/NaOAc reductive cyclization conditions did not yield any reduction products; starting material remained unchanged under these conditions. We attributed this low reactivity to the steric hindrance around the nitro group. Indeed, in the case where $R_1 = CF_3$ (Table 2, entry 11), cyclization could be achieved using $SnCl_2$ in EtOH at 60 °C. However, this process was sluggish, requiring 1−2 days for starting material to be consumed and leading to a mixture of the hydroxamic

dx.doi.org/10.1021/jo200530j |*J. Org. Chem.* 2011, 76, 3484–3497

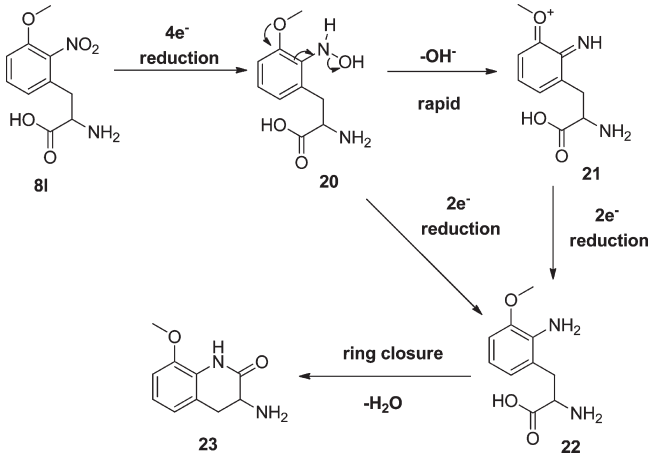
Table 2. Reductive Cyclization of 2-Nitrophenylalanine Derivatives to Hydroxamic Acids Using a $SnCl_2$/NaOAc System



entry	substrate	R_1	R_2	R_3	R_4	% yield of **18a**−***l***[a]	% yield of **19a**−***l***
1	**8a**	H	H	H	Me	86	80
2	**8b**	H	H	H	F	60	73
3	**8c**	H	H	Me	H	45	85
4	**8d**	H	H	Cl	H	42	86
5	**8e**	H	H	CF_3	H	65	94
6	**8f**	H	H	OCF_3	H	72	86
7	**8g**	H	OMe	H	H	75	90
8	**8h**	H	Me	H	H	35	91
9	**8i**	H	Cl	H	H	18	86
10	**8j**	OCF_3	H	H	H	N/A[b]	N/A
11	**8k**	CF_3	H	H	H	0[c]	N/A
12	**8*l***	OMe	H	H	H	0[c]	N/A

[a] Values represent isolated yields obtained after chromatographic purification. [b] A mixture of desired product and lactam was obtained. The mixture could not be separated chromatographically. [c] No reaction, starting material remained.

Scheme 4. Proposed Reduction Mechanism for Electron-Rich Aromatic Nitro Groups



acid and the lactam derived from over-reduction. For R_1 = OMe (Table 2, entry 12), the use of higher reaction temperatures gave complete conversion to the lactam product, and the desired hydroxamic acid product was never observed. In such electron-rich ortho-substituted systems, lone pair donation from the electron-donating group may result in rapid elimination of the hydroxyl group of the hydroxylamine (Scheme 4). The cationic intermediate thus formed (**21**) can then undergo a second reduction to give the aniline **22**, which would subsequently cyclize to lactam **23**. Clearly, for substrates bearing R_1 substituents, an alternative strategy was required.

Activated Ester Strategy: Increasing Cyclization Rate. We postulated that more rapid cyclization of the challenging ortho-substituted substrates such as **8j**, **8k**, and **8*l***, through use of an ester in place of the carboxylic acid, would minimize the problem of over-reduction and subsequent isolation of the lactam by-product; elimination of the hydroxylamine oxygen atom, either via the lone pair participation mechanism described in Scheme 4 or by direct reduction, is much less favored in the cyclized hydroxamic acid product **28a** as compared with the uncyclized systems **26a** or **27a** (Scheme 5).

To test this hypothesis, amino acid **8j** was *N*-protected as the Boc derivative, and converted to the methyl ester (**24a**) and the corresponding trifluoroethyl ester (**25a**) (Scheme 5). These compounds were subjected to a screen of various reductive cyclization conditions and the outcome was monitored by LC-MS (Table 3). Treatment of methyl ester **24a** and trifluoroethyl ester **25a** with $SnCl_2$ at 60 °C gave sluggish reactions, which required 24 h for the majority of the starting materials to be consumed (Table 3, entries 1 and 2). In both cases, significant amounts of the over-reduced lactam **29** were observed. Trifluoroethyl ester substrate **25a** did give improved results over the simple methyl ester, however (Table 3, entries 1 and 2). We therefore sought improved conditions to further minimize the formation of lactam **29**.

Selective reduction of nitroaromatics to hydroxylamines using Pt-catalyzed hydrogenation procedures has been reported.[18] The key to selectivity in these examples was the use of solvent additives such as *N*-methylmorpholine, pyridine, or DMSO, which act to dope the Pt catalyst. Upon further investigation of this strategy, we found that use of pyridine as the hydrogenation solvent was optimal for these cyclic hydroxamic acid systems. Subjecting the *N*-Boc-protected trifluoroethyl ester **25a** to catalytic hydrogenation conditions using 5% Pt/C in pyridine solvent gave excellent results (Table 3, entry 4). This reagent system provided clean conversion to the desired product **28a**, with no lactam byproduct **29** observed (Table 3, entry 4 and Table 4, entry 1). Under these conditions, reductive cyclization

dx.doi.org/10.1021/jo200530j |*J. Org. Chem.* 2011, 76, 3484–3497

Scheme 5. Activated Ester Strategy for Increasing Cyclization Rate

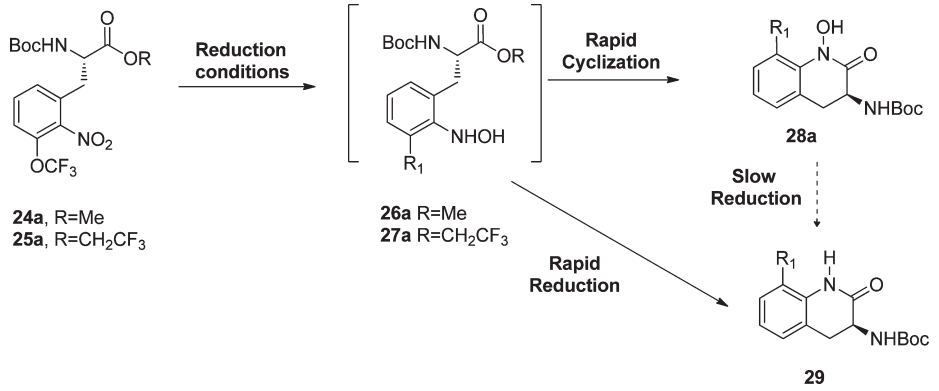


Table 3. Reductive Cyclization of Ester Substrates Using Hydrogenation Conditions

entry	substrate	conditions	product ratio[a] (**28a**:**29**)
1	**24a**	$SnCl_2$, EtOH, 60 °C, 24 h	2:1
2	**25a**	$SnCl_2$, EtOH, 60 °C, 24 h	4:1[b]
3	**24a**	H_2 (30 psi), 5% Pt/C, pyridine, 3 h	2:1
4	**25a**	H_2 (30 psi), 5% Pt/C, pyridine, 3 h	1:0
5	**8j**	H_2 (30 psi), 5% Pt/C, pyridine, 3 h	1:2.3

[a] Values represent ratios obtained from the UV trace of LC-MS analysis. [b] Approximately 20% starting material **25a** remains.

of methyl ester substrate **24a** gave inferior selectivity (Table 3, entry 3), although complete consumption of starting material was observed in only 3 h. The pyridine solvent is crucial to the success of the reaction, as it provides milder reaction conditions by slightly poisoning the hydrogenation catalyst. Employing other solvents such as MeOH produced **29** as a major byproduct. Use of the ester is also key to the success of this transformation: under these conditions, the parent amino acid **8j** yields the undesired lactam as the major product (Table 3, entry 5).

Upon the successful application of these conditions to the efficient synthesis of **28a**, we sought to apply these conditions to the synthesis of further examples of electronically activated and/or sterically hindered substrates. Trifluoroethyl esters **25b**−**f** were prepared and subjected to these hydrogenation conditions (Table 4). Gratifyingly, cyclized hydroxamic products **28b**−**f** were obtained in good yields and again no lactam byproduct was observed. These Boc-protected products were readily deprotected with acid to give **30b**−**f**. In the case of **25d** (R_1 = OPh; Table 4, entry 4), the cyclization reaction proceeded sluggishly, resulting in only 33% yield of the desired product **28d** after 10 h. Starting material **25d** could be recovered and recycled. We attributed this sluggish reaction to the considerable steric hindrance around the nitro group in this molecule. In the remainder of the examples in Table 4, complete conversion of starting material to cyclized product was observed.

In conclusion, we have described two efficient asymmetric synthetic approaches toward the biologically active cyclic hydroxamic acids, both employing a selective nitro group reductive cyclization. In the case of unhindered substrates, a buffered $SnCl_2$ reduction system efficiently provides the desired product. We have also demonstrated that the more challenging ortho-substituted, electron-rich cyclic *N*-aryl hydroxamic acids can be accessed by reductive cyclization of activated trifluoroethyl ester substrates under mild hydrogenation conditions. Both approaches furnish the hydroxamic acid product without production of the undesired lactam or other byproduct.

EXPERIMENTAL SECTION

General Experimental Details. Unless otherwise stated, all starting materials and solvents were obtained from commercial sources and used without further purification. Proton and carbon NMR spectra were obtained using 500 and 400 MHz machines. Enantiomeric excess values were measured using either Chiral SFC [Chiralcel OD-H column (4.6 mm × 25 cm)] or Chiral HPLC [Chirobiotic V column, 4.6 mm × 25 cm]. Flash chromatography was carried out on either an ISCO or BiotageCompanion automated purification system using prepacked ISCO brand silica gel cartridges.

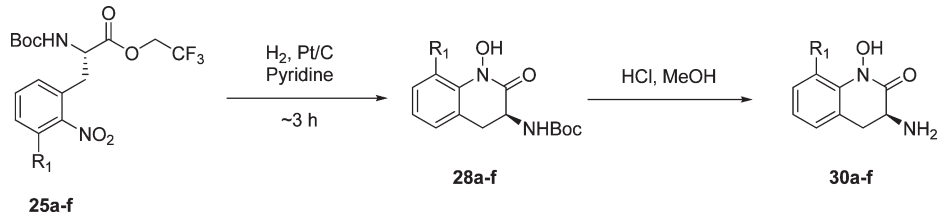
Preparation of 2-Nitrobenzyl Bromides: Preparation of 5a−k

2-(Bromomethyl)-1-methyl-3-nitrobenzene (5a): To a solution of 2-methyl-6-nitrobenzoic acid (5 g, 28 mmol) in THF (25 mL) cooled to 0 °C was added $NaBH_4$ (3.13 g, 82.8 mmol) in small portions. BF_3−Me_2O (7.60 mL, 82.8 mmol) was then added dropwise at 0 °C, and the reaction mixture was allowed to stir overnight, while warming from 0 °C to rt. The reaction mixture was cooled with ice−water, and solid NH_4Cl was added in small portions. Water (100 mL) and EtOAc (500 mL) were added and the water layer was basified using solid $NaHCO_3$. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The crude product mixture was purified on a silica gel column (80 g), eluting with 30% EtOAc/heptane, to give (2-methyl-6-nitrophenyl)methanol (3.90 g, 85% yield) as a light yellow solid. To a solution of (2-methyl-6-nitrophenyl)methanol (3.90 g, 23.3 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added a solution of 1 M PBr_3 in CH_2Cl_2 (46.7 mL, 46.7 mmol). The reaction mixture was allowed to stir overnight at rt, then was diluted with 200 mL of CH_2Cl_2 and poured onto ice−water. After neutralization with solid $NaHCO_3$, the organic layer was separated and washed with H_2O (2 × 25 mL) and saturated aq NaCl (1 × 25 mL), dried over Na_2SO_4, and concentrated in vacuo. The crude product mixture was purified on a silica gel column (120 g), eluting with 20% EtOAc/heptane to give 2-(bromomethyl)-1-methyl-3-nitrobenzene (4.6 g, 86% yield) as a light yellow solid. ^1H NMR (500 MHz, $CDCl_3$) δ 2.54 (s, 3H), 4.73 (s, 2H), 7.35−7.39 (m, 1H), 7.47 (d, J = 7.8 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 140.5, 135.5, 130.2, 129.3, 123.1, 24.9, 19.6. Anal. Calcd for $C_8H_8BrNO_2$: C, 41.77; H, 3.50; Br, 34.73, N, 6.09. Found: C, 42.00; H, 3.58; Br, 34.52; N, 5.99.

2-(Bromomethyl)-1-fluoro-3-nitrobenzene (5b): To a solution of 2-fluoro-6-nitrobenzoic acid (2.7 g, 15 mmol) in anhydrous THF

dx.doi.org/10.1021/jo200530j |*J. Org. Chem.* 2011, 76, 3484–3497

Table 4. Reductive Cyclization of Trifluoroethyl Ester Substrates to Hydroxamic Acids



25a-f 28a-f 30a-f

entry	substrate	R_1	% yield of **28a−f**[a]	% yield of **30a−f**
1	**25a**	OCF_3	88	82
2	**25b**	OMe	64	70
3	**25c**	CF_3	66	56
4	**25d**	OPh	33[b]	94
5	**25e**	Me	46	100
6	**25f**	Cl	60	69

[a] Values represent isolated yields after chromatographic purification. [b] 30% of starting material **25d** was recovered unchanged after 10 h.

(5 mL) at 0 °C was added sodium borohydride (1.67 g, 43.8 mmol) in two portions. After all the gas evolution subsided, $BF_3 \cdot OMe_2$ (4.1 mL, 43.8 mmol) was added dropwise at 0 °C. The reaction was stirred at 0 °C for 30 min, then warmed to rt and stirred overnight. The mixture was quenched with aq ammonium chloride (10 mL). The aqueous layer was extracted with EtOAc (50 mL), then washed with brine (3 × 50 mL) and water (3 × 50 mL). The organic layer was dried over sodium sulfate and purified by flash chromatography on silica gel to provide (2-fluoro-6-nitrophenyl)methanol in 88% yield. To a solution of (2-fluoro-6-nitrophenyl)methanol (2.1 g, 12 mmol) in 8 mL of anhydrous CH_2Cl_2 was added CBr_4 (10.3 g, 30.7 mmol) and PPh_3 (8.1 g, 30.7 mmol) and the reaction was stirred for 2 h at rt. The mixture was diluted with EtOAc (50 mL), then washed with brine (3 × 50 mL) and water (3 × 50 mL). The organic layer was dried over sodium sulfate and concentrated under reduced pressure. The crude product mixture was purified by flash chromatography on silica gel eluting with 0−50% EtOAc/heptane to give 2-(bromomethyl)-1-fluoro-3-nitrobenzene in 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 1H), 7.46 (dt, J = 5.5, 8.3 Hz, 1H), 7.42−7.34 (m, 1H), 4.80 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 130.4, 121.4, 121.4, 121.3, 121.1, 19.4.

2-(Bromomethyl)-4-methyl-1-nitrobenzene (5c): To a solution of (5-methyl-2-nitrophenyl)methanol (5.30 g, 31.7 mmol) in CH_2Cl_2 (100 mL) was added CBr_4 (13.3 g, 50.7 mmol, 1.6 equiv) then PPh_3 (17.0 g, 50.7 mmol, 1.6 equiv). The reaction was allowed to stir at rt for 16 h. The reaction mixture was adsorbed onto silica and purified by flash chromatography on silica gel (120 g) eluting with 0−20% EtOAc/heptane to give 2-(bromomethyl)-4-methyl-1-nitrobenzene (7.29 g, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.3 Hz, 1H), 7.36 (d, J = 1.2 Hz, 1H), 7.28 (dd, J = 1.7, 8.3 Hz, 1H), 4.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 145.1, 133.0, 132.8, 130.1, 125.7, 29.3, 21.3. Anal. Calcd for $C_8H_8BrNO_2$: C, 41.77; H, 3.50; N, 6.09. Found: C, 41.99; H, 3.55; N, 6.03.

2-(Bromomethyl)-4-chloro-1-nitrobenzene (5d): To a solution of (5-chloro-2-nitrophenyl)methanol (1.04, 5.54 mmol) in CH_2Cl_2 (20 mL) was added CBr_4 (3.34 g, 9.98 mmol, 1.8 equiv) then PPh_3 (2.63 g, 9.98 mmol, 1.8 equiv). The reaction was allowed to stir at rt for 16 h. The reaction mixture was adsorbed onto silica and purified by flash chromatography on silica gel (40 g) eluting with 0−20% EtOAc/heptane to give 2-(bromomethyl)-4-chloro-1-nitrobenzene (0.7 g, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.6 Hz, 1H), 7.56 (s, 1H), 7.43 (dd, J = 2.1, 8.8 Hz, 1H), 4.77 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 135.0, 132.7, 129.8, 127.2, 28.2. Anal. Calcd for $C_7H_5BrClNO_2$: C, 33.57; H, 2.01; N, 5.59. Found: C, 33.69; H, 1.95; N, 5.46.

2-(Bromomethyl)-1-nitro-4-(trifluoromethyl)benzene (5e): To a solution of 2-methyl-1-nitro-4-(trifluoromethyl)benzene (6.25 g, 30.5 mmol, 1 equiv) in DMF (10 mL) was added DMF−DMA (9.06 mL, 60.9 mmol, 2 equiv). The reaction mixture was heated at 100 °C for 24 h. The DMF was evaporated off and the residue was dissolved in 1:1 THF−H_2O (10 mL:10 mL). $NaIO_4$ was added to the solution and the mixture was allowed to stir at rt for 18 h. The mixture was then filtered to remove the solids. Water was added to the filtrate, which was then extracted with EtOAc. The EtOAc layer was dried ($MgSO_4$), filtered, and concentrated to give crude 2-nitro-5-(trifluoromethyl)benzaldehyde. To a solution of the crude 2-nitro-5-(trifluoromethyl)benzaldehyde in THF (100 mL) at 0 °C was added $NaBH_4$ (2.35 g, 61 mmol, 2 equiv). The mixture was allowed to stir at rt for 2 h then quenched slowly with water and 1 M HCl. The mixture was then extracted with EtOAc, dried ($MgSO_4$), filtered and concentrated. The crude product mixture was purified by flash chromatography on silica gel (80 g) eluting with 0−100% EtOAc/heptane to give [2-nitro-5-(trifluoromethyl)phenyl]methanol (3.66 g, 54% over 3 steps). To a solution of [2-nitro-5-(trifluoromethyl)-phenyl]methanol (3.66 g, 16.6 mmol, 1 equiv) in CH_2Cl_2 (20 mL) was added CBr_4 (7.14 g, 21.5 mmol, 1.3 equiv) then PPh_3 (5.64 g, 21.5 mmol, 21.5 equiv). The reaction was allowed to stir at rt for 16 h. The reaction mixture was adsorbed onto silica and purified by flash chromatography on silica gel (80 g) eluting with 0−20% EtOAc/heptane to give 2-(bromomethyl)-1-nitro-4-(trifluoromethyl)benzene (3.72 g, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 1.6 Hz, 1H), 7.72 (dd, J = 1.8, 8.6 Hz, 1H), 4.79 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 135.1, 133.8, 129.6, 126.6, 126.0, 123.9, 27.4. Anal. Calcd for $C_8H_5BrF_3NO_2$: C, 33.83; H, 1.77; N, 4.93. Found: C, 33.91; H, 1.71; N, 4.86.

2-(Bromomethyl)-1-nitro-4-(trifluoromethoxy)benzene (5f): To a solution of methyl 2-amino-5-(trifluoromethoxy)benzoate (15 g, 63.80 mmol) in toluene (150 mL) was added *m*-CPBA (44.02 g, 255 mmol) at 0 °C. The reaction mixture was stirred at rt for 12 h, then was concentrated and adjusted to basic pH with aq $NaHCO_3$ solution. The mixture was extracted with EtOAc and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated to obtain crude methyl 2-nitro-5-(trifluoromethoxy)benzoate (13.5 g). To a solution of methyl 2-nitro-5-(trifluoromethoxy)benzoate (5.0 g, 19 mmol) in THF (150 mL)

dx.doi.org/10.1021/jo200530j |*J. Org. Chem.* 2011, 76, 3484–3497

was added a solution of $LiBH_4$ in THF (2 M, 10.4 mL, 20.8 mmol) at 0 °C. The reaction mixture was stirred at rt for 6 h. The mixture was quenched with 1 N HCl solution at −40 °C and extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to obtain crude material, which was purified by flash chromatography on silica gel, eluting with 5% EtOAc in petroleum ether to afford [2-nitro-5-(trifluoromethoxy)phenyl]methanol (1.6 g, 35% yield). To a solution of [2-nitro-5-(trifluoromethoxy)phenyl]methanol (1.5 g, 10 mmol) in toluene (20 mL) was added PBr_3 (2.9 mL, 30.0 mmol) at 0 °C and the reaction mixture was stirred at rt for 48 h. The reaction mixture was then concentrated, quenched with water, and extracted with EtOAc. The organic layer was dried over Na_2SO_4, filtered, and concentrated to obtain crude product, which was purified by silica gel chromatography, eluting with 5% EtOAc in petroleum ether to afford 2-(bromomethyl)-1-nitro-4-(trifluoromethoxy)benzene (640 mg, 31% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 9.0 Hz, 1H), 7.42 (d, J = 2.3 Hz, 1H), 7.36−7.26 (m, 1H), 4.81 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 145.6, 135.9, 128.0, 124.2, 120.8, 120.3, 28.2. Anal. Calcd for $C_8H_5BrF_3NO_3$: C, 32.04; H, 1.58; N, 4.59. Found: C, 32.03; H, 1.68; N, 4.68.

1-(Bromomethyl)-4-methoxy-2-nitrobenzene (5g): To a solution of (4-methoxy-2-nitrophenyl)methanol (5.00 g, 27.3 mmol, 1 equiv) in Et_2O at 0 °C was added PBr_3 (8.87 g, 32.8 mmol, 1.2 equiv). The mixture was allowed to stir for 3 h then poured onto ice−water. The aqueous layer was extracted with Et_2O, washed with brine, dried ($MgSO_4$), filtered, and concentrated. The crude product mixture was purified by flash chromatography on silica gel (40 g), eluting with 0−50% EtOAc/heptane to give 1-(bromomethyl)-4-methoxy-2-nitrobenzene (4.4 g, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 2.7 Hz, 1H), 7.47 (d, J = 8.2 Hz, 1H), 7.14 (dd, J = 2.7, 8.6 Hz, 1H), 4.81 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 148.3, 133.3, 124.4, 119.6, 110.0, 55.7, 28.8. Anal. Calcd for $C_8H_8BrNO_3$: C, 39.05; H, 3.28; N, 5.69. Found: C, 39.20; H, 3.24; N, 5.61.

1-(Bromomethyl)-4-methyl-2-nitrobenzene (5h): To a solution of (4-methyl-2-nitrophenyl)methanol (5.28 g, 31.6 mmol) in CH_2Cl_2 (100 mL) was added CBr_4 (16.9 g, 50.5 mmol, 1.6 equiv) then PPh_3 (13.3 g, 50.5 mmol, 1.6 equiv). The reaction was allowed to stir at rt for 16 h. The reaction mixture was adsorbed onto silica and purified by flash chromatography on silica gel (120 g) eluting with 0−20% EtOAc/heptane to give 1-(bromomethyl)-4-methyl-2-nitrobenzene (2.87 g, 39.5%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.49−7.38 (m, 2H), 4.81 (s, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 140.4, 134.4, 132.4, 129.9, 125.8, 28.9, 21.0. Anal. Calcd for $C_8H_8BrNO_2$: C, 41.77; H, 3.50; N, 6.09. Found: C, 42.23 H, 3.16; N, 6.05.

1-(Bromomethyl)-4-chloro-2-nitrobenzene (5i): To a solution of (4-chloro-2-nitrophenyl)methanol (1.26 g, 6.72 mmol) in CH_2Cl_2 (20 mL) was added CBr_4 (4.05 g, 12.1 mmol, 1.8 equiv) then PPh_3 (3.17 g, 12.1 mmol, 1.8 equiv). The reaction was allowed to stir at rt for 16 h. The reaction mixture was adsorbed onto silica and purified by flash chromatography on silica gel (40 g) eluting with 0−20% EtOAc/heptane to give 1-(bromomethyl)-4-chloro-2-nitrobenzene (1.68 g, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 2.0 Hz, 1H), 7.59−7.53 (m, 1H), 7.53−7.47 (m, 1H), 4.76 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4, 135.6, 134.0, 133.8, 131.6, 125.9, 28.1.

1-(Bromomethyl)-2-nitro-3-(trifluoromethoxy)benzene (5j): To a suspension of sodium perborate (3.59 g, 22.2 mmol, 5 equiv) in trifluoroacetic acid (6 mL) was added 2-amino-3-(trifluoromethoxy)-benzoic acid (0.982 g, 4.43 mmol, 1 equiv). The mixture was heated at reflux overnight. The mixture was cooled and poured onto water. The aqueous layer was then extracted with Et_2O and the organic layer was dried ($MgSO_4$), filtered, and concentrated to give 2-nitro-3-(trifluoromethoxy)-benzoic acid (quantitative yield). To a solution of 2-nitro-3-(trifluoromethoxy)benzoic acid (1.30 g, 5.16 mmol, 1 equiv) in THF (3 mL) at 0 °C was added $NaBH_4$ (593 mg, 15.5 mmol, 3 equiv) then $BF_3 \cdot OMe_2$ (1.45 mL, 15.5 mmol, 3 equiv). The mixture was allowed to stir at rt then quenched with saturated aq NH_4Cl solution. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated to give [2-nitro-3-(trifluoromethoxy)phenyl]methanol (870 mg, 71% yield). To a solution of [2-nitro-3-(trifluoromethoxy)phenyl]methanol (870 mg, 3.67 mmol, 1 equiv) in CH_2Cl_2 (70 mL) at 0 °C was added PBr_3 (2.05 g, 7.34 mmol, 2 equiv) and the reaction was allowed to stir at rt overnight. The reaction mixture was quenched by dropwise addition of saturated aq $NaHCO_3$ until the pH reached 8, followed by dilution with CH_2Cl_2 (10 mL). The separated aqueous phase was washed with EtOAc (2 × 10 mL) and the combined organic layers were washed with water (10 mL), dried over Na_2SO_4, filtered, and concentrated to give 1-(bromomethyl)-2-nitro-3-(trifluoromethoxy)benzene (780 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.49 (m, 1H), 7.48−7.44 (m, 1H), 7.37 (td, J = 1.6, 8.2 Hz, 1H), 4.44 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 140.7, 132.4, 132.1, 129.5, 120.6, 120.3, 25.5.

1-(Bromomethyl)-2-nitro-3-(trifluoromethyl)benzene (5k): A suspension of $NaBO_3$ (22.49 g, 146.2 mmol) in AcOH (30 mL) was heated at 85 °C. A solution of 2-amino-3-(trifluoromethyl)benzoic acid (5.0 g, 24.37 mmol) in acetic acid (20 mL) was then added and the reaction mixture was heated at 95 °C for 24 h. The reaction mixture was poured into water, then extracted with EtOAc and diethyl ether. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to afford crude compound, which was purified by flash chromatography on silica gel, eluting with 10% MeOH in CH_2Cl_2, to afford 2-nitro-3-(trifluoromethyl)benzoic acid (2.1 g, 36.6%). To a solution of 2-nitro-3-(trifluoromethyl)benzoic acid (0.50 g, 2.1 mmol) in dry THF (20.0 mL) was added BH_3−DMS (0.40 mL, 4.2 mmol) in a small amount of THF (5.0 mL) dropwise at 0 °C. The reaction mixture was slowly heated to 60 °C and stirred for 2 h. (The reaction progressed to completion with the formation of two nonpolar spots by TLC.) The reaction mixture was poured into water and 1 N HCl, then extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, concentrated, and purified by flash chromatography on silica gel to afford [2-nitro-3-(trifluoromethyl)phenyl]methanol (300 mg, 64%). To a solution of [2-nitro-3-(trifluoromethyl)phenyl]methanol (0.15 g, 0.67 mmol) in CH_2Cl_2 was added PPh_3 and CBr_4 at 0 °C and the reaction was stirred for 20 min. The reaction mixture was washed with water, dried over Na_2SO_4, filtered, and concentrated to obtain crude product, which was purified by flash chromatography on silica gel, eluting with 10% EtOAc in petroleum ether to give 1-(bromomethyl)-2-nitro-3-(trifluoromethyl)-benzene (100 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, J = 1.0, 7.8 Hz, 1H), 7.70−7.65 (m, 1H), 7.60 (dd, J = 0.6, 7.8 Hz, 1H), 4.37 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.3, 131.1, 129.4, 127.5, 123.4, 123.4, 121.9, 25.0.

Asymmetric Alkylation Reactions: Preparation of 7a−k

***tert*-Butyl N-(diphenylmethylidene)-2-methyl-6-nitro-L-phenylalaninate (7a)—General Procedure A:** To a solution of 2-(bromomethyl)-1-methyl-3-nitrobenzene (**5a**) (1.02 g, 4.41 mmol, 1 equiv) in CH_2Cl_2 (10 mL) cooled to −30 °C was added *tert*-butyl *N*-(diphenylmethylidene)glycinate (1.43 g, 4.86 mmol, 1.1 equiv) and (−)-(*O*)-(9)-allyl-*N*-(9-anthracenylmethyl)cinchodinium bromide (281 mg, 0.44 mmol, 0.1 equiv). CsOH−H_2O (1.10 g, 6.62 mmol, 1.5 equiv) was added and the mixture was allowed to stir for 18 h. The reaction mixture was washed with water, dried (Na_2SO_4), filtered, and concentrated. The crude mixture was purified by flash chromatography on silica gel, eluting with CH_2Cl_2 (isocratic) to give *tert*-butyl *N*-(diphenylmethylidene)-2-methyl-6-nitro-L-phenylalaninate (**7a**) (1.41 g, 72% yield, 91% ee). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47 (s, 9H), 2.38 (s, 3H), 3.54 (dd, J = 13.9, 3.4 Hz, 1H), 3.67−3.72 (m, 1H), 4.28 (dd, J = 10.5, 3.4 Hz, 1H), 7.20−7.40 (m, 12H), 7.48−7.52 (m, 1H), 7.55−7.62 (m, 5H), 7.81−7.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 170.9, 170.6, 151.7, 140.9, 139.1, 135.9, 134.5,

132.7,130.5, 130.2, 129.0, 128.2, 127.6, 127.0, 122.5, 81.6, 66.2, 31.3, 28.3. Anal. Calcd for $C_{27}H_{28}N_2O_4$: C, 72.95; H, 6.35; N, 6.30. Found: C, 72.94; H, 6.51; N, 6.70.

***tert*-Butyl *N*-(diphenylmethylidene)-2-fluoro-6-nitro-L-phenylalaninate (7b):** The title compound was prepared from **5b** (1.2 g, 5.1 mmol, 1 equiv) according to general procedure A to give *tert*-butyl *N*-(diphenylmethylidene)-2-fluoro-6-nitro-L-phenylalaninate (**7b**) (1.8 g, 79% yield, 89% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84−7.74 (m, 1H), 7.63−7.57 (m, 1H), 7.54−7.51 (m, 1H), 7.47 (dd, J = 0.6, 7.4 Hz, 1H), 7.37−7.15 (m, 7H), 6.66 (d, J = 7.0 Hz, 2H), 4.25 (ddd, J = 0.9, 4.5, 9.2 Hz, 1H), 3.81−3.42 (m, 2H), 1.59−1.20 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 169.9, 160.2, 150.8, 139.1, 135.8, 130.3, 130.0, 128.8, 128.5, 128.2, 127.8, 127.4, 122.2, 120.3, 119.8, 119.6, 81.5, 65.1, 28.0; HRMS (m/z) $[M + H]^+$ calcd for $C_{26}H_{26}FN_2O_4$ 449.1871, found 449.1861.

***tert*-Butyl *N*-(diphenylmethylidene)-5-methyl-2-nitro-L-phenylalaninate (7c):** The title compound was prepared from **5c** (4.19 g, 18.2 mmol, 1 equiv) according to general procedure A to give *tert*-butyl *N*-(diphenylmethylidene)-5-methyl-2-nitro-L-phenylalaninate (**7c**) (5.97 g, 74% yield, 100% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 1H), 7.61−7.54 (m, 2H), 7.42−7.25 (m, 6H), 7.18 (d, J = 1.8 Hz, 1H), 7.11 (dd, J = 1.5, 8.3 Hz, 1H), 6.63 (d, J = 7.2 Hz, 2H), 4.32 (dd, J = 4.3, 9.4 Hz, 1H), 3.69 (dd, J = 4.2, 13.2 Hz, 1H), 3.39 (dd, J = 9.4, 13.3 Hz, 1H), 2.30 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.3, 147.2, 143.5, 139.2, 136.0, 134.9, 133.6, 130.2, 128.7, 128.4, 128.1, 127.9, 127.9, 127.4, 124.8, 81.3, 65.8, 36.6, 28.0, 21.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{27}H_{28}N_2O_4$ 445.2121, found, 445.2117. $[\alpha]^{20}_D$ −187.9 (c 0.28, MeOH).

***tert*-Butyl 5-chloro-*N*-(diphenylmethylidene)-2-nitro-L-phenylalaninate (7d):** The title compound was prepared from **5d** (1.33 g, 5.31 mmol, 1 equiv) according to general procedure A to give *tert*-butyl 5-chloro-*N*-(diphenylmethylidene)-2-nitro-L-phenylalaninate (**7d**) (1.24 g, 50% yield, 75% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.6 Hz, 1H), 7.57−7.50 (m, 2H), 7.41−7.22 (m, 8H), 6.72 (d, J = 6.6 Hz, 2H), 4.27 (dd, J = 4.3, 9.0 Hz, 1H), 3.63 (dd, J = 4.5, 13.5 Hz, 1H), 3.42 (dd, J = 9.0, 13.7 Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 170.1, 148.1, 139.2, 138.9, 136.2, 135.9, 134.1, 130.6, 130.3, 129.0, 128.8, 128.5, 128.2, 127.7, 126.3, 81.9, 65.8, 36.5, 28.2. Anal. Calcd for $C_{26}H_{25}ClN_2O_4$: C, 67.17; H, 5.42; N, 6.03. Found: C, 66.96; H, 5.38; N, 5.93.

***tert*-Butyl *N*-(diphenylmethylidene)-2-nitro-5-(trifluoromethyl)-L-phenylalaninate (7e):** The title compound was prepared from **5e** (40.8 g, 143 mmol, 1 equiv) according to general procedure A to give *tert*-butyl *N*-(diphenylmethylidene)-2-nitro-5-(trifluoromethyl)-L-phenylalaninate (**7e**) (51.56 g, 72% yield, 90% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.84 (m, 1H), 7.70−7.65 (m, 1H), 7.60−7.24 (m, 9H), 6.71−6.59 (m, 2H), 4.30−4.21 (m, 1H), 3.65−3.57 (m, 1H), 3.53−3.44 (m, 1H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 170.0, 152.0, 139.0, 137.8, 134.7, 134.2, 133.9, 132.6, 131.4, 130.8, 130.3, 128.9, 128.5, 128.5, 128.2, 127.6, 124.3, 123.1, 82.1, 65.8, 36.1, 28.2.

***tert*-Butyl *N*-(diphenylmethylidene)-2-nitro-5-(trifluoromethoxy)-L-phenylalaninate (7f):** The title compound was prepared from **5f** (810 mg, 2.70 mmol, 1 equiv) according to general procedure A to give *tert*-butyl *N*-(diphenylmethylidene)-2-nitro-5-(trifluoromethoxy)-L-phenylalaninate (**7f**) (700 mg, 50.4% yield, 86% ee). ^{1}H NMR (400 MHz, CD_3OD) δ 8.03−7.96 (m, 1H), 7.54−7.44 (m, 2H), 7.43−7.18 (m, 8H), 6.71−6.52 (m, 2H), 4.38−4.22 (m, 1H), 3.69−3.57 (m, 1H), 3.43−3.31 (m, 1H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 172.7, 170.3, 151.3, 147.9, 138.9, 137.7, 136.3, 135.9, 132.6, 130.6, 129.8, 128.8, 128.6, 128.3, 127.9, 127.2, 127.1, 125.3, 121.6, 119.7, 81.9, 65.4, 35.9, 27.0.

***tert*-Butyl *N*-(diphenylmethylidene)-*O*-methyl-2-nitro-L-tyrosinate (7g):** The title compound was prepared from **5g** (2.5 g, 10.1 mmol, 1 equiv) according to general procedure A to give *tert*-butyl *N*-(diphenylmethylidene)-*O*-methyl-2-nitro-L-tyrosinate (**7g**) (4.15 g, 89% yield, 94% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58−7.51 (m, 2H), 7.38−7.21 (m, 8H), 6.96 (dd, J = 2.7, 8.6 Hz, 1H), 6.63 (d, J = 6.6 Hz, 2H), 4.26 (dd, J = 4.1, 9.2 Hz, 1H), 3.79 (s, 3H), 3.59 (dd, J = 4.1, 13.5 Hz, 1H), 3.30 (dd, J = 9.4, 13.7 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 170.7, 158.8, 150.1, 139.6, 136.4, 135.2, 130.6, 129.0, 128.7, 128.5, 128.2, 127.7, 125.8, 119.5, 109.4, 81.6, 66.3, 56.1, 36.2, 28.3; HRMS (m/z) $[M + H]^+$ calcd for $C_{27}H_{29}N_2O_5$ 461.2070, found 461.2081; $[\alpha]^{20}_D$ −171.9 (c 0.725, MeOH).

***tert*-Butyl *N*-(diphenylmethylidene)-4-methyl-2-nitro-L-phenylalaninate (7h):** The title compound was prepared from **5h** (2.45 g, 10.65 mmol, 1 equiv) according to general procedure A to give *tert*-butyl *N*-(diphenylmethylidene)-4-methyl-2-nitro-L-phenylalaninate (**7h**) (4.2 g, 89% yield, 93% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.61−7.54 (m, 2H), 7.42−7.24 (m, 10H), 6.64 (d, J = 7.0 Hz, 2H), 4.30 (dd, J = 4.1, 9.2 Hz, 1H), 3.65 (dd, J = 4.1, 13.5 Hz, 1H), 3.36 (dd, J = 9.3, 13.4 Hz, 1H), 2.38 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.2, 149.2, 139.1, 137.6, 135.9, 133.7, 133.2, 130.3, 130.1, 128.6, 128.3, 128.0, 127.8, 127.3, 124.7, 81.2, 65.9, 36.0, 27.9, 20.6; HRMS (m/z) $[M + H]^+$ calcd for $C_{27}H_{28}N_2O_4$ 445.2121, found 445.2135; $[\alpha]^{20}_D$ −120 (c 0.23, MeOH).

***tert*-Butyl 4-chloro-*N*-(diphenylmethylidene)-2-nitro-L-phenylalaninate (7i):** The title compound was prepared from **5i** (1.5 g, 3.2 mmol, 1 equiv) according to general procedure A to give *tert*-butyl 4-chloro-*N*-(diphenylmethylidene)-2-nitro-L-phenylalaninate (**7i**) (1.19 g, 49% yield, 90% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 2.1 Hz, 1H), 7.59−7.49 (m, 2H), 7.41−7.24 (m, 8H), 6.66 (d, J = 6.8 Hz, 2H), 4.26 (dd, J = 4.1, 9.2 Hz, 1H), 3.61 (dd, J = 4.2, 13.4 Hz, 1H), 3.35 (dd, J = 9.2, 13.5 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 170.2, 150.0, 139.2, 136.0, 135.4, 133.3, 132.7, 132.3, 130.6, 129.0, 128.8, 128.5, 128.2, 127.6, 124.8, 81.9, 65.9, 36.1, 28.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{26}H_{26}ClN_2O_4$ 465.1575, found 465.1573.

***tert*-Butyl *N*-(diphenylmethylidene)-2-nitro-3-(trifluoromethoxy)-L-phenylalaninate (7j):** The title compound was prepared from **5j** (3.0 g, 10 mmol, 1 equiv) according to general procedure A to give *tert*-butyl *N*-(diphenylmethylidene)-2-nitro-3-(trifluoromethoxy)-L-phenylalaninate (**7j**) (4.8 g, 92% yield, 96% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64−7.57 (m, 2H), 7.45−7.23 (m, 9H), 6.69 (d, J = 7.0 Hz, 2H), 4.23 (dd, J = 5.3, 8.2 Hz, 1H), 3.31−3.17 (m, 2H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 169.8, 144.6, 140.2, 139.2, 135.9, 133.2, 132.6, 130.8, 130.7, 130.6, 130.2, 129.0, 128.8, 128.5, 128.2, 127.5, 119.5, 120.3, 82.0, 66.0, 34.8, 28.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{27}H_{26}N_2O_5F_3$ 515.1788, found 515.1775; $[\alpha]^{20}_D$ −138.68 (c 0.61, MeOH).

***tert*-Butyl *N*-(diphenylmethylidene)-2-nitro-3-(trifluoromethyl)-L-phenylalaninate (7k):** The title compound was prepared from **5k** (970 mg, 3.4 mmol, 1 equiv) according to general procedure A to give *tert*-butyl *N*-(diphenylmethylidene)-2-nitro-3-(trifluoromethyl)-L-phenylalaninate (**7k**) (1.4 g, 82% yield, 96% ee). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.95−7.84 (m, 1H), 7.76−7.68 (m, 2H), 7.53−7.29 (m, 8H), 6.67−6.48 (m, 2H), 4.17−4.07 (m, 1H), 3.26−3.04 (m, 2H), 1.37 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.7, 169.0, 147.3, 138.5, 137.3, 135.1, 131.2, 131.0, 130.6, 129.6, 128.7, 128.4, 128.3, 128.2, 126.8, 126.2, 123.5, 120.7, 120.7, 120.3, 81.3, 65.5, 33.8, 27.5; HRMS (m/z) $[M + H]^+$ calcd for $C_{27}H_{26}N_2O_4F_3$ 499.1839, found 499.1841.

Determination of ee for Asymmetric Alkylation Reactions. Chiral SFC was used to determine ee values of the products **7a**−**d** and **7f**−**j** (Chiralcel OD-H (4.6 mm × 25 cm) column, mobile phase 95/5 CO_2/ propanol, flow rate 2.5 mL/min). In the case of **7e** and **7k**, chiral HPLC was used to determine ee (Chirobiotic V column, 4.6 mm × 25 cm, mobile phase 50/50 MeOH/MeCN, flow rat: 1 mL/min) after conversion to **8e** and **8k**, respectively.

Racemic alkylation products were prepared as standards according to the following general procedure: To a solution of the relevant alkyl bromide **5a**−**k** (1 equiv) in CH_2Cl_2 (10 mL) cooled to −30 °C was added *tert*-butyl *N*-(diphenylmethylidene)glycinate (1.1 equiv) and tetrabutylammonium bromide (0.1 equiv). CsOH (1.5 equiv) was then added and the mixture was allowed to stir for 18 h. The reaction mixture was washed with water, dried (Na_2SO_4), filtered, and concentrated. The crude mixture was purified by flash chromatography on silica gel eluting with CH_2Cl_2 (isocratic) to give the respective racemic products of **7a**−**k**.

Preparation of Chiral Amino Acids 8a−k

2-Methyl-6-nitro-L-phenylalanine (8a)—General Procedure B: To a solution of *tert*-butyl *N*-(diphenylmethylidene)-2-methyl-6-nitro-L-phenylalaninate (**7a**) (190 mg, 0.43 mmol, 1 equiv) in CH_2Cl_2 (5 mL) was added TFA (5 mL). The reaction was allowed to stir at rt for 18 h. The reaction mixture was concentrated to remove TFA. The residue was partitioned between 4 M HCl and Et_2O. The aqueous layer was washed several times with Et_2O. The aqueous layer was then concentrated to give 2-methyl-6-nitro-L-phenylalanine (**8a**) (95 mg, 99% yield) as the HCl salt. ^{1}H NMR (500 MHz, CD_3OD) δ 2.53 (s, 3H), 3.43 (dd, J = 14.2, 7.1 Hz, 1H), 3.62 (dd, J = 14.3, 8.9 Hz, 1H), 4.26 (t, J = 8.0 Hz, 1H), 7.44 (t, J = 7.9 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 169.8, 151.2, 140.7, 135.5, 128.3, 122.9, 52.2, 29.6, 19.1; LC-MS m/e 224 (M + 1). Anal. Calcd for $C_{10}H_{13}ClN_2O_4$: C, 46.08; H, 5.03; Cl, 13.60; N, 10.75. Found; C, 45.89; H, 4.92; Cl, 13.92; N, 10.58. $[\alpha]^{20}_D$ −62.6 (c 0.11, MeOH).

2-Fluoro-6-nitro-L-phenylalanine (8b): The title compound was prepared from **7b** (1.5 g, 3.3 mmol, 1 equiv) according to general procedure B to give 2-fluoro-6-nitro-L-phenylalanine (**8b**) (55 mg, 66% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.92 (td, J = 1.3, 8.0 Hz, 1H), 7.64−7.49 (m, 2H), 4.27 (dd, J = 7.0, 8.4 Hz, 1H), 3.61 (ddd, J = 2.0, 8.4, 13.9 Hz, 1H), 3.47−3.37 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 169.3, 161.9, 150.3, 130.1, 121.1, 120.8, 120.5, 52.3, 26.3; HRMS (m/z) $[M + H]^+$ calcd for $C_9H_9FN_2O_4$ 228.0546, found 228.0544.

5-Methyl-2-nitro-L-phenylalanine (8c): The title compound was prepared from **7c** (5.92 g, 13.3 mmol, 1 equiv) according to general procedure B to give 5-methyl-2-nitro-L-phenylalanine (**8c**) (3.46 g, 100% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 8.04 (d, J = 8.4 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.36 (s, 1H), 4.31 (t, J = 7.4 Hz, 1H), 3.65 (dd, J = 7.0, 13.9 Hz, 1H), 3.38 (dd, J = 7.8, 13.9 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 171.3, 148.5, 146.9, 135.2, 131.7, 131.0, 126.9, 54.8, 35.4, 21.5; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{12}N_2O_4$ 225.0875, found 225.0884. $[\alpha]^{20}_D$ −28.5 (c 0.435, MeOH).

5-Chloro-2-nitro-L-phenylalanine (8d). The title compound was prepared from **7d** (560 mg, 2.29 mmol, 1 equiv) according to general procedure B to give 5-chloro-2-nitro-L-phenylalanine (**8d**) (360 mg, 56% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.04 (d, J = 8.6 Hz, 1H), 7.75 (d, J = 2.3 Hz, 1H), 7.60 (dd, J = 2.3, 9.0 Hz, 1H), 4.12 (t, J = 7.4 Hz, 1H), 3.52 (dd, J = 7.4, 14.1 Hz, 1H), 3.33 (dd, J = 7.4, 14.1 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.5, 148.4, 138.9, 133.7, 129.4, 127.6, 52.9, 33.2. Anal. Calcd for $C_9H_{10}Cl_2N_2O_4$: C, 38.46; H, 3.59; N, 9.97. Found C, 38.49; H, 3.48; N, 10.06.

2-Nitro-5-(trifluoromethyl)-L-phenylalanine (8e): The title compound was prepared from **7e** (6.33 g, 12.7 mmol, 1 equiv) according to general procedure B to give 2-nitro-5-(trifluoromethyl)-L-phenylalanine (**8e**) (3.49 g, 87% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 8.26 (d, J = 8.6 Hz, 1H), 8.01−7.85 (m, 2H), 4.37 (s, 1H), 3.72 (s, 1H), 3.58−3.45 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 168.3, 151.5, 134.3, 131.3, 131.0, 130.3, 126.0, 123.1, 52.8, 33.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{27}H_{26}N_2O_4F_3$ 499.1839, found 499.1833.

2-Nitro-5-(trifluoromethoxy)-L-phenylalanine (8f): The title compound was prepared from **7f** (2 g, 3.89 mmol, 1 equiv) according to general procedure B to give 2-nitro-5-(trifluoromethoxy)-L-phenylalanine (**8f**) (0.8 g, 70% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 8.30−8.22 (m, 1H), 7.56−7.46 (m, 2H), 4.43−4.30 (m, 1H), 3.75−3.62 (m, 1H), 3.54−3.43 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 169.2, 151.8, 147.2, 133.2, 127.6, 124.8, 121.5, 120.3, 52.8, 33.5; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{10}F_3N_2O_5$ 295.0536, found 295.0531.

***O*-Methyl-2-nitro-L-tyrosine (8g):** The title compound was prepared from **7g** (3.6 g, 7.81 mmol, 1 equiv) according to general procedure B to give *O*-methyl-2-nitro-L-tyrosine (**8g**) (1.24 g, 57% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.63 (d, J = 2.5 Hz, 1H), 7.44 (d, J = 8.6 Hz, 1H), 7.28 (dd, J = 2.7, 8.6 Hz, 1H), 4.30 (t, J = 7.4 Hz, 1H), 3.58 (dd, J = 7.0, 14.3 Hz, 1H), 3.35 (t, J = 7.8 Hz, 1H), 3.38−3.33 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 170.7, 161.0, 151.0, 135.2, 122.5, 120.7, 111.2, 56.3, 54.2, 34.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{13}N_2O_5$ 241.0818, found 241.0823; $[\alpha]^{20}_D$ +0.157 (c 0.58, MeOH).

4-Methyl-2-nitro-L-phenylalanine (8h): The title compound was prepared from **7h** (4.3 g, 9.49 mmol, 1 equiv) according to general procedure B to give 4-methyl-2-nitro-L-phenylalanine (**8h**) (2.29 g, 93% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.94 (s, 1H), 7.58−7.50 (m, 1H), 7.41 (d, J = 7.8 Hz, 1H), 4.32 (t, J = 7.5 Hz, 1H), 3.61 (dd, J = 7.2, 14.1 Hz, 1H), 3.35 (dd, J = 7.8, 14.1 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 171.1, 150.6, 141.4, 135.9, 134.5, 128.3, 126.9, 54.6, 34.9, 20.9; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{12}N_2O_4$ 225.0875, found 225.0876; $[\alpha]^{20}_D$ +16.1 (c 0.385, MeOH).

4-Chloro-2-nitro-L-phenylalanine (8i): The title compound was prepared from **7i** (23 mg, 0.094 mmol, 1 equiv) according to general procedure B to give 4-chloro-2-nitro-L-phenylalanine (**8i**) (24 mg, 91% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, J = 2.0 Hz, 1H), 7.79 (dd, J = 2.3, 8.6 Hz, 1H), 7.65 (d, J = 8.6 Hz, 1H), 4.07 (t, J = 7.4 Hz, 1H), 3.46 (dd, J = 7.4, 14.1 Hz, 1H), 3.32 (dd, J = 7.4, 14.1 Hz, 1H); HRMS (m/z) $[M + H]^+$ calcd for $C_9H_{10}ClN_2O_4$ 245.0323, found 245.0319.

2-Nitro-3-(trifluoromethoxy)-L-phenylalanine hydrochloride (8j): To a solution of *tert*-butyl *N*-(diphenylmethylidene)-2-nitro-3-(trifluoromethoxy)-L-phenylalaninate (**7j**) (2.3 g, 4.5 mmol, 1 equiv) in CH_2Cl_2 (20 mL) was added TFA (3 mL). The reaction was allowed to stir at rt for 18 h. The reaction mixture was concentrated to remove TFA, and the residue was partitioned between 4 M HCl and Et_2O. The aqueous layer was washed several times with Et_2O, and then concentrated to give 2-nitro-3-(trifluoromethoxy)-L-phenylalanine (**8j**) (1.48 g, 74% yield) as the HCl salt. ^{1}H NMR (400 MHz, CD_3OD) δ 7.75−7.69 (m, 1H), 7.62−7.54 (m, 2H), 4.28 (t, J = 7.4 Hz, 1H), 3.38−3.34 (m, 1H), 3.25−3.15 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 170.0, 145.5, 141.3, 133.3, 131.0, 130.8, 122.1, 120.1, 54.0, 32.5; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{10}F_3N_2O_5$ 295.0536, found 295.0525; $[\alpha]^{20}_D$ +6.55 (c 0.57, MeOH).

2-Nitro-3-(trifluoromethyl)-L-phenylalanine (8k): The title compound was prepared from **7k** (1.4 g, 2.8 mmol, 1 equiv) according to general procedure B to give 2-nitro-3-(trifluoromethyl)-L-phenylalanine (**8k**) (598 mg, 77% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.02−7.95 (m, 2H), 7.91−7.84 (m, 1H), 4.27−4.11 (m, 1H), 3.29−3.14 (m, 1H), 3.13−2.99 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.5, 169.3, 136.6, 131.8, 129.3, 126.9, 120.9, 52.2, 30.9, 22.5; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{10}F_3N_2O_4$ 279.0587, found 279.0586.

$SnCl_2$ Reductive Cyclization Procedure: Preparation of Hydroxamic Acids 19a−i

(3*S*)-3-Amino-1-hydroxy-5-methyl-3,4-dihydroquinolin-2(1*H*)-one (19a)—General Procedure C (preparation of di-Boc-protected hydroxamic acid intermediate): To a solution of 2-methyl-6-nitro-L-phenylalanine (**8a**) (450 mg, 1.73 mmol, 1 equiv) in THF:MeOH (50 mL:50 mL) at 0 °C was added $SnCl_2$ (1.64 g, 8.63 mmol, 5 equiv) and $NaOAc \cdot 3H_2O$ (2.35 g, 17.3 mmol, 10 equiv). The mixture was allowed to stir, gradually warming to rt over 5 h. NEt_3 (2.4 mL, 17.3 mmol, 10 equiv) and Boc_2O (1.13 g, 5.13 mmol, 3 equiv) were then

added and the mixture was allowed to stir overnight at rt. The mixture was concentrated and the residue was taken up in EtOAc and H_2O. The organic layer was washed several times with water, dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by flash chromatography on silica gel, eluting with 0−100% EtOAc/heptane (containing 1% NEt_3) to give di-Boc-protected product **18a** (660 mg, 89% yield). **General Procedure D:** To a solution of product **18a** (600 mg, 1.53 mmol, 1 equiv) in Et_2O (10 mL) was added 2 M HCl/Et_2O (10 mL). The reaction mixture was stirred overnight at rt. The solid precipitate was filtered off and washed with Et_2O to give (3*S*)-3-amino-1-hydroxy-5-methyl-3,4-dihydroquinolin-2(1*H*)-one (**19a**) (280 mg, 80% yield). ^{1}H NMR (500 MHz, CD_3OD) δ 2.36 (s, 3H), 2.89 (t, J = 14.2 Hz, 1H), 3.40 (dd, J = 15.0, 4.3 Hz, 1H), 4.14 (br s, 1H), 7.00−7.04 (m, 1H), 7.21−7.29 (m, 2H); ^{13}C NMR (500 MHz, CD_3OD) δ 139.1, 136.1, 127.8, 126.2, 118.8, 111.6, 99.9, 49.0, 27.0, 18.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{12}N_2O_2$ 193.0971, found 193.0970; $[\alpha]^{20}_D$ −18.3 (c 0.11, MeOH)

(3*S*)-3-Amino-5-fluoro-1-hydroxy-3,4-dihydroquinolin-2(1*H*)-one (19b): 2-Fluoro-6-nitro-L-phenylalanine (**8b**) (307 mg, 1.34 mmol, 1 equiv) was treated according to general procedure C to give di-Boc-protected product (320 mg, 60% yield). The di-Boc-protected product (150 mg, 0.51 mmol) was treated according to general procedure D to give (3*S*)-3-amino-5-fluoro-1-hydroxy-3,4-dihydroquinolin-2(1*H*)-one (**19b**) (72 mg, 73% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.39−7.28 (m, 1H), 7.18 (d, J = 8.2 Hz, 1H), 6.89 (t, J = 8.7 Hz, 1H), 4.35 (dd, J = 6.6, 14.6 Hz, 1H), 3.53 (dd, J = 6.6, 15.2 Hz, 1H), 2.93 (t, J = 14.9 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 161.7, 159.5, 140.4, 129.7, 111.0, 109.5, 107.4, 48.5, 22.0; HRMS (m/z) $[M + H]^+$ calcd for $C_9H_{10}FN_2O_2$ 197.0721, found 197.0716.

(3*S*)-3-Amino-1-hydroxy-6-methyl-3,4-dihydroquinolin-2(1*H*)-one hydrochloride (19c): 5-Methyl-2-nitro-L-phenylalanine (**8c**) (925 mg, 4.13 mmol, 1 equiv) was treated according to general procedure C to give di-Boc-protected product **18c** (724 mg, 44% yield). Diboc-protected product **18c** (256 mg, 0.65 mmol, 1 equiv) was treated according to general procedure D to give (3*S*)-3-amino-1-hydroxy-6-methyl-3,4-dihydroquinolin-2(1*H*)-one hydrochloride (**19c**) (126 mg, 85% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.27 (d, J = 8.4 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 7.13 (s, 1H), 4.30 (dd, J = 6.6, 14.4 Hz, 1H), 3.23 (dd, J = 6.6, 14.8 Hz, 1H), 3.14 (t, J = 14.6 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 162.9, 137.8, 135.8, 130.2, 129.9, 120.9, 115.0, 50.4, 30.6, 20.9; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{12}N_2O_2$ 193.0977, found 193.0970; $[\alpha]^{20}_D$ −55.7 (c 0.28, MeOH).

(3*S*)-3-Amino-6-chloro-1-hydroxy-3,4-dihydroquinolin-2(1*H*)-one (19d): 5-Chloro-2-nitro-L-phenylalanine (**8d**) (320 mg, 1.3 mmol, 1 equiv) was treated according to general procedure C to give di-Boc-protected product **18d** (230 mg, 43% yield). Di-Boc-protected product **18d** (180 mg, 0.43 mmol, 1 equiv) was treated according to general procedure D to give (3*S*)-3-amino-6-chloro-1-hydroxy-3,4-dihydroquinolin-2(1*H*)-one (**19d**) (93 mg, 86% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.95 (s, 1H), 8.69 (br s, 3H), 7.43 (d, J = 2.0 Hz, 1H), 7.38−7.32 (m, 1H), 7.22 (d, J = 8.6 Hz, 1H), 4.36 (dd, J = 6.6, 14.4 Hz, 1H), 3.25−3.00 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 137.7, 128.5, 128.1, 122.8, 115.5, 48.5, 29.1. Anal. Calcd for $C_9H_{10}Cl_2N_2O_2$: C, 43.40; H, 4.05; N, 11.25. Found C, 43.46; H, 3.60; N, 11.03. HRMS (m/z) $[M + H]^+$ calcd for $C_9H_{10}ClN_2O_2$ 213.0425, found 213.0420.

(3*S*)-3-Amino-1-hydroxy-6-(trifluoromethyl)-3,4-dihydroquinolin-2(1*H*)-one (19e). 2-Nitro-5-(trifluoromethyl)-L-phenylalanine **8e** (457 mg, 1.64 mmol, 1 equiv) was treated according to general procedure C to give di-Boc protected product **18e** (424 mg, 65% yield). Di-Boc-protected product **18e** (226 mg, 0.5 mmol, 1 equiv) was treated according to general procedure D to give (3*S*)-3-amino-1-hydroxy-6-(trifluoromethyl)-3,4-dihydroquinolin-2(1*H*)-one (**19e**) (134 mg, 94% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.15 (br s, 1H), 8.88 (br s, 3H), 7.74 (s, 1H), 7.69 (d, J = 8.6 Hz, 1H), 7.42 (d, J = 8.6 Hz, 1H), 4.44 (dd, J = 6.4, 14.6 Hz, 1H), 3.44−3.30 (m, 1H), 3.29−3.14 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.8, 143.0, 126.0, 125.9, 124.6, 124.3, 121.7, 114.2, 48.4, 29.1. Anal. Calcd for $C_{10}H_{10}F_3N_2O_2Cl$: C, 42.49; H, 3.57; N, 9.91. Found: C, 42.21; H, 3.35; N, 9.70.

(3*S*)-3-Amino-1-hydroxy-6-(trifluoromethoxy)-3,4-dihydroquinolin-2(1*H*)-one (19f): 2-Nitro-5-(trifluoromethoxy)-L-phenylalanine (**8f**) (203 mg, 0.67 mmol, 1 equiv) was treated according to general procedure C to give di-Boc protected product **18f** (203 mg, 72% yield). Di-Boc-protected product **18f** (106 mg, 0.22 mmol, 1 equiv) was treated according to general procedure D to give (3*S*)-3-amino-1-hydroxy-6-(trifluoromethoxy)-3,4-dihydroquinolin-2(1*H*)-one (**19f**) (61 mg, 89% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.01 (br s, 1H), 8.77 (br s, 3H), 7.40 (s, 1H), 7.31 (s, 2H), 4.40 (dd, J = 6.6, 14.4 Hz, 1H), 3.32−3.21 (m, 1H), 3.20−3.06 (m, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.3, 144.5, 138.9, 122.8, 122.0, 121.8, 121.5, 115.3, 48.4, 29.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{10}F_3N_2O_3$ 263.0638, found 263.0640.

(3*S*)-3-Amino-1-hydroxy-7-methoxy-3,4-dihydroquinolin-2(1*H*)-one (19g): 4-Methyl-2-nitro-L-phenylalanine (**8g**) (1.2 g, 4.33 mmol, 1 equiv) was treated according to general procedure C to give di-Boc protected product **18g** (1.33 g, 75% yield). Di-Boc-protected product **18g** (600 mg, 1.47 mmol, 1 equiv) was treated according to general procedure D to give (3*S*)-3-amino-1-hydroxy-7-methoxy-3,4-dihydroquinolin-2(1*H*)-one (**19g**) (323 mg, 90% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.20 (d, J = 8.2 Hz, 1H), 6.95 (d, J = 2.5 Hz, 1H), 6.69 (dd, J = 2.5, 8.4 Hz, 1H), 4.29 (dd, J = 6.4, 14.6 Hz, 1H), 3.81 (s, 3H), 3.25−3.16 (m, 1H), 3.13−3.00 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.0, 159.5, 140.3, 129.2, 112.0, 108.8, 100.0, 55.6, 48.6, 28.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{13}N_2O_3$ 209.0920, found 209.0915; $[\alpha]^{20}_D$ −36.79 (c 0.41, MeOH).

(3*S*)-3-Amino-1-hydroxy-7-methyl-3,4-dihydroquinolin-2(1*H*)-one hydrochloride (19h): 4-Methyl-2-nitro-L-phenylalanine (**8h**) (2.27 g, 10.2 mmol, 1 equiv) was treated according to general procedure C to give di-Boc protected product **18h** (1.40 g, 35% yield). Di-Boc-protected product **18h** (529 mg, 1.35 mmol, 1 equiv) was treated according to general procedure D to afford (3*S*)-3-amino-1-hydroxy-7-methyl-3,4-dihydroquinolin-2(1*H*)-one hydrochloride (**19h**) (289 mg, 91% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.23 (s, 1H), 7.18 (d, J = 7.6 Hz, 1H), 6.96 (dd, J = 0.7, 7.5 Hz, 1H), 4.30 (dd, J = 6.6, 14.6 Hz, 1H), 3.25 (dd, J = 6.5, 14.7 Hz, 1H), 3.12 (t, J = 14.7 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 163.2, 140.2, 140.0, 129.2, 126.4, 118.0, 115.5, 50.5, 30.2, 21.6; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{12}N_2O_2$ 193.0977, found 193.0980; $[\alpha]^{20}_D$ −29.1 (c 0.45, MeOH).

(3*S*)-3-Amino-7-chloro-1-hydroxy-3,4-dihydroquinolin-2(1*H*)-one (19i): 4-Chloro-2-nitro-L-phenylalanine (**8i**) (403 mg, 1.4 mmol, 1 equiv) was treated according to general procedure C to give di-Boc protected product **18i** (107 mg, 18% yield). Di-Boc-protected product **18i** (77 mg, 0.19 mmol, 1 equiv) was treated according to general procedure D to provide (3*S*)-3-amino-7-chloro-1-hydroxy-3,4-dihydroquinolin-2(1*H*)-one (**19i**) (40 mg, 86% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.02 (br s, 1H), 8.73 (br s, 2H), 7.32 (d, J = 7.8 Hz, 1H), 7.20 (s, 1H), 7.10 (d, J = 7.8 Hz, 1H), 4.36 (dd, J = 5.7, 14.4 Hz, 1H), 3.20 (dd, J = 6.2, 15.2 Hz, 1H), 3.11−2.97 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.5, 141.0, 133.2, 130.4, 123.8, 119.6, 113.4, 48.5, 28.9; HRMS (m/z) $[M + H]^+$ calcd for $C_9H_{10}ClN_2O_2$ 213.0425, found 213.0423.

Preparation of Methyl *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethoxy)-L-phenylalaninate (24a): To a solution of *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethoxy)-L-phenylalanine (183 mg, 0.465 mmol, 1 equiv; see below for preparation) in CH_2Cl_2 (3 mL) was added EDCI (109 mg, 0.558 mmol, 1 equiv), DMAP (29 mg, 0.233 mmol, 0.5 equiv), and MeOH (3 mL). The

reaction was allowed to stir at rt overnight. The mixture was then washed with brine, dried ($MgSO_4$), filtered, and concentrated. The crude product mixture was purified by flash chromatography on silica gel (12 g) eluting with 0−40% EtOAc/heptane to give methyl *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethoxy)-L-phenylalaninate (**24a**) (119 mg, 63% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.8 Hz, 1H), 7.39−7.26 (m, 2H), 5.20−5.09 (m, 1H), 4.62−4.52 (m, 1H), 3.21−3.10 (m, 1H), 3.03−2.92 (m, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 153.8, 143.9, 139.2, 130.5, 130.1, 128.2, 118.9, 119.2, 79.3, 52.9, 51.6, 33.3, 27.1. Anal. Calcd for $C_{16}H_{19}F_3N_2O_7$: C, 47.06; H, 4.69; N, 6.86. Found: C, 47.20; H, 4.33; N, 6.55.

Preparation of Trifluoroethyl Ester Amino Acids 25a−f

Table 4, entry 1: *N*-(*tert*-Butoxycarbonyl)-2-nitro-3-(trifluoromethoxy)-L-phenylalanine: To a solution of 2-nitro-3-(trifluoromethoxy)-L-phenylalanine in water (10 mL) was added NEt_3 (0.85 mL, 6.05 mmol, 4 equiv) and Boc_2O (363 mg, 1.66 mmol, 1.1 equiv) and the reaction was stirred at rt overnight. The reaction was acidified with 10% citric acid to pH ∼5, and extracted with EtOAc. The organic layers were washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product mixture was purified on silica gel eluting with 5% CH_3OH/CH_2Cl_2 to give *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethoxy)-L-phenylalanine (510 mg, 86% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.66−7.57 (m, 1H), 7.47 (d, J = 8.0 Hz, 2H), 4.41 (dd, J = 4.7, 10.0 Hz, 1H), 3.24 (dd, J = 4.7, 14.4 Hz, 1H), 2.96 (dd, J = 10.0, 14.4 Hz, 1H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 174.0, 157.5, 145.8, 141.0, 133.6, 132.5, 131.3, 121.1, 121.5, 80.6, 55.0, 34.2, 28.6; HRMS (m/z) $[M + Na]^+$ calcd for $C_{17}H_{17}F_3N_2O_7Na$ 417.0880, found 417.0882; $[\alpha]^{20}_D$ +5.64 (c 0.55, MeOH).

2,2,2-Trifluoroethyl *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethoxy)-L-phenylalaninate (25a): To a solution of *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethoxy)-L-phenylalanine (450 mg, 1.14 mmol, 1 equiv) in THF (10 mL) was added NEt_3 (0.41 mL, 2.85 mmol, 2.5 equiv) and 2,2,2-trifluoroethyl trifluoromethanesulfonate (344 mg, 1.48 mmol, 1.3 equiv). The reaction was heated at 60 °C overnight. The reaction mixture was partitioned between EtOAc and water, and the organic layer was washed with water, dried ($MgSO_4$), filtered, and concentrated. The crude product mixture was purified by chromatography on silica gel (12 g), eluting with 0−100% EtOAc/heptane to give 2,2,2-trifluoroethyl *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethoxy)-L-phenylalaninate (**25a**) as a white solid (429 mg, 79% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.69−7.59 (m, 1H), 7.56−7.42 (m, 2H), 4.63 (q, J = 8.8 Hz, 2H), 4.49 (dd, J = 5.4, 9.9 Hz, 1H), 3.24−3.16 (m, 1H), 3.06 (dd, J = 10.0, 14.3 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 169.8, 156.3, 144.6, 139.9, 132.2, 131.8, 131.6, 130.1, 124.7, 120.4, 79.8, 60.7, 54.0, 32.3, 27.4; HRMS (m/z) $[M + Na]^+$ calcd for $C_{17}H_{18}F_6N_2O_7Na$ 499.0910, found 499.0894; $[\alpha]^{20}_D$ +4.00 (c 0.55, MeOH).

Table 4, entry 2: *tert*-Butyl *N*-(diphenylmethylidene)-3-methoxy-2-nitro-L-phenylalaninate: To a solution of 1-(bromomethyl)-3-methoxy-2-nitrobenzene (494 mg, 2.01 mmol, 1 equiv) in CH_2Cl_2 (10 mL) cooled to −30 °C was added *tert*-butyl *N*-(diphenylmethylidene)glycinate (890 mg, 3.01 mmol, 1.5 equiv) and (−)-(*O*)-(9)-allyl-*N*-(9-anthracenylmethyl)cinchodinium bromide (128 mg, 0.201 mmol, 0.1 equiv). CsOH (439 mg, 2.61 mmol, 1.3 equiv) was then added and the mixture was allowed to stir for 18 h. The reaction mixture was washed with water, dried (Na_2SO_4), filtered, and concentrated. The crude mixture was purified by flash chromatography on silica gel eluting with CH_2Cl_2 (isocratic) to give *tert*-butyl *N*-(diphenylmethylidene)-3-methoxy-2-nitro-L-phenylalaninate (870 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.58 (m, 2H), 7.41−7.18 (m, 7H), 6.86 (d, J = 8.2 Hz, 2H), 6.71 (d, J = 7.0 Hz, 1H), 4.21 (dd, J = 4.7, 8.8 Hz, 1H), 3.85 (s, 3H), 3.34−2.95 (m, 2H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 170.2, 150.9, 139.5, 136.2, 131.7, 130.5, 130.4, 130.3, 129.1, 128.7, 128.4, 128.2, 127.8, 123.9, 110.7, 81.8, 77.6, 76.9, 66.3, 56.6, 34.7, 28.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{27}H_{29}N_2O_5$ 461.20701, found 461.2069; $[\alpha]^{20}_D$ −128.8 (c 0.182, MeOH).

***N*-(*tert*-Butoxycarbonyl)-3-methoxy-2-nitro-L-phenylalanine:** To a solution of *tert*-butyl *N*-(diphenylmethylidene)-3-methoxy-2-nitro-L-phenylalaninate (396 mg, 0.86 mmol, 1 equiv) in CH_2Cl_2 (20 mL) was added TFA (3 mL). The reaction was allowed to stir at rt for 18 h. The reaction mixture was concentrated to remove TFA. The residue was partitioned between 4 M HCl and Et_2O. The aqueous layer was washed several times with Et_2O. The aqueous layer was then concentrated to give 3-methoxy-2-nitro-L-phenylalanine (**8l**) as the HCl salt. The amino acid was dissolved in THF (10 mL) and 1 M NaOH (10 mL). Boc_2O (375 mg, 1.72 mmol, 2 equiv) was added and the mixture was allowed to stir at rt overnight. The reaction mixture was neutralized using aq NH_4Cl solution and extracted with EtOAc. The organic layers were dried ($MgSO_4$), filtered, and concentrated to give *N*-(*tert*-butoxycarbonyl)-3-methoxy-2-nitro-L-phenylalanine (240 mg).

2,2,2-Trifluoroethyl *N*-(*tert*-butoxycarbonyl)-3-methoxy-2-nitro-L-phenylalaninate (25b): To a solution of *N*-(*tert*-butoxycarbonyl)-3-methoxy-2-nitro-L-phenylalanine (100 mg, 0.294 mmol, 1 equiv) in THF (10 mL) was added NEt_3 (0.102 mL, 0.735 mmol, 2.5 equiv) and trifluoroethyl trifluoromethanesulfonate (89 mg, 0.382 mmol, 1.3 equiv). The reaction was heated at 60 °C overnight. The reaction mixture was partitioned between EtOAc and water. The organic layer was washed with water, dried (MgSO4), filtered, and concentrated. The crude product mixture was purified on a 12 g silica column eluting with 0−100% EtOAc/heptane to give 2,2,2-trifluoroethyl *N*-(*tert*-butoxycarbonyl)-3-methoxy-2-nitro-L-phenylalaninate (**25b**) as a white solid (84 mg, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, J = 8.1 Hz, 1H), 7.00−6.87 (m, 2H), 5.17 (d, J = 7.6 Hz, 1H), 4.67−4.57 (m, 1H), 4.57−4.43 (m, 2H), 3.88 (s, 3H), 3.16−3.06 (m, 1H), 2.95 (dd, J = 8.5, 14.3 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 155.2, 151.2, 142.3, 131.4, 129.6, 122.3, 122.8, 111.7, 80.7, 61.6, 56.6, 54.2, 33.3, 28.4. Anal. Calcd for $C_{17}H_{21}F3N_2O_7$: C, 48.34; H, 5.01; N, 6.63. Found: C, 48.55; H, 5.00; N, 6.54. $[\alpha]^{20}_D$ −6.6 (c 0.11, MeOH).

Table 4, entry 3: *N*-(*tert*-Butoxycarbonyl)-2-nitro-3-(trifluoromethyl)-L-phenylalanine: To a solution of 2-nitro-3-(trifluoromethyl)-L-phenylalanine (**8k**) (1.5 g, 5.39 mmol) in dioxane and water (1:1) (100 mL) was added Et_3N (4.3 mL 32.34 mmol) followed by Boc_2O (2.9 mL 13.47 mmol) at rt and the reaction was stirred for 1 h. The reaction mixture was quenched with saturated NH_4Cl solution and extracted with EtOAc. The organic solution was dried over Na_2SO_4, filtered, and concentrated to obtain crude *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethyl)-L-phenylalanine, which was used without further purification.

2,2,2-Trifluoroethyl *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethyl)-L-phenylalaninate (25c): To a solution of *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethyl)-L-phenylalanine (0.1 g, 0.264 mmol) in dry THF (20 mL) was added Et_3N (0.08 mL, 0.65 mmol) followed by trifluoroethyl trifluoromethanesulfonate (0.08 mL, 0.343 mmol), and the mixture was heated at reflux for 12 h. The reaction mixture was quenched with water and extracted with EtOAc. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product mixture was purified by flash chromatography on silica gel eluting with EtOAc to give 2,2,2-trifluoroethyl *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethyl)-L-phenylalaninate (**25c**) as a white solid (0.120 g, 99%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.01−7.77 (m, 2H), 7.66−7.54 (m, 1H), 4.85−4.66 (m, 2H), 4.42−4.28 (m, 1H), 3.11−2.96 (m, 2H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.6, 155.1, 147.2, 136.5, 131.5, 130.7, 126.3, 124.6, 121.9, 120.3, 78.4, 60.2, 53.4, 31.3, 27.9; HRMS (m/z) $[M + NH_4]^+$ calcd for $C_{17}H_{22}F_6N_3O_6$ 478.1407, found 478.1409.

Table 4, entry 4: 3-Fluoro-2-nitro-L-phenylalanine: To a solution of 1-(bromomethyl)-3-fluoro-2-nitrobenzene (3.72 g, 15.9 mmol, 1 equiv) in CH_2Cl_2 (30 mL) cooled to −30 °C was added *tert*-butyl

N-(diphenylmethylidene)glycinate (6.23 g, 20.7 mmol, 1.3 equiv) and (−)-(*O*)-(9)-allyl-*N*-(9-anthracenylmethyl)cinchodinium bromide (1.01 g, 1.59 mmol, 0.1 equiv). $CsOH·H_2O$ (3.47 g, 20.7 mmol, 1.3 equiv) was then added and the mixture was allowed to stir for 18 h. The reaction mixture was washed with water, dried (Na_2SO_4), filtered, and concentrated. The crude mixture was purified by flash chromatography on silica gel eluting with CH_2Cl_2 (isocratic) to give *tert*-butyl *N*-(diphenylmethylidene)-3-fluoro-2-nitro-L-phenylalaninate (1.72 g, 32%). To a solution of *tert*-butyl *N*-(diphenylmethylidene)-3-fluoro-2-nitro-L-phenylalaninate (678 mg, 1.5 mmol, 1 equiv) was added TFA (4 mL) and the reaction was allowed to stir at rt overnight, then concentrated to remove TFA. The residue was partitioned between 4 M HCl and Et_2O. The aqueous layer was washed several times with Et_2O, and concentrated to give 3-fluoro-2-nitro-L-phenylalanine (273 mg, 68% yield, 96% ee). ^{1}H NMR (400 MHz, CD_3OD) δ 7.80−7.51 (m, 1H), 7.45−7.26 (m, 2H), 4.26 (t, J = 7.4 Hz, 1H), 3.36 (dd, J = 7.2, 14.6 Hz, 1H), 3.20 (dd, J = 7.7, 14.7 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 169.2, 153.1, 133.2, 133.1, 130.2, 127.3, 116.7, 53.2, 31.7; HRMS (m/z) $[M + H]^+$ calcd for $C_9H_{10}N_2O_4F$ 229.0619, found 229.0620; $[\alpha]^{20}_D$ +13.3 (c 0.35, MeOH).

***N*-(*tert*-Butoxycarbonyl)-3-fluoro-2-nitro-L-phenylalanine:** To solution of 3-fluoro-2-nitro-L-phenylalanine (1.91 g, 1.5 mmol, 1 equiv) in water (10 mL) was added NEt_3 (3.5 mL, 25.1 mmol, 3 equiv) and Boc_2O (2.8 mg, 12.6 mmol, 1.1 equiv) and the reaction was stirred at room temperature overnight. The reaction was acidified with 10% citric acid to pH ∼5, and extracted with EtOAc. The organic layers were washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product mixture was purified on silica gel eluting with 0−40% EtOAc/heptane to give *N*-(*tert*-butoxycarbonyl)-3-fluoro-2-nitro-L-phenylalanine (1.84 g, 67% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.59−7.37 (m, 1H), 7.36−7.15 (m, 2H), 4.44−4.28 (m, 1H), 3.24−3.18 (m, 1H), 2.97 (?, 1H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 173.0, 156.4, 155.2, 138.1, 132.7, 132.0, 127.3, 115.3, 79.5, 53.9, 33.1, 27.4; HRMS (m/z) $[M + Na]^+$ calcd for $C_{15}H_{20}N_2O_6Na$ 347.1213, found 347.1203; $[\alpha]^{20}_D$ +33 (c 0.46, MeOH).

***N*-(*tert*-Butoxycarbonyl)-2-nitro-3-phenoxy-L-phenylalanine:** To a solution of *N*-(*tert*-butoxycarbonyl)-3-fluoro-2-nitro-L-phenylalanine (400 mg, 1.2 mmol, 1 equiv) in DMF (2 mL) was added phenol (206 mg, 2.19 mmol, 1.8 equiv) and Cs_2CO_3 (1.19 g, 3.65 mmol, 3 equiv). The reaction was heated at 70 °C for 18 h. The reaction mixture was diluted with water and the aqueous layer was washed with EtOAc (1×) to remove excess phenol. The aqueous phase was then acidified with 10% citric acid to pH 6 and extracted with EtOAc. The combined organic layers were washed twice with brine, dried (MgSO4), filtered, and concentrated to give *N*-(*tert*-butoxycarbonyl)-2-nitro-3-phenoxy-L-phenylalanine (347 mg, 70% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.38−7.29 (m, 3H), 7.23−7.18 (m, 1H), 7.19−7.10 (m, 1H), 7.03−6.98 (m, 2H), 6.84−6.78 (m, 1H), 4.43−4.03 (m, 1H), 3.25−3.17 (m, 1 H), 2.91−2.81 (m, 1 H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 175.8, 156.3, 155.9, 148.4, 141.8, 132.1, 130.5, 129.6, 125.6, 124.1, 118.6, 117.3, 78.8, 55.8, 34.0, 27.3; HRMS (m/z) $[M + Na]^+$ calcd for $C_{20}H_{22}N_2O_7Na$ 425.1319, found 425.1309; $[\alpha]^{20}_D$ −5 (c 0.42, MeOH).

2,2,2-Trifluoroethyl *N*-(*tert*-butoxycarbonyl)-2-nitro-3-phenoxy-L-phenylalaninate (25d): To a solution of *N*-(*tert*-butoxycarbonyl)-2-nitro-3-phenoxy-L-phenylalanine (280 mg, 0.862 mmol, 1 equiv) in THF (5 mL) was added NEt_3 (0.309 mL, 2.16 mmol, 2.5 equiv) and trifluoroethyl trifluoromethanesulfonate (260 mg, 1.12 mmol, 1.3 equiv). The reaction was heated at 60 °C overnight. The reaction mixture was partitioned between EtOAc and water. The organic layer was washed with water, dried ($MgSO_4$), filtered, and concentrated. The crude product mixture was purified by chromatography on silica (12 g), eluting with 0−100% EtOAc/heptane to give 2,2,2-trifluoroethyl *N*-(*tert*-butoxycarbonyl)-2-nitro-3-phenoxy-L-phenylalaninate (**25d**) as a white solid (280 mg, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.28 (m, 3H), 7.22−7.14 (m, 1H), 7.10−6.98 (m, 3H), 6.85 (dd, J = 0.9, 8.3 Hz, 1H), 5.24−5.14 (m, 1H), 4.71−4.60 (m, 1H), 4.57−4.45 (m, 2H), 3.23−3.11 (m, 1H), 3.09−2.98 (m, 1H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 155.5, 154.9, 149.3, 143.6, 131.1, 130.0, 126.7, 124.7, 124.0, 121.2, 119.5, 117.8, 80.6, 61.0, 54.0, 33.3, 28.2; HRMS (m/z) $[M + Na]^+$ calcd for $C_{22}H_{23}N_2O_7F_3Na$ 507.1349, found 507.1351; $[\alpha]^{20}_D$ −7.6 (c 0.63, MeOH).

Table 4, entry 5: 1-(Bromomethyl)-3-methyl-2-nitrobenzene: To a solution of (3-methyl-2-nitrophenyl)methanol (2.5 g, 15 mmol, 1 equiv) in CH_3CN (50 mL) was added CBr_4 (4.96 g, 15 mmol, 1 equiv) followed by PPh_3 (3.92 g, 15 mmol, 1 equiv). The reaction was allowed to stir at rt for 18 h. The reaction mixture was washed with water, dried ($MgSO_4$), filtered, and concentrated. The crude product mixture was purified via chromatography (40 g silica), eluting with 0−30% EtOAc/heptane to give 1-(bromomethyl)-3-methyl-2-nitrobenzene (2.56 g, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.29 (m, 2H), 7.25−7.20 (m, 1H), 4.42 (s, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 132.1, 131.0, 131.0, 129.8, 129.2, 27.2, 17.9. Anal. Calcd for $C_8H_8NO_2Br$: C, 41.77; H, 3.51; N, 6.09. Found: C, 41.86; H, 3.69; N, 6.09.

***tert*-Butyl *N*-(diphenylmethylidene)-3-methyl-2-nitro-L-phenylalaninate.** To a solution of 1-(bromomethyl)-3-methyl-2-nitrobenzene (1.21 g, 5.26 mmol, 1 equiv) in CH_2Cl_2 (30 mL) cooled to −30 °C was added *tert*-butyl *N*-(diphenylmethylidene)glycinate (2.06 g, 6.84 mmol, 1.3 equiv) and (−)-(*O*)-(9)-allyl-*N*-(9-anthracenylmethyl)cinchodinium bromide (335 mg, 0.525 mmol, 0.1 equiv). CsOH (1.13 g, 6.84 mmol, 1.3 equiv) was added and the mixture was allowed to stir for 18 h. The reaction mixture was washed with water, dried (Na_2SO_4), filtered, and concentrated. The crude mixture was purified by flash chromatography on silica gel eluting with CH_2Cl_2 (isocratic) to give *tert*-butyl *N*-(diphenylmethylidene)-3-methyl-2-nitro-L-phenylalaninate (620 mg, 27%, 96% ee). ^{1}H NMR (400 MHz, CD_3OD) δ 7.50−7.41 (m, 1H), 7.39−7.29 (m, 2H), 4.24−4.13 (m, 1H), 3.25−3.19 (m, 1H), 3.08 (dd, J = 8.1, 14.7 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 169.0, 139.1, 132.8, 129.7, 127.1, 126.6, 126.3, 34.0, 28.8, 21.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{27}H_{29}N_2O_4$ 445.2121, found 445.2129; $[\alpha]^{20}_D$ −211 (c 0.28, MeOH).

3-Methyl-2-nitro-L-phenylalanine hydrochloride: To a solution of *tert*-butyl *N*-(diphenylmethylidene)-3-methyl-2-nitro-L-phenylalaninate (289 mg, 0.65 mmol) in CH_2Cl_2 (7 mL) was added TFA (7 mL). The reaction was allowed to stir at rt for 18 h, then concentrated to remove TFA. The residue was partitioned between 4 M HCl and Et_2O. The aqueous layer was washed several times with Et_2O and then concentrated to give 3-methyl-2-nitro-L-phenylalanine (140 mg, 96% yield) as its HCl salt. ^{1}H NMR (400 MHz, CD_3OD) δ 7.50−7.41 (m, 1H), 7.39−7.29 (m, 2H), 4.24−4.13 (m, 1H), 3.25−3.19 (m, 1H), 3.08 (dd, J = 8.1, 14.7 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 169.0, 139.1, 132.8, 129.7, 127.1, 126.6, 126.3, 34.0, 28.8, 21.2; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{12}N_2O_4$ 225.0877, found 225.0869; $[\alpha]^{20}_D$ +1.25 (c 0.32, MeOH).

2,2,2-Trifluoroethyl *N*-(*tert*-butoxycarbonyl)-3-methyl-2-nitro-L-phenylalaninate (25e): To a solution of 3-methyl-2-nitro-L-phenylalanine (115 mg, 0.51 mmol, 1 equiv) in water (10 mL) was added NEt_3 (0.2 mL, 1.47 mmol, 3 equiv) and Boc_2O (164 mg, 0.735 mmol, 1.5 equiv) and the reaction was stirred at room temperature overnight. The reaction was acidified with 10% citric acid to pH ∼5, then extracted with EtOAc. The organic layers were washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product mixture was purified by chromatography on silica gel, eluting with 0−40% EtOAc/heptane to give *N*-(*tert*-butoxycarbonyl)-3-methyl-2-nitro-L-phenylalanine (141 mg, 85% yield). To a solution of *N*-(*tert*-butoxycarbonyl)-3-methyl-2-nitro-L-phenylalanine (91 mg, 0.28 mmol, 1 equiv) in THF (5 mL) was added NEt_3 (0.1 mL, 0.70 mmol, 2.5 equiv) and trifluoroethyl trifluoromethanesulfonate (85 mg, 0.365 mmol, 1.3 equiv). The reaction was heated at 60 °C overnight. The reaction

mixture was partitioned between EtOAc and water. The organic layer was washed with water, dried ($MgSO_4$), filtered, and concentrated. The crude product mixture was purified by silica gel chromatography (12 g silica), eluting with 0−100% EtOAc/heptane to give 2,2,2-trifluoroethyl *N*-(*tert*-butoxycarbonyl)-3-methyl-2-nitro-L-phenylalaninate (**25e**) as a white solid (81 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.28 (m, 1H), 7.18 (d, J = 7.4 Hz, 2H), 5.13 (d, J = 7.4 Hz, 1H), 4.60 (d, J = 6.2 Hz, 1H), 4.53−4.40 (m, 2H), 3.13−3.04 (m, 1H), 2.94 (dd, J = 8.6, 14.1 Hz, 1H), 2.29 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 155.2, 152.1, 130.6, 130.6, 130.3, 128.9, 128.1, 121.4, 80.7, 61.3, 54.3, 33.7, 28.4, 17.9; HRMS (m/z) $[M + Na]^+$ calcd for $C_{17}H_{21}F_3N_2O_6Na$ 429.1243, found 429.1248; $[\alpha]^{20}_D$ +2.9 (c 0.25, MeOH).

Table 4, entry 6: *N*-(*tert*-Butoxycarbonyl)-3-chloro-2-nitro-L-phenylalanine: To a solution of 3-chloro-2-nitro-L-phenylalanine (1.5 g, 5.36 mmol) in water:dioxane (1:2) (27 mL) was added NEt_3 (3.0 mL, 21 mmol) and Boc_2O (3.04 mL, 13.4 mmol) at rt and the reaction was stirred for 30 min. The reaction mixture was concentrated, diluted with EtOAc, and washed with saturated aq NH_4Cl solution. The organic layer was dried over Na_2SO_4, filtered, and concentrated to obtain crude compound, which was triturated with *n*-pentane to afford *N*-(*tert*-butoxycarbonyl)-3-chloro-2-nitro-L-phenylalanine (1.2 g, 66% yield).

2,2,2-Trifluoroethyl *N*-(*tert*-butoxycarbonyl)-3-chloro-2-nitro-L-phenylalaninate (25f): To a solution of *N*-(*tert*-butoxycarbonyl)-3-chloro-2-nitro-L-phenylalanine (1 g, 2.91 mmol) and Et_3N (1.0 mL, 7.267 mmol) in THF (25 mL) was added 2,2,2-trifluoroethyl trifluoromethanesulfonate (1.18, 4.941 mmol). The mixture was stirred at 60 °C for 12 h. The reaction mixture was cooled to rt and the solvent was evaporated. The residual oil was partitioned between EtOAc and water, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated to obtain crude compound. The crude product was triturated with *n*-pentane to afford 2,2,2-trifluoroethyl *N*-(*tert*-butoxycarbonyl)-3-chloro-2-nitro-L-phenylalaninate (**25f**) (560 mg, 45% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 7.0 Hz, 3H), 5.16−5.02 (m, 1H), 4.67−4.56 (m, 1H), 4.49 (dd, J = 2.1, 8.4 Hz, 2H), 3.18−3.06 (m, 1H), 3.03−2.90 (m, 1H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 154.9, 131.2, 130.4, 129.8, 129.7, 124.1, 121.2, 81.0, 61.3, 54.0, 33.8, 28.3. Anal. Calcd for $C_{16}H_{18}ClF_3N_2O_6$: C, 45.03; H, 4.25; N, 6.56. Found: C, 44.85; H, 4.06; N. 6.50.

Reductive Cyclization of Trifluoroethyl Ester Amino Acids: Preparation of 28a−f

***tert*-Butyl [(3*S*)-1-hydroxy-2-oxo-8-(trifluoromethoxy)-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (28a)—General Procedure E:** To a solution of 2,2,2-trifluoroethyl *N*-(*tert*-butoxycarbonyl)-2-nitro-3-(trifluoromethoxy)-L-phenylalaninate (**25a**) (324 mg, 0.68 mmol, 1 equiv) in pyridine (10 mL) was added 5% Pt/C catalyst (33 mg). The reaction was shaken on a Parr shaker at 30 psi of H_2 for 3 h. The reaction mixture was filtered through Celite and concentrated. The crude product mixture was purified by flash chromatography on silica gel (25 g) eluting with 0−100% EtOAc/heptane to give *tert*-butyl [(3*S*)-1-hydroxy-2-oxo-8-(trifluoromethoxy)-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (**28a**) (218 mg, 88% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.30−7.24 (m, 2H), 7.21−7.14 (m, 1H), 4.38 (dd, J = 7.0, 13.3 Hz, 1H), 3.15−2.99 (m, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 168.2, 157.9, 138.7, 133.2, 128.8, 127.8, 126.5, 123.5, 123.3, 120.7, 80.8, 51.4, 33.2, 28.6; HRMS (m/z) $[M + Na]^+$ calcd for $C_{15}H_{17}F_3N_2O_5Na$ 385.0981, found 385.0983; $[\alpha]^{20}_D$ −25.95 (c 0.42, MeOH).

***tert*-Butyl [(3*S*)-1-hydroxy-8-methoxy-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (28b):** The title compound was prepared from **25b** (29 mg, 0.069 mmol) according to general procedure E to give *tert*-butyl [(3*S*)-1-hydroxy-8-methoxy-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (**28b**) (13.4 mg, 64% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.16−7.09 (m, 1H), 7.00 (d, J = 8.2 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 6.84 (d, J = 7.4 Hz, 1H), 4.37−4.24 (m, 1H), 3.88 (s, 3H), 3.03−2.89 (m, J = 9.4 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 167.6, 150.3, 128.3, 127.3, 126.1, 119.3, 112.1, 79.2, 55.3, 50.6, 32.1, 27.1.

***tert*-Butyl [(3*S*)-1-hydroxy-2-oxo-8-(trifluoromethyl)-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (28c):** The title compound was prepared from **25c** (100 mg, 0.217 mmol) according to general procedure E to give *tert*-butyl [(3*S*)-1-hydroxy-2-oxo-8-(trifluoromethyl)-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (**28c**) (50 mg, 66% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.71−7.63 (m, 1 H), 7.54−7.47 (m, 1 H), 7.28−7.21 (m, 1 H), 4.47−4.35 (m, 1 H), 3.17−2.97 (m, 2 H), 1.47 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 155.5, 132.0, 127.8, 126.6, 125.4, 124.8, 122.1, 119.6, 80.7, 49.6, 33.3, 28.5; HRMS (m/z) $[M + Na]^+$ calcd for $C_{15}H_{17}F_3N_2NaO_4$ 369.1033, found 369.1037.

***tert*-Butyl [(3*S*)-1-hydroxy-2-oxo-8-phenoxy-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (28d):** The title compound was prepared from **25d** (80 mg, 0.16 mmol) according to general procedure E to give *tert*-butyl [(3*S*)-1-hydroxy-2-oxo-8-phenoxy-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (**28d**) (20 mg, 33% yield) and **25d** (24 mg, 30% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.35−7.22 (m, 2H), 7.15−6.98 (m, 3H), 7.00−6.89 (m, 2H), 6.89−6.76 (m, 1H), 4.49−4.28 (m, 1H), 3.09−2.95 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 167.2, 157.9, 156.3, 145.7, 131.2, 129.2, 127.4, 125.6, 122.8, 122.4, 120.9, 117.4, 79.4, 50.3, 32.1, 27.2; HRMS (m/z) $[M + Na]^+$ calcd for $C_{20}H_{22}N_2O_5Na$ 393.1421, found 393.1412; $[\alpha]^{20}_D$ −57.2 (c 0.63, MeOH).

***tert*-Butyl [(3*S*)-1-hydroxy-8-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (28e):** The title compound was prepared from **25e** (70 mg, 0.17 mmol) according to general procedure E to give *tert*-butyl [(3*S*)-1-hydroxy-8-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (**28e**) (23 mg, 46% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.12−7.07 (m, 1H), 7.07−7.02 (m, 1H), 7.02−6.95 (m, 1H), 4.31 (s, 1H), 3.07−2.76 (m, 2H), 2.45 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 167.7, 156.7, 137.8, 131.5, 128.4, 125.8, 125.3, 125.0, 79.6, 50.3, 32.6, 27.5, 19.8; HRMS (m/z) $[M + Na]^+$ calcd for $C_{15}H_{20}N_2O_4Na$ 315.1315, found 315.1320; $[\alpha]^{20}_D$ −31.6 (c 0.28, MeOH).

***tert*-Butyl [(3*S*)-8-chloro-1-hydroxy-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (28f):** The title compound was prepared from **25f** (0.45 g, 1.03 mmol) according to general procedure E to give *tert*-butyl [(3*S*)-8-chloro-1-hydroxy-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (**28f**) (0.2 g, 60% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.35−7.28 (m, 1H), 7.20−7.13 (m, 1H), 7.10−7.01 (m, 1H), 4.40−4.23 (m, 1H), 3.06−2.93 (m, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 168.2, 156.4, 136.6, 130.7, 128.7, 126.3, 126.0, 124.0, 79.7, 50.5, 32.5, 27.5; HRMS (m/z) $[M + Na]^+$ calcd for $C_{14}H_{17}ClN_2O_4Na$ 335.0769, found 335.0796.

Preparation of 30a−e

(3*S*)-3-Amino-1-hydroxy-8-(trifluoromethoxy)-3,4-dihydroquinolin-2(1*H*)-one (30a)—General Procedure F: To a solution of *tert*-butyl [(3*S*)-1-hydroxy-2-oxo-8-(trifluoromethoxy)-1,2,3,4-tetrahydroquinolin-3-yl]carbamate (**28a**) (178 mg, 0.49 mmol) in Et_2O was added 2 M HCl in Et_2O. The reaction mixture was allowed to stir overnight at rt. The solid precipitate was filtered and washed with Et_2O to give (3*S*)-3-amino-1-hydroxy-8-(trifluoromethoxy)-3,4-dihydroquinolin-2(1*H*)-one (**30a**) (120 mg, 82% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.39−7.30 (m, 2H), 7.30−7.22 (m, 1H), 4.37 (dd, J = 7.2, 13.5 Hz, 1H), 3.28−3.19 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 163.4, 137.7, 131.7, 127.0, 126.0, 125.3, 123.0, 120.8, 48.9, 29.8; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_9F_3N_2O_3$ 263.0638, found 263.0633; $[\alpha]^{20}_D$ −25.37 (c 0.46, MeOH).

(3*S*)-3-Amino-1-hydroxy-8-methoxy-3,4-dihydroquinolin-2(1*H*)-one (30b): The title compound was prepared from **28b** (13 mg, 0.042 mmol) according to general procedure F to give (3*S*)-3-amino-1-hydroxy-8-methoxy-3,4-dihydroquinolin-2(1*H*)-one (**30b**) (7.1 mg, 70%

yield). ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.38 (br s, 1H), 8.61 (br s, 3H), 7.20−7.11 (m, 1H), 7.10−7.01 (m, 1H), 6.92 (d, J = 7.7 Hz, 1H), 4.40−4.22 (m, 1H), 3.81 (s, 3H), 3.16−2.99 (m, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.8, 150.0, 128.3, 126.2, 125.3, 119.7, 113.0, 56.2, 48.5, 29.7; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{13}N_2O_3$ 209.0920, found 209.0918.

(3*S*)-3-Amino-1-hydroxy-8-(trifluoromethyl)-3,4-dihydroquinolin-2(1*H*)-one (30c): The title compound was prepared from **28c** (50 mg, 0.144 mmol) according to general procedure F to give (3*S*)-3-amino-1-hydroxy-8-(trifluoromethyl)-3,4-dihydroquinolin-2(1*H*)-one (**30c**) (20 mg, 56% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.12−10.93 (m, 1H), 8.74−8.59 (m, 2H), 7.76−7.71 (m, 1H), 7.69−7.64 (m, 1H), 7.39−7.25 (m, 1H), 4.57−4.41 (m, 1H), 3.27−3.05 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 162.9, 137.0, 131.7, 127.6, 125.0, 124.7, 124.4, 122.0, 48.4, 29.7; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{10}F_3N_2O_2$ 247.0687, found 247.0689.

(3*S*)-3-Amino-1-hydroxy-8-phenoxy-3,4-dihydroquinolin-2(1*H*)-one (30d): The title compound was prepared from **28d** (280 mg, 0.75 mmol) according to general procedure F to give (3*S*)-3-amino-1-hydroxy-8-phenoxy-3,4-dihydroquinolin-2(1*H*)-one (**30d**) (190 mg, 94% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.36−7.24 (m, 2H), 7.17−7.03 (m, 3H), 6.96−6.92 (m, 2H), 6.92−6.88 (m, 1H), 4.43−4.26 (m, 1H), 3.23−3.15 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 163.4, 157.7, 146.2, 130.8, 129.3, 126.3, 125.0, 123.0, 122.7, 121.4, 117.6, 49.0, 29.9; HRMS (m/z) $[M + H]^+$ calcd for $C_{15}H_{15}N_2O_3$ 271.1077, found 271.1077; $[\alpha]^{20}_D$ −38.3 (c 0.34, MeOH).

(3*S*)-3-Amino-1-hydroxy-8-methyl-3,4-dihydroquinolin-2(1*H*)-one (30e): The title compound was prepared from **28e** (12 mg, 0.041 mmol) according to general procedure F to afford (3*S*)-3-amino-1-hydroxy-8-methyl-3,4-dihydroquinolin-2(1*H*)-one (**30e**) (10 mg,100% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.20−7.09 (m, 2H), 7.09−7.01 (m, 1H), 4.30−4.07 (m, 1H), 3.19−3.07 (m, 2H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 164.3, 137.5, 132.2, 128.6, 125.6, 125.5, 123.5, 49.4, 30.6, 19.8; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{13}N_2O_2$ 193.0971, found 193.0971; $[\alpha]^{20}_D$ −9.25 (c 0.4, MeOH).

(3*S*)-3-Amino-8-chloro-1-hydroxy-3,4-dihydroquinolin-2(1*H*)-one hydrochloride (30f): The title compound was prepared from **28f** (200 mg, 0.641 mmol) according to general procedure F to afford (3*S*)-3-amino-8-chloro-1-hydroxy-3,4-dihydroquinolin-2(1*H*)-one as its hydrochloride salt (**30f**) (110 mg, 69% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.00 (br s, 1H), 7.42 (d, J = 7.9 Hz, 1H), 7.33 (d, J = 7.4 Hz, 1H), 7.22−7.04 (m, 1H), 4.40 (dd, J = 7.0, 13.0 Hz, 1H), 3.34−3.05 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 136.4, 130.9, 126.9, 126.6, 126.1, 122.6, 48.1, 29.6. Anal. Calcd for $C_9H_{10}Cl_2N_2O_2$: C, 43.40; H, 4.05; N, 11.25. Found: C, 43.10; H, 3.81; N, 11.06. $[\alpha]^{20}_D$ −6.23 (c 0.39, MeOH).

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra for all compounds and chiral SFC and HPLC traces. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

We thank Professor Andrew Myers for helpful discussions. We also thank Geeta Yalamanchi and Qi Yan for analytical services. We are grateful to Dr. R. Bagepalli Madhu, Mr. C. Suresh Kumar, Mr. K. Venkateswarlu, Mr. B. Rajasekhara Rao, and Mrs. C. Aruna of GVK Biosciences Private Limited for resynthesis support. We thank Dr. Katherine E. Brighty for her editing assistance.

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