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Bifunctional-Thiourea-Catalyzed Diastereo- and Enantioselective Aza-Henry Reaction

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In memoriam Professor Kiyoshi Tanaka

Abstract: Bifunctional thiourea **1a** catalyzes aza-Henry reaction of nitroalkanes with *N*-Boc-imines to give *syn*-β-nitroamines with good to high diastereo- and enantioselectivity. Apart from the catalyst, the reaction requires no additional reagents such as a Lewis acid or a Lewis base. The N-protecting groups of the imines have a determining effect on the chirality of the products, that is, the reaction of *N*-Boc-imines gives *R* adducts as major products, whereas the same reaction of *N*-phosphonoylimines furnishes the corresponding *S* adducts. Various types of nitroalkanes bearing aryl, alcohol, ether, and ester groups can be used as nucleophiles, providing access to a wide range of useful chiral building blocks in good yield and high enantiomeric excess. Synthetic versatility of the addition products is demonstrated by the transformation to chiral piperidine derivatives such as CP-99,994.

Keywords: asymmetric catalysis · C–C Coupling · enantioselectivty · nitroamines · nucleophilic addition

Introduction

The development of stereoselective carbon–carbon bond-forming reactions that create contiguous stereogenic centers bearing heteroatom functionality can provide valuable building blocks for organic synthesis. The aza-Henry (nitro-Mannich) reaction, that is, nucleophilic addition of nitroalkanes to imines,[1] is a useful carbon–carbon bond-forming process. The thus-obtained β-nitroamines can be transformed into valuable compounds such as vicinal diamines and α-amino acids by reduction[2] and Nef reaction[3] of the nitro moiety (Scheme 1). The class of diamines is of particular interest owing to their broad utility as biologically active natural products, drug candidates, and, more recently, chiral ligands for asymmetric reactions.[4] Although a variety of synthetic procedures have been devised to carry out the Mannich reaction enantioselectively,[5] until quite recently the enantioselective aza-Henry reaction was unknown. Therefore, considerable effort has been directed toward the development of catalytic asymmetric aza-Henry reaction over the past several years.[6–10] As a result, two groups achieved initial breakthroughs in this field. Shibasaki et al. reported that heterobimetallic complexes with lanthanide BINOL (2,2′-dihydroxy-1,1′-binaphthyl) systems promoted the aza-Henry reaction of *N*-phosphinoylimines with nitromethane to give β-nitroamines with high enantioselectivity.[6] Jørgensen et al. also developed a catalytic asymmetric version of this reaction with (*N*-*p*-methoxybenzyl)-α-imino esters and bis-oxazoline copper(II) complexes.[7] Recently, we[8] and Johnston et al.[9] independently reported enantioselective aza-Henry reactions with different organocatalysts. However, each reaction is limited to a few substrates or moderate enantioselectivity. To improve the enantioselectivity of the aza-Henry adducts, we continued studies focusing on the effects of *N*-substituents of imines. During that time, Jacobsen et al. discovered that aza-Henry reaction catalyzed by a combination of chiral thiourea (10 mol %) and tertiary amine (100 mol %) proceeded with high enantio- and diastereoselectivity to provide *syn*-β-nitroamines as major products with up to 97 % *ee*.[10] Here we present the reaction of *N*-Boc imines with various nitroalkanes in the presence of bifunctional thiourea catalyst **1a**,[11] which proceeded efficiently without any external amine to give the desired adducts with high diastereo- and enantioselectivity (Scheme 1). In addition, successful transformation of the obtained prod-

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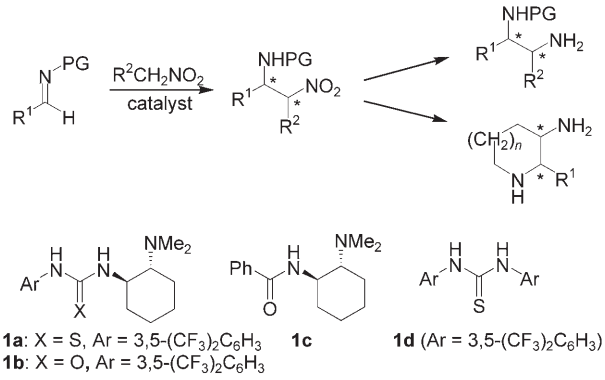


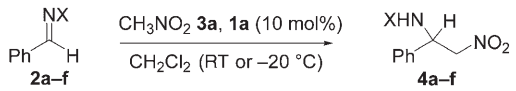
Scheme 1. Top: Aza-Henry reaction and subsequent conversion of the resuling β-nitroamines into valuable compounds such as vicinal diamines. Bottom: Chiral urea and amide catalysts **1a–d** used in the reaction.

ucts into chiral piperidine derivatives such as CP-99,994 is also described.

Results and Discussion

Enantioselective aza-Henry reaction of nitromethane 3a with aldimines 2a–f: We initially screened several imines **2a–f** that had electron-withdrawing groups in the presence of thiourea **1a** (10 mol%) and nitromethane **3a** (10 equiv) in dichloromethane at room temperature (Table 1). Among

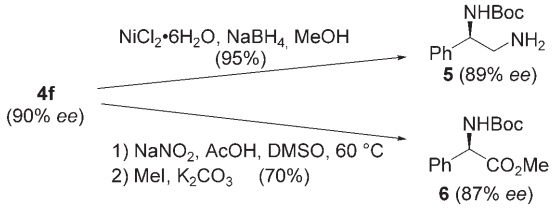
Table 1. Enantioselective aza-Henry reaction of imines **2a-f** with nitromethane **3a**.[a]



Entry	**2** (X)	Time [h]	Product	Yield [%][b]	*ee* [%][c]
1	**2a** (Ts)	4.5	**4a**	99	4
2	**2b** ($P(O)Ph_2$)	24	**4b**	87	67 (*S*)
3	**2c** (Ac)	24	**4c**	95	63
4	**2d** (CO_2Me)	24	**4d**	64	83
5	**2e** (CO_2Bn)	24	**4e**	68	85
6	**2f** (Boc)	24	**4f**	76	90 (*R*)
7[d]	**2f** (Boc)	24	**4f**	90	94 (*R*)

[a] The reaction was carried out with imines **2a–f** and nitromethane (**3a**, 10 equiv) in CH_2Cl_2 at room temperature in the presence of **1** (10 mol%). [b] Yield of isolated product after chromatography. [c] Enantiomeric excess was determined by HPLC analysis of **4a–f** on a chiral column. [d] The reaction was carried out at −20°C.

the imines examined, *N*-Boc imines **2f** gave the best results in terms of chemical yield and enantiomeric excess (**4f**: 76%, 90% *ee*), while the reactions with *N*-alkoxycarbonyl imines **2d–f** tended to provide the desired products with good enantioselectivity compared with the other imines **2a–c** (Table 1, entries 1–6). From the standpoint of synthetic advantages of *N*-protecting groups in the following transformation, *N*-Boc imines would be the best choice as starting material. To demonstrate its utility, the obtained β-nitroamine **4f** (90% *ee*) was treated with $NiCl_2$ and $NaBH_4$ in MeOH[2a] to give the desired *N*-Boc-*vic*-diamine **5**[12] in 95% yield with 89% *ee* (Scheme 2). Furthermore, Nef reaction ($NaNO_2$ and AcOH

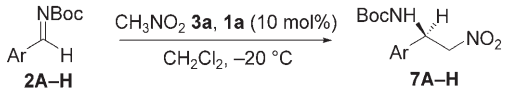


Scheme 2. Transformation of β-nitroamine **4f** into **5** and **6**.

in DMSO)[3b] and subsequent methylation of **4f** gave α-phenylglycine derivative **6**[13] in 70% yield with 87% *ee*. The absolute configuration of **4f** was unambiguously determined to be *R* by comparison of its $[\alpha]_D$ value with authentic data [**5**: $[\alpha]_D^{25}=39.6$ ($c=1.10$, $CHCl_3$), lit.:[12] $[\alpha]_D^{25}=44$ ($c=1.1$, $CHCl_3$); **6**: $[\alpha]_D^{22}=111$ (87% *ee*, $c=1.00$, $CHCl_3$), lit.:[13] $[\alpha]_D=132.3$ ($c=1.1$, $CHCl_3$)]. It is noteworthy that aza-Henry reaction with *N*-phosphinoylimine **2b**[6a] afforded the corresponding antipode adduct (*S*)-**4b**[8] under the same reaction conditions as with **2f**. These results indicate that the substituents X on the nitrogen atom of imines **2a–f** have a determinant effect on the absolute configuration of the addition products and the enantiomeric excess. Furthermore, the selectivity (*ee*) was improved by simply decreasing the reaction temperature to −20°C, whereby β-nitroamine **4f** was obtained in 90% yield with 94% *ee* (Table 1, entry 7).

Having established the optimal reaction conditions of **4f** with nitromethane **3a**, we next examined the aza-Henry reaction of other *N*-Boc imines **2A–H** under the same reaction conditions; representative results are shown in Table 2. The reaction proceeded smoothly with imine **2A** bearing an electron-withdrawing group to give product **7A** in 80% yield with 98% *ee* (Table 2, entry 1). In the case of imines

Table 2. Thiourea-catalyzed enantioselective aza-Henry reaction of *N*-Boc imines **2A–H** with **3a**.[a]

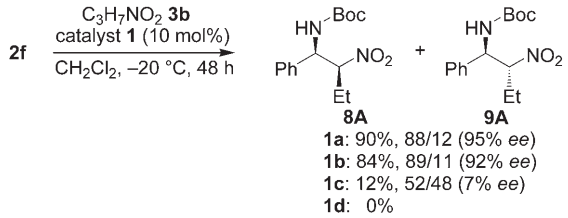


Entry	**2** (Ar)	Time [h]	Product	Yield [%][b]	*ee* [%][c]
1	**2A** (p-$CF_3C_6H_4$)	24	**7A**	80	98
2	**2B** (p-MeC_6H_4)	24	**7B**	82	93
3	**2C** (p-$MeOC_6H_4$)	60	**7C**	71	95
4	**2D** (1-naphthyl)	24	**7D**	85	95
5	**2E** (2-naphthyl)	48	**7E**	85	85
6	**2F** (2-furyl)	60	**7F**	81	91
7	**2G** (3-pyridyl)	24	**7G**	89	98
8	**2H** (2-thyenyl)	24	**7H**	83	83

[a] The reaction was carried out with imines **2A–H** and nitromethane **3a** (10 equiv) in CH_2Cl_2 at −20°C in the presence of **1** (10 mol%). [b] Yield of isolated product after chromatography. [c] Enantiomeric excess was determined by HPLC analysis of **7A–H** on a chiral column.

2B and **2C** bearing an electron-donating group, the reaction required a prolonged reaction time, but the corresponding products **7B** and **7C** were obtained with 93 and 95% *ee*, respectively (Table 2, entries 2 and 3). On the other hand, *N*-Boc imines **2D–H** bearing a naphthyl or heteroaromatic ring provided the corresponding α-nitroamines **7D–H** in good yield, but the enantioselectivities of **7D–H** were somewhat affected by the linked position of the naphthyl group (85–95% *ee*, Table 2, entries 4 and 5) and the heteroatom of the heteroaromatic rings (83–98% *ee*, Table 2, entries 6–8). Although we have no reasonable explanation for these results at this stage, the various β-nitroamines **7** could be synthesized in good yields with up to 98% *ee* by just using 10 mol% of bifunctional thiourea catalyst **1a** without any additional reagents such as a Lewis acid or a Lewis base.

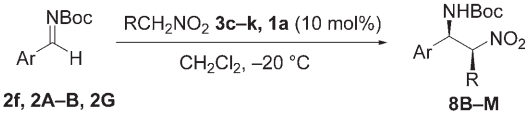
Enantioselective aza-Henry reaction of nitroalkanes 3b–k withaldimines 2: Having succeeded in the development of enantioselective aza-Henry reaction of nitromethane (**3a**) with several *N*-Boc imines **2A–H**, we next investigated whether the same reaction of nitroalkanes **3b–k** proceeded in a diastereo- and enantioselective manner to provide *syn*- or *anti*-β-nitroamine **8** or **9** as a major product. In the beginning, the reaction of nitropropane **3b** with *N*-Boc imine **2f** was carried out under the same reaction conditions as that of **3a** (Scheme 3). Thiourea **1a** efficiently prompted the reaction to furnish a mixture of β-nitroamines **8A** and **9A** in 90% yield with good diastereoselectivity (*syn*-**8A**/*anti*-**9A** 88/12). In addition, the *ee* of the major product **8A** was high (95%). To clarify the effects of bifunctional thiourea **1a** on the diastereo- and enantioselectivity, we carried out the same reaction with other catalysts **1b–d** (Scheme 1). The use of urea **1b**[11] for the aza-Henry reaction gave *syn*-β-nitroamine **8A** as a major product in a similar diastereomeric ratio (d.r. = 89/11) but with a somewhat lower enantioselectivity (92% *ee*). In contrast, the same reaction with **1c**,[11] which has an amide group in the place of the urea moiety, did not proceed smoothly and led to a 52/48 mixture of **8A** and **9A** in only 12% yield. Furthermore, the enantioselectivity for **8A** was only 7% *ee*. Thiourea catalyst **1d** without a tertiary amino group has no catalytic activity. These results indicate the following characteristics of the thiourea-catalyzed aza-Henry reaction: 1) Since the reaction hardly occurs at −20 °C with only a tertiary amine as catalyst, thiourea and urea moieties should play a important role in promoting the reaction; 2) Although thiourea catalysts without a tertiary amino group have no catalytic activity, the urea and thiourea moieties have crucial effects on the diastereo- and enantioselectivity.



Scheme 3. Aza-Henry reaction of nitropropane (**3b**) with catalysts **1a–d**.

Once the optimal conditions were established, the scope and limitations of the reaction with various nitroalkanes **3c–k** were examined. Table 3 shows representative results. In all cases, the corresponding *syn*-β-nitroamines **8B–M** were obtained as major products in good yields with good diastereo- and enantioselectivity (89–99% *ee*). The reactions of **2f** with nitroalkanes **3c–e** bearing different alkyl chains under the same conditions gave the desired products **8B–D** with high enantioselectivities, while the diastereoselectivity somewhat decreased for **3e** (Table 3, entries 1–3). Functionalized nitroalkanes such as **3f–k** would be more promising nucleophiles from the viewpoint of utility of these products as synthetic intermediates. To synthesize 1,3-amino alcohols, 2-nitroethanol **3f** was treated with imine **2f** in the presence of **1a**, and this provided the desired product **8E** with good enantioselectivity, but with moderate diastereoselectivity (Table 3, entry 4). However, using benzyl ether derivative **3g** overcame the problem and provided **8F** with improved diastereoselectivity (Table 3, entry 5). Similarly, high stereoselectivities (d.r. and *ee*) were consistently obtained in the reaction of **2f** with several nitroalkanol derivatives **3h–k** bearing a longer carbon chain (Table 3, entries 6–9). It is also noteworthy that unlike 2-nitroethanol (**3f**), 4-nitrobutanol **3j** could be employed in the aza-Henry reaction to yield the corre-

Table 3. Enantio- and diastereoselective aza-Henry reaction of *N*-Boc imines **2f**, **2A**, **2B**, and **2G** with prochiral nitroalkanes **3c–k**.[a]



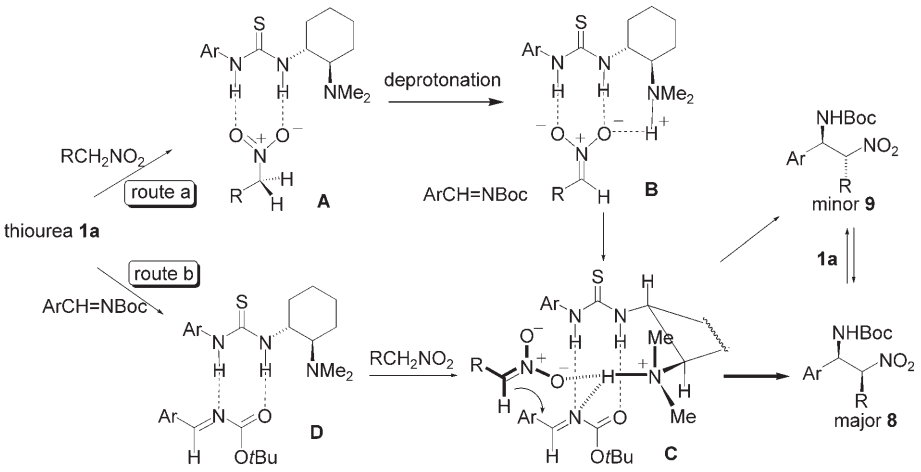
2f, 2A–B, 2G → **8B–M**

Entry	2	3 (R)	Product	Yield [%][b]	d.r. (**8**/**9**)[c]	*ee* [%][d]
1	**2f**	**3c** (CH_3)	**8B**	92	90/10	93
2		**3d** (C_5H_{11})	**8C**	82	93/7	99
3		**3e**(CH_2Ph)	**8D**	84	83/17	97
4		**3f** (CH_2OH)	**8E**	75	75/25	90
5		**3g** (CH_2OBn)	**8F**	80	86/14	95
6		**3h** [$(CH_2)_2OBn$]	**8G**	86	93/7	94
7		**3i** [$(CH_2)_3OBn$]	**8H**	80	91/9	92
8		**3j** [$(CH_2)_3OH$]	**8I**	80	92/8	89
9		**3k** [$(CH_2)_3OTf$]	**8J**	78	93/7	90
10	**2A**	**3e** (CH_2Ph)	**8K**	94	97/3	95
11	**2B**	**3e** (CH_2Ph)	**8L**	90	93/7	92
12	**2G**	**3e** (CH_2Ph)	**8M**	93	83/17	93

[a] The reaction was carried out with *N*-Boc imines **2** and nitroalkanes **3c–k** (2–10 equiv) in CH_2Cl_2 at −20 °C in the presence of **1** (10 mol%). [b] Yield of isolated product after chromatography. [c] Diastereomeric ratio was determined by ^1H NMR and HPLC analysis. [d] Enantiomeric excess of **8** was determined by HPLC analysis of **8B–M** on a chiral column.

sponding adduct **8I** with high stereoselectivities (Table 3, entry 8: d.r. 92/8, 89% *ee*). Next, we examined other *N*-Boc imines **2A**, **2B**, and **2G** as reaction partners (Table 3, entries 10–12). This revealed that phenyl groups with electron-withdrawing or electron-donating substituents and pyridyl groups on the imines had marginal effects on both stereoselectivities, and the corresponding adducts **8K–M** were obtained as major products with up to 95% *ee* and 97/3 d.r. These results demonstrate that the scope of the reaction is quite broad with respect to the nitroalkanes and *N*-Boc imines. To the best of our knowledge, this is the first report of highly diastereo- and enantioselective aza-Henry reaction of various functionalized nitroalkanes to give *N*-protected imines.

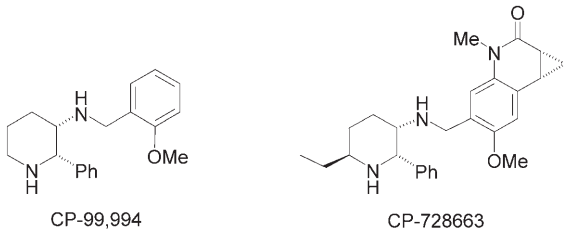
The absolute configuration of **8B** was determined by ^{1}H NMR spectroscopy and HPLC analysis,[9] and those of the other adducts **8A** and **8C–M** were deduced on the basis of this result. To account for the current highly stereoselective reaction, we propose a ternary complex **C** of catalyst **1a**, imine **2f**, and nitronate of **3** as a plausible transition state, in which **2f** and the nitronate anion may coordinate to a thiourea moiety and a tertiary amino group of **1a** by hydrogen bonding[14] (Scheme 4). Ternary complex **C** can be



Scheme 4. Proposed reaction process of the thiourea-catalyzed aza-Henry reaction.

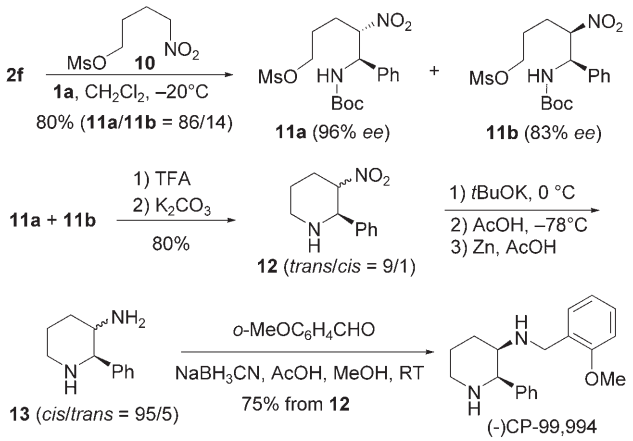
considered to be generated through route a or route b. In the former, thiourea catalyst **1a** first activates nitroalkane **3** by hydrogen-bonding interaction (**A**), which is followed by intra- or intermolecular deprotonation by the amino group of **1a** to generate nitronate complex **B**. Subsequent coordination of imine **2f** to the thiourea moiety in place of the generated nitronate produces complex **C**. On the other hand, complex **C** might be formed by the successive interaction of imine **2f** and nitroalkane **3** with thiourea catalyst **1a** via coordination and deprotonation (**D**→**C**). In any event, the thiourea moiety of **1a** would play a crucial role in activation of *N*-Boc imine **2** in the nucleophilic addition step and/or nitroalkane **3** in the deprotonation step. If complex **C** were predominantly produced, *syn*-β-nitroamines **8** should be obtained enantioselectively. Furthermore, to determine whether *syn*-β-nitroamines **8** are the kinetically or thermodynamically controlled products, a 90/10 mixture of **8B** and **9B** was subjected to the reaction conditions (10 mol% of **1a**, CH_2Cl_2, ca. 20°C, 48 h). However, neither enantioselectivity nor diastereoselectivity of the products **8B** and **9B** changed, and the *ee* and *dr* values remained constant. In contrast, treatment of the same mixture with thiourea **1a** (10 mol%) at room temperature for 48 h resulted in a significant decrease in *dr* (**8B**/**9B**) from 90/10 to 64/36, but the *ee* values of **8B** and **9B** did not change at all. These results reveal that the retro aza-Henry reaction seems not to occur even at room temperature, but epimerization of the C2 position of the products, undoubtedly induced by the thiourea catalyst at elevated temperature, lowers the diastereoselectivity.

Asymmetric synthesis of biologically important piperidines from β-nitroamines: Asymmetric synthesis of 2,3-disubstituted and 2,3,6-trisubstituted piperidines is becoming increasingly important, since their unique biological activities, such as neurokinin-1 (NK-1) receptor antagonist behavior, have been demonstrated in medicinal research.[15] Although the physiological role of the NK-1 receptor remains to be more clearly defined, selective NK-1 receptor antagonists such as CP-99,994 may be of potential therapeutic value (Scheme 5).[16] Although various types of asymmetric syntheses of CP-99,994 have been reported,[17] there are still problems to be solved in terms of overall yield, enantioselectivity, and operational simplicity. By using the aza-Henry reaction established above, we planned a five-step synthesis of chiral CP-99,994 without any separation of diastereomers (Scheme 6).



Scheme 5. Asymmetric synthesis of (−)-CP-99,994.

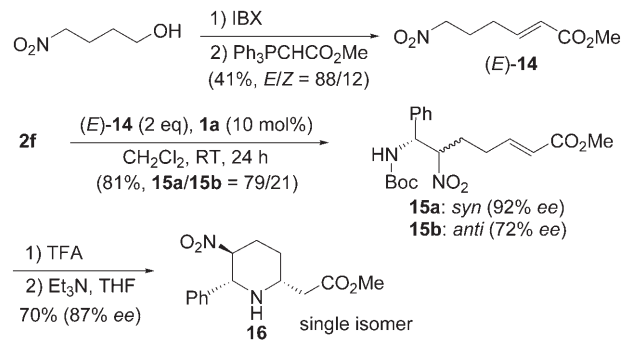
To this end, mesylate **10**, prepared from a known nitroalcohol,[18] was treated with imine **2f** at −20°C in the presence of thiourea **1a** (10 mol%) to give aza-Henry adducts **11** as a mixture of diastereomers (**11a**/**11b** = 86/14) in 80% yield.



Scheme 6. Potent neurokinin-1 (NK-1) receptor antagonists.

The enantiomeric excesses of **11a** and **11b** were 96% *ee* and 83% *ee*, respectively. Removal of the *N*-Boc group from **11** with TFA and subsequent treatment of the crude product with aqueous K_2CO_3 gave the cyclized products **12** as a 9/1 mixture of *trans* and *cis* isomers in 80% yield. Epimerization of the C3 position of **12** was successfully performed by the kinetically controlled protonation protocol. Thus, successive treatment of **12** with *t*BuOK (2.0 equiv) in THF at 0°C and AcOH at −78°C provided the desired *cis*-**12** as a major product (*cis*/*trans* = 95/5). It is noteworthy that our successful result is in sharp contrast with the previous report[19] in which the 2-piperidinone derivative of *trans*-**12** failed to epimerize into the corresponding *cis* isomer by a similar procedure. Since *cis*-**12** thus obtained was liable to isomerize into *trans*-**12**, crude *cis*-**12** was directly reduced with zinc in AcOH without any purification to afford diamine **13**. Finally, the 3-aminopiperidine **13** was treated with *o*-anisaldehyde in the presence of $NaBH_3CN$ and AcOH to give (−)-CP-99,994: $[\alpha]_D^{20} \approx 63$ ($c = 0.27$, $CHCl_3$) [lit.:[17f] (+)-CP-99,994: $[\alpha]_D^{20} = +67.2$ ($c = 1.0$, $CHCl_3$)] as a single product in 75% yield from **12**. The ^{1}H NMR data of the synthetic compound were identical with those reported in the literature.[17]

The same method was applied to the preparation of 2,3,6-trisubstituted piperidine **16** (Scheme 7). The requisite nitroester (*E*)-**14** was synthesized from a known nitroalcohol[18] in two steps (oxidation with 2-iodoxybenzoic acid (IBX) and then Wittig olefination). The aza-Henry reaction of imine **2f** with (*E*)-**14**, which was carried out at room temperature due to the prolonged reaction time at −20°C, gave adducts **15a** and **15b** as a mixture of diastereomers (**15a**/**15b** = 79/21) in 81% yield. Although the *ee* of the major adduct **15a** was still high (92%), that of the minor adduct **15b** became somewhat low (72% *ee*). It is noteworthy that the major product could be obtained with high enantioselectivity even at room temperature. Successive treatment of **15** with TFA and Et_3N induced intramolecular Michael addition of primary amine to α,β-unsaturated ester to furnish cyclized adducts **16**. Although the obtained crude products consisted of several diastereoisomers of the C3 and C6 positions, purification by column chromatography on SiO_2 provided the thermodynamically stable (2*S*,3*R*,6*S*)-piperidine **16** as a single product in 70% yield with 87% *ee*.



Scheme 7. Asymmetric synthesis of 2,6-*cis*-piperidine derivative **16**.

Conclusion

We have demonstrated that bifunctional thiourea catalyst **1a** catalyzes the aza-Henry reaction of nitroalkanes with *N*-Boc imines to give *syn*-β-nitroamines with good diastereoselectivity and high enantioselectivity. Similar to the previously reported Michael reaction of malonates to give nitroalkenes,[11] the urea and thiourea groups were revealed to play a crucial role both for activating substrates and inducing chirality. Various types of nitroalkanes bearing aryl, alcohol, ether, and ester groups were shown to participate in the reaction with high stereoselectivity. In addition, the reaction required no additional reagents other than the catalyst. It was also revealed that *syn*-β-nitroamines thus obtained could be prepared with good to high enantioselectivity even at room temperature. The synthetic utility of this methodology was demonstrated by further application to the enantioselective synthesis of (−)-CP-99,994 and 2,3,6-trisubstituted piperidines.

Experimental Section

General: Nominal (LRMS) and high-resolution mass spectra (HRMS) were recorded on a JEOL JMS-01SG-2 or JMS-HX/HX 110A mass spectrometer. ^{1}H and ^{13}C NMR spectra were registered on a JEOL JNM-LA500 spectrometer in $CDCl_3$ or some other suitable solvent with TMS as internal standard. IR spectra were obtained in $CHCl_3$ solution on a JASCO FT-IR-410 spectrometer. Melting points were recorded on a YANAGIMOTO micro melting point apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$, unless otherwise noted, with a JASCO DIP-360 digital polarimeter. For column chromatography, Kanto Silica Gel 60 (spherical, 63–210 μm) was employed and preparative TLC (PTLC) was carried out on Silica Gel 60 (Merck). Diastereomer ratios were determined by ^{1}H NMR analysis. Enantiomer ratios were determined by chiral HPLC on a Shimadzu SPD-10A with Daicel Chemical Industries, Ltd., Chiralpak AD, AD-H, AS-H and Chiralcel OD, OD-H, OJ, and OJ-H (0.46 × 25 cm). Unless otherwise noted, materials were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used without purification.

Materials: Imines **2a–f** and **2A–G** were prepared according to literature procedures.[6,8–10,20] Nitroalkanes **3e**, **3g–i**, **3j–k** and **10** were prepared according to literature procedure.[18,21]

Typical procedure for enantioselective aza-Henry reaction of nitromethane with imines 2a–f at room temperature: $MeNO_2$ (10 equiv, 0.11 mL) was added to a stirred solution of imine **2** (0.2 mmol) and thiourea (0.1 equiv, 8.3 mg) in CH_2Cl_2 (0.4 mL), and the mixture was stirred for 24 h (4.5 h for **4a**). Then the reaction mixture was condensed in vacuo, and the obtained residue was purified by column chromatography on silica gel to afford desired product **4**.

***N*-(2-Nitro-1-phenylethyl)] *p*-toluenesulfonamide (4a)**: $MeNO_2$ (10 equiv, 0.11 mL) was added to a stirred solution of *N*-tosylimine **2a** (0.2 mmol, 51.8 mg) and **1a** (0.1 equiv, 8.3 mg) in CH_2Cl_2 (0.40 mL), and the mixture was stirred for 4.5 h. Then the reaction mixture was condensed in vacuo, and the obtained residue was purified by column chromatography on silica gel ($CHCl_3$/acetone 4/1 as eluant) to afford desired product **4a** (63.3 mg, 99%).

(*S*)-*N*-(2-Nitro-1-phenylethyl)] diphenylphosphinamide (4b): $MeNO_2$ (10 equiv, 0.11 mL) was added to a stirred solution of *N*-phosphinoylimine **2b** (0.2 mmol, 61.1 mg) and **1a** (0.1 equiv, 8.3 mg) in CH_2Cl_2 (0.40 mL), and the mixture was stirred for 24 h. Then the reaction mixture was condensed in vacuo, and the obtained residue was purified by column chromatography on silica gel ($CHCl_3$/acetone, 10/1 as eluant) to afford desired product **4b** (63.7 mg, 87%). HPLC analysis (Chiralcel OD-H, hexane/2-propanol 90/10, flow rate = 1.0 mL min^{-1}, λ = 210 nm): retention time t_r (major) = 13.9 min, t_r (minor) = 21.9 min; m.p. 197–198 °C ($CHCl_3$/hexane); $[\alpha]_D^{28} = +33.2$ (76% *ee*, $c = 0.90$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.93–7.67 (m, 4H), 7.59–7.10 (m, 11H), 4.97–4.77 (m, 3H), 4.36 ppm (dd, J = 8.2, 7.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.04, 137.99, 132.44, 132.36, 132.3, 131.8, 131.7, 131.3, 130.8, 129.1, 128.7, 128.6, 128.5, 126.4, 80.8, 80.7, 53.3, 53.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3371, 3063, 3034, 2991, 1555 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 367 [*M*+H]$^+$ (76), 154 (100); HRMS (FAB$^+$) calcd for $[C_{20}H_{20}N_2O_3P]^+$: 367.1211; found: 367.1210.

***N*-(2-Nitro-1-phenylethyl)acetamide (4c)**: $MeNO_2$ (10 equiv, 0.11 mL) was added to a stirred solution of *N*-Ac-imine **2c** (0.2 mmol, 29.4 mg) and **1a** (0.1 equiv, 8.3 mg) in CH_2Cl_2 (0.40 mL), and the mixture was stirred for 24 h. Then the reaction mixture was condensed in vacuo, and the obtained residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH 20/1 as eluant) to afford desired product **4c** (39.6 mg, 95%). HPLC analysis (Chiralpak AD-H, hexane/EtOH 80/20, flow rate = 0.8 mL min^{-1}, λ = 210 nm): t_r (major) = 10.2, t_r (minor) = 11.3 min; m.p. 166–169 °C (AcOEt); $[\alpha]_D^{25} = 30.8$ (63% *ee*, $c = 1.00$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.47–7.28 (m, 5H), 6.23 (d, J = 7.3 Hz, 1H), 5.80–5.58 (m, 1H), 4.93 (dd, J = 6.3, 13.0 Hz, 1H), 4.75 (dd, J = 5.7, 13.0 Hz, 1H), 2.07 ppm (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.0, 136.4, 129.2, 128.8, 126.4, 78.1, 51.2, 23.0 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3437, 3013, 2925, 2848, 1681, 1557, 1496 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 209 [*M*+H]$^+$ (68), 154 (100); elemental analysis (%) calcd for $C_{10}H_{12}N_2O_3$: C 57.69, H 5.81, N 13.45; Found: C 57.96, H 5.71, N 13.15.

Methyl 2-nitro-1-phenylethylcarbamate (4d): $MeNO_2$ (10 equiv, 0.11 mL) was added to a stirred solution of *N*-methoxycarbonylimine **2d** (0.2 mmol, 32.6 mg) and **1a** (0.1 equiv, 8.3 mg) in CH_2Cl_2 (0.40 mL), and the mixture was stirred for 24 h. Then the reaction mixture was condensed in vacuo, and the obtained residue was purified by column chromatography on silica gel (hexane/AcOEt 3/1 as eluant) to afford desired product **4d** (28.5 mg, 64%). HPLC analysis (Chiralpak AD-H, hexane/EtOH 70/30, flow rate = 0.8 mL min^{-1}, λ = 210 nm): t_r (major) = 12.2, t_r (minor) = 11.2 min; m.p. 102–110 °C ($CHCl_3$/hexane); $[\alpha]_D^{21} = 31.8$ (83% *ee*, $c = 1.05$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.43–7.27 (m, 5H), 5.66 (d, J = 6.7 Hz, 1H), 5.45 (d, J = 5.5 Hz, 1H), 4.92–4.80 (m 1H), 4.77–4.64 (m, 1H), 3.69 ppm (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 156.2, 136.6, 129.2, 128.8, 126.3, 78.6, 53.1, 52.6 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 34.38, 3030, 2958, 1725, 1558, 1504 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 225 [*M*+H]$^+$ (100); elemental analysis (%) calcd for $C_{10}H_{12}N_2O_4$: C 53.57, H 5.39, N 12.42; found: C 53.49, H 5.33, N 12.50.

Benzyl 2-nitro-1-phenylethylcarbamate (4e): $MeNO_2$ (10 equiv, 0.11 mL) was added to a stirred solution of *N*-Cbz-imine **2e** (0.2 mmol, 47.9 mg) and **1a** (0.1 equiv, 8.3 mg) in CH_2Cl_2 (0.40 mL), and the mixture was stirred for 24 h. Then the reaction mixture was condensed in vacuo, and the obtained residue was purified by column chromatography on silica gel (hexane/AcOEt 5/1 as eluant) to afford desired product **4e** (40.6 mg, 68%). HPLC analysis (Chiralpak AD-H, hexane/EtOH 70/30, flow rate = 1 mL min^{-1}, λ = 210 nm): t_r (major) = 23.1, t_r (minor) = 30.3 min; m.p. 93–94 °C ($CHCl_3$/hexane); $[\alpha]_D^{23} = 11.0$ (85% *ee*, $c = 0.98$, $CHCl_3$); ^{1}H NMR (500 MHz, [D$_6$]DMSO) δ = 8.24 (d, J = 9.2 Hz, 1H), 7.52–7.11 (m, 10H), 5.33 (dt, J = 4.7, 9.5 Hz, 1H), 5.01 (d, J = 12.5 Hz, 1H), 4.97 (d, J = 12.8 Hz, 1H), 4.91 (dd, J = 4.6, 13.1 Hz, 1H), 4.75 ppm (dd, J = 10.2, 13.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 155.5, 136.5, 135.8, 129.3, 128.9, 128.6, 128.4, 128.2, 126.3, 78.6, 67.4, 53.1 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3437, 3031, 1723, 1558, 1500 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 301 [*M*+H]$^+$ (27), 91 (100); elemental analysis (%) calcd for $C_{16}H_{16}N_2O_4$: C 63.99, H 5.37, N 9.33; found: C 63.93, H 5.43, N 9.37.

***tert*-Butyl (1*R*)-2-nitro-1-phenylethylcarbamate (4f)**: $MeNO_2$ (10 equiv, 0.11 mL) was added to a stirred solution of *N*-Boc-imine **2f** (0.2 mmol, 41.1 mg) and **1a** (0.1 equiv, 8.3 mg) in CH_2Cl_2 (0.40 mL), and the mixture was stirred for 24 h. Then the reaction mixture was condensed in vacuo, and the obtained residue was purified by column chromatography on silica gel (hexane/AcOEt 5/1 as eluant) to afford desired product **4f** (40.4 mg, 76%). HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, flow rate = 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 11.8, t_r (minor) = 14.3 min; m.p. 108–109 °C ($CHCl_3$/hexane); $[\alpha]_D^{23} = 23.7$ (90% *ee*, $c = 0.98$, $CHCl_3$); ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 7.76 (d, J = 9.16 Hz, 1H), 7.51–7.11 (m, 5H), 5.27 (dt, J = 5.0, 9.4 Hz, 1H), 4.86 (dd, J = 4.9, 13.2 Hz, 1H), 4.72 (dd, J = 10.4, 12.8 Hz, 1H), 1.33 ppm (s, 9H); ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 155.1 138.8, 128.9, 128.2, 127.0, 78.82, 78.76, 52.6, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3442, 3029, 2981, 2932, 1713, 1557, 1492 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 267 [*M*+H]$^+$ (10), 150 (100); elemental analysis (%) calcd for $C_{13}H_{18}N_2O_4$: C 58.63, H 6.81, N 10.2; found: C 58.53, H 6.85, N 10.41.

***tert*-Butyl (*R*)-2-amino-1-phenylethylcarbamate (5)**: $NaBH_4$ (12 equiv, 90.8 mg) was added to a stirred suspension of **4f** (53.3 mg, 0.20 mmol, 90% *ee*) and $NiCl_2 \cdot 6H_2O$ (1.0 equiv, 47.5 mg) in MeOH (1.1 mL) at 0 °C. After 60 min, the reaction mixture was quenched with a saturated NH_4Cl solution, and the aqueous phase was extracted with $CHCl_3$. The combined organic layers were dried over K_2CO_3, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH 5/1 as eluant) to afford desired product **7** (44.7 mg, 95%, 89% *ee*). HPLC analysis (Chiralcel OJ-H, hexane/2-propanol 70/30 with 0.1 vol% diethylamine, flow rate = 0.8 mL min^{-1}): t_r (major) = 14.0, t_r (minor) = 12.7 min; m.p. 70–72 °C (EtOH/hexane); $[\alpha]_D^{25} = 39.6$ (89% *ee*, $c = 1.10$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.12 (m, 5H), 5.46 (brs, 1H), 4.68 (brs, 1H), 3.01 (brs, 2H), 1.73 (brs, 2H), 1.43 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 155.7, 140.8, 128.7, 127.4, 126.4, 79.5, 56.4, 47.1, 28.3 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3439, 30009, 2979, 2875, 1707, 1495 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 237 [*M*+H]$^+$ (66), 181 (100); HRMS (FAB$^+$) calcd for $[C_{13}H_{21}N_2O_2]^+$: 237.1603; found: 237.1600; elemental analysis (%) calcd for $C_{13}H_{20}N_2O_2$: C 66.07, H 8.53, N 11.85; found: C 65.95, H 8.42, N 11.57.

(*R*)-*N*-(*tert*-Butoxycarbonyl)phenylglycine methyl ester (6): A solution of **4f** (53.3 mg, 0.20 mmol, 90% *ee*), sodium nitrite (3 equiv, 41.4 mg), and acetic acid (10 equiv, 0.11 mL) in DMSO (1.4 mL) was heated at 60 °C for 14 h. After the mixture had been cooled to room temperature, 1 N HCl solution (1.5 mL) was added to the solution, and the aqueous phase was extracted with $CHCl_3$. The combined organic phases were washed with brine and dried over $MgSO_4$. After filtration and evaporation of $CHCl_3$ in vacuo, K_2CO_3 (20 equiv, 552 mg) and MeI (16 equiv, 0.20 mL) were added to the obtained residue, and the mixture stirred for 3.5 h. Then water was added to the reaction mixture, and the aqueous phase extracted with Et_2O. The combined organic phases were washed with brine and dried over $MgSO_4$. After filtration and concentration in vacuo, the residual oil was purified by column chromatography on silica gel (hexane/AcOEt 5/1 as eluant) to afford desired product **8** (36.9 mg, 70%, 87% *ee*). HPLC analysis (Chiralcel OD-H, hexane/2-propanol 99.5/0.5, flow rate = 1.0 mL min^{-1}): t_r (major) = 18.5, t_r (minor) = 21.0 min; m.p. 105–106 °C ($CHCl_3$/hexane); $[\alpha]_D^{22} = 111$ (87% *ee*, $c = 1.00$, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.17 (m, 5H), 5.57 (d, J = 6.1 Hz, 1H), 5.33 (d, J = 7.3 Hz, 1H), 3.72 (s, 3H), 1.43 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.7, 154.8, 136.9, 128.9, 128.5, 127.1, 80.1, 57.5, 52.6, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3438, 3030, 3010, 2981, 2958, 2934, 1742, 1711 cm^{-1}; MS (FAB$^+$): m/z (%): 266 $[M+H]^+$ (26), 210 (100); elemental analysis (%) calcd for $C_{14}H_{19}NO_4$: C 63.38, H 7.22, N 5.28; found: C 63.09, H 7.00, N 5.34.

Typical procedure for enantioselective aza-Henry reaction of $MeNO_2$ with *N*-Boc-imines at −20 °C: $MeNO_2$ (10 equiv, 0.11 mL) was added to a stirred solution of benzaldehyde *N*-(*tert*-butoxycarbonyl) imine **2f**, **2A**–**H** (0.2 mmol) and **1a** (0.1 equiv, 8.3 mg) in CH_2Cl_2 (0.4 mL) at −20 °C, and the mixture was stirred for 24 h to 60 h. Then the reaction mixture was condensed in vacuo, and the obtained residue was purified by column chromatography on silica gel (hexane/EtOAc 5/1 as eluant) to afford desired product **4f, 7A**–**H**.

***tert*-Butyl (*R*)-2-nitro-1-phenylethylcarbamate (4f)**: According to the typical procedure, imine **2f** (0.2 mmol, 41.1 mg) and $MeNO_2$ were stirred for 24 h and converted to the product **4f** (47.9 mg, 90%) as a white solid. HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, flow rate = 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 9.0, t_r (minor) = 11.2 min; m.p. 107–108 °C (hexane/EtOAc); $[\alpha]_D^{30}$ = 25.3 (94% *ee*, c = 1.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (m, 5H), 5.38 (brs, 1H), 5.28 (brs, 1H), 4.69–4.87 (m, 2H), 1.44 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.9, 137.0, 129.3, 128.9, 126.4, 80.8, 79.0, 52.9, 28.3 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3442, 3027, 2981, 1713, 1557, 1164 cm^{-1}; MS (FAB$^+$): m/z (%): 267 $[M+H]^+$ (100); HRMS (FAB$^+$) calcd for $[C_{13}H_{19}N_2O_4]^+$: 267.1345; found: 267.1352; elemental analysis (%) calcd for $C_{13}H_{18}N_2O_4$: C 58.63, H 6.81, N 10.52; found: C 58.84, H 6.82, N 10.77.

***tert*-Butyl (*R*)-2-nitro-1-(*p*-trifluoromethylphenyl)ethylcarbamate (7A)**: According to the typical procedure, imine **2A** (0.2 mmol, 55.2 mg) and $MeNO_2$ were stirred for 24 h and converted to the product **7A** (53.5 mg, 80%) as a white solid. HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, flow rate = 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 8.3, t_r (minor) = 6.6 min; m.p. 143–144 °C (hexane/EtOAc); $[\alpha]_D^{27}$ = 11.0 (98% *ee*, c = 0.99, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18 (s, 4H), 5.33 (d, J = 5.8 Hz, 1H), 5.22 (brs, 1H), 4.83 (s, 1H), 4.68 (dd, J = 12.4, 5.7 Hz, 1H), 2.34 (s, 3H), 1.44 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.8, 138.7, 133.9, 129.9, 126.3, 80.6, 78.9, 52.6, 28.2 21.0 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3442, 3027, 2981, 1713, 1557, 1164 cm^{-1}; MS (FAB$^-$): m/z (%): 333 $[M-H]^-$ (76), 216 (100); HRMS (FAB$^-$) calcd for $[C_{14}H_{16}F_3N_2O_4]^-$: 333.1062; found: 333.1054; elemental analysis (%) calcd for $C_{14}H_{17}F_3N_2O_4$: C 50.30, H 5.13, N 8.38; found: C 50.03, H 5.13, N 8.34.

***tert*-Butyl (*R*)-2-nitro-1-(4-methylphenyl)ethylcarbamate (7B)**: According to the typical procedure, imine **2B** (0.2 mmol, 43.8 mg) and $MeNO_2$ were stirred for 24 h and converted to the product **7B** (46.2 mg, 82%) as a white solid. HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, flow rate = 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 9.1, t_r (minor) = 10.9 min; m.p. 135–136 °C (hexane/EtOAc); $[\alpha]_D^{27}$ = 28.0 (93% *ee*, c = 1.01, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18 (s, 4H), 5.33 (d, J = 5.8 Hz 1H), 5.22 (brs, 1H), 4.83 (s, 1H), 4.68 (dd, J = 12.4, 5.7 Hz, 1H), 2.34 (s, 3H), 1.44 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.8, 138.7, 133.9, 129.9, 126.3, 80.6, 78.9, 52.6, 28.2, 21.0 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3442, 3027, 2981, 1713, 1557, 1164 cm^{-1}; MS (FAB$^+$): m/z (%): 281 $[M+H]^+$ (35), 164 (100); HRMS (FAB$^+$) calcd for $[C_{14}H_{21}N_2O_4]^+$: 281.1501; found: 281.1499; elemental analysis (%) calcd for $C_{14}H_{20}N_2O_4$: C 59.99, H 7.19, N 9.99; found: C60.25, H 7.31, N 9.84.

***tert*-Butyl (*R*)-2-nitro-1-(*p*-methoxyphenyl)ethylcarbamate (7C)**: According to the typical procedure, imine **2C** (0.2 mmol, 59.2 mg) and $MeNO_2$ were stirred for 60 h and converted to the product **7C** (42.3 mg, 71%) as a white solid. HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, flow rate = 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 14.0, t_r (minor) = 13.2 min; m.p. 145–146 °C (hexane/EtOAc); $[\alpha]_D^{27}$ = 36.0 (95% *ee*, c = 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.22 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 5.31 (s, 1H), 5.23 (d, J = 7.0 Hz, 1H), 4.83 (s, 1H), 4.66 (dd, J = 12.0, 5.3 Hz, 1H), 3.80 (s, 3H), 1.44 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.8, 154.8, 128.9, 127.6, 114.6, 80.6, 78.9, 55.3, 52.4, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3443, 3027, 2980, 1712, 1557, 1164 cm^{-1}; MS (FAB$^+$): m/z (%): 297 $[M+H]^+$ (45), 180 (100); elemental analysis (%) calcd for $C_{14}H_{20}N_2O_5$: C 56.75, H 6.80, N 9.45; found: C 56.50, H6.60, N 9.33.

***tert*-Butyl (*R*)-2-nitro-1-(1-naphthyl)ethylcarbamate (7D)**: According to the typical procedure, imine **2D** (0.2 mmol, 51.1 mg) and $MeNO_2$ were stirred for 24 h and converted to the product **7D** (53.4 mg, 85%) as a white solid. HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, flow rate = 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 10.2, t_r (minor) = 7.5 min; m.p. 177–178 °C (hexane/EtOAc); $[\alpha]_D^{28}$ = 6.13 (95% *ee*, c = 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.12 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.84 (dd, J = 5.7, 3.5 Hz, 1H), 7.61 (t, J = 7.3 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.45 (m, 2H), 6.27 (s, 1H), 5.37 (d, J = 4.9 Hz, 1H), 4.88 (brs, 2H), 1.43 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.7, 134.1, 132.6, 130.3, 129.5, 129.3, 127.3, 126.3, 125.2, 123.3, 122.2, 80.7, 78.2, 49.2, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3440, 3030, 2982, 1713, 1558, 1164 cm^{-1}; MS (FAB$^-$): m/z (%): 315 $[M-H]^-$ (90), 153 (100); HRMS (FAB$^-$) calcd for $[C_{17}H_{19}N_2O_4]^-$: 315.1345; found: 315.1344; elemental analysis (%) calcd for $C_{17}H_{20}N_2O_4$: C 64.54, H 6.37, N 8.86; found: C 64.38, H 6.34, N 8.76.

***tert*-Butyl (*R*)-2-nitro-1-(2-naphthyl)ethylcarbamate (7E)**: According to the typical procedure, imine **2E** (0.2 mmol, 51.1 mg) and $MeNO_2$ were stirred for 48 h and converted to the product **7E** (53.7 mg, 85%) as a white solid. HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, flow rate = 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 14.6, t_r (minor) = 11.7 min; m.p. 168–169 °C (hexane/EtOAc); $[\alpha]_D^{28}$ = 28.6 (88% *ee*, c = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (s, 1H), 7.86 (s, 1H), 7.83 (m, 2H), 7.77 (s, 1H), 7.52 (m, 2H), 7.40 (dd, J = 8.6, 1.5 Hz, 1H), 5.47 (m, 2H), 4.95 (brs, 1H), 4.80 (m, 1H), 1.45 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.7, 134.1, 132.6, 130.3, 129.6, 129.3, 127.3, 126.3, 125.3, 123.2, 122.2, 80.8, 78.2, 49.2, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3440, 3027, 2982, 1714, 1557, 1163 cm^{-1}; MS (FAB$^-$): m/z (%): 315 $[M-H]^-$ (75), 153 (100); HRMS (FAB$^-$) calcd for $[C_{17}H_{19}N_2O_4]^-$: 315.1345; found: 315.1354.

***tert*-Butyl (*R*)-2-nitro-1-(2-furyl)ethylcarbamate (7F)**: According to the typical procedure, imine **2F** (0.20 mmol, 39.1 mg) and $MeNO_2$ were stirred for 60 h and converted to the product **7F** (41.1 mg, 81%) as a white solid. HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, flow rate = 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 9.1, t_r (minor) = 13.9 min; m.p. 98–100 °C (hexane/EtOAc); $[\alpha]_D^{28}$ = 6.13 (79% *ee*, c = 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 (d, J = 1.5 Hz, 1H), 6.53 (m, 1H), 6.31 (d, J = 3.1 Hz, 1H), 5.47 (d, J = 6.1 Hz, 1H), 5.32 (s, 1H), 4.85 (s, 1H), 4.73 (dd, J = 13.0, 5.7 Hz, 1H), 1.46 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.7, 149.5, 142.9, 110.7, 107.8, 80.8, 76.5, 47.1, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3443, 3029, 2982, 1714, 1559, 1162 cm^{-1}; MS (FAB$^-$): m/z (%): 255 $[M-H]^-$ (85), 153 (100); HRMS (FAB$^-$) calcd for $[C_{11}H_{15}N_2O_5]^-$: 255.0981; found: 255.0974; elemental analysis (%) calcd for $C_{11}H_{16}N_2O_5$: C 51.56, H 6.29, N 10.93; found: C 51.62, H 6.10, N 10.66.

***tert*-Butyl (*R*)-2-nitro-1-(3-pyridyl)ethylcarbamate (7G)**: According to the typical procedure, imine **2G** (0.20 mmol, 41.2 mg) and $MeNO_2$ were stirred for 24 h and converted to the product **7G** (47.2 mg, 89%) as a white solid. HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, flow rate = 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 24.1, t_r (minor) = 19.4 min; m.p. 151–152 °C (hexane/EtOAc); $[\alpha]_D^{28}$ = 21.0 (98% *ee*, c = 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.63 (d, J = 21.4 Hz, 2H), 7.70 (d, J = 7.9 Hz, 1H), 7.34 (dd, J = 7.5, 4.7 Hz, 1H), 5.73 (s, 1H), 5.43 (s, 1H), 4.91 (s, 1H), 4.76 (d, J = 8.9 Hz, 1H), 1.44 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.7, 149.7, 148.0, 134.4, 133.1, 123.9, 81.0, 78.2, 50.7, 28.1 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3440, 3029, 2982, 1714, 1560, 1163 cm^{-1}; MS (FAB$^-$): m/z (%): 266 $[M-H]^-$ (50), 153 (100); HRMS (FAB$^-$) calcd for $[C_{12}H_{16}N_3O_4]^-$: 266.1141; found: 266.1143; elemental analysis (%) calcd for $C_{12}H_{17}N_3O_4$: C 53.92, H 6.41, N 15.72; found: C 53.72, H 6.43, N 15.68.

***tert*-Butyl (*R*)-2-nitro-1-(2-thienyl)ethylcarbamate (7H)**: According to the typical procedure, imine **2H** (0.20 mmol, 42.2 mg) and $MeNO_2$ were stirred for 24 h and converted to the product **7H** (49.0 mg, 90%) as a white solid. HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, flow rate = 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 11.2, t_r (minor) = 14.7 min; m.p. 113–114 °C (hexane/EtOAc); $[\alpha]_D^{30}$ = 5.4 (83% *ee*, c = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (dd, J = 4.9, 1.2 Hz, 1H), 7.00 (m,

2H), 5.62 (m, 1H), 5.32 (brs, 1H), 4.83 (m, 2H), 1.46 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.8, 140.3, 127.6, 126.0, 125.6, 81.1, 78.8, 49.1, 28.4 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 2959, 2928, 2360, 1716, 1559, 1161 cm^{-1}; MS (FAB$^-$): *m*/*z* (%): 271 [*M*−H]$^-$ (50), 153 (100); HRMS (FAB$^-$) calcd for $[C_{11}H_{15}N_2O_4S]^-$: 271.0753; found: 271.0747.

Typical procedure for enantioselective aza-Henry reaction of nitro substrates with *N*-Boc-imines: Nitro substrate (**3b**–**k**, 2.0–5.0 equiv) was added to a stirred solution of benzaldehyde *N*-(*tert*-butoxycarbonyl) imines **2f**, **2A**–**B, 2G** (0.2 mmol) and thiourea (0.1 equiv, 8.3 mg) in CH_2Cl_2 (0.4 mL), and the mixture was stirred for 24 h to 72 h at the −20 °C. Then the reaction mixture was condensed in vacuo and the obtained residue was purified by column chromatography on silica gel (hexane/EtOAc 5/1 as eluant) to afford desired products **8A**–**M, 9A.**

***tert*-Butyl (1*R*,2*S*)-2-nitro-1-phenylbutylcarbamate (8A) and *tert*-Butyl (1*R*,2*R*)-2-nitro-1-phenylbutyl carbamate (9A)**: According to the typical procedure, imine **2f** (0.20 mmol, 41.1 mg) and nitro compound **3b** were converted to products **8A** and **9A** as white solids (53.0 mg, 90%) and a **8A**/**9A** (88/12) mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The *ee* of major diastereomer **8A** was determined to be 95% by chiral HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, 1 mL min^{-1}, λ = 210 nm): t_r (major) = 5.3 min, t_r (minor) = 5.8 min; and that of the the minor diastereomer **9A** was determined to be 79% (Chiralpak AD, hexane/*i*PrOH 85/15, 1 mL min^{-1}, λ = 210 nm): t_r (major) = 15.1 min, t_r (minor) = 13.0 min; m.p. 156–157 °C (hexane/EtOAc); $[\alpha]_D^{30}$ = 29.6 (*c* = 1.01, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 730–7.40 (m, 3H), 7.22–7.26 (m, 2H), 5.14–5.20 (brs, 1H), 5.10–5.14 (m, 1H), 4.74 (brs, 1H), 1.84–1.92 (m, 2H), 1.43 (s, 9H), 0.96–1.03 ppm (t, *J* = 3.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.9, 136.7, 129.0, 128.7, 126.9, 93.0, 74.8, 56.8, 28.2, 24.8, 10.4 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3441, 2961, 2928, 1713, 1491, 1423 cm^{-1}; MS (FAB$^-$): *m*/*z* (%): 293 [*M*−H]$^-$ (100); HRMS (FAB$^-$) calcd for $[C_{15}H_{21}N_2O_4]^-$: 293.1501; found: 293.1509; elemental analysis (%) calcd for $C_{15}H_{22}N_2O_4$: C 61.21, H 7.53, N 9.52; found: C 60.43, H 6.87, N 9.53.

***tert*-Butyl (1*R*,2*S*)-2-nitro-1-phenylpropylcarbamate (8B)**: According to the typical procedure, imine **2f** (0.20 mmol, 41.1 mg) and nitro compound **3c** were converted to the product **8B** (51.5 mg, 92%) as a white solid and a 90/10 mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The major diastereomer was determined to have 93% *ee* by chiral HPLC analysis (Chiralpak AD-H, hexane/*i*PrOH 90/10, 1 mL min^{-1}, λ = 210 nm): t_r (major) = 10.7 min, t_r (minor) = 9.9 min; and the minor diastereomer was determined to have 83% *ee* under the same HPLC analysis conditions: t_r (major) = 13.0 min, t_r (minor) = 15.8 min; m.p. 143–144 °C (hexane/EtOAc); $[\alpha]_D^{30}$ = 22.0 (*c* = 1.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28–7.34 (m, 3H), 7.18–7.21 (m, 2H), 5.32 (brs, 1H), 5.16 (dd, *J* = 8.8, 5.8 Hz, 1H), 4.88 (brs, 1H), 1.49 (d, *J* = 6.7 Hz, 3H), 1.39 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 155.2, 136.7, 129.3, 129.0, 127.2, 86.0, 80.0, 57.7, 28.4, 15.5 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3439, 2982, 2937, 1713, 1554 cm^{-1}; MS (FAB$^-$): *m*/*z* (%): 279 [*M*−H]$^-$ (90), 153 (100); HRMS (FAB$^-$) calcd for $[C_{14}H_{19}N_2O_4]^-$: 279.1345; found: 279.1350; elemental analysis (%) calcd for $C_{14}H_{20}N_2O_4$: C 59.99, H 7.19, N 9.99; found: C 59.84, H 6.92, N 9.92.

***tert*-Butyl (1*R*,2*S*)-2-nitro-1-phenylhexylcarbamate (8C)**: According to the typical procedure, imine **2f** (0.20 mmol, 41.1 mg) and nitro compound **3d** were converted to product **8C** as a white solid (55.0 mg, 82%) and a 93/7 mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The major diastereomer was determined to have 99% *ee* by chiral HPLC analysis (Chiralpak AD-H, hexane/*i*PrOH 80/20, 0.5 mL min^{-1}, λ = 210 nm): t_r (major) = 13.8 min, t_r (minor) = 10.2 min; and the minor diastereomer was determined to have 97% *ee* under the same HPLC analysis conditions: t_r (major) = 12.7 min, t_r (minor) = 15.6 min; m.p. 113–114 °C (hexane/EtOAc); $[\alpha]_D^{30}$ = 14.7 (*c* = 1.14, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$):δ = 7.28–7.38 (m, 3H), 7.19–7.26 (m, 2H), 5.02–5.29 (m, 2H), 4.72–4.78 (brs, 1H), 1.76–2.04 (m, 2H), 1.43 (s, 9H), 1.24–1.35 (m, 6H), 0.84–0.87 ppm (t, *J* = 6.71, 10.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.9, 136.7, 129.0, 128.7, 126.9, 126.3, 91.5, 80.5, 56.9, 31.0, 29.7, 28.2, 25.5, 22.2, 13.8 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3440, 3026, 1714, 1554, 1211, 1023 cm^{-1}; MS (FAB$^-$): *m*/*z* (%): 335 [*M*−H]$^-$ (100); HRMS (FAB$^-$) calcd for $[C_{18}H_{27}N_2O_4]^-$: 335.1971; found: 335.1978; elemental analysis (%) calcd for $C_{18}H_{28}N_2O_4$: C 64.26, H 8.39, N 8.33; found: C 63.78, H 8.30, N 8.27.

***tert*-Butyl (1*R*,2*S*)-2-nitro-1,3-diphenylpropylcarbamate (8D)**: According to the typical procedure, imine **2f** (0.20 mmol, 41.1 mg) and nitro compound **3e** were converted to the product **8D** as a white solid (60.0 mg, 84%) and a 83/17 mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The major diastereomer was determined to have 97% *ee* by chiral HPLC analysis (Chiralpak AD-H, hexane/EtOH 85/15, 0.5 mL min^{-1}, λ = 210 nm): t_r (major) = 14.3 min, t_r (minor) = 15.2 min; and the minor diastereomer was determined to have 78% *ee* under the same HPLC analysis conditions: t_r (major) = 17.7 min, t_r (minor) = 16.2 min; m.p. 189–190 °C (hexane/EtOAc); $[\alpha]_D^{30}$ = 51.6 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$):δ = 7.33–7.41 (m, 3H), 7.26–7.31 (m, 4H), 7.12–7.25 (m, 3H), 5.19–5.30 (m, 2H), 4.99–5.10 (brs, 1H), 3.25–3.35 (m, 1H), 3.13–3.20 (dd, *J* = 3.5, 14.8 Hz, 1H), 1.46 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 155.0, 136.4, 135.5, 129.2, 129.0, 128.9, 128.8, 127.5, 127.0, 92.7, 80.8, 57.3, 36.2, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3436, 3019, 1715, 1556, 1369, 1162 cm^{-1}; MS (FAB$^-$): *m*/*z* (%): 355 [*M*−H]$^-$ (100); HRMS (FAB$^-$) calcd for $[C_{20}H_{23}N_2O_4]^-$: 355.1658; found: 355.1651; elemental analysis (%) calcd for $C_{20}H_{24}N_2O_4$: C 67.40, H 6.79, N 7.86; found: C 67.26, H 6.67, N 7.82.

***tert*-Butyl (1*R*,2*S*)-3-hydroxy-2-nitro-1-phenylpropylcarbamate (8E)**: According to the typical procedure, imine **2f** (0.20 mmol, 41.1 mg) and nitro compound **3f** were converted to the product **8E** as a white solid (44.5 mg, 75%) and a 75/25 mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The major diastereomer was determined to have 90% *ee* by chiral HPLC analysis (Chiralpak AD-H, 85/15 hexane/EtOH, 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 14.9 min, t_r (minor) = 10.4 min; and the minor diastereomer was determined to have 82% *ee* under the same HPLC analysis conditions: t_r (major) = 12.1 min, t_r (minor) = 21.5 min; m.p. 103–109 °C (hexane/EtOAc); $[\alpha]_D^{30}$ = 24.5 (*c* = 0.85, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$):δ = 7.27–7.41 (m, 5H), 5.41–5.66 (m, 1H), 5.19–5.35 (m, 1H), 4.77–5.03 (m, 1H), 4.06–4.19 (m, 2H), 3.48–3.97 (m, 1H), 1.44 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 156.3, 136.4, 129.3, 128.7, 126.3, 91.6, 81.4, 61.5, 58.7, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3437, 3019, 1714, 1555, 1360, 1060 cm^{-1}; MS (FAB$^-$): *m*/*z* (%): 295 [*M*−H]$^-$ (45), 153 (100); HRMS (FAB$^-$) calcd for $[C_{14}H_{19}N_2O_5]^-$: 295.1294; found: 295.1297; elemental analysis (%) calcd for $C_{14}H_{20}N_2O_5$: C 56.75, H 6.80, N 9.45; found: C 55.48, H 6.58, N 9.57.

***tert*-Butyl (1*R*,2*S*)-3-benzyloxy-2-nitro-1-phenylpropylcarbamate (8F)**: According to the typical procedure, imine **2f** (0.20 mmol, 41.1 mg) and nitro compound **3g** were converted to the product **8F** as a white solid (61.5 mg, 80%) and a 86/14 mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The major diastereomer was determined to have 95% *ee* by chiral HPLC analysis (Chiralpak AD-H, hexane/*i*PrOH 85/15, flow rate = 0.5 mL min^{-1}, λ = 210 nm): t_r (major) = 26.8 min, t_r (minor) = 30.2 min; and the minor diastereomer was determined to have 89% *ee* under the same HPLC analysis conditions: t_r (major) = 24.7 min, t_r (minor) = 28.4 min; m.p. 101–102 °C (hexane/EtOAc); $[\alpha]_D^{30}$ = 12.4 (*c* = 1.03, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30–7.37 (m, 6H), 7.21–7.25 (m, 4H), 5.58 (brs, 1H), 5.10–5.25 (m, 1H), 5.06 (brs, 1H), 4.46–4.53 (s, 2H), 3.67–4.03 (m, 2H), 1.41 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.9, 136.9, 136.6, 129.2, 128.6, 127.9, 127.8, 126.7, 126.2, 90.7, 80.5, 73.6, 68.6, 56.8, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3436, 3010, 1715, 1561, 1369, 1097 cm^{-1}; MS (FAB$^-$): *m*/*z* (%): 385 [*M*−H]$^-$ (100); HRMS (FAB$^-$) calcd for $[C_{21}H_{25}N_2O_5]^-$: 385.1763; found: 385.1786; elemental analysis (%) calcd for $C_{21}H_{26}N_2O_5$: C 65.27, H 6.78, N 7.25; found: C 66.41, H 6.70, N 6.69.

***tert*-Butyl (1*R*,2*S*)-4-benzyloxy-2-nitro-1-phenylbutylcarbamate (8G)**: According to the typical procedure, imine **2f** (0.20 mmol, 41.1 mg) and nitro compound **3h** were converted to the product **8G** as a white solid (68.5 mg, 86%) and a 93/7 mixture of diastereomers by ^{1}H NMR ($CDCl_3$) analysis. The major diastereomer was determined to have 94% *ee* by chiral HPLC analysis (Chiralpak AD-H, 85/15 hexane/EtOH, 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 9.6 min, t_r (minor) = 12.3 min; and the minor diastereomer was determined to have 98% *ee* under the same HPLC analysis condition: t_r (major) = 15.5 min, t_r (minor) = 11.3 min; m.p. 69–70 °C (hexane/EtOAc); $[\alpha]_D^{30}$ = 35.0 (*c* = 1.22, $CHCl_3$); ^{1}H NMR

(500 MHz, $CDCl_3$): $\delta = 7.26$–7.37 (m, 8H), 7.20–7.25 (m, 2H), 5.15–5.28 (m, 2H), 5.08 (brs, 1H), 4.42–4.49 (m, 2H), 3.36–3.61 (m, 2H), 2.13–2.36 (m, 2H), 1.43 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 154.9$, 137.8, 136.7, 129.0, 128.6, 128.5, 127.9, 126.9, 88.3, 80.4, 73.3, 65.8, 56.9, 30.3, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3437$, 3028, 1714, 1555, 1369, 1163 cm^{-1}; MS (FAB^-): m/z (%): 399 $[M-H]^-$ (100); HRMS (FAB^-) calcd for $[C_{22}H_{27}N_2O_5]^-$: 399.1920; found: 399.1925; elemental analysis (%) calcd for $C_{14}H_{20}N_2O_4$: C 59.99, H 7.19, N 9.99; found: C 59.84, H 6.92, N 9.92.

***tert*-Butyl (1*R*,2*S*)-5-benzyloxy-2-nitro-1-phenylpentylcarbamate (8H)**: According to the typical procedure, imine **2f** (0.20 mmol, 41.1 mg) and nitro compound **3i** were converted to the product **8H** as a white solid (66.0 mg, 80%) and a 91/9 mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The major diastereomer was determined to have 92% *ee* by chiral HPLC analysis (Chiralpak AD-H, 80:20 hexane/EtOH, 0.5 mL min^{-1}, $\lambda = 210$ nm): t_r (major) = 14.8 min, t_r (minor) = 13.7 min; and the minor diastereomer was determined to have 73% *ee* under the same HPLC analysis conditions: t_r (major) = 17.8 min, t_r (minor) = 16.5 min; m.p. 75–76 °C (hexane/EtOAc); $[\alpha]_D^{30} = 3.91$ ($c = 0.72$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$):$\delta = 7.27$–7.35 (m, 7H),M 7.15–7.24 (m, 3H), 5.05–5.29 (m, 2H), 4.72–4.99 (brs, 1H), 4.42–4.50 (s, 2H), 3.33–3.46 (m, 2H), 1.99–2.30 (m, 2H), 1.53–1.75 (m, 2H), 1.41 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 154.9$, 138.2, 136.7, 129.0, 128.7, 128.6, 128.5, 127.7, 126.9, 91.2, 80.5, 72.9, 68.9, 65.8, 56.9, 28.2, 26.0 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3436$, 3026, 1715, 1554, 1368, 1164 cm^{-1}; MS (FAB^-): m/z (%): 413 $[M-H]^-$ (100); HRMS (FAB^-) calcd for $[C_{23}H_{29}N_2O_5]^-$: 413.2076; found: 413.2070; elemental analysis (%) calcd for $C_{23}H_{30}N_2O_5$: C 66.98, H 7.05, N 7.00; found: C 66.18, H 6.96, N 6.76.

***tert*-Butyl (1*R*,2*S*)-5-hydroxy-2-nitro-1-phenylpentylcarbamate (8I)**: According to the typical procedure, imine **2f** (0.20 mmol, 41.1 mg) and nitro compound **3j** were converted to the product **8I** as a white solid (51.5 mg, 80%) and a 92/8 mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The major diastereomer was determined to have 89% *ee* by chiral HPLC analysis (Chiralpak AD-H, 85/15 hexane/EtOH, 1.0 mL min^{-1}, $\lambda = 210$ nm): t_r (major) = 6.2 min, t_r (minor) = 8.0 min; and the minor diastereomer was determined to have 87% *ee* under the same HPLC analysis conditions: t_r (major) = 15.8 min, t_r (minor) = 17.0 min; m.p. 155–156 °C (hexane/EtOAc); $[\alpha]_D^{30} = 3.72$ ($c = 1.50$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$):$\delta = 7.31$–7.40 (m, 3H), 7.21–7.26 (m, 2H), 5.13–5.24 (m, 2H), 4.92 (brs, 1H), 3.63–3.72 (m, 2H), 3.1.96–2.17 (m, 2H), 1.64–1.66 (m, 1H), 1.54–1.59 (m, 1H), 1.43 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 155.0$, 136.7, 129.1, 128.9, 126.9, 91.1, 83.8, 61.7, 56.9, 28.6, 28.2 26.5 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3033$, 2959, 2927, 1731, 1554, 1376, 1161, 1046 cm^{-1}; MS (FAB^-): m/z (%): 323 $[M-H]^-$ (100); HRMS (FAB^-) calcd for $[C_{16}H_{24}N_2O_5]^-$: 323.1607; found: 323.1617.

***tert*-Butyl (1*R*,2*S*)-2-nitro-1-phenyl-5-(trifluoromethanesulfonyloxy)pentylcarbamate (8J)**: According to the typical procedure, imine **2f** (0.20 mmol, 41.1 mg) and nitro compound **3k** were converted to the product **8J** as a white solid (71.0 mg, 78%) and a 93/7 mixture of diastereomers by ^{1}H NMR ($CDCl_3$) analysis. The major diastereomer was determined to have 90% *ee* by chiral HPLC analysis (Chiralpak AD-H, hexane/*i*PrOH 85/15, 1.0 mL min^{-1}, $\lambda = 210$ nm): t_r (major) = 13.7 min, t_r (minor) = 9.1 min; and the minor diastereomer was determined to have 55% *ee* under the same HPLC analysis conditions: t_r (major) = 15.2 min, t_r (minor) = 19.2 min; m.p. 94–95 °C (hexane/EtOAc); $[\alpha]_D^{30} = 8.42$ ($c = 0.95$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$):$\delta = 7.32$–7.40 (m, 3H), 7.22–7.26 (d, $J = 7.0$ Hz, 2H), 5.06–5.24 (m, 2H), 4.80–4.95 (brs, 1H), 4.29–4.36 (m, 2H), 1.94–2.27 (m, 2H), 1.76–1.92 (m, 2H), 1.43 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 161.9$, 154.9, 136.3, 129.2, 126.9, 126.4, 90.6, 80.7, 74.7, 67.8, 56.9, 28.2, 24.8 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3443$, 3024, 1714, 1556, 1393, 1164, 1052 cm^{-1}; MS (FAB^-): m/z (%): 305 $[M-HOTf]^-$ (100); HRMS (FAB^-) calcd for $C_{16}H_{21}N_2O_4$ $[M-HOTf)]^-$: 305.1501; found: 305.1515.

***tert*-Butyl (1*R*,2*S*)-2-nitro-1-(*p*-triflouromethylphenyl)-1,3-diphenylpropylcarbamate (8K)**: According to the typical procedure, imine **2A** (0.20 mmol, 54.6 mg) and nitro compound **3e** were converted to the product **8K** (79.5 mg, 94%) as a white solid and a 97/3 mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The major diastereomer was determined to have 95% *ee* by chiral HPLC analysis (Chiralpak AD-H, hexane/*i*PrOH 90/10, 1.0 mL min^{-1}, $\lambda = 210$ nm): t_r (major) = 12.9 min, t_r (minor) = 9.9 min; and the minor diastereomer was determined to have 87% *ee* under the same HPLC analysis conditions: t_r (major) = 10.8 min, t_r (minor) = 28.7 min; m.p. 205–206 °C (hexane/EtOAc); $[\alpha]_D^{30} = 50.0$ ($c = 0.10$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.62$–7.65 (dd, $J = 12.8$, 7.9 Hz, 2H), 7.39–7.42 (d, $J = 7.9$ Hz, 1H), 7.25–7.37 (m, 4H), 7.12–7.16 (m, 2H), 5.29 (brs, 1H), 5.21 (s, 1H), 5.04–5.13 (m, 1H), 3.15–3.38 (m, 2H), 1.44 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 172.7$, 154.8, 134.9, 129.2, 129.0, 128.8, 127.7, 126.7, 126.1, 92.2, 81.2, 56.8, 37.5, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3438$, 2932, 1715, 1557 cm^{-1}; MS (FAB^-): m/z (%): 423 $[M-H]^-$ (60), 153 (100); HRMS (FAB^-) calcd for $[C_{21}H_{22}F_3N_2O_4]^-$: 423.1532; found: 423.1528; elemental analysis (%) calcd for $C_{21}H_{23}N_2O_4$: C 59.43, H 5.46, N 6.60; found: C 59.21, H 5.44, N 6.47.

***tert*-Butyl (1*R*,2*S*)-1-(*p*-methylphenyl)-2-nitro-1,3-diphenylpropylcarbamate (8L)**: According to the typical procedure, imine **2B** (0.20 mmol, 43.8 mg) and nitro compound **3e** were converted to the product **8L** (66.5 mg, 90%) as a white solid and a 93/7 mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The major diastereomer was determined to have 92% *ee* by chiral HPLC analysis (Chiralpak AD-H, hexane/*i*PrOH 95/5, 1.0 mL min^{-1}, $\lambda = 210$ nm): t_r (major) = 24.7 min, t_r (minor) = 22.4 min; and the minor diastereomer was determined to have 57% *ee* under the same HPLC analysis conditions: t_r (major) = 34.1 min, t_r (minor) = 21.6 min; m.p. 156–157 °C (hexane/EtOAc); $[\alpha]_D^{30} = 73.0$ ($c = 0.20$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.26$–7.29 (m, 3H), 7.14–7.17 (m, 6H), 5.19 (brs, 2H), 5.05–5.09 (m, 1H), 3.14–3.30 (m, 2H), 2.34 (s, 3H), 1.44 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 155.0$, 138.8, 135.5, 133.3, 129.8, 128.8, 127.4, 126.8, 126.2, 92.8, 80.6, 57.1, 36.2, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3025$, 2360, 1714, 1556, 1162 cm^{-1}; MS (FAB^-): m/z (%): 369 $[M-H]^-$ (80), 153 (100); HRMS (FAB^-) calcd for $[C_{21}H_{25}N_2O_4]^-$: 369.1814; found: 369.1819; elemental analysis (%) calcd for $C_{21}H_{26}N_2O_4$: C 68.09, H 7.07, N 7.56; found: C 68.01, H 7.00, N 7.50.

***tert*-Butyl (1*R*,2*S*)-2-nitro-1-(3-pyridine)-1,3-diphenylpropylcarbamate (8M)**: According to the typical procedure, imine **2G** (0.20 mmol, 41.2 mg) and nitro compound **3e** were converted to the product **8M** (66.5 mg, 93%) as a white solid and a 83/17 mixture of diastereomers by ^{1}H NMR ([D$_6$]DMSO) analysis. The major diastereomer was determined to have 93% *ee* by chiral HPLC analysis (Chiralpak AD-H, hexane/*i*PrOH 90/10, 1 mL min^{-1}, $\lambda = 210$ nm): t_r (major) = 23.9 min, t_r (minor) = 20.4 min; and the minor diastereomer was determined to have 65% *ee* under the same HPLC analysis conditions: t_r (major) = 44.0 min, t_r (minor) = 30.4 min; m.p. 169–170 °C (hexane/EtOAc); $[\alpha]_D^{30} = 26.1$ ($c = 0.72$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.55$–8.58 (d, $J = 12.8$ Hz, 2H), 7.57–7.62 (m, 1H), 7.27–7.34 (m, 4H), 7.14–7.17 (dd, $J = 11.1$, 7.2 Hz, 2H), 5.92 (brs, 1H), 5.19–5.23 (m, 1H), 5.04–5.06 (m, 1H), 3.29–3.40 (m, 1H), 3.16–3.19 (dd, $J = 14.7$, 3.7 Hz, 1H), 1.44 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 149.9$, 134.3, 133.8, 129.2, 129.0, 128.8, 128.6, 128.0, 127.7, 123.8, 92.9, 81.8, 59.5, 38.6, 28.2 ppm; IR ($CHCl_3$): $\tilde{\nu} = 3437$, 2984, 2360, 1715, 1557 cm^{-1}; MS (FAB^-): m/z (%): 356 $[M-H]^-$ (75), 153 (100); HRMS (FAB^-) calcd for $[C_{19}H_{22}N_3O_4]^-$: 356.1610; found: 356.1622; elemental analysis (%) calcd for $C_{19}H_{23}N_3O_4$: C 63.85, H 6.49, N 10.97; found: C 63.65, H 6.70, N 10.97.

***tert*-Butyl (1*R*,2*S*)-5-(methanesulfonyloxy)-2-nitro-1-phenylpentylcarbamate (11)**: 4-*O*-methanesulfonyl-1-nitrobutane[7] (**10**, 0.60 mmol, 1.5 equiv, 118.2 mg) was added to a stirred solution of imine **2f** (0.40 mmol, 82.3 mg) and **1a** (0.1 equiv, 16.5 mg) in CH_2Cl_2 (0.8 mL, 0.5 M) at −20 °C and then stirred for 72 h. The reaction mixture was concentrated in vacuo, and the obtained residue was purified by flash column chromatography on silica gel (hexane/EtOAc 2/1 as eluant) to afford desired product **11** as a white solid (131.9 mg, 80%) as a 80/20 (**11a**/**11b**) mixture of diastereomers by ^{1}H NMR ($CDCl_3$) analysis. The major diastereomer **11a** was determined to have 96% *ee* by chiral HPLC analysis (Chiralpak AD, hexane/*i*PrOH 90/10, flow rate = 1.0 mL min^{-1}, $\lambda = 210$ nm): t_r (major) = 39.8 min, t_r (minor) = 36.4 min; and the minor diastereomer **11b** was determined to have 83% *ee* under the same HPLC analysis conditions: t_r (major) = 64.0 min, t_r (minor) = 81.0 min; m.p. 85–86 °C (hexane/EtOAc); $[\alpha]_D^{25} = -24.4$ ($c = 0.82$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.29$–7.40 (m, 3H), 7.21–7.27 (m, 2H), 5.20–5.27

(m, 1H), 5.07–5.20 (m, 1H), 4.90 (brs, 1H), 4.18–4.31 (m, 2H), 3.01 (s, 3H), 2.04–2.18 (m, 2H), 1.76–1.84 (m, 2H), 1.43 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 155.0, 136.3, 129.1, 126.9, 126.3, 90.5, 80.6, 68.2, 56.8, 37.3, 28.1, 26.2, 25.4 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3036, 2927, 1735, 1231 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 403 [*M*+H]$^+$ (7), 347 (100); HRMS (FAB$^+$) calcd for $[C_{17}H_{27}N_2O_7S]^+$: 403.1539; found: 403.1534; elemental analysis (%) calcd for $C_{17}H_{26}N_2O_7S$: C 50.73, H 6.51, N 6.96; found: C 50.57, H 6.24, N 7.00.

(2*R*,3*S*)-3-Nitro-2-phenylpiperidine (12): Trifluoroacetic acid (TFA, 280.2 mg, 2.0 mmol, 10 equiv) was added to a stirred ice-cooled solution of **11** (80.4 mg, 0.2 mmol, mixture of diastereomers **11a**/**11b** = 86/14) in CH_2Cl_2 (1.0 mL), and stirring was continued for 3 h under a N_2 atmosphere. After addition of saturated aqueous K_2CO_3 (5 mL), the aqueous phase was extracted with AcOEt. The combined organic phases were washed with brine, dried (Na_2SO_4), and concentrated in vacuo, and the crude material was purified by column chromatography on silica gel (hexane/EtOAc 1/1 as eluant) to give **12** as a colorless oil (33.0 mg, 80%) as a 9/1 (*trans*/*cis*) mixture of diastereomers by ^{1}H NMR ($CDCl_3$) analysis. The major diastereomer was determined to have 94% *ee* by chiral HPLC analysis (Chiralpak AD-H, hexane/*i*PrOH 90/10, 1.0 mL min^{-1}, λ = 210 nm): t_r (major) = 16.1 min, t_r (minor) = 14.7 min; and the minor diastereomer was determined to have 98% *ee* under the same HPLC analysis condition: t_r (major) = 18.5 min, t_r (minor) = 20.1 min; $[\alpha]_D^{25}$ = +48.9 (94% *ee*, *c* = 1.21, $CHCl_3$); *trans* isomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28–7.38 (m, 5H), 4.58 (ddd, *J* = 9.8, 9.5, 4.3 Hz, 1H), 4.02 (d, *J* = 9.5 Hz, 1H), 3.16 (brd, *J* = 11.9 Hz, 1H), 2.85 (ddd, *J* = 11.9, 11.9, 2.7, 1H), 2.43 (m, 1H), 2.12 (ddd, *J* = 12.5, 12.5, 4.3 Hz, 1H), 1.89 (m, 1H), 1.67–1.83 ppm (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.7, 128.8, 127.5, 122.2, 89.3, 64.9, 46.3, 30.9, 24.4 ppm; IR ($CDCl_3$): $\tilde{\nu}$ = 3694, 3027, 1603, 1556; MS (FAB$^+$): m/*z* (%): 207 [*M*+H]$^+$ (100), 160 (28); HRMS (FAB$^+$) calcd for $[C_{11}H_{25}N_2O_2]^+$: 207.1134; found: 207.1137. *cis* isomer: $[\alpha]_D^{25}$ = +17.5 (*c* = 0.24, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27–7.37 (m, 5H), 4.95 (brs, 1H), 4.13 (brs, 1H), 3.43 (brd, *J* = 13.1 Hz, 1H), 2.87 (ddd, *J* = 12.8, 13.1, 3.1 Hz 1H), 2.50 (brs, 1H), 2.48 (brd, *J* = 15.0, 1H), 2.14 (m, 1H), 2.03 (m, 1H), 1.60 ppm (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.5, 128.7, 127.9, 125.8, 84.0, 61.2, 46.0, 28.8, 20.1 ppm; IR ($CDCl_3$): $\tilde{\nu}$ = 3693, 3028, 1601, 1552 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 207 [*M*+H]$^+$ (100), 91 (44); HRMS (FAB$^+$) calcd for $[C_{11}H_{25}N_2O_2]^+$: 207.1134; found: 207.1132.

(2*R*,3*R*)-3-[*N*-(2-methoxybenzyl)amino]-2-phenylpiperidine ((−)-CP-99,994): *t*BuOK (22.5 mg, 0.20 mmol) was added to a solution of the 9/1 mixture of diastereomers of **12** (20.7 mg, 0.10 mmol) in THF (0.5 mL) at 0 °C under N_2 atmosphere. After the mixture was stirred at this temperature for 1 h, the temperature was reduced to −78 °C, and AcOH (0.1 mL) was added. After stirring for 1 h at this temperature, the mixture was allowed to warm slowly to room temperature. The reaction was quenched with saturated aqueous Na_2CO_3 (5 mL), and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo to give *cis*-**12**. Zn (156 mg, 2.40 mmol) and AcOH (0.3 mL) were added to a stirred solution of the obtained *cis*-**12** in THF (1.0 mL). After stirring the mixture at room temperature under N_2 atmosphere for 8 h, it was quenched with saturated aqueous $NaHCO_3$ (5 mL) and extracted with $CHCl_3$. The combined organic layers were washed with brine, dried (K_2CO_3), and concentrated in vacuo to give **13** as a pale yellow oil. *o*-Anisaldehyde (13.6 mg, 0.10 mmol) was added to a solution of the obtained **13** in 1,2-dichloroethane (DCE, 1.0 mL). After stirring the mixture for 1 h at room temperature, $NaBH_3CN$ (6.9 mg, 0.11 mmol), AcOH (6.8 μL, 0.11 mmol) and MeOH (0.4 mL) were added. After stirring for 6 h at room temperature, the mixture was basified with aqueous $NaHCO_3$ and solid K_2CO_3 (ca. 240 mg) and extracted with $CHCl_3$. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography on silica gel (AcOEt/hexane/MeOH/TEA 100/50/5/1 as eluant) to give (−)-CP-99,994 as a colorless oil (22.3 mg, 75% from **12**): $[\alpha]_D^{20}$ = 63.0 (*c* = 0.27, $CHCl_3$) (lit.:[17f] $[\alpha]_D^{20}$ = +67.2 (*c* = 1.0, $CHCl_3$) as (+)-CP-99,994); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.21–7.31 (m, 5H), 7.15 (td, *J* = 7.9, 1.5 Hz, 1H), 6.97 (dd, *J* = 7.3, 1.5 Hz, 1H), 6.80 (brt, *J* = 7.3 Hz, 1H), 6.68 (brd, *J* = 8.2 Hz, 1H), 3.88 (d, *J* = 2.4 Hz, 1H), 3.67 (d, *J* = 13.7 Hz, 1H), 3.45 (s, 3H), 3.41 (d, *J* = 13.7, 1H), 3.27 (brd, *J* = 12.5 Hz, 1H), 2.75- 2.85 (m, 2H), 2.14 (brd, *J* = 14.6 Hz, 1H), 1.92 (m, 1H), 1.64–1.74 (brs, 2H), 1.61 (tt, *J* = 13.4, 3.7 Hz, 1H), 1.40 ppm (brd, *J* = 13.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 157.7, 142.5, 129.6, 128.3, 128.2, 127.8, 126.6, 126.3, 120.0, 109.8, 63.9, 54.70, 54.65, 47.7, 46.7, 28.1, 20.3 ppm; IR ($CDCl_3$): $\tilde{\nu}$ = 3320, 3064, 2939, 1601, 1493, 1462 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 297 [*M*+H]$^+$ (92), 121 (100); HRMS (FAB$^+$) calcd for $[C_{19}H_{25}N_2O]^+$: 297.1967; found: 297.1975.

Methyl *trans*-6-nitro-2-hexenoate ((*E*)-14): IBX (1.5 equiv, 5.83 g) was added to a stirred solution of 4-nitro-1-butanol (1.57 g, 13.2 mmol), DMSO (7 mL), and THF (7 mL). After 2 h, saturated aqueous $NaHCO_3$ was added to the reaction mixture, which was extracted with Et_2O. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to afford the crude aldehyde (1.20 g). The crude aldehyde was dissolved in benzene (20 mL) and the Wittig reagent (1.5 equiv, 5.12 g) was added to the reaction mixture at room temperature. After 20 h, the reaction mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/AcOEt 3/1 as eluant) to afford (*Z*)-**14** (130 mg, 5%) and (*E*)-**14** (893 mg, 36%). *E* isomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.91 (dt, *J* = 15.6, 7.0 Hz, 1H), 5.90 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.42 (t, *J* = 6.9 Hz, 2H), 3.74 (s, 3H), 2.41–2.29 (m, 2H), 2.27–2.13 ppm (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 166.5, 145.7, 122.8, 74.4, 51.5, 28.4, 25.4 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 1719, 1660, 1555 cm^{-1}; MS (CI$^+$): *m*/*z* (%): 174 [*M*+H]$^+$ (100); HRMS (CI$^+$) calcd for $[C_7H_{12}NO_4]^+$: 174.0766; found: 174.0763. *Z isomer*: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.21 (ddd, *J* = 11.4, 7.8, 7.6 Hz, 1H), 5.89 (dt, *J* = 11.3, 1.5 Hz, 1H), 4.42 (t, *J* = 7.0 Hz, 2H), 3.72 (s, 3H), 2.77 (ddt, *J* = 1.5, 7.5, 7.5 Hz, 2H), 2.19 (ddt, *J* = 7.0, 7.3, 7.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 166.4, 146.6, 121.4, 74.6, 51.1, 26.2, 25.3 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 1718, 148, 1554 cm^{-1}; MS (CI$^+$): *m*/*z* (%): 174 [*M*+H]$^+$ (32), 42 (100); HRMS (CI$^+$) calcd for $[C_7H_{12}NO_4]^+$: 174.0766; found: 174.0768.

Methyl (6*R*,7*S*)-*trans*-7-[*N*-(*tert*-butoxycarbonyl)amino]-6-nitro-7-phenyl-2-heptenoate (15): **1a** (0.1 equiv, 5.5 mg) was added to a stirred solution of *N*-Boc-imine **2f** (0.13 mmol, 27.1 mg) and nitroalkane (*E*)-**14** (2 equiv, 49.5 mg) in CH_2Cl_2 (0.26 mL) at room temperature, and the mixture was stirred for 24 h. Then the reaction mixture was purified by column chromatography on silica gel (hexane/AcOEt 5/1 as eluant) to afford a 79/21 mixture of diastereomers of **15** (40.7 mg, 81%). HPLC analysis (Chiralpak AS-H, hexane/EtOH 90:10, flow rate = 1.0 mL min^{-1}): **15a** (92% *ee*): t_r (major) = 9.1 min, t_r (minor) = 14.8 min; **15b** (72% *ee*): (t_r major) = 12.4 min, t_r (minor) = 7.4 min. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.44–7.28 (m, 3H), 7.25–7.17 (m, 2H), 6.91–6.78 (m, 1H), 5.84 (d, *J* = 15.9 Hz, 1H), 5.24–5.06 (m, 2H), 4.81 (brs, 1H), 3.74 (s, 3H), 2.42–2.10 (m, 3H), 2.03–1.89 (m, 1H), 1.43 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): Major isomer (**15a**): δ = 166.6, 155.0, 145.8, 136.4, 128.9, 128.7, 126.8, 122.6, 90.4, 80.4, 56.8, 51.4, 28.3, 28.1, 28.0 ppm. Minor isomer (**15b**): δ = 166.5, 155.0, 145.4, 137.1, 129.0, 128.5, 126.3, 122.7, 91.0, 80.3, 56.0, 51.4, 29.3, 28.0, 27.9 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3443, 3028, 3006, 2979, 1716, 1554 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 379 [*M*+H]$^+$ (6), 212 (100); HRMS (FAB$^+$) calcd for $[C_{19}H_{27}N_2O_6]^+$: 379.1869; found: 379.1866.

Methyl 2-[(2*S*,3*R*,6*S*)-5-nitro-6-phenylpiperidin-2-yl]acetate (16): TFA (0.20 mL) was added to a stirred solution of **15** (37.8 mg, 0.10 mmol, **15a**/**15b** 79/21) in CH_2Cl_2 (0.20 mL) at 0 °C. After 2 h, the reaction mixture was concentrated in vacuo. The residual solid was dissolved in THF (1.0 mL), and then TEA (5 equiv, 0.070 mL) was added to the mixture. After 2 h, saturated aqueous $NaHCO_3$ was added to the reaction mixture, and the aqueous phase was extracted with $CHCl_3$. The combined organic extract was dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was purified by column chromatography on silica gel (hexane/AcOEt 3/1 as eluant) to afford desired product **16** (19.6 mg, 70%). HPLC analysis (Chiralpak AD, hexane/EtOH 90:10, flow rate = 1.0 mL min^{-1}): t_r (major) = 12.4, t_r (minor) = 15.1 min; m.p. 114 °C ($CHCl_3$/hexane); $[\alpha]_D^{23}$ = +16.7 (87% *ee*, *c* = 1.01, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.27 (m, 5H), 4.54 (ddd, *J* = 4.0, 9.8, 11.9 Hz, 1H), 4.13 (d, *J* = 9.8 Hz, 1H), 3.66 (s, 3H), 3.31–3.17 (m, 1H), 2.54–2.47 (m, 1H), 2.47–2.38 (m, 2H), 2.33 (s, 1H), 2.27–2.11 (m, 1H), 1.93–1.83 (m, 1H),

1.52–1.36 ppm (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.3, 138.7, 128.80, 128.75, 127.6, 89.2, 64.5, 52.7, 51.7, 40.1, 30.5, 30.2 ppm; IR ($CHCl_3$): $\tilde{\nu}$ = 3330, 3030, 2952, 2950, 1731, 1550 cm^{-1}; MS (FAB$^+$): *m*/*z* (%): 279 $[M+H]^+$ (100); HRMS (FAB$^+$) calcd for $[C_{14}H_{19}N_2O_4]^+$: 279.1345; found: 279.1342; elemental analysis (%) calcd for $C_{14}H_{18}N_2O_4$: C 60.40, H 6.52, N 10.07; found: C 60.12, H 6.55, N 9.99.

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