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Enantioselective Conjugate Addition of 2-Acetyl Azaarenes to β,β-Disubstituted Nitroalkene for the Construction of All-Carbon Quaternary Stereocenters

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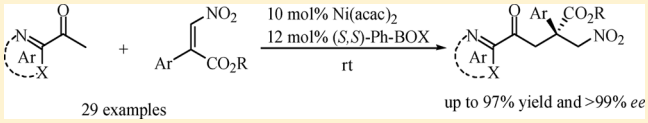
Supporting Information

ABSTRACT: The first highly enantioselective conjugate addition of 2-acetyl azaarenes to α-substituted-β-nitroacrylates was successfully realized under mild conditions by a Ni(II)-bisoxazoline complex, providing the desired adducts bearing an all-carbon quaternary stereocenter in high yield with excellent enantioselectivity. The products obtained in this system could be readily converted into optically active $\beta^{2,2}$-amino esters, succinates, lactones, and lactams.

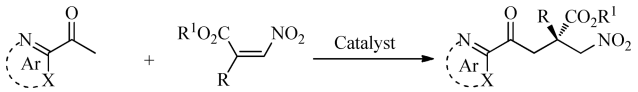


Aromatic N-heterocycles (azaarenes), including pyridine, pyrimidine, quinoline, oxazole, thiazole, and so on, are ubiquitous structural motifs in pharmaceuticals and other biologically active compounds.[1] It has been reported that the majority of all known active pharmaceutical ingredients (APIS) contain an aromatic N-heterocycle.[2] On the other hand, approximately half of all APIs are chiral compounds. Therefore, the development of efficient methodologies for incorporating an aromatic N-heterocycle in chiral molecules is highly valuable and desirable in medicinal chemistry and organic synthesis.

All-carbon quaternary stereocenters are widely present in a number of natural products, therapeutic agents, and other functional molecules.[3] Over the past several decades, studies on the construction of all-carbon quaternary stereocenters with high levels of stereocontrol have been a longstanding and challenging topic owing to the high steric hindrance, and hence become a research focus in organic synthesis.[4] So far, there are a plethora of methods explored for this purpose, such as alkylation,[5] allylic alkylation,[6] conjugate addition,[7] rearrangement,[8] desymmetrization,[9] and so on.[10] Among them, asymmetric conjugate addition (ACA) of carbon-based nucleophiles with suitable unsaturated carbonyl acceptors is one straightforward and efficient strategy for the construction of quaternary carbon stereocenters. In the past few years, β,β-disubstituted nitroalkene as a Michael acceptor has received increasing attention for attaining this goal, because the resulting products could be transformed to β-amino acid derivatives, lactones, and related bioactive compounds bearing quaternary carbon stereocenters.[11] To date, only a few examples concerning α-phenyl β-nitroacrylate have been reported by Xiao,[12a,b] Jia,[12c] Wennemers,[12d] Gong,[12e] and other groups,[12f] affording efficient approaches to the construction of hetero-quaternary or all-carbon quaternary stereocenters. In addition, β,β-disubstituted unsaturated carbonyl compounds bearing a β-CF_3 group have also been employed to the conjugate addition for the construction of trifluoromethylated all-carbon quaternary stereocenters by several groups.[13] Despite these notable advances, the method for the formation of quaternary carbon stereocenters, particularly acyclic all-carbon quaternary stereocenters, is still limited,[14] and hence remains highly desirable and challenging.

We have recently found a highly enantioselective conjugate addition between a 2-acetyl azaarene as a nucleophile and a β-CF_3-β-disubstituted nitroalkene by employing a Ni(acac)$_2$-BOX complex.[15] Inspired by this success, we envisioned that α-phenyl-β-nitroacrylate as a Michael acceptor could also proceed smoothly with 2-acetyl azaarene to deliver the enantioselective adducts containing an all-carbon quaternary stereocenter (Scheme 1). To the best of our knowledge, the method for

Scheme 1. Strategy for the Formation of All-Carbon Quaternary Stereocenters



incorporating various aromatic N-heterocycles and an all-carbon quaternary stereocenter in an organic molecule is relatively unexplored, and of great significance in medicinal and organic chemistry. Herein, we report the first asymmetric conjugate addition of various 2-acetyl azaarenes to α-substituted β-nitroacrylates catalyzed by a Ni(II)-bisoxazoline complex, in which the resulting products could be readily converted into versatile optically active compounds bearing an all-carbon quaternary stereocenter such as pyrrolidine, succinate, lactone, and lactams.

We started our study from the reaction of commercially available 2-acetyl pyridine **1a** with α-phenyl-β-nitroacrylate methyl ester **2a** in *i*-PrOH at 0 °C using 10 mol % of chiral Ni(acac)$_2$−bisoxazoline complexes based on our previous

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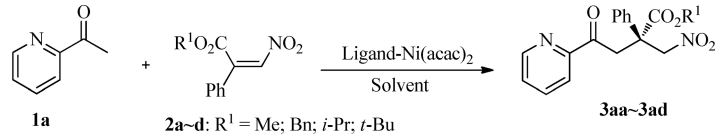
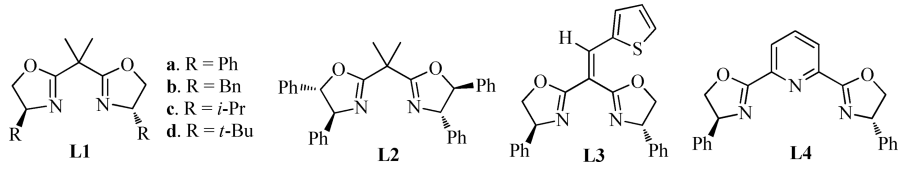
Table 1. Optimization of Reaction Conditions[a]





entry	L	R^1	solvent	T (°C)	time (h)	yield[b] (%)	ee[c] (%)
1	**L1a**	Me	*i*-PrOH	0	24	90 (**3aa**)	84
2	**L1b**	Me	*i*-PrOH	0	24	78 (**3aa**)	36
3	**L1c**	Me	*i*-PrOH	0	24	72 (**3aa**)	14
4	**L1d**	Me	*i*-PrOH	0	24	88 (**3aa**)	0
5	**L2**	Me	*i*-PrOH	0	24	59 (**3aa**)	0
6	**L3**	Me	*i*-PrOH	0	24	51 (**3aa**)	83
7	**L4**	Me	*i*-PrOH	0	24	57 (**3aa**)	2
8	**L1a**	Bn	*i*-PrOH	0	24	92 (**3ab**)	97
9	**L1a**	*i*-Pr	*i*-PrOH	0	24	90 (**3ac**)	97
10	**L1a**	*t*-Bu	*i*-PrOH	0	24	93 (**3ad**)	98
11	**L1a**	*t*-Bu	MeOH	0	24	55 (**3ad**)	84
12	**L1a**	*t*-Bu	EtOH	0	24	90 (**3ad**)	95
13	**L1a**	*t*-Bu	CH_2Cl_2	0	24	89 (**3ad**)	92
14	**L1a**	*t*-Bu	toluene	0	24	84 (**3ad**)	97
15	**L1a**	*t*-Bu	Et_2O	0	24	89 (**3ad**)	98
16	**L1a**	*t*-Bu	*i*-PrOH	−10	48	93 (**3ad**)	99
17	**L1a**	*t*-Bu	*i*-PrOH	rt	12	95 (**3ad**)	97
18[d]	**L1a**	*t*-Bu	*i*-PrOH	rt	24	94 (**3ad**)	96
19[e]	**L1a**	*t*-Bu	*i*-PrOH	rt	48	85 (**3ad**)	92

[a]Reaction conditions unless noted otherwise: **1a** (0.20 mmol), **2** (0.30 mmol), **L** (0.024 mmol), $Ni(acac)_2$ (0.020 mmol) in *i*-PrOH (2 mL) under nitrogen at 0 °C for 24 h. [b]Isolated yield. [c]Determined by HPLC using a chiralcel OD-H column. [d]5 mol % catalyst loading. [e]2.5 mol % catalyst loading.

work.[15] The results are summarized in Table 1. Evans' ligands were first screened (entries 1−4), and (*S*,*S*)-Ph-BOX (**L1a**) afforded the best yield and enantioselectivity (entry 1, 90% yield and 84% *ee*). Other bisoxazoline ligands **L2**, **L3**, and **L4** were also examined and gave lower yields or *ee* values (entries 5−7). Subsequently, the effect of the ester group on the reaction was tested. When replacing the methyl group of *α*-phenyl-*β*-nitroacrylate (**2a**) with more sterically hindered benzyl, *iso*-propyl, and *tert*-butyl groups, the enantioselectivity increased gradually while high reactivity was still maintained (entries 8−10); particularly, **2d** with a *tert*-butyl group afforded the highest *ee* value (98%). In addition, other Lewis acids including $Ni(ClO_4)_2{\cdot}6H_2O$, $Ni(OTf)_2$, $Cu(OTf)_2$, $Ni(OAc)_2{\cdot}4H_2O$, and $Zn(OTf)_2$ were examined, and most of them did not promote the reaction except that $Ni(OAc)_2{\cdot}4H_2O$ offered an excellent enantioselectivity, but moderate yield (entry 13, 45% yield and 98% *ee*; see the Supporting Information, Table S1).[16] A simple survey of solvent demonstrated that high to excellent enantioselectivities were achieved for the screened solvents (entries 11−15, 84−98% *ee*); however, *i*-PrOH was finally chosen as the optimal solvent in terms of the reactivity and safety. Moreover, the effect of temperature and catalyst loading on the reaction was tested. When the reaction proceeded at −10 °C for 48 h or room temperature for 12 h, 99% *ee* and 97% *ee* values were obtained, respectively, indicating that the decreased temperature could result in a little improvement in enantioselectivity but at the expense of the reactivity (entries 16 and 9 vs entry 17). When the catalyst loading was reduced to 5 and 2.5 mol %, a longer reaction time was needed for ensuring high yields while the enantioselectivity dropped slightly (entries 18 and 19, 96% and 92% *ee*). Consequently, the reaction would be carried out in *i*-PrOH at room temperature using 10 mol % of $Ni(acac)_2$ and 12 mol % of **L1a**.

Under optimal reaction conditions, the scope of nitroacrylate was next explored, and the results are shown in Table 2. First, a series of different substituted phenyl *β*-nitroacrylates (**2e**−**2j**) were applied to the reaction with 2-acetyl pyridine. Both the yields and enantioselectivities are generally excellent for nitroacrylate substrates bearing either electron-withdrawing or electron-donating groups on the phenyl ring (entries 1−6, 93−97% yield, 97−99% *ee*). Subsequently, *α*-heteroaryl-substituted *β*-nitroacrylates were used in this reaction, which also afforded excellent results (entries 7 and 8, 92% yield and 95% *ee*, 96% yield and 96% *ee*, respectively). Notably, the reaction of styryl-substituted nitroacrylate (**2m**) with **1a** proceeded for only 4 h to give the adduct **3am** in 95% yield with 95% *ee* (entry 9), exhibiting higher reactivity than *α*-aryl-substituted nitroalkenes. Furthermore, different substituted 2-acetyl-pyridine derivatives **1b**, **1c**, and **1d** were subjected to this reaction condition. 2-Acetyl 5-Me-pyridine **1b** and 2-acetyl 5-Br-pyridine **1c** were well tolerant with the reaction (entries 10−11); however, no

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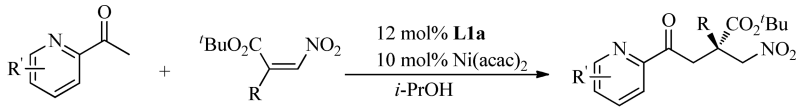
Table 2. Substrate Scope of Nitroacrylate[a]

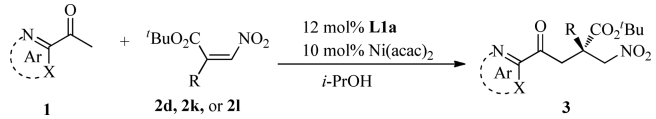


1a R' = H; **1b** R' = 5-Me; **1c** R' = 5-Br; **1d** R' = 6-Br — **2** — **3**

entry	1	R	time (h)	yield[b] (%)	ee[c] (%)
1	**1a**	4-MeC_6H_4 (**2e**)	12	97 (**3ae**)	97
2	**1a**	4-$MeOC_6H_4$ (**2f**)	12	95 (**3af**)	98
3	**1a**	4-FC_6H_4 (**2g**)	12	95 (**3ag**)	98
4	**1a**	4-BrC_6H_4 (**2h**)	12	93 (**3ah**)	99 (*R*)
5	**1a**	4-$CF_3C_6H_4$ (**2i**)	12	94 (**3ai**)	97
6	**1a**	4-$NO_2C_6H_4$ (**2j**)	12	97 (**3aj**)	97
7	**1a**	2-furyl (**2k**)	12	92 (**3ak**)	95
8	**1a**	2-thienyl (**2l**)	12	96 (**3al**)	96
9	**1a**	styryl (**2m**)	4	95 (**3am**)	95
10	**1b**	Ph (**2d**)	12	90 (**3bd**)	93
11	**1c**	Ph (**2d**)	12	94 (**3cd**)	98
12	**1d**	Ph (**2d**)	12		
13[d]	**1a**	Me (**2n**)	12(48)	95(93) (**3an**)	66(80)
14[d]	**1a**	*n*-C_7H_{15} (**2o**)	12(48)	93(89) (**3ao**)	43(75)
15	**1a**	cyclohexyl (**2p**)	72	84 (**3ap**)	94

[a]Reaction conditions: unless stated otherwise, **1** (0.20 mmol), **2** (0.30 mmol), **L1a** (0.024 mmol), $Ni(acac)_2$ (0.020 mmol) in *i*-PrOH (2 mL) under nitrogen at rt. [b]Isolated yield. [c]Determined by HPLC using a chiral column. [d]The numbers in paretheses were obtained when reactions were conducted at 0 °C.

Table 3. Substrate Scope of Azaarenes[a]



1 — **2d, 2k,** or **2l** — **3**

entry	1 (azaarenes)	R	time (h)	yield[b] (%)	ee[c] (%)
1	2-pyrazinyl (**1e**)	Ph (**2d**)	36	85 (**3ed**)	99
2	2-pyrimidinyl (**1f**)	Ph (**2d**)	48	86 (**3fd**)	93
3	2-quinolinyl (**1g**)	Ph (**2d**)	12	97 (**3gd**)	99
4	2-quinoxalinyl (**1h**)	Ph (**2d**)	12	90 (**3hd**)	98
5	2-oxazolyl (**1i**)	Ph (**2d**)	12	86 (**3id**)	98
6	2-thiazolyl (**1j**)	Ph (**2d**)	12	96 (**3jd**)	>99
7	2-benzothiazolyl (**1k**)	Ph (**2d**)	12	92 (**3kd**)	99
8	*N*-Me-2-imidazolyl (**1l**)	Ph (**2d**)	12	92 (**3ld**)	>99
9	*N*-Bn-2-benzimidazolyl (**1m**)	Ph (**2d**)	48	85 (**3md**)	99
10	*N*-Me-2-imidazolyl (**1n**)	2-furyl (**2k**)	48	85 (**3lk**)	>99
11	*N*-Me-2-imidazolyl (**1n**)	2-thienyl (**2l**)	48	88 (**3ll**)	>99

[a]Reaction conditions: **1** (0.20 mmol), **2** (0.30 mmol), **L1a** (0.024 mmol), $Ni(acac)_2$ (0.020 mmol) in *i*-PrOH (2 mL) under nitrogen at rt. [b]Isolated yield. [c]Determined by HPLC using a chiral column.

reaction occurred with 2-acetyl 6-Br-pyridine **1d** (entry 12). This result may be attributed to that the key intermediate metal enolate could not be formed because the pyridine N atom coordinating to the Ni(II) center was retarded by the adjacent 6-Br atom. Unfortunately, methyl- and *n*-heptyl-substituted substrates **2n** and **2o** furnished only moderate enantioselectivities (66% *ee* and 43% *ee*). Lowering the reaction temperature to 0 °C led to an obvious improvement of the enantioselectivity (80% *ee* and 75% *ee*), albeit with a decrease of the reactivity (entries 13 and 14). When using the bulky cyclohexyl-substituted nitroacrylate **2p**, the reaction was prolonged to 72 h at rt and afforded a 94% *ee* of product **3ap** with 84% yield (entry 15). These results suggested that a steric effect could be mainly responsible for the excellent enantioselectivity of the reaction.

To explore the generality of the catalytic asymmetric conjugate addition, we next investigated other available 2-acetyl azaarenes. As shown in Table 3, six-membered N-heterocycles containing, for example, 2-pyrazinyl, 2-pyrimidinyl, 2-quinolinyl, and 2-quinoxalinyl groups (**1e**−**1h**) were well compatible with the reaction, delivering the desired adducts in high yields with excellent enantioselectivities (entries 1−4, 85−97% yield and 93−99% *ee*). To our excitement, in the case of five-membered N-heterocycles containing **1i**−**1o**, both the high yields and excellent enantioselectivities were also achieved (entries 5−9, 85−96% yield and 98 to >99% *ee*). It is worth noting that *N*-methyl-2-acetylimidazole **1l** and *N*-benzyl-2-

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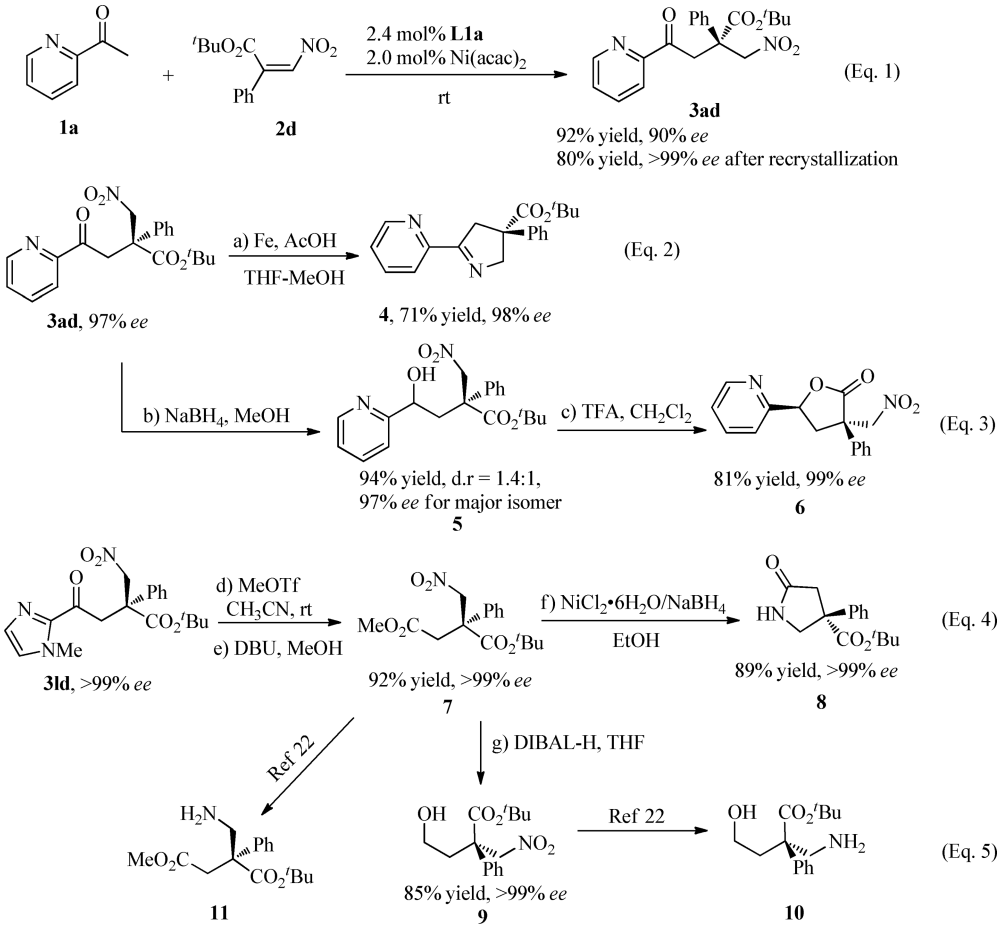
Scheme 2. Transformations of the Products



acetyl benzimidazole **1m** were very competent substrates in terms of the enantioselectivity (entries 8 and 9). Furthermore, when *N*-Me-2-acetyl imidazole reacted with α-2-furyl- and 2-thienyl-substituted β-nitroacrylates (**2k** and **2l**), a nearly perfect level of the enantioselectivity was achieved[17] (entries 10 and 11, >99% *ee* values).

To show the practicality of the present reaction, a gram-scale experiment was tested. As shown in Scheme 2 (eq 1), the catalytic asymmetric conjugate addition of **1a** with **2d** was accomplished at room temperature within 60 h in 92% yield with a 90% *ee* value by using only a 2.0 mol % of catalyst loading. Optically pure **3ad** (>99% *ee*) could be obtained in 80% yield after a single recrystallization from methanol.

Significantly, product **3**, containing multiple functional groups, such as NO_2, C═O, and CO_2R, could be converted into many useful intermediates for the synthesis of β-amino ester, succinates, lactams, and other biologically active compounds, as shown in Scheme 2. For example, **3ad** was treated by a one-pot procedure of reduction/ring-closure process (Fe/AcOH), which afforded pyrroline derivative **4** (eq 2).[14] The reduction of product **3ad** with $NaBH_4$ in MeOH produced the diastereoisomers **5**, whose major isomer was separated by column chromatography, followed by treatment with TFA, which led to γ-lactone **6** (eq 3). Notably, the acyl imidazole moiety is easily transformed into a variety of carbonyl-containing derivatives such as aldehydes, ketones, and esters.[18,17c] As expected, 2-acetyl imidazole **3ld** was treated sequentially with MeOTf and then DBU in methanol in one-pot to give the succinate ester **7** bearing an all-carbon quaternary stereocenter in 92% yield and >99% *ee* (Scheme 2, eq 4).[19] Succinates are valuable chiral building blocks for the synthesis of β-amino acids, peptidomimics, and other bioactive derivatives.[20] To our knowledge, the approach to the succinates bearing an all-carbon quaternary stereocenter has been rarely reported.[21] Subsequently, treatment of **7** with $NaBH_4/NiCl_2\cdot 6H_2O$ in EtOH afforded γ-lactam **8**, or reduction of **7** with DIBAL-H led to δ-nitro alcohol **9** in 85% yield with >99% *ee* (Scheme 2, eq 5). Moreover, the selective reduction of **7** and **9** would generate the corresponding amino ester **11** and amino alcohol **10** according to a literature procedure.[22] In general, these transformations could lead to many biologically active compounds bearing an all-carbon quaternary stereocenter with retention of the enantiopurity including amino esters, succinates, γ-lactones, γ-lactams, and others.

The absolute configuration of **3ah** was determined to be *R* based on X-ray crystallographic analysis.[23] The configurations of the other adducts were assigned by analogy. A plausible asymmetric induction model was proposed. As shown in Figure 1, 2-acetyl pyridine coordinates with the Ni(II)/BOX complex to form enolate; subsequently, the enolate preferentially approaches β-nitroacrylate from the *Si*-face to form the major *R*-configured product **3ah** because the *Re*-face attack is unfavorable due to the steric hindrance between the phenyl group of ligand **L1a** and β-nitroacrylate. Considering that the excellent enantioselectivities achieved by various aryl and cyclohexyl vs methyl and heptyl group nitroacrylates, as well as $-CO_2{}^t$Bu vs $-CO_2$Me, CO_2Bn, $CO_2{}^i$Pr substrates, the steric effect could play a much more important role in the

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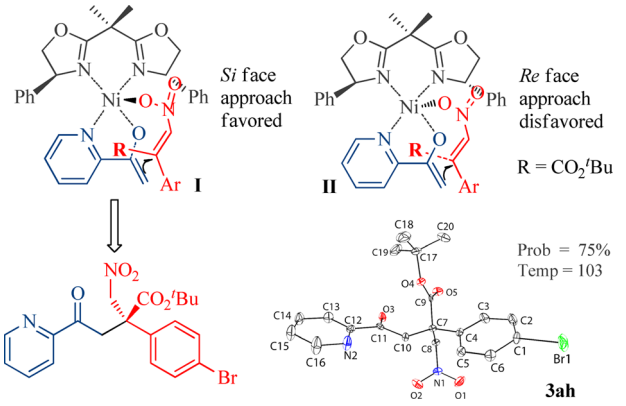
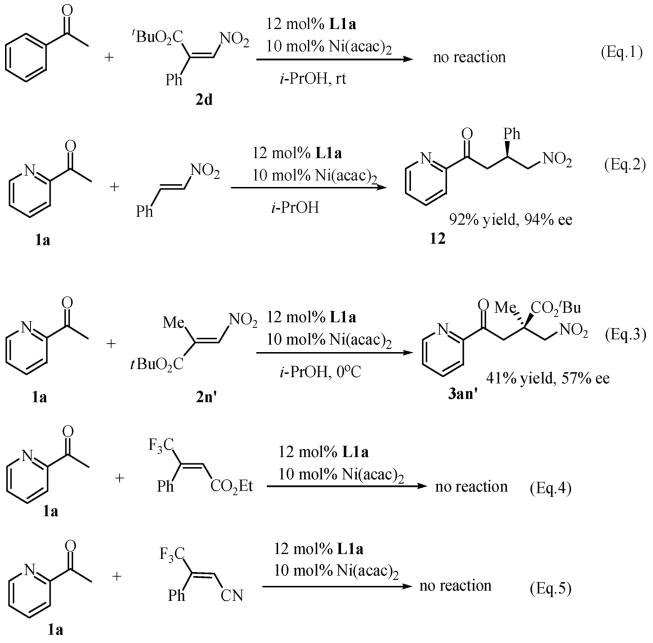


Figure 1. Plausible asymmetric induction model and the X-ray structure of **3ah**.

stereoselectivity-determining step. The formation of enolates was easily confirmed by the following control experiments (Scheme 3): (1) Acetophenone did not occur with α-phenyl β-

Scheme 3. Control Experiments



nitroacrylate **2d** under the same condition. (2) The reaction of 2-acetyl pyridine with 2-phenyl nitro alkene proceed smoothly to give the desired adduct **12** bearing a tertiary stereocenter in 92% yield with 94% *ee*. (3) When *E*-nitroacrylate **2n′** was reacted with 2-acetyl pyridine under the same condition, product **3an′** with an inverse configuration was afforded in 41% yield and 57% *ee*. The nitro group is required in this transformation, which had been confirmed and elucidated in our previous work.[15] For example, when other substrates with $-CO_2Et$ or $-CN$ substituents were employed in this reaction, no reaction was observed (eqs 4 and 5). In addition, based on some reports in the literatures,[24] the counterion acac could coordinate to the Ni(II) center and form complex intermediates in a solution, providing a well-defined chiral environment. The detailed mechanism remains to be further studied.

In summary, we have developed a highly enantioselective conjugate addition of 2-acetyl azaarenes to α-substituted β-nitroacrylates. The reaction was conducted at room temperature using a chiral Ni(II)-BOX complex, providing a variety of aromatic N-heterocycle-containing compounds bearing an all-carbon quaternary stereocenter in high yields with excellent enantioselectivities (up to >99% *ee*). The method features high yield and excellent enantioselectivity, broad substrate scope, inexpensive catalysts, and mild conditions. More importantly, the present method provides an easy approach to optically active $\beta^{2,2}$-amino ester, pyrrolidine, succinate, γ-lactam, and γ-lactone derivatives bearing all-carbon quaternary stereocenters, exhibiting versatile synthetic potentials. Further extension of this methodology in organic synthesis is currently underway.

EXPERIMENTAL SECTION

General. ^{1}H NMR spectra were recorded on a 300 MHz spectrometer in $CDCl_3$, and ^{13}C NMR spectra were recorded on a 75 MHz spectrometer using tetramethylsilane (TMS) as internal standard. HRMS data were obtained by electrospray ionization (ESI) sources with a time-of-flight mass analyzer. Optical rotations were measured on a PerkinElmer 341 LC polarimeter. The enantiomeric excesses of (*R*)- and (*S*)-enantiomers were determined by HPLC analysis over a chiral column with a UV detector. The absolute configuration of the major enantiomer was assigned by X-ray diffraction analysis. Solvents were purified and dried by standard procedures.

General Procedure for the Catalytic Conjugate Addition Reaction. To a Schlenk tube were added ligand **L1a** (0.024 mmol), $Ni(acac)_2$ (0.020 mmol), and *i*-PrOH (2 mL) sequentially under a nitrogen atmosphere. After the solution was stirred at room temperature for 1 h, 2-acetyl azaarene **1** (0.20 mmol) was added, and after stirring for 20 min, α-substituted-β-nitroacrylate **2** (0.30 mmol) was finally added. The reaction proceeded at 0 °C or rt for 4−72 h, and then the solvent was removed under vacuum to give the crude product, which was purified by flash column chromatography on silica gel (eluted with ethyl acetate/petroleum ether (1/10−1/5, v/v) to yield the desired adduct.

Procedure of the Gram-Scale Experiment. To a Schlenk tube were added ligand **L1a** (0.24 mmol), $Ni(acac)_2$ (0.2 mmol), and *i*-PrOH (20 mL) under a nitrogen atmosphere. After the solution was stirred for 1 h at room temperature, 2-acetyl pyridine **1a** (10 mmol) was added, the resulting mixture was stirred for another 30 min, α-phenyl-β-nitroacrylate **2d** (15 mmol) was finally added, and the mixture was stirred for 60 h at room temperature. The solvent was evaporated under vacuum, H_2O (30 mL) was added, and extracted with CH_2Cl_2 (20 mL × 3). The organic layer was combined and dried over anhydrous Na_2SO_4, and then concentrated to give the crude product, which was purified by flash column chromatography on silica gel (eluted with ethyl acetate/petroleum ether (1/10, v/v) to yield the adduct **3ad** (3.40 g, 92% yield, 90% *ee*). After one single recrystallization from MeOH, **3ad** (2.96 g) was achieved in 80% yield with >99% *ee*.

*(R)-Methyl 2-Nitromethyl-4-oxo-2-phenyl-4-(pyridin-2-yl) Butanoate (**3aa**).* White solid, Mp: 126−127 °C, 69 mg, 90% yield; $[\alpha]_D^{20}$ = +76.0 (*c* 1.0, CH_2Cl_2); 84% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 16.00 min, *t* (major) = 22.20 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (d, *J* = 3.3 Hz, 1H), 8.04 (d, *J* = 7.7 Hz, 1H), 7.85 (t, *J* = 7.4 Hz, 1H), 7.64−7.28 (m, 6H), 5.36 (ABd, *J* = 12.4 Hz, 1H), 5.35 (ABd, *J* = 12.4 Hz, 1H), 4.69 (d, *J* = 19.4 Hz, 1H), 4.25 (d, *J* = 19.3 Hz, 1H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.8, 172.1, 152.7, 149.1, 136.9, 129.1, 128.4, 127.7, 126.0, 121.8, 79.5, 53.0, 50.8, 40.3; ESI-HRMS Calcd for $C_{17}H_{17}N_2O_5$ $[M + H]^+$: 329.1132, Found: 329.1127.

*(R)-Benzyl 2-Nitromethyl-4-oxo-2-phenyl-4-(pyridin-2-yl) Butanoate (**3ab**).* Colorless oil, 74 mg, 92% yield. $[\alpha]_D^{20}$ = +56.8 (*c* 0.75, CH_2Cl_2); 97% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-

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J. Org. Chem. 2017, 82, 7353−7362

H column, *n*-hexane/*i*-PrOH = 85:15, 1.0 mL/min, 254 nm; *t* (minor) = 13.52 min, *t* (major) = 17.47 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (dq, *J* = 4.7, 0.9 Hz, 1H), 7.98 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.49 (ddd, *J* = 7.5, 4.8, 1.3 Hz, 1H), 7.44−7.30 (m, 5H), 7.26−7.16 (m, 3H), 7.14−7.09 (m, 2H), 5.39 (s, 2H), 5.23−5.08 (m, 2H), 4.67 (d, *J* = 19.4 Hz, 1H), 4.30 (d, *J* = 19.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.8, 171.4, 152.7, 149.0, 136.9, 136.8, 135.0, 129.0, 128.4, 128.3, 128.1, 127.6, 126.0, 121.8, 79.5, 67.6, 51.0, 40.3; ESI-HRMS Calcd for $C_{23}H_{21}N_2O_5$ $[M + H]^+$: 405.1445, Found: 405.1444.

*(R)-iso-Propyl 2-Nitromethyl-4-oxo-2-phenyl-4-(pyridin-2-yl) Butanoate (**3ac**).* Colorless oil, 64 mg, 90% yield. $[\alpha]_D^{20}$ = +69.0 (*c* 1.0, CH_2Cl_2); 97% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 7.79 min, *t* (major) = 10.08 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78−8.68 (m, 1H), 8.07−7.99 (m, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.54−7.42 (m, 3H), 7.42−7.28 (m, 3H), 5.38 (s, 2H), 5.08 (hept, *J* = 6.2 Hz, 1H), 4.61 (d, *J* = 19.3 Hz, 1H), 4.27 (d, *J* = 19.3 Hz, 1H), 1.17−1.08 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.8, 170.9, 152.8, 149.1, 137.2, 136.9, 128.9, 128.2, 127.6, 125.9, 121.6, 79.6, 69.7, 50.9, 40.2, 21.3, 21.2; ESI-HRMS Calcd for $C_{19}H_{21}N_2O_5$ $[M + H]^+$: 357.1445, Found: 357.1444.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(pyridin-2-yl) Butanoate (**3ad**).* White solid, Mp: 88−89 °C, 70 mg, 95% yield. $[\alpha]_D^{20}$ = +76.0 (*c* 1.0, CH_2Cl_2); 97% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 8.24 min, *t* (major) = 12.69 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.4 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.82 (dd, *J* = 10.9, 4.5 Hz, 1H), 7.46 (d, *J* = 7.3 Hz, 3H), 7.42−7.28 (m, 3H), 5.37 (ABd, *J* = 12.4 Hz, 1H), 5.33 (ABd, *J* = 12.4 Hz, 1H), 4.55 (d, *J* = 19.2 Hz, 1H), 4.25 (d, *J* = 19.2 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.8, 170.1, 152.8, 149.0, 137.5, 136.8, 128.8, 128.0, 127.5, 125.8, 121.5, 82.5, 79.6, 51.3, 40.2, 27.4; ESI-HRMS Calcd for $C_{20}H_{23}N_2O_5$ $[M + H]^+$: 371.1601, Found: 371.1599.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-tolyl-4-(pyridin-2-yl) Butanoate (**3ae**).* White solid, Mp: 104−105 °C, 75 mg, 97% yield. $[\alpha]_D^{20}$ = +84.7 (*c* 0.45, CH_2Cl_2); 97% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (major) = 6.02 min, *t* (minor) = 8.16 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73−8.70 (m, 1H), 8.05 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.52−7.48 (m, 1H), 7.39−7.28 (m, 2H), 7.23−7.10 (m, 2H), 5.43−5.22 (m, 2H), 4.53 (d, *J* = 19.3 Hz, 1H), 4.22 (dd, *J* = 19.3, 0.7 Hz, 1H), 2.33 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.9, 170.4, 153.0, 149.0, 137.8, 136.9, 134.5, 129.6, 127.5, 125.7, 121.6, 82.5, 79.8, 51.1, 40.3, 27.5, 20.9; ESI-HRMS Calcd for $C_{21}H_{25}N_2O_5$ $[M + H]^+$: 385.1757, Found: 385.1754.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-(p-methoxylphenyl)-4-(pyridin-2-yl) Butanoate (**3af**).* White solid, Mp: 131−132 °C, 76 mg, 95% yield. $[\alpha]_D^{20}$ = +89.0 (*c* 0.83, CH_2Cl_2); 98% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 8.26 min, *t* (major) = 10.26 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76−8.68 (m, 1H), 8.09−7.99 (m, 1H), 7.90−7.79 (m, 1H), 7.56−7.44 (m, 1H), 7.43−7.32 (m, 2H), 6.95−6.82 (m, 2H), 5.40−5.20 (m, 2H), 4.50 (d, *J* = 19.2 Hz, 1H), 4.21 (dd, *J* = 19.2, 0.7 Hz, 1H), 3.79 (d, *J* = 0.7 Hz, 3H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.9, 170.4, 159.2, 153.0, 149.1, 136.9, 129.5, 127.5, 127.1, 121.6, 114.2, 82.5, 79.8, 55.2, 50.8, 40.3, 27.5; ESI-HRMS Calcd for $C_{21}H_{25}N_2O_6$ $[M + H]^+$: 401.1707, Found: 401.1704.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-(p-fluorophenyl)-4-(pyridin-2-yl) Butanoate (**3ag**).* White solid, Mp: 101−102 °C, 74 mg, 95% yield. $[\alpha]_D^{20}$ = +66.7 (*c* 0.45, CH_2Cl_2); 98% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 6.35 min, *t* (major) = 8.08 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.72−8.69 (m, 1H), 8.05 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.85 (td, *J* = 7.7, 1.7 Hz, 1H), 7.55−7.40 (m, 3H), 7.14−7.01 (m, 2H), 5.40−5.24 (m, 2H), 4.50 (d, *J* = 19.2 Hz, 1H), 4.22 (dd, *J* = 19.2, 0.8 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 170.1, 162.3 (d, $J_{C\text{-}F}$ = 247.9 Hz), 152.8, 149.1, 136.9, 133.4 (d, $J_{C\text{-}F}$ = 3.4 Hz), 127.7 (d, $J_{C\text{-}F}$ = 8.2 Hz), 127.6, 121.6, 115.8 (d, $J_{C\text{-}F}$ = 21.5 Hz), 82.9, 79.4, 50.9, 40.3, 27.5; ESI-HRMS Calcd for $C_{20}H_{22}FN_2O_5$ $[M + H]^+$: 389.1507, Found: 389.1501.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-(p-bromophenyl)-4-(pyridin-2-yl) Butanoate (**3ah**).* White solid, Mp: 144−146 °C, 83 mg, 93% yield. $[\alpha]_D^{20}$ = +68.5 (*c* 0.50, CH_2Cl_2); 99% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 95:5, 0.6 mL/min, 254 nm; *t* (minor) = 15.42 min, *t* (major) = 24.64 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.74−8.70 (m, 1H), 8.05 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.86 (td, *J* = 7.7, 1.7 Hz, 1H), 7.56−7.47 (m, 3H), 7.39−7.30 (m, 2H), 5.39−5.23 (m, 2H), 4.48 (d, *J* = 19.2 Hz, 1H), 4.20 (dd, *J* = 19.2, 0.7 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 169.8, 152.8, 149.1, 137.0, 136.8, 132.1, 127.7, 127.6, 122.4, 121.7, 83.0, 79.4, 51.1, 40.2, 27.5; ESI-HRMS Calcd for $C_{20}H_{22}BrN_2O_5$ $[M + H]^+$: 449.0707, Found: 449.0708.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-(p-trifluoromethylphenyl)-4-(pyridin-2-yl) Butanoate (**3ai**).* White solid, Mp: 138−140 °C, 82 mg, 94% yield. $[\alpha]_D^{20}$ = +63.5 (*c* 0.40, CH_2Cl_2); 97% *ee*, determined by HPLC analysis [Daicel Chiralcel AD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 8.92 min, *t* (major) = 11.52 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76−8.70 (m, 1H), 8.05 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.87 (td, *J* = 7.7, 1.7 Hz, 1H), 7.63 (q, *J* = 8.6 Hz, 4H), 7.57−7.51 (m, 1H), 5.39 (d, *J* = 12.6 Hz, 1H), 5.32 (dd, *J* = 12.6, 0.8 Hz, 1H), 4.53 (d, *J* = 19.2 Hz, 1H), 4.25 (dd, *J* = 19.2, 0.8 Hz, 1H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5, 169.6, 152.7, 149.1, 141.7, 137.0, 130.4 (q, $J_{C\text{-}F}$ = 32.8 Hz), 127.7, 126.5, 125.9 (q, $J_{C\text{-}F}$ = 3.6 Hz), 123.8 (q, $J_{C\text{-}F}$ = 272.1 Hz), 121.7, 83.3, 79.4, 51.4, 40.2, 27.5; ESI-HRMS Calcd for $C_{21}H_{22}F_3N_2O_5$ $[M + H]^+$: 439.1475, Found: 439.14754.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-(p-nitrophenyl)-4-(pyridin-2-yl) Butanoate (**3aj**).* Yellow solid, Mp: 133−135 °C, 81 mg, 97% yield. $[\alpha]_D^{20}$ = +62.7 (*c* 0.70, CH_2Cl_2); 97% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 80:20, 1.0 mL/min, 254 nm; *t* (minor) = 9.17 min, *t* (major) = 14.04 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (dd, *J* = 3.9, 0.8 Hz, 1H), 8.30−8.21 (m, 2H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.88 (td, *J* = 7.8, 1.7 Hz, 1H), 7.72−7.63 (m, 2H), 7.58−7.51 (m, 1H), 5.37 (ABd, *J* = 12.7 Hz, 1H), 5.36 (ABd, *J* = 12.6 Hz, 1H), 4.52 (d, *J* = 19.2 Hz, 1H), 4.26 (d, *J* = 19.2 Hz, 1H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.2, 169.2, 152.6, 149.2, 147.6, 144.9, 137.0, 127.8, 127.2, 124.0, 121.8, 83.7, 79.2, 51.6, 40.3, 27.5; ESI-HRMS Calcd for $C_{20}H_{22}N_3O_7$ $[M + H]^+$: 416.1452, Found: 416.1449.

*(S)-tert-Butyl 2-Nitromethyl-4-oxo-2-(2-furyl)-4-(pyridin-2-yl) Butanoate (**3ak**).* White solid, Mp: 82−83 °C, 66 mg, 92% yield. $[\alpha]_D^{20}$ = +36.1 (*c* 0.98, CH_2Cl_2); 95% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 95:5, 0.8 mL/min, 254 nm; *t* (major) = 11.21 min, *t* (minor) = 18.32 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (d, *J* = 4.6 Hz, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.85 (td, *J* = 7.7, 1.7 Hz, 1H), 7.56−7.47 (m, 1H), 7.40 (d, *J* = 1.2 Hz, 1H), 6.45−6.33 (m, 2H), 5.39−5.24 (m, 2H), 4.34−4.14 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.1, 167.9, 152.8, 150.5, 149.1, 142.7, 136.9, 127.6, 121.7, 110.7, 108.0, 83.2, 77.2, 49.0, 39.6, 27.6; ESI-HRMS Calcd for $C_{18}H_{21}N_2O_6$ $[M + H]^+$: 361.1394, Found: 361.1394.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-(2-thienyl)-4-(pyridin-2-yl) Butanoate (**3al**).* White solid, Mp: 77−79 °C, 72 mg, 96% yield. $[\alpha]_D^{20}$ = +58.5 (*c* 0.52, CH_2Cl_2); 96% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 80:20, 1.0 mL/min, 254 nm; *t* (minor) = 5.90 min, *t* (major) = 9.15 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78−8.63 (m, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 7.84 (td, *J* = 7.7, 1.4 Hz, 1H), 7.52−7.47 (m, 1H), 7.32−7.22 (m, 1H), 7.13 (d, *J* = 3.6 Hz, 1H), 6.98 (dd, *J* = 4.9, 3.9 Hz, 1H), 5.39 (ABd, *J* = 12.4 Hz, 1H), 5.34 (ABd, *J* = 12.4 Hz, 1H), 4.50 (d, *J* = 19.2 Hz, 1H), 4.29 (d, *J* = 19.2 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.3, 169.1, 152.7, 149.1, 141.1, 136.8, 127.5, 126.9, 125.4, 125.4, 121.6, 83.2, 79.7, 49.9, 41.6, 27.5; ESI-HRMS Calcd for $C_{18}H_{21}N_2O_5S$ $[M + H]^+$: 377.1166, Found: 377.1162.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-styryl-4-(pyridin-2-yl) Butanoate (**3am**).* Light yellow solid, Mp: 82−84 °C, 75 mg, 95% yield. $[\alpha]_D^{20}$ = +51.8 (*c* 1.0, CH_2Cl_2); 95% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10,

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1.0 mL/min, 254 nm; t (minor) = 7.41 min, t (major) = 8.27 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (dd, J = 4.7, 0.6 Hz, 1H), 8.04 (d, J = 7.8 Hz, 1H), 7.85 (td, J = 7.7, 1.7 Hz, 1H), 7.52−7.48 (m, 1H), 7.40−7.26 (m, 5H), 6.68 (d, J = 16.3 Hz, 1H), 6.36 (d, J = 16.3 Hz, 1H), 5.18 (ABd, J = 12.3 Hz, 2H), 5.14 (ABd, J = 12.3 Hz, 2H), 4.06 (s, 2H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 169.7, 152.9, 149.0, 136.9, 136.1, 132.1, 128.6, 128.2, 127.5, 127.0, 126.6, 121.7, 82.9, 78.7, 49.7, 40.9, 27.7; ESI-HRMS Calcd for $C_{22}H_{25}N_2O_5$ $[M + H]^+$: 397.1757, Found: 397.1754.

*(S)-tert-Butyl 2-Nitromethyl-4-oxo-2-methyl)-4-(pyridin-2-yl) Butanoate (**3an**).* White solid, Mp: 98−100 °C, 58 mg, 95% yield. $[\alpha]_D^{20}$ = −10.0 (c 0.60, CH_2Cl_2); 66% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 95:5, 0.8 mL/min, 254 nm; t (minor) = 9.42 min, t (major) = 10.20 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.69−8.67 (m, 1H), 8.03 (dt, J = 7.9, 1.1 Hz, 1H), 7.85 (td, J = 7.7, 1.7 Hz, 1H), 7.52−7.46 (m, 1H), 4.97 (d, J = 11.9 Hz, 1H), 4.84 (d, J = 11.9 Hz, 1H), 3.76 (ABd, J = 11.9 Hz, 1H), 3.74 (ABd, J = 11.9 Hz, 1H), 1.45 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.7, 172.1, 152.9, 149.0, 136.9, 127.4, 121.6, 82.2, 79.8, 44.2, 42.3, 27.7, 22.2; ESI-HRMS Calcd for $C_{15}H_{21}N_2O_5$ $[M + H]^+$: 309.1445, Found: 309.1442.

*(S)-tert-Butyl 2-Nitromethyl-4-oxo-2-heptyl-4-(pyridin-2-yl) Butanoate (**3ao**).* Colorless oil, 73 mg, 93% yield. $[\alpha]_D^{20}$ = −8.3 (c 1.43, CH_2Cl_2); 43% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 95:5, 0.8 mL/min, 254 nm; t (major) = 6.25 min, t (minor) = 6.82 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70−8.66 (m, 1H), 8.03 (dt, J = 7.9, 1.1 Hz, 1H), 7.84 (td, J = 7.7, 1.7 Hz, 1H), 7.52−7.47 (m, 1H), 5.03 (ABd, J = 11.9 Hz, 1H), 4.94 (ABd, J = 11.9 Hz, 1H), 3.77 (ABd, J = 19.3 Hz, 1H), 3.71 (ABd, J = 19.4 Hz, 1H), 1.80−1.64 (m, 2H), 1.45 (s, 9H), 1.27 (s, 10H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.9, 171.4, 153.0., 149.0, 136.8, 127.4, 121.6, 82.2, 47.6, 41.5, 35.6, 31.6, 29.5, 28.8, 27.8, 23.5, 22.5, 14.0; ESI-HRMS Calcd for $C_{21}H_{33}N_2O_5$ $[M + H]^+$: 393.2384, Found: 393.2384.

*(S)-tert-Butyl 2-Nitromethyl-4-oxo-2-cyclohexyl-4-(pyridin-2-yl) Butanoate (**3ap**).* White solid, mp: 78−80 °C, 63 mg, 84% yield; $[\alpha]_D^{20}$ = −25.2 (c 0.65, CH_2Cl_2), 94% *ee*, determined by HPLC analysis [Daicel Chiralcel AD-H column, *n*-hexane/*i*-PrOH = 90:10, 0.5 mL/min, 254 nm; t (minor) = 9.31 min, t (major) = 13.3 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 (d, J = 4.1 Hz, 1H), 8.02 (d, J = 7.8 Hz, 1H), 7.83 (td, J = 7.7, 1.7 Hz, 1H), 7.51−7.41 (m, 1H), 5.06 (s, 2H), 3.96−3.71 (m, 2H), 2.02−1.63 (m, 6H), 1.46 (s, 9H), 1.30−1.00 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.5, 170.4, 153.2, 148.9, 136.8, 127.3, 121.6, 82.3, 75.8, 50.8, 42.7, 39.4, 27.9, 27.9, 27.8, 26.8, 26.2; ESI-HRMS Calcd for $C_{20}H_{28}N_2O_5$ $[M + H]^+$: 377.2071, Found: 377.2068.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(5-methylpyridin-2-yl) Butanoate (**3bd**).* White solid, Mp: 119−121 °C, 69 mg, 90% yield. $[\alpha]_D^{20}$ = +62.3 (c 0.53, CH_2Cl_2); 93% *ee*, determined by HPLC analysis [Daicel Chiralcel AD-H column, *n*-hexane/*i*-PrOH = 80:20, 0.8 mL/min, 254 nm; t (minor) = 9.47 min, t (major) = 11.18 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58−8.49 (m, 1H), 7.96 (d, J = 7.9 Hz, 1H), 7.69−7.59 (m, 1H), 7.51−7.28 (m, 5H), 5.38−5.27 (m, 2H), 4.51 (d, J = 19.2 Hz, 1H), 4.21 (d, J = 19.1 Hz, 1H), 2.44 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 170.3, 150.8, 149.5, 138.0, 137.7, 137.2, 128.9, 128.1, 125.9, 121.4, 82.6, 79.8, 51.4, 40.2, 27.5, 18.7; ESI-HRMS Calcd for $C_{21}H_{25}N_2O_5$ $[M + H]^+$: 385.1758, Found: 385.1755.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(5-bromopyridin-2-yl) Butanoate (**3cd**).* Colorless crystal, Mp: 136−137 °C, 84 mg, 94% yield. $[\alpha]_D^{20}$ = +47.1 (c 0.24, CH_2Cl_2); 98% *ee*, determined by HPLC analysis [Daicel Chiralcel AD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; t (minor) = 10.57 min, t (major) = 11.37 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, J = 1.5 Hz, 1H), 7.97 (dt, J = 18.2, 5.2 Hz, 2H), 7.50−7.30 (m, 5H), 5.42−5.23 (m, 2H), 4.50 (d, J = 19.3 Hz, 1H), 4.17 (d, J = 19.2 Hz, 1H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0, 170.1, 151.2, 150.3, 139.7, 137.4, 128.9, 128.2, 125.8, 122.9, 82.8, 79.6, 51.3, 40.2, 27.5; ESI-HRMS Calcd for $C_{20}H_{22}BrN_2O_5$ $[M + H]^+$: 449.0707, Found: 449.0705.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(2-pyrazinyl) Butanoate (**3ed**).* White solid, Mp: 75−76 °C, 63 mg, 85% yield. $[\alpha]_D^{20}$ = +18.0 (c 1.23, CH_2Cl_2); 99% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; t (major) = 9.39 min, t (minor) = 16.88 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.24 (d, J = 1.4 Hz, 1H), 8.80 (d, J = 2.4 Hz, 1H), 8.68 (dd, J = 2.4, 1.5 Hz, 1H), 7.49−7.29 (m, 5H), 5.36 (d, J = 12.5 Hz, 2H), 4.52 (d, J = 19.3 Hz, 1H), 4.17 (d, J = 19.3 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.4, 169.9, 148.2, 147.2, 143.6, 143.4, 137.3, 129.0, 128.3, 125.7, 83.5, 79.4, 51.3, 40.3, 27.5; ESI-HRMS Calcd for $C_{19}H_{22}N_3O_5$ $[M + H]^+$: 372.1554, Found: 372.1550.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(pyrimidin-2-yl) Butanoate (**3fd**).* Colorless oil, 64 mg, 86% yield. $[\alpha]_D^{20}$ = +69.1 (c 0.55, CH_2Cl_2); 93% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 80:20, 1.0 mL/min, 254 nm; t (minor) = 14.26 min, t (major) = 18.86 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00−8.92 (m, 2H), 7.55−7.27 (m, 7H), 5.35 (s, 2H), 4.58 (d, J = 19.4 Hz, 1H), 4.24 (d, J = 19.3 Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.5, 169.8, 159.5, 157.6, 137.3, 128.9, 128.2, 125.7, 123.3, 83.1, 79.3, 51.4, 41.5, 27.5; ESI-HRMS Calcd for $C_{19}H_{22}N_3O_5$ $[M + H]^+$: 372.1554, Found: 372.1551.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(2-quinolyl) Butanoate (**3gd**).* Colorless oil, 82 mg, 97% yield. $[\alpha]_D^{20}$ = +36.4 (c 0.55, CH_2Cl_2); 99% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; t (minor) = 6.86 min, t (major) = 8.39 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, J = 8.4 Hz, 2H), 8.11 (d, J = 8.5 Hz, 1H), 7.88−7.76 (m, 2H), 7.70−7.59 (m, 1H), 7.58−7.48 (m, 2H), 7.45−7.30 (m, 3H), 5.43 (ABd, J = 12.4 Hz, 1H), 5.40 (ABd, J = 12.5 Hz, 1H), 4.77 (d, J = 19.2 Hz, 1H), 4.41 (d, J = 19.2 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.2, 170.3, 152.5, 147.1, 137.7, 137.0, 130.7, 130.1, 129.7, 128.9, 128.7, 128.1, 127.6, 125.9, 117.8, 82.7, 79.7, 51.6, 40.0, 27.5; ESI-HRMS Calcd for $C_{24}H_{25}N_2O_5$ $[M + H]^+$: 421.1758, Found: 421.1755.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(2-quinoxalinyl) Butanoate (**3hd**).* Light yellow oil, 76 mg, 90% yield. $[\alpha]_D^{20}$ = +41.2 (c 0.89, CH_2Cl_2); 98% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; t (minor) = 8.72 min, t (major) = 20.90 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.49 (s, 1H), 8.40−8.06 (m, 2H), 8.05−7.77 (m, 2H), 7.53−7.29 (m, 5H), 5.40 (s, 2H), 4.71 (d, J = 19.2 Hz, 1H), 4.31 (d, J = 19.2 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 170.0, 145.9, 144.1, 142.7, 140.9, 137.4, 132.4, 130.8, 130.5, 129.4, 129.0, 128.2, 125.8, 83.0, 79.4, 51.4, 40.1, 27.5; ESI-HRMS Calcd for $C_{23}H_{23}N_3NaO_5$ $[M + Na]^+$: 444.1530, Found: 444.1534.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(2-oxazolyl) Butanoate (**3id**).* White solid, Mp: 85−86 °C, 62 mg, 86% yield. $[\alpha]_D^{20}$ = +66.2 (c 0.60, CH_2Cl_2); 98% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 80:20, 1.0 mL/min, 254 nm; t (minor) = 7.83 min, t (major) = 12.16 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 0.5 Hz, 1H), 7.43−7.29 (m, 6H), 5.39−5.25 (m, 2H), 4.38 (d, J = 18.9 Hz, 1H), 4.09 (d, J = 18.9 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.2, 169.5, 157.5, 142.0, 136.8, 129.3, 129.0, 128.4, 125.6, 83.3, 79.1, 51.3, 41.3, 27.5; ESI-HRMS Calcd for $C_{18}H_{21}N_2O_6$ $[M + H]^+$: 361.1394, Found: 361.1389.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(2-thiazolyl) Butanoate (**3jd**).* Light yellow solid, Mp: 58−60 °C, 72 mg, 96% yield. $[\alpha]_D^{20}$ = +140.2 (c 0.55, CH_2Cl_2); >99% *ee*, determined by HPLC analysis [Daicel Chiralcel AD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; t (major) = 11.66 min, t (minor) = 13.27 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, J = 3.0 Hz, 1H), 7.71 (d, J = 3.0 Hz, 1H), 7.45−7.26 (m, 5H), 5.35 (s, 2H), 4.47 (d, J = 18.9 Hz, 1H), 4.20 (d, J = 18.9 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.9, 169.7, 166.1, 144.9, 137.1, 1289.0, 128.3, 126.6, 125.7, 125.6, 83.1, 79.4, 51.3, 40.7, 27.5; ESI-HRMS Calcd for $C_{18}H_{21}N_2O_5S$ $[M + H]^+$: 377.1166, Found: 377.1164.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(2-benzothiazolyl) Butanoate (**3kd**).* White solid, Mp: 90−91 °C, 79 mg, 92% yield. $[\alpha]_D^{20}$

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J. Org. Chem. 2017, 82, 7353−7362

= +42.0 (*c* 0.75, CH_2Cl_2); 99% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 6.80 min, *t* (major) = 8.19 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26−8.19 (m, 1H), 8.01−7.94 (m, 1H), 7.63−7.50 (m, 2H), 7.50−7.43 (m, 2H), 7.43−7.29 (m, 3H), 5.38 (s, 2H), 4.61 (d, *J* = 19.0 Hz, 1H), 4.31 (d, *J* = 19.0 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.5, 169.7, 165.4, 153.4, 137.3, 137.1, 129.0, 128.3, 127.9, 127.1, 125.8, 125.6, 122.4, 83.2, 79.4, 51.5, 41.0, 27.5; ESI-HRMS Calcd for $C_{22}H_{23}N_2O_5S$ $[M + H]^+$: 427.1322, Found: 427.1319.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(N-methyl-2-imidazolyl) Butanoate (**3ld**).* White solid, Mp: 120−121 °C, 69 mg, 92% yield. $[\alpha]_D^{20}$ = +77.6 (*c* 0.41, CH_2Cl_2); >99% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 10.35 min, *t* (major) = 13.18 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45−7.27 (m, 5H), 7.17 (s, 1H), 7.05 (s, 1H), 5.32 (ABd, *J* = 12.3 Hz, 1H), 5.29 (ABd, *J* = 12.4 Hz, 1H), 4.42 (d, *J* = 18.7 Hz, 1H), 4.16 (d, *J* = 18.7 Hz, 1H), 3.98 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.4, 170.2, 142.5, 137.3, 129.4, 128.8, 128.1, 127.3, 125.8, 82.6, 79.8, 51.3, 41.0, 36.0, 27.5; ESI-HRMS Calcd for $C_{19}H_{24}N_3O_5$ $[M + H]^+$: 374.1710, Found: 374.1707.

*(S)-tert-Butyl 2-Nitromethyl-4-oxo-2-furyl-4-(N-methyl-2-imidazolyl) Butanoate (**3lk**).* White solid, Mp: 110−111 °C, 62 mg, 85% yield. $[\alpha]_D^{20}$ = +41.9 (*c* 0.42, CH_2Cl_2); >99% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 80:20, 1.0 mL/min, 254 nm; *t* (minor) = 9.47 min, *t* (major) = 11.96 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 1.2 Hz, 1H), 7.17 (s, 1H), 7.06 (s, 1H), 6.47−6.24 (m, 2H), 5.32 (ABd, *J* = 12.3 Hz, 1H), 5.26 (ABd, *J* = 12.3 Hz, 1H), 4.12 (d, *J* = 1.5 Hz, 2H), 3.99 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.6, 167.9, 150.2, 142.6, 142.3, 129.4, 127.3, 110.7, 108.0, 83.1, 77.4, 49.0, 40.4, 36.1, 27.6; ESI-HRMS Calcd for $C_{17}H_{22}N_3O_6$ $[M + H]^+$: 364.1501, Found: 364.1501.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-thienyl-4-(N-methyl-2-imidazolyl) Butanoate (**3ll**).* White solid, Mp: 109−110 °C, 67 mg, 88% yield. $[\alpha]_D^{20}$ = +49.4 (*c* 0.5, CH_2Cl_2); >99% *ee*, determined by HPLC analysis [Daicel Chiralcel AS-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 14.04 min, *t* (major) = 15.84 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 5.2, 1.1 Hz, 1H), 7.19 (d, *J* = 0.8 Hz, 1H), 7.11 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.07 (s, 1H), 6.98 (dd, *J* = 5.1, 3.7 Hz, 1H), 5.44−5.22 (m, 2H), 4.38 (d, *J* = 18.7 Hz, 1H), 4.21 (d, *J* = 18.6 Hz, 1H), 3.99 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.8, 169.1, 142.4, 140.8, 129.5, 127.3, 126.9, 125.5, 125.4, 83.2, 79.8, 49.9, 42.4, 36.1, 27.5; ESI-HRMS Calcd for $C_{17}H_{22}N_3O_5S$ $[M + H]^+$: 380.1275, Found: 380.1271.

*(R)-tert-Butyl 2-Nitromethyl-4-oxo-2-phenyl-4-(N-Bn-2-benzimidazolyl) Butanoate (**3md**).* White solid, Mp: 119−120 °C, 85 mg, 85% yield. $[\alpha]_D^{20}$ = +45.6 (*c* 0.35, CH_2Cl_2); 99% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 80:20, 1.0 mL/min, 254 nm; *t* (minor) = 8.46 min, *t* (major) = 15.77 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02−7.91 (m, 1H), 7.50−7.28 (m, 8H), 7.26−7.18 (m, 3H), 7.07 (d, *J* = 6.0 Hz, 2H), 5.92 (ABd, *J* = 15.8 Hz, 1H), 5.81 (ABd, *J* = 15.8 Hz, 1H), 5.26 (s, 2H), 4.65 (d, *J* = 19.2 Hz, 1H), 4.37 (d, *J* = 19.0 Hz, 1H), 1.26 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.3, 170.0, 145.1, 141.8, 137.1, 136.7, 136.4, 128.9, 128.7, 128.2, 127.7, 126.5, 125.9, 124.1, 122.2, 111.1, 82.8, 79.8, 51.3, 48.6, 42.2, 27.4; ESI-HRMS Calcd for $C_{29}H_{30}N_3O_5$ $[M + H]^+$: 500.2180, Found: 500.2179.

*(R)-5-(2-Pyridinyl)-3-phenyl-3-(t-butyloxy carbonyl)-3,4-dihydro-2H-pyrrole (**4**).* To the dry round-bottom flask was added **3ad** (60 mg, 0.16 mmol, 97% *ee*), THF (2 mL), MeOH (1 mL), AcOH (144 μL, 16 equiv), and Fe powder (403 mg, 45 equiv) successively at room temperature, and the resulting mixture was refluxed for 12 h under nitrogen atmosphere. After cooling to room temperature, a solution of saturated $NaHCO_3$ (aq. 10 mL) was added and stirred for another 30 min at room temperature, and the reaction mixture was filtrated through Celite and washed with ethyl acetate (20 mL). The water layer was extracted with ethyl acetate (20 mL × 3). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum/ethyl acetate = 95/5) to give (*R*)-**4** (37.1 mg, 71% yield). Light yellow oil, $[\alpha]_D^{20}$ = −10.9 (*c* 0.38 CH_2Cl_2); 98% *ee*, determined by HPLC analysis [Daicel Chiralcel AD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 7.63 min, *t* (major) = 12.27 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67−8.64 (m, 1H), 8.13 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.73 (td, *J* = 7.7, 1.8 Hz, 1H), 7.37−7.28 (m, 5H), 7.27−7.18 (m, 1H), 5.02 (dt, *J* = 16.6, 1.5 Hz, 1H), 4.43 (dt, *J* = 16.7, 1.9 Hz, 1H), 4.27−4.10 (m, 1H), 3.51 (dt, *J* = 17.9, 1.9 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 173.4, 152.6, 149.0, 142.4, 136.2, 128.4, 126.8, 126.3, 124.7, 121.6, 81.3, 70.5, 58.5, 45.0, 27.6; ESI-HRMS Calcd for $C_{20}H_{23}N_2O_2$ $[M + H]^+$: 323.1754, Found: 323.1752.

*(R)-tert-Butyl 2-Nitromethyl-4-hydroxy-2-phenyl-4-(2-pyridinyl) Butanoate (**5**).* To a stirred solution of **3ad** (148 mg, 0.4 mmol) in anhydrous MeOH (5 mL) was added $NaBH_4$ (16 mg, 0.4 mmol) in portions at 0 °C, and stirred for another 15 min. The reaction mixture was treated with a saturated aqueous NH_4Cl solution at 0 °C. The two phases were separated, and the aqueous phase was extracted with ethyl acetate (10 mL × 3). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography to afford the pure β-nitroacrylic esters **5**. Colorless oil, 144 mg, 94% yield (the ratio of diastereomers, 1.4:1), 40% isolated yield for major isomer. $[\alpha]_D^{20}$ = −24.6 (*c* 1.0, CH_2Cl_2, major isomer). 97% *ee*, determined by HPLC analysis [Daicel Chiralcel AS-H column, *n*-hexane/*i*-PrOH = 88:22, 1.0 mL/min, 254 nm; *t* (minor) = 7.77 min, *t* (major) = 9.12 min]. (major isomer) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (d, *J* = 4.5 Hz, 1H), 7.62 (td, *J* = 7.7, 1.2 Hz, 1H), 7.48−7.27 (m, 5H), 7.22−6.96 (m, 2H), 5.84 (d, *J* = 14.4 Hz, 1H), 5.37 (d, *J* = 14.4 Hz, 1H), 4.67 (s, 1H), 4.43 (d, *J* = 10.4 Hz, 1H), 2.66 (d, *J* = 14.8 Hz, 1H), 2.44 (dd, *J* = 15.0, 11.0 Hz, 1H), 1.38 (s, 9H); (major isomer) ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 160.9, 147.9, 138.0, 136.7, 129.0, 127.3, 125.7, 122.4, 120.0, 82.2, 78.0, 68.9, 52.8, 42.7, 27.4; ESI-HRMS Calcd for $C_{20}H_{25}N_2O_5$ $[M + H]^+$: 373.1758, Found: 373.1754.

*(3R,5S)-5-(2-Pyridinyl)-3-nitromethyl-3-phenyl-dihydrofuran-2-one (**6**).* To a 25 mL round-bottom flask were added β-nitroacrylic esters **5** (major isomer, 80 mg, 0.21 mmol), 10 mL of CH_2Cl_2, and 2 mL of TFA at room temperature. The reaction mixture was stirred for 24 h at 30 °C, and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum/ethyl acetate, 1:2, (v/v)) to give the lactone **6** (52 mg, 81% yield). White solid, Mp: 58−59 °C, $[\alpha]_D^{20}$ = +8.7 (*c* 0.31, CH_2Cl_2); 99% *ee*, determined by HPLC analysis [Daicel Chiralcel AS-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 254 nm; *t* (minor) = 37.24 min, *t* (major) = 55.44 min]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.5 Hz, 1H), 7.43 (td, *J* = 7.8, 1.6 Hz, 1H), 7.28 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.19 (dd, *J* = 9.6, 5.7 Hz, 3H), 7.13−7.02 (m, 2H), 5.75 (dd, *J* = 8.9, 3.0 Hz, 1H), 4.94 (d, *J* = 14.2 Hz, 1H), 4.79 (d, *J* = 14.2 Hz, 1H), 3.51 (dd, *J* = 13.8, 3.2 Hz, 1H), 3.28 (dd, *J* = 13.8, 9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.3, 157.8, 149.1, 136.4, 134.5, 128.9, 128.5, 126.3, 122.6, 119.8, 80.7, 77.4, 50.6, 37.0. ESI-HRMS Calcd for $C_{16}H_{15}N_2O_4$ $[M + H]^+$: 299.1026, Found: 299.1024.

*(R)-tert-Butyl 4-Methyl 2-(nitromethyl)-2-phenylsuccinate (**7**).* To a 25 mL oven-dried vial under a N_2 atmosphere were added **3ld** (93 mg, 0.25 mmol), 30 mg of 4 Å MS, and 2.0 mL of acetonitrile. After stirring for 10 min, MeOTf (45 mg, 0.275 mmol) was added. The reaction mixture was stirred for 12 h at room temperature before MeOH (1.0 mL) and DBU (0.1 mL) were added. The reaction was stirred for another 1 h at room temperature. Then, the resulting mixture was separated with water, and the aqueous phase was extracted with CH_2Cl_2 (10 mL × 3). The combined organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum/ethyl/acetate, 1/10 (v/v)) to give the succinate **7** (74 mg, 92% yield). White solid, Mp: 80−81 °C, $[\alpha]_D^{20}$ = −62.4 (*c* 0.50, CH_2Cl_2); >99% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 210 nm; *t* (minor) = 6.31 min, *t* (major) = 7.45 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.26 (m, 5H), 5.34 (q, *J* = 13.1 Hz, 2H), 3.68 (s, 3H), 3.44 (ABd, *J* = 17.2 Hz, 1H), 3.29 (ABd, *J* = 17.3 Hz, 1H), 1.40 (s,

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J. Org. Chem. 2017, 82, 7353−7362

9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 169.6, 136.9, 129.0, 128.3, 125.5, 83.1, 78.8, 51.8, 51.4, 36.9, 27.5; ESI-HRMS Calcd for $C_{16}H_{21}NNaO_6$ $[M + Na]^+$: 346.1261, Found: 346.1263.

*(R)-tert-Butyl 5-Oxo-3-phenylpyrrolidine-3-carboxylate (**8**).* To a suspension of succinate **7** (40 mg, 0.12 mmol, major isomer) and $NiCl_2{\cdot}6H_2O$ (43 mg, 0.18 mmol) in ethanol (2 mL) was added $NaBH_4$ (68 mg, 1.8 mmol) at 0 °C, and the mixture was stirred for 9 h at room temperature. Then, the reaction mixture was quenched with a solution of saturated aqueous NH_4Cl and extracted with CH_2Cl_2(10 mL × 3). The organic layers were washed with brine, dried over Na_2SO_4, and concentrated under vacuum. The crude product was purified with flash chromatography on silica gel (ethyl acetate/petroleum ether, 1:1 (v/v)) to afford the lactam **8** (29 mg, 89% yield). White solid, Mp: 122−124 °C, 99.2% *ee*. $[\alpha]_D^{20}$ = −8.6 (*c* 0.62, CH_2Cl_2); determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 80:20, 1.0 mL/min, 210 nm; *t* (minor) = 6.82 min, *t* (major) = 8.30 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.22 (m, 5H), 6.33 (s, 1H), 4.32 (d, *J* = 9.8 Hz, 1H), 3.61(d, *J* = 9.8 Hz, 1H), 3.27 (d, *J* = 16.7 Hz, 1H), 2.75 (d, *J* = 16.7 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.4, 172.0, 140.3, 128.5, 127.3, 125.8, 81.9, 55.0, 50.6, 39.9, 27.4. ESI-HRMS Calcd for $C_{15}H_{20}NO_3$ $[M + H]^+$: 262.1438, Found: 262.1436.

*(R)-tert-Butyl 4-Hydroxy-2-(nitromethyl)-2-phenylbutanoate (**9**).* To a round-bottom flask were added succinate **7** (72 mg, 0.22 mmol) and anhydrous THF (5 mL) under a nitrogen atmosphere, followed by addition of DIBAL-H (0.48 mL in THF, 0.48 mmol) at 0 °C. The reaction mixture was stirred for another 24 h at 0 °C. H_2O (10 mL) was added to the reaction mixture, and extracted with CH_2Cl_2 (10 mL × 3). The organic layer was dried over Na_2SO_4, filtered, and concentrated under vacuum, and the crude product was purified with flash chromatography on silica gel (ethyl acetate/petroleum ether, 1:5 (v/v)) to afford the product **9**. Colorless oil, 55 mg, 85% yield. $[\alpha]_D^{20}$ = +5.0 (*c* 0.18, CH_2Cl_2); 99.5% *ee*, determined by HPLC analysis [Daicel Chiralcel OD-H column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, 210 nm; *t* (major) =11.70 min, *t* (minor) = 14.96 min]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.27 (m, 3H), 7.24 (dd, *J* = 6.8, 1.7 Hz, 2H), 5.33−5.10 (m, 2H), 3.67 (dd, *J* = 11.1, 5.5 Hz, 1H), 3.49 (s, 1H), 2.60−2.28 (m, 2H), 1.97 (s, 1H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 137.8, 128.9, 127.9, 125.8, 82.8, 79.5, 58.9, 53.0, 36.4, 27.6; ESI-HRMS Calcd for $C_{15}H_{22}NO_5$ $[M + H]^+$: 296.1492, Found: 296.1485.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01014.

Crystallographic data for **3ah** (CIF)

X-ray data for compound **3ah**, HPLC data, and ^{1}H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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