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Asymmetric Construction of Functionalized 1,2-Dihydropyridine and Pyridine Derivatives with Adjacent Stereocenters via a Unified Metal-Free Catalytic Approach

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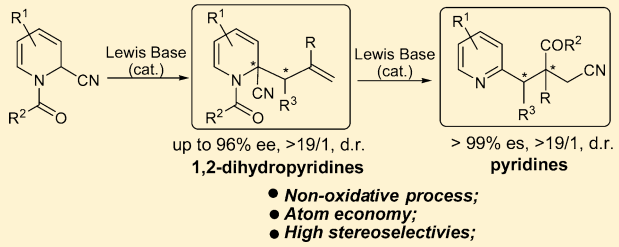
Supporting Information

ABSTRACT: A novel asymmetric catalytic approach for the construction of enantioenriched functionalized 1,2-dihydropyridines and pyridine derivatives incorporating adjacent quaternary and tertiary stereocenters has been reported. This process involved a metal-free catalytic asymmetric allylic alkylation and a stereospecifically nonoxidative aromatization approach for the desired chiral molecules.

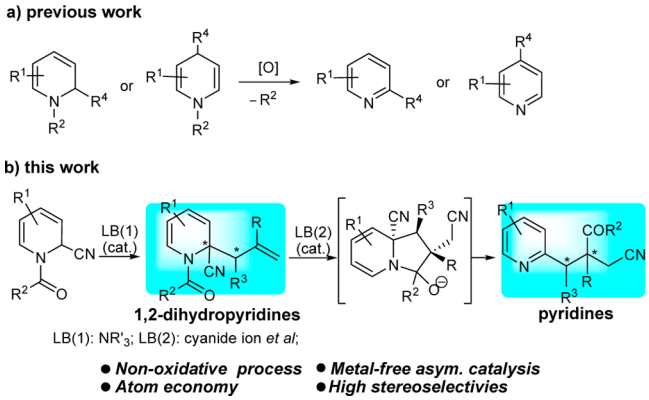


The substituted pyridine motif is among the most common heterocyclic frameworks found in the wide-ranging biological activities associated with both naturally occurring and synthetic compounds.[1] Its dihydro analogues also are known to possess a wide range of biological and pharmacological actions.[2] In addition, pyridines and dihydropyridines are important building blocks in the preparation of azaheterocyclic scaffolds.[3] Therefore, the efficient methods for the synthesis of these compounds are of great value.[3,4]

It is well documented that readily available pyridines can serve as convenient synthetic precursors to chiral dihydropyridines, while dihydropyridines in turn may also be converted to substituted pyridines through oxidation.[4a,b] Although numbers of asymmetric catalytic methods have been developed to build enantioenriched dihydropyridines from pyridine derivatives and other resources,[5] to the best of our knowledge, an asymmetric catalytic approach for dihydropyridines bearing adjacent tertiary−quaternary carbon centers has not been developed.[6] On the other hand, despite the fact that the oxidation of dihydropyridines into substituted pyridines has been well established (Scheme 1, a), the conversion of enantiomerically pure dihydropyridines into substituted pyridines incorporating chiral carbon centers is unexploited.[7] Furthermore, the oxidative aromatization process generally requires stoichiometric oxidants and dismantles N substituents that would produce unwanted waste in terms of the inherent nature of oxidative mechanism and thereby is not in accord with atom economical and sustainable synthesis.

We recently disclosed a novel metal-free intramolecular carbocyanation strategy for the construction of an aromatic N-heterocyclic motif by combining a nucleophilic cyanation and subsequent rearomatization process.[8] Because of the great importance of nitrogen-containing compounds and the growing demand for creating chiral molecules containing heteroaromatic motifs,[9] we decided to explore a unified and asymmetric protocol to constructing various substituted functionalized 1,2-dihydropyridine and pyridine derivatives incorporating contiguous stereocenters from α-cyano-substituted 1,2-dihydropyridines through a metal-free catalytic asymmetric allylic alkylation (AAA) and subsequent Lewis base-mediated intramolecular acylcyanation of activated alkenes (Scheme 1, b).[10] This unified metal-free protocol not only represented the first catalytic asymmetric approach to constructing enantioenriched 1,2-dihydropyridines incorporating adjacent quaternary and tertiary stereocenters but also provided an alternative nonoxidative aromatization approach to furnishing functionalized pyridines with pendant chiral scaffolds with high efficiency and atom economy in a stereospecific manner. Herein, we report our preliminary results on this subject.

Scheme 1. Synthetic Strategies



Our initial investigations commenced with the identification of the model reaction of metal-free catalytic AAA reaction between Morita−Baylis−Hillman (MBH) adducts and α-

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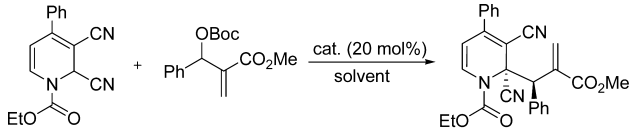
cyano-substituted 1,2-dihydropyridines, which can be prepared readily from Reissert reaction of available pyridine derivatives.[5h] The preliminary results revealed that the substituent patterns and electronic properties of substituents at the 1,2-dihydropyridine ring system are essential for accomplishing this allylic alkylation.[11] Nevertheless, to our delight, 3-cyano-4-phenyl dihydropyridine **1a** was found be a suitable model substrate for further evaluation. Treatment of dihydropyridine **1a** with MBH adduct **2a** in toluene provided the desired 2,2-disubstituted 1,2-dihydropyridine **3a** bearing adjacent quaternary and tertiary stereocenters in 67% yield (major isomer) with moderate diastereoselectivity and good enantioselectivity in the presence of a catalytic amount of quinidine (20 mol %) (Table 1, entry 1). Evaluation of other cinchona alkaloid catalysts revealed that hydroquinidine afforded superior results with regard to the chemical outcome and stereoinduction, while catalysts such as quinine, cinchonine, $(DHQ)_2PHAL$, etc. gave relatively low stereoselectivities (Table 1, entries 1−9). In the presence of hydroquinidine, various solvents were examined, and obvious improvements in both chemical and optical yields were observed in *o*-xylene.[11] Further performance of this allylc alkylation at low temperatures with less solvent furnished desired product **3a** in 91% yield with high stereoselectivities (90% ee and 18:1 dr) (Table 1, entry 10).

Table 1. Studies of Asymmetric Allylic Alkylation[a]



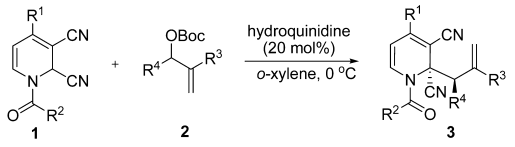
1a **2a** **3a**

entry	catalyst	solvent	yield (%)[b]	dr[c]	ee (%)[d]
1	quinidine	toluene	67	6.5:1	83
2	hydroquinidine	toluene	70	7.5:1	87
3	quinine	toluene	77	5.4:1	−58
4	cinchonidine	toluene	74	4.8:1	−3
5	cinchonine	toluene	20	nd	55
6	$(DHQD)_2AQN$	toluene	60	3.6:1	7
7	$(DHQ)_2AQN$	toluene	64	4.9:1	35
8	$(DHQD)_2PHAL$	toluene	70	3.5:1	31
9	$(DHQ)_2PHAL$	toluene	64	3:1	74
10[e]	hydroquinidine	*o*-xylene	91	18:1	90

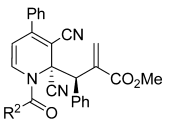
[a]Performed with **1a** (0.2 mmol), **2a** (0.26 mmol), and catalyst (20 mol %) in solvent (c = 0.5 M) at 30 °C over 36 h. Abbreviations: $(DHQD)_2AQN$, hydroquinidine anthraquinone-1,4-diyl diether; $(DHQ)_2AQN$, hydroquinine anthraquinone-1,4-diyl diether; $(DHQD)_2PHAL$, hydroquinidine 1,4-phthalazinediyl diether; $(DHQ)_2PHAL$, hydroquinine 1,4-phthalazinediyl diether. [b]Isolated yield of the major isomer. [c]The dr values were determined by ^1H NMR analysis. [d]The ee values of major isomers were determined by chiral HPLC analysis. [e]Run at 0 °C in 60 h (c = 1.0 M).

Having established the optimal reaction condition, we next examined the substrate scope of hydroquinidine-catalyzed enantioselective allylic alkylation reactions of MBH carbonates **2** with 1,2-dihydropyridines **1**, and the results are illustrated in Table 2. In general, high yields and stereoselectivities were observed for a broad range of 2,2-disubstituted dihydropyridines. At first, 2-cyano-substituted dihydropyridines with different acyl substituents (R^2) at the nitrogen were investigated to elucidate the effect of R^2 groups on the reaction outcome and stereoselective induction.[12] Aside from *N*-carboethoxy-substituted compound **1a**, both *N*-carboisobutoxy compound **1b** and *N*-carboallyloxy-substituted compound **1c** also furnished functionalized dihydropyridines **3b** and **3c** in high yields with excellent diastereoselectivities and high enantioselectivities (94 and 90% ee, respectively). The substituents (R^1) at the 4 position of dihydropyridines had distinct effects on the reaction outcome and diastereoselectivity. Substrates bearing aromatic substituents are superior to their alkyl analogue, while the electronic properties of the aromatic substituents of dihydropyridines did not affect the allylic alkylation reaction (**3d**−**3h**). Next, the reactions of a variety of MBH carbonates **2** with dihydropyridine **1a** were surveyed to explore the generality of this transformation. MBH carbonates with different electron-withdrawing groups (R^3) have been applied in the developed process (**3i**−**3k**). Substrate **1a** reacted with MBH carbonate with a ketone moiety to give product **3i** in good yield with high enantioselectivity and relatively low diastereoselectivity, while treatment of dihydropyridine **1a** and MBH carbonates, including cyano and *tert*-butyl esters as EWG groups, did not provide any desired products. The aryl moieties in MBH carbonates **2** were well-tolerated, and an array of MBH carbonates provided the desired congested products **3** in high yields and enantioselectivities (up to 94% ee, **3l**−**3o**), with the

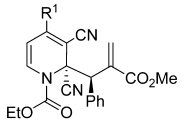
Table 2. Substrate Scope of Asymmetric Allylic Alkylation[a]



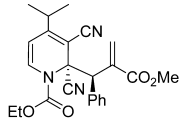
1 **2** **3**



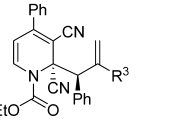
3a (R^2 = OEt): 91%, 90% ee, 18/1 d.r.
3b (R^2 = O*i*Bu): 91%, 94% ee, 18/1 d.r.
3c (R^2 = OAllyl): 86%, 90% ee, >19/1 d.r.



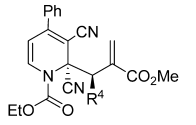
3d (R^1 = 4-MeOC$_6$H$_4$): 90%, 94% ee, 17/1 d.r.
3e (R^1 = 4-MeC$_6$H$_4$): 89%, 93% ee, 18/1 d.r.
3f (R^1 = 4-CF$_3$C$_6$H$_4$): 68%, 94% ee, >19/1 d.r.
3g (R^1 = 2-MeC$_6$H$_4$): 87%, 90% ee, 19/1 d.r.



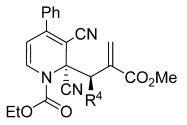
3h: 67%, 90% ee, 10/1 d.r.



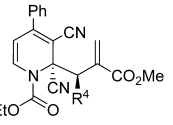
3i (R^3 = COMe): 76%, 91% ee, 5/1 d.r.
3j (R^3 = CO$_2$*t*Bu): nd
3k (R^3 = CN): nd



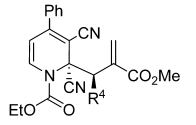
3l (R^4 = 4-BrC$_6$H$_4$): 91%, 94% ee, 18/1 d.r.
3m[b] (R^4 = 4-MeOC$_6$H$_4$): 72%, 88% ee, 9/1 d.r.



3n (R^4 = 3-BrC$_6$H$_4$): 86%, 96% ee, 14/1 d.r.
3o (R^4 = 3-MeOC$_6$H$_4$): 86%, 92% ee, 15/1 d.r.



3p[c] (R^4 = 2-BrC$_6$H$_4$): 83% (42%), 71% (95%) ee, >19/1 d.r.



3q (R^4 = 2-naphthyl): 91%, 94% ee, 11/1 d.r.

[a]Reactions were performed with **1** (0.2 mmol), **2** (0.26 mmol), and hydroquinidine (20 mol %) at 0 °C in *o*-xylene (c = 1.0 M). Yields shown are of isolated products of major isomers. The ee values of major isomers were determined by chiral HPLC analysis. The dr values were determined by ^1H NMR analysis. [b]Run at 0 °C for 72 h and at 30 °C for 24 h. [c]The data in parentheses were provided from recrystallization.

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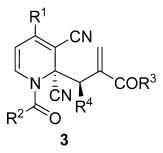
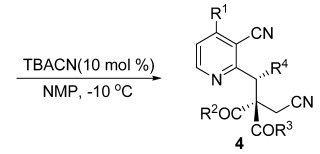
exception that *o*-bromo-substituted dihydropyridine provided moderate enantioselectivity. However, enantioenriched product **3p** can be obtained in excellent optical purity from a single recrystallization. 2-Naphthyl-substituted MBH carbonate could also be applied to the present transformation to deliver desired product **3q** in high yield with high enantionselectivity and slightly decreased diastereoselectivity. Treatment of alkyl-substituted MBH carbonate with substrate **1a** provided a complex mixture. The absolute configuration of the allylation product was determined on the basis of X-ray crystal structural analysis of compound **3n**,[13] and the absolute configuration of other products was assigned by analogy.

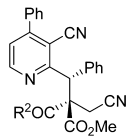
With this well-established asymmetric alkylation in hand, we turned our attention to the catalytic conversion of enantioenriched allylic-substituted dihydropyridines into functionalized pyridines with pendant chiral scaffolds via an intramolecular acylcyanation (for details, see Table S4). To our delight, the desired acylcyanation occurred and gave rise to highly functionalized pyridine product **4a** in good yield with perfect stereospecificity in the presence of TBACN (10 mol %, TBACN = tetrabutylammonium cyanide) with NMP as a medium (**4a** in Table 3). Under the optimal reaction conditions, the substrate scope of catalyzed asymmetric acylcyanation was examined. The results are summarized in Table 3. All examined allylic dihydropyridines displayed almost complete enantiospecificity. Enantioenriched *N*-carboisobutoxy and *N*-carboallyloxy dihydropyridines **3b** and **3c** furnished functionalized pyridines **3b** and **3c** in good to moderate yields with excellent stereospecificities (up to 99% es and 19:1 dr). Allyl-substituted dihydropyridines including aromatic substituents provided excellent stereospecificities, regardless of the electronic properties of the aromatic system (R^1), while an electron-rich aromatic system gave yields superior to that of an electron-deficient analogue (**4d**–**4g**). Allylic dihydropyridine possessing an alkyl group at the 4 position delivered desired product **4h** in good yield with complete stereospecificity. Treatment of dihydropyridine possessing a ketone moiety as the EWG group gave moderate diastereoselectivity (**4i**). The broad scope of the process was further illustrated by the asymmetric acylcyanation of allylic dihydropyridines bearing various aromatic groups in good to high yields and excellent stereospecificity (**4l**–**4q**).

This methodology also could be extended to other α-cyano-substituted 1,2-dihydropyridines with different substitution patterns. In our preliminary study, the products of AAA reaction between 5-substituted 1,2-dihydropyridines **1** and MBH carbonate **2** were found to be unstable,[11] thereby impeding the preparation of functionalized pyridines, including chiral scaffolds via a subsequent asymmetric acylcyanation process. Pleasingly, 5-substituted pyridines **4r** and **4s** incorporating adjacent chiral quaternary and tertiary stereocenters can be readily prepared in moderate yields with high enantioselectivities and excellent diastereoselectivities from substrate **1** and MBH carbonate **2** through the quick purification and subsequent acylcyanation of the allylic alkylation products of α-cyano-substituted 1,2-dihydropyridines (Scheme 2), which further expanded the applicability of this synthetic strategy remarkably.

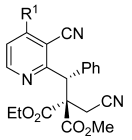
Table 3. Substrate Scope of Asymmetric Acylcyanation[a]



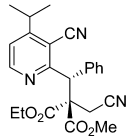




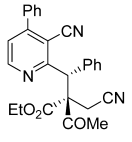
4a (R^2 = OEt): 71%, >99% es, >19/1 d.r.
4b (R^2 = O*i*Bu): 70%, >99% es, >19/1 d.r.
4c[b] (R^2 = OAllyl): 53%, >99% es, >19/1 d.r.



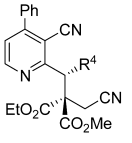
4d (R^1 = 4-MeOC$_6$H$_4$): 67%, 99% es, 15/1 d.r.
4e (R^1 = 4-MeC$_6$H$_4$): 69%, >99% es, 19/1 d.r.
4f[c] (R^1 = 4-CF$_3$C$_6$H$_4$): 50%, >99% es, 19/1 d.r.
4g (R^1 = 2-MeC$_6$H$_4$): 69%, >99% es, 12/1 d.r.



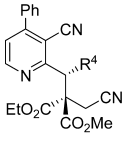
4h 80%, >99% es, 13/1 d.r.



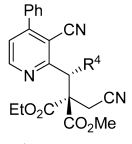
4i 83%, >99% es, 9/1 d.r.



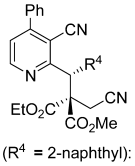
4l (R^4 = 4-BrC$_6$H$_4$): 73%, >99% es, 19/1 d.r.
4m (R^4 = 4-MeOC$_6$H$_4$): 60%, >99% es, 19/1 d.r.



4n (R^4 = 3-BrC$_6$H$_4$): 70%, 99% es, 15/1 d.r.
4o (R^4 = 3-MeOC$_6$H$_4$): 71%, >99% es, 19/1 d.r.



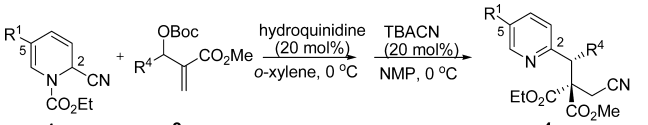
4p (R^4 = 2-BrC$_6$H$_4$): 83%, 99% es, >19/1 d.r.



4q (R^4 = 2-naphthyl): 61%, >99% es, 18/1 d.r.

[a]Reactions were performed with **3** (0.1 mmol) and TBACN (10 mol %) at −10 °C in NMP (*c* = 0.1 M) for 12 h. Yields shown are of isolated products. es = (product ee/starting material ee) × 100%. The ee values were determined by chiral HPLC analysis. The dr values were determined by ^{1}H NMR analysis. [b]Performed with DMF. [c]TBACN (15 mol %) was employed.

Scheme 2. One-Pot Synthesis of Compound 4



4r (R^1 = CON(CH$_2$)$_4$O, R^4 = Ph): 42% yield, 90% ee, >19/1 d.r.
4s (R^1 = CON(*i*Pr)$_2$, R^4 = 4-BrC$_6$H$_4$): 49% yield, 87% ee, >19/1 d.r

On the basis of the observation described above and the previous results, a possible reaction pathway for the intramolecular acylcyanation reaction is proposed (Scheme 3). An enolate (**I**) was first generated from the Michael addition of cyanide ion to the activated C═C bond of enantioenriched 1,2-dihydropyridine **3** in this transformation. Because of the facial selectivity of enolate (**I**), subsequently a tandem intramolecular condensation between the enolate (*si*-face) with the amide group proceeded stereospecifically and gave intermediate **II**, which followed an elimination to afford desired product **4** with cyanide ion. This result was supported by the X-ray crystal structural analyses of enantioenriched 1,2-dihydropyridine **3n** and racemic 5-substituted analogue **4t** [R^1 = CON(*i*Pr)$_2$, R^2 = OEt, R^3 = OMe, and R^4 = Ph].[16]

Finally, the utility of this method was demonstrated by the palladium-catalyzed decarboxylative allylation of pyridine

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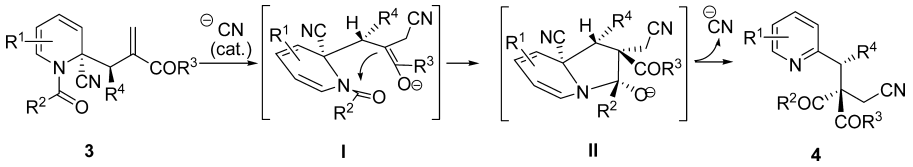
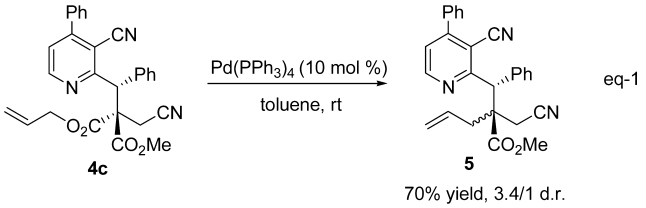
Scheme 3. Proposed Mechanism



derivative **4c**, which delivered functionalized pyridine **5** bearing a γ,δ-unsaturated moiety in 70% yield (eq 1).



In conclusion, a unified and novel catalytic approach by utilizing a metal-free AAA reaction and stereospecifically intramolecular acylcyanation reaction has been developed, which provided facile access to preparing enantioenriched functionalized 1,2-dihydropyridines and enantiomerically pure pyridine derivatives bearing adjacent quaternary and tertiary carbon centers under neutral and mild conditions with high stereoselectivities. The scope and versatility of the process were demonstrated. Further extension of this synthetic strategy also has been demonstrated.

EXPERIMENTAL SECTION

General Procedure for the Allylic Alkylation Reaction of MBH Adducts 2 with Compound 1. To a dried 10 mL reaction tube under a N_2 atmosphere were added compound **1** (0.2 mmol),[14] MBH carbonate **2** (0.26 mmol),[15] and *o*-xylene (0.2 mL). After being stirred at 0 °C for 10 min, the mixture was supplemented with catalyst (20 mol %). The reaction was monitored by TLC. Upon completion, the reaction mixture was concentrated *in vacuo*. The crude mixture was purified by column chromatography [silica gel, EtOAc/petroleum ether (60−90 °C)] to provide the following compounds.

*Ethyl 2,3-Dicyano-2-[2-(methoxycarbonyl)-1-phenylallyl]-4-phenylpyridine-1(2H)-carboxylate (Table 2, **3a**).* Yellow solid (83 mg, 91%); mp 59−60 °C; 90% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 90:10 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 35.4 min (minor), and t_R = 38.1 min (major)]: $[\alpha]_D^{25}$ = −76 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59−7.57 (m, 2H), 7.45−7.43 (m, 3H), 7.42−7.35 (m, 3H),7.24 (d, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 7.1 Hz, 2H), 6.76 (s, 1H), 6.71 (s, 1H), 5.81 (d, *J* = 7.8 Hz, 1H), 5.18 (s, 1H), 4.39−4.31 (m, 2H). 3.75 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 151.8, 149.3, 136.3, 135.4, 134.4, 131.9, 131.6, 130.8, 130.7, 129.2, 129.1, 128.9, 128.2, 116.2, 115.0, 107.9, 95.9, 64.8, 61.0, 52.6, 47.9, 14.2; HRMS (ESI) calcd for $C_{27}H_{24}N_3O_4$ ($[M + H]^+$) 454.1761, found 454.1760.

*Isobutyl 2,3-Dicyano-2-[2-(methoxycarbonyl)-1-phenylallyl]-4-phenylpyridine-1(2H)-carboxylate (Table 2, **3b**).* Yellow solid (87 mg, 91%); mp 119−121 °C; 94% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak OD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 22.6 min (minor), and t_R = 43.3 min (major)]: $[\alpha]_D^{25}$ = −66 (*c* = 0.55, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59−7.57 (m, 2H), 7.45−7.42 (m, 3H), 7.42−7.34 (m, 3H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.22−7.19 (m, 2H), 6.75 (s, 1H), 6.72 (s, 1H), 5.82 (d, *J* = 7.8 Hz, 1H), 5.19 (s, 1H), 4.12 (dd, *J* = 10.4, 6.7 Hz, 1H), 4.02 (dd, *J* = 10.4, 6.7 Hz, 1H), 3.74 (s, 3H), 2.11−2.03 (m, 1H), 1.01 (d, *J* = 1.2 Hz, 3H), 1.00 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 151.9, 149.3, 136.3, 135.4, 134.4, 131.8, 131.7, 130.8, 130.7, 129.2, 129.1, 128.9, 128.2, 116.2, 115.0, 108.1, 96.1, 74.8, 60.9, 52.7, 47.9, 27.9, 19.2, 19.1; HRMS (ESI) calcd for $C_{29}H_{28}N_3O_4$ ($[M + H]^+$) 482.2074, found 482.2062.

*Allyl 2,3-Dicyano-2-[2-(methoxycarbonyl)-1-phenylallyl]-4-phenylpyridine-1(2H)-carboxylate (Table 2, **3c**).* Yellow solid (80 mg, 86%); mp 109−111 °C; 90% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AS-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 23.8 min (minor), and t_R = 28.3 min (major)]: $[\alpha]_D^{25}$ = −92 (*c* = 0.90, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59−7.56 (m, 2H), 7.45−7.43 (m, 3H), 7.42−7.34 (m, 3H), 7.25 (d, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 7.1 Hz, 2H), 6.75 (s, 1H), 6.72 (s, 1H), 6.03−5.95 (m, 1H), 5.83 (d, *J* = 7.8 Hz, 1H), 5.43 (dd, *J* = 17.2, 0.9 Hz, 1H), 5.36 (d, *J* = 10.4 Hz, 1H), 5.18 (s, 1H), 4.80−4.72 (m, 2H), 3.74 (s, 3H); ^{13}CNMR (125 MHz, $CDCl_3$) δ 167.6, 151.6, 149.2, 136.2, 135.4, 134.3, 131.7, 131.7, 130.8, 130.7, 129.2, 129.1, 128.9, 128.2, 120.5, 116.2, 114.9, 108.3, 96.2, 69.1, 61.1, 52.7, 47.9; HRMS (ESI) calcd for $C_{28}H_{24}N_3O_4$ ($[M + H]^+$) 466.1761, found 466.1754.

*Ethyl 2,3-Dicyano-2-[2-(methoxycarbonyl)-1-phenylallyl]-4-(4-methoxyphenyl)pyridine-1(2H)-carboxylate (Table 2, **3d**).* Yellow solid (87 mg, 90%); mp 110−112 °C; 94% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 21.4 min (minor), and t_R = 22.8 min (major)]: $[\alpha]_D^{25}$ = −257 (*c* = 0.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62−7.51 (m, 2H), 7.47−7.40 (m, 3H), 7.22 (d, *J* = 7.7 Hz, 1H), 7.16 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.74 (s, 1H), 6.70 (s, 1H), 5.82 (d, *J* = 7.7 Hz, 1H), 5.16 (s, 1H), 4.34 (q, *J* = 6.9 Hz, 2H), 3.80 (s, 3H), 3.74 (s, 3H), 1.39 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 161.5, 151.8, 148.7, 136.4, 134.5, 131.6, 131.3, 130.7, 129.9, 129.0, 128.9, 127.4, 116.7, 115.1, 114.3, 107.9, 94.3, 64.7, 60.9, 55.5, 52.5, 47.9, 14.1; HRMS (ESI) calcd for $C_{28}H_{26}N_3O_5$ ($[M + H]^+$) 484.1867, found 484.1858.

*Ethyl 2,3-Dicyano-2-[2-(methoxycarbonyl)-1-phenylallyl]-4-(p-tolyl)pyridine-1(2H)-carboxylate (Table 2, **3e**).* Yellow solid (83 mg, 89%); mp 55−56 °C; 93% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 16.4 min (minor), and t_R = 18.1 min (major)]: $[\alpha]_D^{25}$ = −169 (*c* = 0.67, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60−7.52 (m, 2H), 7.48−7.38 (m, 3H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 6.75 (s, 1H), 6.71 (s, 1H), 5.81 (d, *J* = 7.8 Hz, 1H), 5.17 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.74 (s, 3H), 2.35 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 151.8, 149.2, 141.1, 136.3, 134.4, 132.4, 131.7, 131.5, 130.7, 129.6, 129.1, 129.0, 128.1, 116.4, 115.0, 108.0, 95.2, 64.8, 60.9, 52.6, 47.9, 21.5, 14.2; HRMS (ESI) calcd for $C_{28}H_{26}N_3O_4$ ($[M + H]^+$) 468.1918, found 468.1909.

*Ethyl 2,3-Dicyano-2-[2-(methoxycarbonyl)-1-phenylallyl]-4-[4-(trifluoromethyl)phenyl]pyridine-1(2H)-carboxylate (Table 2, **3f**).* Yellow solid (71 mg, 68%); mp 55−57 °C; 94% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 13.6 min (minor), and t_R = 14.9 min (major)]: $[\alpha]_D^{25}$ = −176 (*c* = 0.80, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.59−7.57 (m, 2H), 7.46−7.43 (m, 3H), 7.32−7.27 (m, 3H), 6.77 (s, 1H), 6.69 (s, 1H), 5.78 (d, *J* = 7.8 Hz, 1H), 5.19 (s, 1H), 4.40−4.32 (m, 2H), 3.76 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.6, 151.8, 148.2, 139.0, 136.3, 134.3, 132.7, 132.6, 132.3, 131.83, 130.8, 129.4, 129.3, 128.7, 126.1 (q, *J* = 3.7 Hz), 115.8, 114.9,

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107.3, 97.1, 65.1, 61.2, 52.7, 47.9, 14.2; HRMS (ESI) calcd for $C_{28}H_{23}F_3N_3O_4$ ([M + H]$^+$) 522.1635, found 522.1629.

*Ethyl 2,3-Dicyano-2-[2-(methoxycarbonyl)-1-phenylallyl]-4-(o-tolyl)pyridine-1(2H)-carboxylate (Table 2, **3g**).* Yellow solid (81 mg, 87%); mp 48−49 °C; 90% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 17.3 min (minor), and t_R = 18.6 min (major)]: $[\alpha]_D^{25}$ = −240 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.0 Hz, 2H), 7.51−7.30 (m, 4H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.18−7.05 (m, 3H), 6.75−6.65 (m, 2H), 5.63−5.57 (m, 1H), 5.21 (s, 1H), 4.46−4.25 (m, 2H), 3.76 (s, 1H), 2.19 (s, 2H), 1.91 (s, 1H), 1.39 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 151.9, 150.9, 136.5, 135.6, 135.3, 135.0, 134.4, 132.5, 131.7, 130.8, 130.6, 130.2, 129.7, 129.1, 128.0, 126.3, 115.2, 108.3, 98.9, 64.8, 60.7, 52.6, 48.6, 19.7, 14.1; HRMS (ESI) calcd for $C_{28}H_{26}N_3O_4$ ([M + H]$^+$) 468.1918, found 468.1917.

*Ethyl 2,3-Dicyano-4-isopropyl-2-[2-(methoxycarbonyl)-1-phenylallyl]pyridine-1(2H)-carboxylate (Table 2, **3h**).* White solid (56 mg, 67%); mp 126−128 °C; 90% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak OD-H, 70:30 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 10.4 min (minor), and t_R = 21.9 min (major)]: $[\alpha]_D^{25}$ = −34 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48−7.43 (m, 2H), 7.39−7.33 (m, 3H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.71 (s, 1H), 6.67 (s, 1H), 5.59 (d, *J* = 8.1 Hz, 1H), 4.99 (s, 1H), 4.37−4.26 (m, 2H), 3.74 (s, 3H), 2.99−2.88 (m, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 5.2 Hz, 3H), 1.03 (d, *J* = 5.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 157.1, 151.8, 136.3, 134.2, 131.8, 131.3, 130.7, 128.9, 128.8, 115.2, 114.9, 103.6, 96.5, 64.6, 60.3, 52.6, 48.4, 20.8, 20.4, 14.2; HRMS (ESI) calcd for $C_{24}H_{26}N_3O_4$ ([M + H]$^+$) 420.1918, found 420.1927.

*Ethyl 2,3-Dicyano-2-(2-methylene-3-oxo-1-phenylbutyl)-4-phenylpyridine-1(2H)-carboxylate (Table 2, **3i**).* Yellow solid (66 mg, 76%); mp 115−116 °c; 91% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 21.6 min (minor), and t_R = 24.1 min (major)]: $[\alpha]_D^{25}$ = −101 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 3.6 Hz, 2H), 7.44−7.41 (m, 3H), 7.40−7.33 (m, 3H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.13 (d, *J* = 7.3 Hz, 2H), 6.85 (s, 1H), 6.60 (s, 1H), 5.79 (d, *J* = 7.8 Hz, 1H), 5.41 (s, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.4, 151.8, 149.5, 144.7, 135.4, 134.8, 131.9, 130.7, 130.6, 129.1, 128.9, 128.8, 128.1, 116.5, 115.2, 107.9, 95.5, 64.7, 60.9, 45.3, 25.9, 14.3; HRMS (ESI) calcd for $C_{27}H_{24}N_3O_3$ ([M + H]$^+$) 438.1812, found 438.1807.

*Ethyl 2-[1-(4-Bromophenyl)-2-(methoxycarbonyl)allyl]-2,3-dicyano-4-phenylpyridine-1(2H)-carboxylate (Table 2, **3l**).* Yellow solid (97 mg, 91%); mp 84−86 °C; 94% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 70:30 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 14.7 min (major), and t_R = 17.3 min (minor)]: $[\alpha]_D^{25}$ = −133 (*c* = 0.57, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.4 Hz, 2H), 7.46−7.38 (m, 5H), 7.23 (d, *J* = 7.7 Hz, 3H), 6.74 (s, 1H), 6.63 (s, 1H), 5.81 (d, *J* = 7.8 Hz, 1H), 5.16 (s, 1H), 4.40−4.30 (m, 2H), 3.74 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.16, 151.70, 149.6, 136.1, 135.2, 133.5, 132.3, 132.2, 131.9, 131.5, 130.8, 129.1, 128.1, 123.5, 116.2, 114.9, 107.9, 95.7, 64.9, 60.7, 52.7, 47.7, 14.2; HRMS (ESI) calcd for $C_{27}H_{23}BrN_3O_4$ ([M + H]$^+$) 532.0866, found 532.0845.

*Ethyl 2,3-Dicyano-2-[2-(methoxycarbonyl)-1-(4-methoxyphenyl)-allyl]-4-phenylpyridine-1(2H)-carboxylate (Table 2, **3m**).* Yellow solid (69 mg, 72%); mp 49−50 °C; 88% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 30.0 min (major), and t_R = 32.4 min (minor)]: $[\alpha]_D^{25}$ = −101 (*c* = 0.70, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.6 Hz, 2H), 7.44−7.34 (m, 3H), 7.26 (d, *J* = 6.7 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 2H), 6.71 (s, 1H), 6.67 (s, 1H), 5.80 (d, *J* = 7.8 Hz, 1H), 5.11 (s, 1H), 4.39−4.28 (m, 2H), 3.83 (s, 3H), 3.73 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 160.2, 151.7, 149.0, 136.7, 135.4, 131.9, 131.7, 131.0, 130.6, 128.9, 128.1, 126.1, 116.1, 115.1, 114.4, 107.9, 96.2, 64.7, 61.0, 55.4, 52.5, 47.3, 14.1; HRMS (ESI) calcd for $C_{28}H_{26}N_3O_5$ ([M + H]$^+$) 484.1867, found 484.1861.

*Ethyl 2-[1-(3-Bromophenyl)-2-(methoxycarbonyl)allyl]-2,3-dicyano-4-phenylpyridine-1(2H)-carboxylate (Table 2, **3n**).* Yellow solid (92 mg, 86%); mp 51−53 °C; 96% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 19.1 min (minor), and t_R = 22.6 min (major)]: $[\alpha]_D^{25}$ = −104 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.54 (s, 1H), 7.45−7.39 (m, 3H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 1H), 6.76 (s, 1H), 6.72 (s, 1H), 5.82 (d, *J* = 7.8 Hz, 1H), 5.13 (s, 1H), 4.41−4.29 (m, 2H), 3.75 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 151.7, 149.7, 136.5, 135.7, 135.2, 134.4, 132.3, 131.8, 131.5, 130.8, 130.7, 129.1, 128.8, 128.2, 122.9, 116.0, 114.7, 107.9, 95.6, 64.9, 60.8, 52.7, 47.8, 14.2; HRMS (ESI) calcd for $C_{27}H_{23}BrN_3O_4$ ([M + H]$^+$) 532.0866, found 532.0846.

*Ethyl 2,3-Dicyano-2-[2-(methoxycarbonyl)-1-(3-methoxyphenyl)-allyl]-4-phenylpyridine-1(2H)-carboxylate (Table 2, **3o**).* Yellow solid (83 mg, 86%); mp 52−54 °C; 92% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 17.2 min (minor), and t_R = 23.1 min (major)]: $[\alpha]_D^{25}$ = −158 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.35 (m, 3H), 7.35−7.30 (m, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.22−7.16 (m, 3H), 7.11 (d, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 6.75 (s, 1H), 6.68 (s, 1H), 5.80 (d, *J* = 7.8 Hz, 1H), 5.16 (s, 1H), 4.40−4.29 (m, 2H), 3.84 (s, 3H), 3.75 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 159.9, 151.8, 149.4, 136.4, 135.8, 135.5, 131.9, 131.6, 130.6, 130.1, 128.9, 128.2, 123.1, 116.3, 116.1, 115.1, 115.0, 107.9, 95.9, 64.8, 61.1, 55.5, 52.6, 47.9, 14.2; HRMS (ESI) calcd for $C_{28}H_{26}N_3O_5$ ([M + H]$^+$) 484.1867, found 484.1865.

*Ethyl 2-[1-(2-Bromophenyl)-2-(methoxycarbonyl)allyl]-2,3-dicyano-4-phenylpyridine-1(2H)-carboxylate (Table 2, **3p**).* Yellow solid (45 mg, 42%); mp 75−77 °C; 95% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AS-H, 90:10 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 38.6 min (major), and t_R = 42.3 min (minor)]: $[\alpha]_D^{25}$ = −129 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.7 Hz, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.46−7.33 (m, 3H), 7.28 (t, *J* = 6.3 Hz, 2H), 7.16 (d, *J* = 7.3 Hz, 2H), 6.76 (s, 1H), 6.55 (s, 1H), 5.99 (s, 1H), 5.86 (d, *J* = 7.8 Hz, 1H), 4.41−4.31 (m, 2H), 3.77 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 151.9, 150.5, 136.1, 135.4, 133.9, 133.7, 132.3, 131.9, 131.3, 130.6, 130.4, 128.8, 128.2, 128.1, 127.9, 116.5, 115.1, 108.4, 94.6, 64.8, 61.1, 52.6, 46.1, 14.2; HRMS (ESI) calcd for $C_{27}H_{23}BrN_3O_4$ ([M + H]$^+$) 532.0866, found 532.0855.

*Ethyl 2,3-Dicyano-2-[2-(methoxycarbonyl)-1-(naphthalen-2-yl)-allyl]-4-phenylpyridine-1(2H)-carboxylate (Table 2, **3q**).* Yellow solid (92 mg, 91%); mp 76−77 °C; 94% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 31.4 min (minor), and t_R = 40.1 min (major)]: $[\alpha]_D^{25}$ = −184 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.88−7.82 (m, 2H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.53−7.49 (m, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.30−7.23 (m, 4H), 7.12 (d, *J* = 7.5 Hz, 2H), 6.78 (s, 2H), 5.80 (d, *J* = 7.8 Hz, 1H), 5.37 (s, 1H), 4.42−4.31 (m, 2H), 3.75 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 151.8, 149.4, 136.5, 135.4, 133.3, 133.2, 131.9, 131. 8, 131.7, 130.6, 128.9, 128.8, 128.2, 128.0, 127.9, 127.5, 126.9, 126.8, 116.2, 115.2, 107.9, 95.9, 64.9, 61.0, 52.6, 48.4, 14.2; HRMS (ESI) calcd for $C_{31}H_{26}N_3O_4$ ([M + H]$^+$) 504.1918, found 504.1917.

General Procedure for Intramolecular Carbocyanation of Compound 3. To a dried 10 mL reaction tube under a N_2 atmosphere were added enantiomerically pure 2,2-disubstituted 1,2-dihydropyridine **3** (0.1 mmol) and NMP or DMF (1.0 mL). After being stirred at −10 °C for 10 min, the mixture was supplemented with TBACN (10 mol %). The reaction was monitored by TLC. Upon

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completion, the reaction mixture was poured into EtOAc (20 mL), washed with saturated brine (3 × 10 mL), and dried over Na_2SO_4. After being filtered and concentrated *in vacuo*, the crude product was purified by column chromatography [silica gel, EtOAc/petroleum ether (60−90 °C)] to provide the desired product.

*1-Ethyl 3-Methyl 2-[(3-Cyano-4-phenylpyridin-2-yl)(phenyl)-methyl]-2-(cyanomethyl)malonate (Table 3, **4a**).* White solid (32 mg, 71%, dr >19:1); mp 128−129 °C; 90% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 70:30 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 14.0 min (major) and t_R = 23.8 min (minor); for the minor diastereomer, t_R = 21.0 min]: $[\alpha]_D^{25}$ = +81 (*c* = 0.60, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 5.2 Hz, 1H), 7.54−7.46 (m, 5H), 7.34 (d, *J* = 5.2 Hz, 1H), 7.33−7.30 (m, 3H), 7.28−7.25 (m, 2H), 5.81 (s, 1H), 4.19−4.08 (m, 2H), 4.13 (d, *J* = 17.0 Hz, 1H), 3.83 (s, 3H), 3.18 (d, *J* = 16.8 Hz, 1H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 167.9, 164.2, 154.5, 150.2, 135.7, 134.9, 130.7, 130.3, 129.2, 128.9, 128.7, 128.6, 122.3, 117.9, 115.6, 108.8, 62.6, 60.3, 53.7, 53.2, 20.9, 13.8; HRMS (ESI) calcd for $C_{27}H_{24}N_3O_4$ ([M + H]$^+$) 454.1761, found 454.1767.

*1-Isobutyl 3-Methyl 2-[(3-Cyano-4-phenylpyridin-2-yl)(phenyl)-methyl]-2-(cyanomethyl)malonate (Table 3, **4b**).* White solid (34 mg, 70%, dr >19:1); mp 41−42 °C; 94% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 95:5 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 74.7 min (major) and t_R = 118.8 min (minor); for the minor diastereomer, t_R = 67.2 min]: $[\alpha]_D^{25}$ = +141 (*c* = 0.48, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 5.1 Hz, 1H), 7.53−7.42 (m, 5H), 7.35−7.28 (m, 4H), 7.25−7.23 (m, 2H), 5.81 (s, 1H), 4.12 (d, *J* = 16.7 Hz, 1H), 3.91 (dd, *J* = 10.4, 6.4 Hz, 1H), 3.82 (s, 3H), 3.77 (dd, *J* = 10.4, 6.6 Hz, 1H), 3.15 (d, *J* = 16.8 Hz, 1H), 1.89−1.81 (m, 1H), 0.85 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 168.1, 164.3, 154.6, 150.3, 135.8, 135.1, 130.8, 130.3, 129.2, 128.9, 128.8, 128.6, 122.4, 117.9, 115.6, 108.9, 72.9, 60.4, 53.6, 53.5, 27.7, 21.0, 19.1, 19.0; HRMS (ESI) calcd for $C_{29}H_{28}N_3O_4$ ([M + H]$^+$) 482.2074, found 482.2076.

*1-Allyl 3-Methyl 2-[(3-Cyano-4-phenylpyridin-2-yl)(phenyl)-methyl]-2-(cyanomethyl)malonate (Table 3, **4c**).* White solid (25 mg, 53%, dr >19:1); mp 51−52 °C; 90% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 21.3 min (major), and t_R = 34.8 min (minor)]: $[\alpha]_D^{25}$ = +178 (*c* = 0.38, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 5.2 Hz, 1H), 7.52−7.45 (m, 5H), 7.34−7.31 (m, 4H), 7.28−7.25 (m, 2H), 5.82 (s, 1H), 5.71−5.63 (m, 1H), 5.23 (dd, *J* = 17.2, 1.1 Hz, 1H), 5.15 (d, *J* = 10.4 Hz, 1H), 4.60−4.49 (m, 2H), 4.11 (d, *J* = 16.7 Hz, 1H), 3.83 (s, 3H), 3.18 (d, *J* = 16.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.1, 167.6, 164.1, 154.5, 150.2, 135.8, 134.9, 130.8, 130.7, 130.3, 129.1, 128.9, 128.7, 128.6, 122.3, 119.5, 117.8, 115.5, 108.8, 67.0, 60.3, 53.7, 53.3, 21.1; HRMS (ESI) calcd for $C_{28}H_{24}N_3O_4$ ([M + H]$^+$) 466.1761, found 466.1765.

*1-Ethyl 3-Methyl 2-{[3-Cyano-4-(4-methoxyphenyl)pyridin-2-yl]-(phenyl)methyl}-2-(cyanomethyl)malonate (Table 3, **4d**).* White solid (32 mg, 67%, dr 15:1); mp 64−65 °C; 93% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 30.4 min (major) and t_R = 67.1 min (minor); for the minor diastereomer, t_R = 32.2 min]: $[\alpha]_D^{25}$ = +59 (*c* = 0.81, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J* = 5.1 Hz, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.35−7.29 (m, 4H), 7.28−7.23 (m, 2H), 6.99 (d, *J* = 8.5 Hz, 2H), 5.80 (s, 1H), 4.17−4.08 (m, 2H), 4.14 (d, *J* = 16.6 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.17 (d, *J* = 16.7 Hz, 1H), 1.08 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 167.9, 164.2, 161.4, 154.0, 150.1, 135.0, 130.7, 130.1, 128.8, 128.7, 127.9, 122.0, 117.9, 115.9, 114.6, 108.3, 62.6, 60.3, 55.5, 53.6, 53.2, 20.9, 13.7; HRMS (ESI) calcd for $C_{28}H_{26}N_3O_5$ ([M + H]$^+$) 484.1867, found 484.1864.

*1-Ethyl 3-Methyl 2-{[3-Cyano-4-(p-tolyl)pyridin-2-yl](phenyl)-methyl}-2-(cyanomethyl)malonate (Table 3, **4e**).* White solid (32 mg, 69%, dr 19:1); mp 144−145 °C; 93% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 21.1 min (major) and t_R = 40.6 min (minor); for the minor diastereomer, t_R = 22.6 min]: $[\alpha]_D^{25}$ = +127 (*c* = 0.69, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 5.2 Hz, 1H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.33−7.30 (m, 4H), 7.30−7.25 (m, 4H), 5.80 (s, 1H), 4.17−4.07 (m, 2H), 4.13 (d, *J* = 16.6 Hz, 1H), 3.82 (s, 3H), 3.17 (d, *J* = 16.8 Hz, 1H). 2.40 (s, 3H), 1.08 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 167.9, 164.2, 154.6, 150.2, 140.7, 134.9, 132.9, 130.7, 129.9, 128.9, 128.7, 128.5, 122.2, 117.9, 115.8, 108.6, 62.6, 60.3, 53.6, 53.2, 21.5, 20.9, 13.8; HRMS (ESI) calcd for $C_{28}H_{26}N_3O_4$ ([M + H]$^+$) 468.1918, found 468.1907.

*1-Ethyl 3-Methyl 2-({3-Cyano-4-[4-(trifluoromethyl)phenyl]-pyridin-2-yl}(phenyl)methyl)-2-(cyanomethylmalonate (Table 3, **4f**).* White solid (26 mg, 50%, dr 19:1); mp 131−132 °C; 94% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 70:30 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 24.6 min (minor), and t_R = 28.9 min (major)]: $[\alpha]_D^{25}$ = +152 (*c* = 0.53, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (d, *J* = 5.2 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.36−7.32 (m, 4H), 7.29−7.26 (m, 2H), 5.79 (s, 1H), 4.19−4.12 (m, 2H), 4.09 (d, *J* = 16.8 Hz, 1H), 3.83 (s, 3H), 3.18 (d, *J* = 16.8 Hz, 1H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 167.9, 164.5, 153.0, 150.6, 139.3, 134.8, 130.8, 129.2, 129.1, 128.9, 126.3 (q, *J* = 3.6 Hz), 122.2, 117.8, 115.3, 108.9, 62.8, 60.4, 53.8, 53.4, 21.1, 13.9; HRMS (ESI) calcd for $C_{28}H_{23}F_3N_3O_4$ ([M + H]$^+$) 522.1635, found 522.1608.

*1-Ethyl 3-Methyl 2-{[3-Cyano-4-(o-tolyl)pyridin-2-yl](phenyl)-methyl}-2-(cyanomethyl)malonate (Table 3, **4g**).* White solid (32 mg, 69%, dr 12:1); mp 47−48 °C; 90% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 15.1 min (major) and t_R = 23.4 min (minor); for the minor diastereomer, t_R = 18.7 min]; $[\alpha]_D^{25}$ = +104 (*c* = 0.63, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 5.1 Hz, 1H), 7.37−7.28 (m, 5H), 7.28−7.23 (m, 3H), 7.22 (d, *J* = 5.1 Hz, 1H), 7.09 (br s, 1H), 5.77 (s, 1H), 4.18−4.08 (m, 2H), 4.11 (d, *J* = 16.7 Hz, 1H), 3.82 (s, 3H), 3.17 (d, *J* = 16.7 Hz, 1H), 2.18−2.01 (m, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 167.8, 155.4, 149.9, 135.8, 135.2, 130.9, 130.8, 130.6, 129.8, 128.9, 128.8, 128.7, 126.3, 123.1, 121.3, 117.8, 114.9, 110.8, 62.6, 60.2, 53.6, 53.2, 20.9, 19.7, 13.8; HRMS (ESI) calcd for $C_{28}H_{26}N_3O_4$ ([M + H]$^+$) 468.1918, found 468.1923.

*1-Ethyl 3-methyl 2-[(3-cyano-4-isopropylpyridin-2-yl)(phenyl)-methyl]-2-(cyanomethyl)malonate (Table 3, **4h**).* White solid (34 mg, 80%, dr 19:1); mp 50−51 °C; 90% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 90:10 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nmat 30 °C, t_R = 22.0 min (major), and t_R = 24.9 min (minor)]: $[\alpha]_D^{25}$ = +150 (*c* = 0.78, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 5.3 Hz, 1H), 7.32−7.29 (m, 3H), 7.24−7.19 (m, 3H), 5.71 (s, 1H), 4.11 (d, *J* = 16.8 Hz, 1H). 4.13−4.04 (m, 2H), 3.82 (s, 3H), 3.32−3.23 (m, 1H), 3.14 (d, *J* = 16.8 Hz, 1H), 1.29 (d, *J* = 6.9 Hz, 3H), 1.24 (d, *J* = 6.8 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 167.7, 163.2, 162.9, 150.5, 135.0, 130.6, 128.8, 128.6, 118.9, 117.9, 114.9, 109.7, 62.5, 60.2, 53.6, 53.1, 32.6, 22.8, 22.2, 20.9, 13.6; HRMS (ESI) calcd for $C_{24}H_{26}N_3O_4$ ([M + H]$^+$) 420.1918, found 420.1921.

*Ethyl 2-[(3-Cyano-4-phenylpyridin-2-yl)(phenyl)methyl]-2-(cyanomethyl)-3-oxobutanoate (Table 3, **4i**).* A colorless oil (36 mg, 83%, dr 9:1); 91% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 23.6 min (major) and t_R = 39.9 min (minor); for the minor diastereomer, t_R = 21.0 min (minor) and t_R = 29.4 min (major)]; $[\alpha]_D^{25}$ = +56 (*c* = 0.55, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (d, *J* = 5.2 Hz, 1H), 7.54−7.45 (m, 5H), 7.35 (d, *J* = 5.2 Hz, 1H), 7.33−7.27 (m, 3H), 7.17 (dd, *J* = 6.1, 3.2 Hz, 2H), 5.74 (s, 1H), 4.18−4.08 (m, 2H), 4.03 (d, *J* = 16.8 Hz, 1H), 3.13 (d, *J* = 16.8 Hz, 1H), 2.46 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.6, 169.1, 164.3, 154.6, 150.3, 135.7, 134.6, 130.7, 130.4, 129.2, 128.9, 128.7,

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128.6, 122.4, 118.1, 115.6, 108.9, 66.4, 62.7, 52.3, 26.9, 20.2, 13.8; HRMS (ESI) calcd for $C_{27}H_{24}N_3O_3$ ([M + H]$^+$) 438.1812, found 438.1806.

*1-Ethyl 3-methyl 2-[(4-Bromophenyl)(3-cyano-4-phenylpyridin-2-yl)methyl]-2-(cyanomethyl)malonate (Table 3, **4l**).* White solid (39 mg, 73%, dr 19:1); mp 59−60 °C; 94% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AS-H, 70:30 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 22.4 min (minor) and t_R = 56.2 min (major); for the minor diastereomer, t_R = 30.6 min (minor) and t_R = 48.5 min (major)]: $[\alpha]_D^{25}$ = +63 (*c* = 0.80, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 5.1 Hz, 1H), 7.58−7.50 (m, 5H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 5.1 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 2H), 5.76 (s, 1H), 4.19−4.08 (m, 2H), 4.02 (d, *J* = 16.8 Hz, 1H), 3.83 (s, 3H), 3.18 (d, *J* = 16.8 Hz, 1H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 167.6, 163.6, 154.6, 150.4, 135.6, 133.9, 132.4, 132.0, 130.4, 129.2, 128.6, 123.2, 122.5, 117.5, 115.5, 108.8, 62.7, 59.9, 53.7, 52.5, 21.2, 13.8; HRMS (ESI) calcd for $C_{27}H_{23}BrN_3O_4$ ([M + H]$^+$) 532.0866, found 532.0865.

*1-Ethyl 3-Methyl 2-[(3-Cyano-4-phenylpyridin-2-yl)(4-methoxyphenyl)methyl]-2-(cyanomethyl)malonate (Table 3, **4m**).* White solid (29 mg, 60%, dr 19:1); mp 52−53 °C; 88% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AS-H, 70:30 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 30.9 min (minor) and t_R = 47.1 min (major); for the minor diastereomer, t_R = 39.9 min]: $[\alpha]_D^{25}$ = +96 (*c* = 0.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, *J* = 5.2 Hz, 1H), 7.56−7.45 (m, 5H), 7.32 (d, *J* = 5.2 Hz, 1H), 7.18 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.75 (s, 1H), 4.16−4.05 (m, 2H), 4.09 (d, *J* = 16.9 Hz, 1H). 3.83 (s, 3H), 3.77 (s, 3H), 3.16 (d, *J* = 16.7 Hz, 1H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 167.9, 164.5, 159.8, 154.5, 150.2, 135.8, 131.9, 130.3, 129.1, 128.6, 126.8, 122.2, 117.9, 115.6, 114.3, 108.7, 62.6, 60.3, 55.3, 53.6, 52.6, 21.0, 13.8; HRMS (ESI) calcd for $C_{28}H_{26}N_3O_5$ ([M + H]$^+$) 484.1867, found 484.1856.

*1-Ethyl 3-Methyl 2-[(3-Bromophenyl)(3-cyano-4-phenylpyridin-2-yl)methyl]-2-(cyanomethyl)malonate (Table 3, **4n**).* White solid (37 mg, 70%, dr 15:1); mp 30−31 °C; 95% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 20.2 min (major) and t_R = 34.1 min (minor); for the minor diastereomer, t_R = 21.7 min (minor) and t_R = 28.8 min (major)]: $[\alpha]_D^{25}$ = +121 (*c* = 0.73, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, *J* = 5.2 Hz, 1H), 7.55−7.48 (m, 5H), 7.47−7.42 (m, 2H), 7.37 (d, *J* = 5.2 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 5.77 (s, 1H), 4.18−4.09 (m, 2H), 4.04 (d, *J* = 16.8 Hz, 1H), 3.84 (s, 3H), 3.20 (d, *J* = 16.8 Hz, 1H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.1, 167.6, 163.3, 154.6, 150.4, 137.1, 135.6, 133.4, 131.9, 130.4, 130.3, 129.6, 129.2, 128.6, 122.9, 122.6, 117.4, 115.4, 108.91, 62.8, 60.2, 53.7, 52.5, 21.1, 13.8; HRMS (ESI) calcd for $C_{27}H_{23}BrN_3O_4$ ([M + H]$^+$) 532.0866, found 532.0862.

*1-Ethyl 3-Methyl 2-[(3-Cyano-4-phenylpyridin-2-yl)(3-methoxyphenyl)methyl]-2-(cyanomethyl)malonate (Table 3, **4o**).* White solid (34 mg, 71%, dr >19:1); mp 42−44 °C; 92% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 24.5 min (major) and t_R = 43.9 min (minor); for the minor diastereomer, t_R = 27.4 min]: $[\alpha]_D^{25}$ = +121 (*c* = 0.73, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 5.2 Hz, 1H), 7.54−7.47 (m, 5H), 7.34 (d, *J* = 5.2 Hz, 1H), 7.24 (t, *J* = 8.0 Hz, 1H), 6.86−6.83 (m, 2H), 6.80 (s, 1H), 5.78 (s, 1H), 4.18−4.08 (m, 2H), 4.13 (d, *J* = 16.5 Hz, 1H), 3.84 (s, 3H), 3.77 (s, 3H), 3.20 (d, *J* = 16.8 Hz, 1H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 167.8, 164.1, 159.8, 154.5, 150.2, 136.3, 135.8, 130.3, 129.9, 129.1, 128.6, 123.1, 122.3, 117.9, 117.1, 115.6, 113.5, 108.8, 62.6, 60.3, 55.4, 53.6, 53.1, 20.9, 13.8; HRMS (ESI) calcd for $C_{28}H_{26}N_3O_5$ ([M + H]$^+$) 484.1867, found 484.1866.

*1-Ethyl 3-Methyl 2-[(2-Bromophenyl)(3-cyano-4-phenylpyridin-2-yl)methyl]-2-(cyanomethyl)malonate (Table 3, **4p**).* White solid (44 mg, 83%, dr >19:1); mp 53−54 °C; 94% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AS-H, 70:30 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 50.5 min (major) and t_R = 89.9 min (minor); for the minor diastereomer, t_R = 46.1 min]: $[\alpha]_D^{25}$ = +121 (*c* = 0.73, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, *J* = 5.2 Hz, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.53−7.48 (m, 5H), 7.35 (d, *J* = 5.2 Hz, 1H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.7 Hz, 1H), 6.18 (s, 1H), 4.22 (d, *J* = 16.2 Hz, 1H), 4.23−4.13 (m, 2H), 3.83 (s, 3H), 3.05 (d, *J* = 16.3 Hz, 1H), 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 167.9, 164.7, 154.9, 150.1, 135.6, 134.7, 134.0, 132.2, 130.4, 130.0, 129.1, 128.6, 127.5, 127.4, 122.6, 118.0, 115.2, 108.7, 62.5, 59.1, 53.9, 51.4, 21.5, 13.7; HRMS (ESI) calcd for $C_{27}H_{23}BrN_3O_4$ ([M + H]$^+$) 532.0866, found 532.0865.

*1-Ethyl 3-Methyl 2-[(3-Cyano-4-phenylpyridin-2-yl)(naphthalen-2-yl)methyl]-2-(cyanomethyl)malonate (Table 3, **4q**).* White solid (31 mg, 61%, dr 18:1); mp 57−58 °C; 94% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AS-H, 70:30 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C; for the major diastereomer, t_R = 22.5 min (major) and t_R = 27.7 min (minor); for the minor diastereomer, t_R = 24.2 min]: $[\alpha]_D^{25}$ = +87 (*c* = 0.70, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (d, *J* = 5.2 Hz, 1H), 7.83−7.76 (m, 3H), 7.71 (s, 1H), 7.51−7.45 (m, 7H), 7.41 (dd, *J* = 8.6, 1.7 Hz, 2H), 7.36 (d, *J* = 5.2 Hz, 2H), 5.95 (s, 1H), 4.23−4.13 (m, 2H), 4.19 (d, *J* = 16.7 Hz, 1H). 3.82 (s, 3H), 3.19 (d, *J* = 16.7 Hz, 1H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 167.9, 164.2, 154.6, 150.3, 135.8, 133.2, 133.1, 132.5, 130.4, 130.3, 129.1, 128.6, 128.3, 127.8, 127.7, 126.9, 126.7, 122.4, 117.9, 115.6, 108.9, 62.7, 60.4, 53.6, 53.5, 21.2, 13.8; HRMS (ESI) calcd for $C_{31}H_{26}N_3O_4$ ([M + H]$^+$) 504.1918, found 504.1917.

General Procedure for Asymmetric Allylic Alkylation−Acylcyanation Reaction. To a dried 10 mL reaction tube under a N_2 atmosphere were added compound **1** (0.2 mmol), MBH carbonate **2** (0.26 mmol), and solvent (2 mL). After being stirred at 0 °C for 10 min, the mixture was supplemented with catalyst (20 mol %). The reaction was monitored by TLC. Upon completion, the reaction mixture was concentrated *in vacuo*. The mixture was purified by column chromatography [silica gel, EtOAc/petroleum ether (60−90 °C)] quickly to provide the crude product. Subsequently, the crude product and NMP (1.0 mL) were added to a dried 10 mL reaction tube under a N_2 atmosphere. After the mixture had been stirred at −10 °C for 10 min, TBACN (20 mol %) was added. The reaction was monitored by TLC. Upon completion, the reaction mixture was poured into EtOAc (20 mL), washed with saturated brine (3 × 10 mL), and dried over Na_2SO_4. After being filtered and concentrated *in vacuo*, the mixture was purified by column chromatography [silica gel, EtOAc/petroleum ether (60−90 °C)] to provide the desired product.

*1-Ethyl 3-Methyl 2-(Cyanomethyl)-2-{[5-(morpholine-4-carbonyl)pyridin-2-yl](phenyl)methyl}malonate (Scheme 2, **4r**).* White solid (39 mg, 42%, dr >19:1); mp 45−46 °C; 90% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 70:30 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 28.1 min (major) and t_R = 35.4 min (minor)]: $[\alpha]_D^{25}$ = +111 (*c* = 0.70, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57−8.55 (m, 1H), 7.64 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.35−7.28 (m, 3H), 7.26−7.21 (m, 2H), 7.19 (d, *J* = 8.1 Hz, 1H), 5.33 (s, 1H), 4.16−4.09 (m, 2H), 3.87 (d, *J* = 16.7 Hz, 1H), 3.75 (s, 3H), 3.79−3.38 (m, 8H), 3.08 (d, *J* = 16.7 Hz, 1H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 167.9, 167.7, 161.4, 146.4, 136.9, 135.9, 130.5, 129.4, 128.8, 128.4, 124.8, 117.9, 66.9, 62.6, 60.0, 55.0, 53.4, 20.9, 13.8; HRMS (ESI) calcd for $C_{25}H_{28}N_3O_6$ ([M + H]$^+$) 466.1973, found 466.1971.

*1-Ethyl 3-Methyl 2-{(4-Bromophenyl)[5-(diisopropylcarbamoyl)-pyridin-2-yl]methyl}-2-(cyanomethyl)malonate (Scheme 2, **4s**).* A colorless oil (55 mg, 49%, dr >19:1); 87% ee. The enantiomeric excess was determined by chiral HPLC analysis [Chiralpak AD-H, 70:30 *n*-hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm at 30 °C, t_R = 21.9 min (major), and t_R = 24.9 min (minor)]: $[\alpha]_D^{20}$ = +107 (*c* = 0.80, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (d, *J* = 1.5 Hz, 1H), 7.55 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 1H), 5.26 (s, 1H), 4.15−4.07 (q, *J* = 7.1 Hz,

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2H), 3.82 (d, J = 16.8 Hz, 1H), 3.76 (s, 3H), 3.72−3.46 (m, 2H), 3.09 (d, J = 16.8 Hz, 1H), 1.61−1.15 (m, 12H), 1.07 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.51, 167.9, 167.8, 159.4, 145.2, 136.2, 134.7, 133.0, 132.4, 131.8, 124.7, 122.7, 117.8, 62.6, 59.7, 54.2, 53.4, 21.1, 20.8 (br s), 13.7; HRMS (ESI) calcd for $C_{27}H_{33}BrN_3O_5$ ($[M + H]^+$) 558.1598, found 558.1591.

*1-Ethyl 3-Methyl 2-(Cyanomethyl)-2-[5-(diisopropylcarbamoyl)-pyridin-2-yl][(phenyl)methyl]malonate (**4t**).* For the procedure, see compound **4r**. DABCO (1,4-diazabicyclo[2.2.2]octane, 20 mol %) was used as a catalyst in the allylic alkylation: white solid (45 mg, 47%, dr >19:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, J = 2.1 Hz, 1H), 7.54 (dd, J = 8.0, 2.2 Hz, 1H), 7.35−7.28 (m, 3H), 7.26−7.20 (m, 2H), 7.13 (d, J = 8.1 Hz, 1H), 5.33 (s, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.92 (d, J = 16.7 Hz, 1H), 3.75 (s, 3H), 3.82−3.50 (m, 2H), 3.07 (d, J = 16.7 Hz, 1H), 1.70−0.90 (m, 12H), 1.07 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 168.1, 167.9, 160.2, 145.0, 137.2, 134.5, 132.8, 130.6, 128.8, 128.4, 124.7, 118.1, 62.5, 60.1, 55.1, 53.3, 20.9 (br s), 20.8, 13.7; HRMS (ESI) calcd for $C_{27}H_{34}N_3O_5$ ($[M + H]^+$) 480.2493, found 480.2502.

Procedure for Chemical Transformation (eq 1). To a dried 10 mL reaction tube under a N_2 atmosphere were added **4c** (0.1 mmol), $Pd(PPh_3)_4$ (10 mol %), and toluene (1.0 mL). After being stirred at rt for 1 h, the reaction mixture was concentrated *in vacuo*. The crude mixture was purified by column chromatography [silica gel, EtOAc/petroleum ether (60−90 °C)] to provide desired product **5** as a colorless oil. Unseparated diastereoisomer (30 mg, 70%, dr 3.4:1). Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (d, J = 5.2 Hz, 1H), 7.52−7.44 (m, 5H), 7.39−7.33 (m, 4H), 7.31 (d, J = 5.2 Hz, 1H), 7.28 (t, J = 6.7 Hz, 1H), 5.85−5.74 (m, 1H), 5.26 (m, 2H), 5.19 (s, 1H), 3.57 (d, J = 17.8 Hz, 1H), 3.55 (s, 3H), 3.36 (d, J = 17.3 Hz, 1H), 2.79 (dd, J = 14.1, 7.4 Hz, 1H), 2.69 (dd, J = 14.3, 7.5 Hz, 1H). Minor diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (d, J = 5.2 Hz, 1H), 7.52−7.44 (m, 5H), 7.39−7.34 (m, 6H), 5.86−5.72 (m, 1H), 5.24 (s, 1H), 5.09 (d, J = 10.1 Hz, 1H), 4.95 (dd, J = 16.9, 1.1 Hz, 1H), 3.75 (s, 3H), 3.58 (d, J = 17.0 Hz, 1H), 2.95 (d, J = 17.0 Hz, 1H), 2.65 (d, J = 7.4 Hz, 2H). Mixture of diastereomers: ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 172.8, 165.2, 163.1, 154.3, 154.3, 150.7, 150.5, 135.9, 135.8, 135.3, 132.0, 131.6, 131.2, 130.8, 130.2, 129.1, 128.8, 128.6, 128.4, 128.2, 122.4, 122.1, 120.9, 120.1, 117.7, 115.69, 109.8, 108.6, 55.2, 55.1, 52.4, 52.3, 52.2, 51.5, 41.5, 40.6, 22.4, 21.9; HRMS (ESI) calcd for $C_{27}H_{24}N_3O_2$ ($[M + H]^+$) 422.1863, found 422.1862.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00791.

Crystallization data (CIF)

Crystallization data (CIF)

Screening and optimization data, NMR and HPLC spectra of products **3a−3i**, **3l−3q**, **4a−4i**, and **4l−4t**, and X-ray structures of compounds **3n** and **4t** (PDF)

NMR spectra of **5** (PDF)

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Notes

The authors declare no competing financial interest.

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(11) See the Supporting Information for the details.

(12) Although *N*-acetyl- and *N*-benzoyl-substituted compounds also furnished the desired functionalized 2-allylic substituted dihydropyr-

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idines, the corresponding conversions into pyridine derivatives failed to give any desired products. For the mechanism, please see the Supporting Information.
(13) See the Supporting Information for X-ray structures. CCDC 1436100 (**3n**) contains the supplementary crystallographic data for this paper.
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(16) The attempts to obtain the X-ray crystal structures of enantioenriched functionalized pyridines with adjacent stereocenters (**4l**, **4n**, or **4p**) were unsuccessful. However, the X-ray crystal structure of racemic analogue **4t** can be obtained. See the Supporting Information for X-ray structures. CCDC 1447044 (**4t**) contains the supplementary crystallographic data for this paper.

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