JOC The Journal of Organic Chemistry

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Palladium-Catalyzed Divergent Imidoylative Cyclization of Multifunctionalized Isocyanides: Tunable Access to Oxazol-5(4*H*)-ones and Cyclic Ketoimines

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Cite This: https://dx.doi.org/10.1021/acs.joc.0c00672 Read Online

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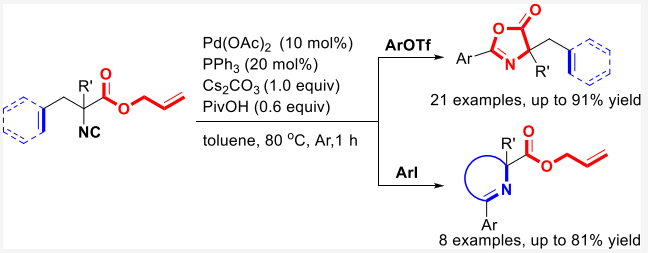
ABSTRACT: A palladium-catalyzed tunable imidoylative cyclization of multifunctionalized isocyanides to construct diverse imine-containing heterocycles has been developed. Oxazol-5(4*H*)-one derivatives were obtained exclusively when allyl-2-benzyl(or allyl)-2-isocyanoacetates were used in the reaction with aryl triflates as electrophiles, whereas cyclic ketoimines were generated in the presence of aryl iodides with the allyl ester group remaining unreacted. The reactions proceeded smoothly under mild conditions with a wide functional group tolerance.



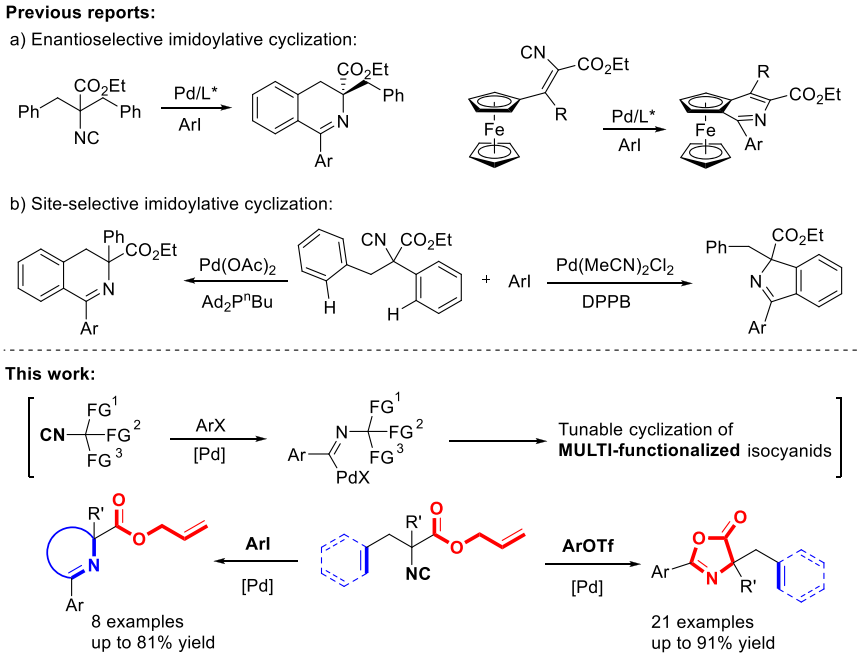
INTRODUCTION

Selective catalytic transformation of organic molecules is one of the most challenging tasks in modern synthetic chemistry.[1] The construction and modification of nitrogen-containing heterocycles are of vital importance, which are ubiquitous in natural products, pharmaceutical chemistry, and material sciences. In this regard, divergent heterocycles could be accessed by conditions-controlled selective reactions from the same molecules, which could facilitate the assembly of complex compounds.[2] For example, a solvent-controlled site-selective (2/3 position) alkenylation reaction of indoles was developed by the Gaunt group in 2005.[3] Tunable cyclization of 2-aryl cyclic 1,3-dicarbonyl compounds with alkynes and alkenes leading to fused or spiro N-heterocycles was reported by the Lam group using palladium or ruthenium catalysis,, respectively.[4] Very recently, Fan and co-workers reported an elegant annulation reaction of 2-arylindazoles with maleimides for the divergent synthesis of indazo-lo[2,3-*a*]pyrrolo[3,4-*c*]-quinolinones or spiroindolo[1,2-*b*]indazole-11,3′-pyrrolidinones, which could be simply switched by resorting to different additives.[5a−d]

In the past decades, isocyanide was widely investigated in transition-metal-catalyzed insertion reactions,[6] multicomponent reactions,[7] cycloaddition reactions,[8] and even biorthogonal reactions[9] because of its diverse reactivities. As an equivalent of carbon monoxide (CO), C1 insertion reactions of isocyanide under palladium catalysis have been applied in the construction of numerous N-containing compounds.[10] Because of the adjustable R group of isocyanides, an efficient access to N-heterocycles by the strategy of functionalized isocyanide was successfully developed, in which multiple atoms (including both nitrogen and carbon atoms of isocyanide) were introduced to the formed cycle, demonstrating the advantage over carbon monoxide-participated carbonylation reactions. For instance, camptothecins,[11] indoles,[12] oxazoles,[13] phenanthridines,[14] *β*-carbolines,[15] tetrasubstituted imidazolones,[16] and cyclic imines[17] were successfully prepared by applying this approach. In 2017, the Zhu group developed the first enantioselective palladium-catalyzed C−H bond imidoylation reaction *via* a desymmetrization strategy (Scheme 1a).[18a] Later on, a site-selective imidoylative cyclization was reported by the same group (Scheme 1b).[19] The selectivity of the formation of six- or five-membered ketoimines was tuned by using bulky Ad_2PnBu or bidentate DPPB as the ligands. However, to the best of our knowledge, selective and tunable cyclization of isocyanides bearing different functional groups, which could offer divergent access to different types of heterocycles, remains unprecedented. Herein, we developed the first palladium-catalyzed imidoylative cyclization of multifunctionalized isocyanides, affording diverse imine-containing heterocycles. Oxazol-5(4*H*)-one derivatives were obtained exclusively when allyl-2-benzyl(allyl)-2-isocyanoacetates were conducted in the reaction with aryl triflates as electrophiles. When aryl iodides were used as the coupling partner, cyclic ketoimines were generated selectively with the allyl ester group remaining unreacted. A wide range of functional groups were

Received: March 14, 2020
Published: May 6, 2020

Scheme 1. Selective Palladium-Catalyzed Imidoylative Cyclization of Functionalized Isocyanides; (a) Enantioselective Imidoylative Cyclization; (b) Site-Selective Imidoylative Cyclization



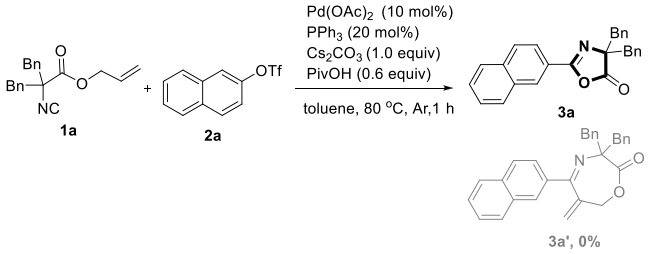
tolerated under mild conditions and the reactions featured an exclusive selectivity.

RESULTS AND DISCUSSION

The study was started with allyl 2-benzyl-2-isocyano-3-phenylpropanoate (**1a**) and naphthalen-2-yl trifluoromethanesulfonate (**2a**) as model substrates in the presence of $Pd(OAc)_2$, PPh_3, Cs_2CO_3, and PivOH. An unexpected product 4,4-dibenzyl-2-(naphthalen-2-yl)oxazol-5(4*H*)-one (**3a**) was generated in 89% yield, whereas the initial designed imidoylative-Heck type product **3a′** was not detected when **1a** was added *via* a syringe pump in 1 h (Table 1, entry 1). In this transformation, the allyl group was released and the C(sp^2)−H bonds remained unreacted, which differed from the previously reported C−H bond imidoylation reaction. Other solvents such as dimethyl sulfoxide (DMSO) and dioxane reduced the efficiency of this transformation (entries 2−3). The product was obtained in 89 and 81% yields, respectively, using 1.0 or 0.3 equiv of PivOH (entries 4−5). The yield decreased sharply in the absence of PivOH (entry 6). The product **3a** was generated in 85 and 52% yield when the reaction was conducted at 70 and 60 °C, respectively (entries 7−8). When the addition time of **1a** was reduced to 0.5 h, **3a** was obtained in only 56% yield and the efficiency of the reaction was not improved by prolonging the time to 1.5 h (entries 9−10).

With the optimized conditions in hand, we first screened the scope of isocyanides with **2a** as the reaction partner (Scheme 2). Both electron-donating and -withdrawing groups on the benzylic ring were well tolerated under the reaction conditions and the products were generated in good to excellent yields (**3a**−**3i**). It should be pointed out that the C−Br bond, which could facilitate further transformations, remained stable in this reaction (**3e**). Tetrasubstituted product **3h** was generated in 66% yield, showing that the reaction was not very sensitive to steric hindrance. 4-Benzyl-4-alkyloxazol-5(4*H*)-ones **3j**−**3l** were afforded in 70, 72, and 86% yields, respectively, when

Table 1. Optimization of the Reaction Conditions[a]



entry	change from the "standard conditions"[a]	yield (%)
1	none	89
2	DMSO as solvent	76
3	dioxane as solvent	69
4	with 1.0 equiv of PivOH	89
5	with 0.3 equiv of PivOH	81
6	without PivOH	45
7	70 °C	85
8	60 °C	52
9	the addition time was 0.5 h	56
10	the addition time was 1.5 h	81

[a]Standard reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), $Pd(OAc)_2$ (0.01 mmol), PPh_3 (0.02 mmol), Cs_2CO_3 (0.1 mmol), PivOH (0.06 mmol), toluene, 80 °C, Ar, A solution of **1a** in toluene (1 mL) was added slowly *via* a syringe pump within 1 h. Isolated yields.

changing one of the benzyl groups to alkyl ones such as Et, Pr, and ^{t}Bu. C2-Phenylated oxazol-5(4*H*)-one **3m** could be prepared smoothly as well using phenyl triflates as the electrophilic coupling partner of **1a** under slightly modified conditions. Substituents on the phenyl ring such as Me, OMe, F, Cl, Br, and CF_3 were well tolerated under the reaction conditions and the corresponding products **3n**−**3t** were generated in 67−83% yields. However, alkenyl triflates were not able to participate in the cyclization reaction. When changing the R^2 group to H, no desired product was generated

https://dx.doi.org/10.1021/acs.joc.0c00672
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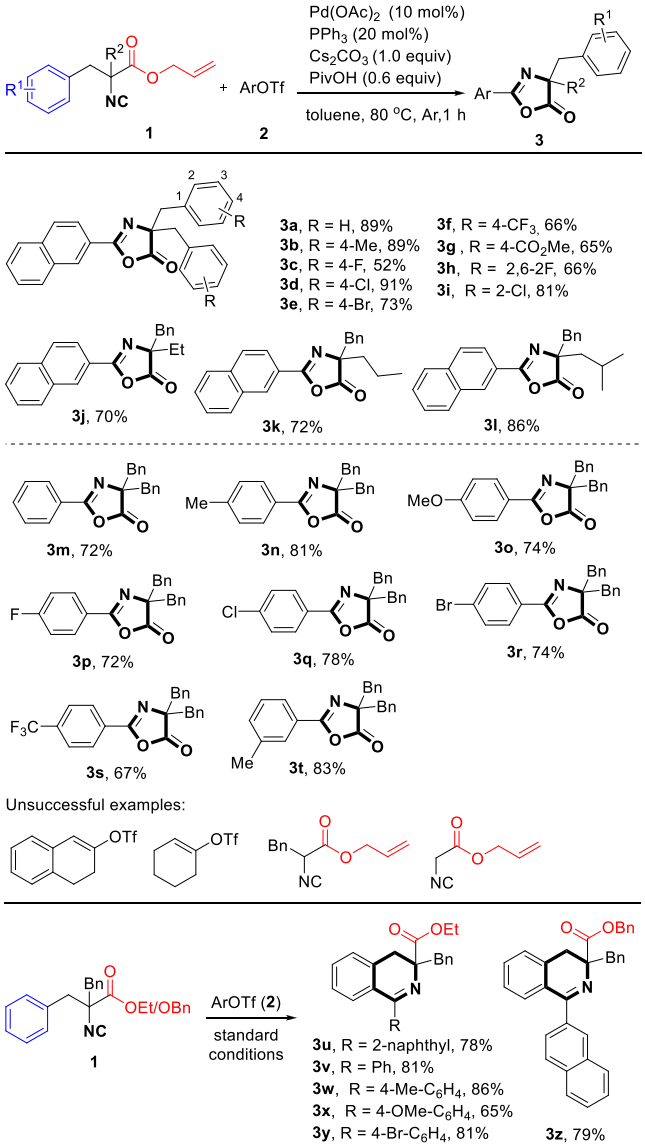
Scheme 2. Synthesis of Multisubstituted Oxazol-5(4*H*)-ones and 3,4-Dihydroisoquinolines Using Aryl Triflates[a]

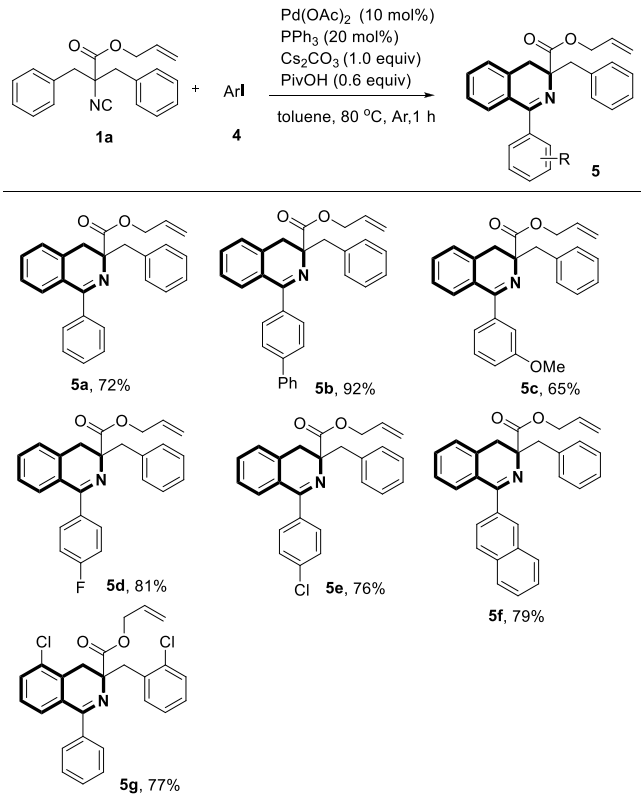


[a]Reaction Conditions. 1 (0.1 mmol), **2** (0.15/0.3 mmol), $Pd(OAc)_2$ (0.01 mmol), PPh_3 (0.02 mmol), Cs_2CO_3 (0.1 mmol), PivOH (0.06 mmol), toluene, 80 °C, Ar. A solution of **1** in toluene (1 mL) was added slowly *via* a syringe pump within 1 h. Isolated yields.

using 2-naphthyl triflate as the coupling partner. Interestingly, the eater group remained unreacted when the allyl moiety of the substrate **1** was changed to ethyl or benzyl groups. 3,4-Dihydroisoquinoline products **3u**–**3z** were afforded exclusively through a C–H bond activation pathway in 65–86% yields, which demonstrated the essential role of the allyl group in the formation of oxazol-5(4*H*)-one scaffolds.

Next, we moved our attention to the study of the reactivity of functionalized isocyanide **1a** with aryl iodides **4** (Scheme 3). To our surprise, 3,4-dihydroquinolines were generated exclusively under the standard conditions with the allyl ester group remaining unreacted. Oxazol-5(4*H*)-one derivatives were not detected in this transformation. Substituents such as Ph, OMe, F, and Cl survived the reaction conditions smoothly and the products **5a**–**5g** were generated in 65–92% yields.

Scheme 3. Synthesis of 3,4-Dihydroisoquinolines from Allyl 2-Benzyl-2-isocyano-3-phenylpropanoates[a]



[a]Reaction Conditions. **1a** (0.1 mmol), **4** (0.15 mmol), $Pd(OAc)_2$ (0.01 mmol), PPh_3 (0.02 mmol), Cs_2CO_3 (0.1 mmol), PivOH (0.06 mmol), toluene, 80 °C, Ar. A solution of **1a** in toluene (1 mL) was added slowly *via* a syringe pump within 1 h. Isolated yields.

Then, the reactivity of isocyanide bearing three functional groups (**6**) under the optimized conditions was investigated (Scheme 4). When iodobenzene was used as the electrophile, the reaction proceeded *via* an imidoylative-Heck pathway, leading to 4-methylene-3,4-dihydro-2*H*-pyrrole derivative **7a**, with the allyl ester and benzyl group remaining unreacted, revealing that the alkene group could trap the imidoyl-palladium intermediate prior to C(sp^2)–H bonds. Tetrasubstituted oxazol-5(4*H*)-one **7b** was afforded in 74% yield when 2-naphthyl triflate was applied as the coupling partner, which was in accordance with the results shown in Scheme 2.

To further demonstrate the practicality of the transformation, tandem reactions were conducted with **9a**′ and **9b**′ as the reaction partner of **1a** respectively. However, a mixture of 3,4-dihydroisoquinoline and oxazol-5(4*H*)-one was generated (not shown). By changing the benzyl groups to ethyl ones, C1-tethered oxindole-oxazolone biheterocycle scaffold **9a** was obtained in 81% yield and a tandem alkyne insertion cascade was realized as well, affording **9b** in 58% yield (Scheme 5).

Gram-scale preparation of oxazol-5(4*H*)-one **3a** was carried out in 54% yield (Scheme 6). The oxazol-5(4*H*)-one ring could be disclosed using methanol and allyl alcohol as nucleophiles, affording amide products **10a** and **10b** in 99 and 44% yields, respectively.

To gain further insight into the mechanism of the formation of oxazol-5(4*H*)-ones, a series of control experiments were conducted. The desired product **3a** was generated in excellent

https://dx.doi.org/10.1021/acs.joc.0c00672
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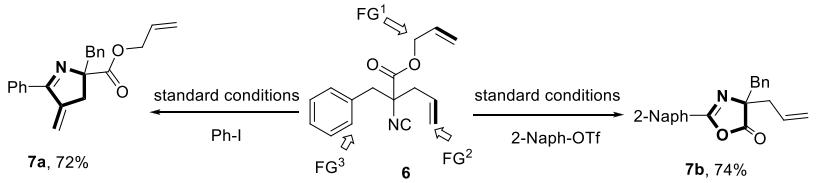
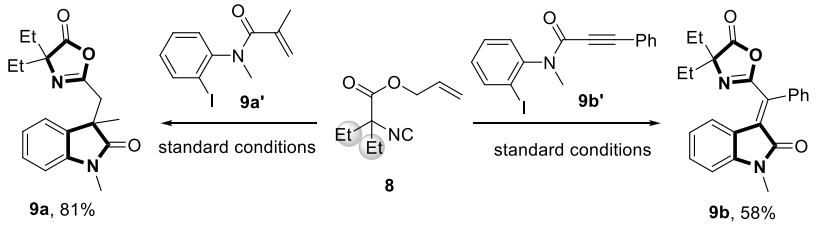
Scheme 4. Cyclization Reactions of Allyl 2-Benzyl-2-isocyano-3-phenylpropanoates[a]



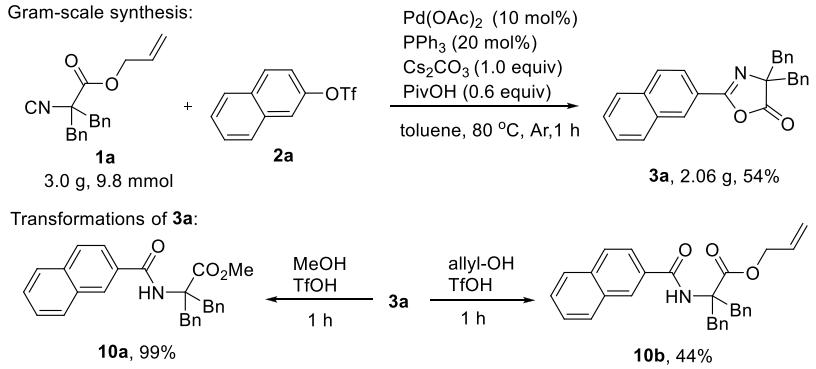
[a]Reaction Conditions. **6** (0.1 mmol), iodobenzene/2-naphthyl triflate (0.15 mmol), $Pd(OAc)_2$ (0.01 mmol), PPh_3 (0.02 mmol), Cs_2CO_3 (0.1 mmol), PivOH (0.06 mmol), toluene, 80 °C, Ar. A solution of **6** in toluene (1 mL) was added slowly *via* a syringe pump within 1 h. Isolated yields.

Scheme 5. Tandem Annulation for the Synthesis of Oxindole-oxazol-5(4*H*)-one Biheterocycles[a]



[a]Reaction Conditions. **8** (0.1 mmol), **9a**/**9a**′ (0.15 mmol), $Pd(OAc)_2$ (0.01 mmol), PPh_3 (0.02 mmol), Cs_2CO_3 (0.1 mmol), PivOH (0.06 mmol), toluene, 80 °C, Ar. A solution of **8** in toluene (1 mL) was added slowly *via* a syringe pump within 1 h. Isolated yields.

Scheme 6. Gram-Scale Preparation and Transformations of 3a



yields when one equivalent of KI or $^nBu_4NI$ was added under standard conditions (Scheme 7a). Additionally, if AgOTf or $AgBF_4$ was added in the reaction for the formation of **5a**, the title product was obtained in 42 and 39% yields, respectively, in which the corresponding oxazol-5(4*H*)-one compounds were not detected (Scheme 7b). These results suggested that the exchange of the counteranion of imidoyl-palladium intermediate was very slow. No product **3a** was detected with 92% of **10b** being recovered by submitting **10b** into the catalytic system under standard conditions (Scheme 7c), suggesting that the possibility of the generation of **10b** followed by intramolecular condensation annulation could be ruled out. Next, 1.0 equiv of $H_2{}^{18}O$ was added in the standard reaction with anhydrous solvent (Scheme 7b). The desired product **3a** was generated in 56% yield and the isotope labeling ratio was 0%, revealing that the oxygen atoms of **3a** were totally from the ester group of **1a**.

Based on the experiments, a possible mechanism of the reactions was depicted in Scheme 8. Oxidative addition of the in situ-generated Pd(0) species to electrophiles afforded aryl-Pd(II) intermediate **II**, followed by isocyanide coordination and migratory insertion to deliver the imidoyl-Pd(II) intermediate **III**. When the coupled anion was iodide, seven-membered palladacycle intermediate (**VI**) was generated and the subsequent reductive elimination afforded the cyclic ketoimine product **5** with Pd(0) being released to complete the catalytic cycle. When aryl triflate was applied in the reaction, the Pd(II) intermediate III was considered to be more ionic, which featured the potential to be attacked by an intramolecular nucleophile (path a). Intermediate **IV** was formed, followed by the release of the allyl group with the assistance of a nucleophile such as H_2O from the reaction system. The product **3m** was given from six-membered palladacycle intermediate **V**, along with the regeneration of Pd(0). However, the possibility that **3m** was delivered from a Pd(IV) intermediate, which was generated *via* an intramolecular oxidative addition of species **III**, could not be ruled out at this stage. The allyl group was revealed to be essential for the formation of oxazol-5(4*H*)-ones. The pivalic acid might play the role of assisting the release of the allyl group.

CONCLUSIONS

In summary, we have developed an efficient and practical method for the tunable preparation of oxazol-5(4*H*)-ones and cyclic ketoimines *via* a palladium-catalyzed selective imidoylative cyclization of multifunctionalized isocyanides. Oxazol-5(4*H*)-one derivatives were obtained exclusively when allyl-2-

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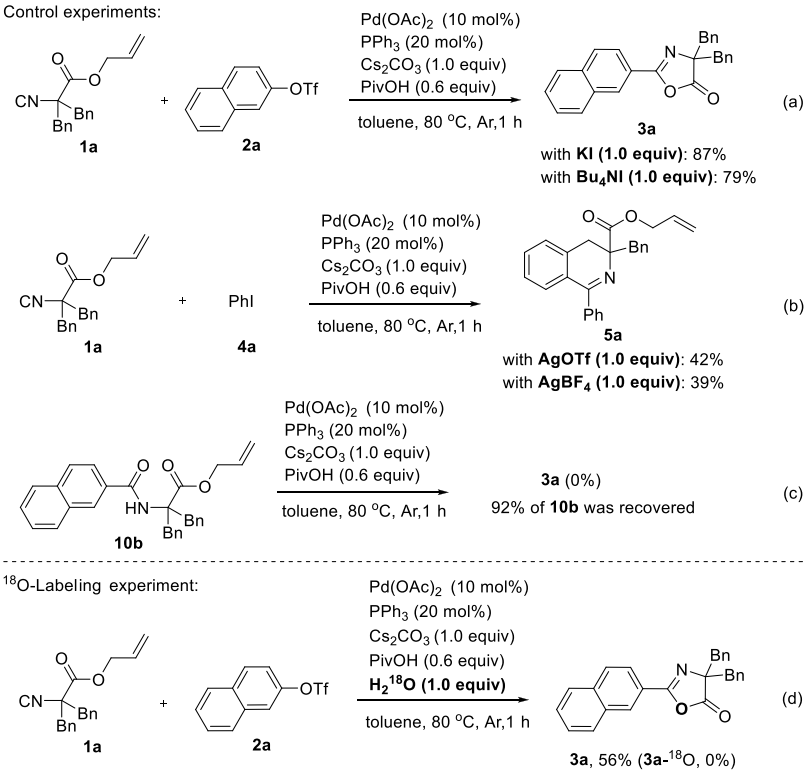
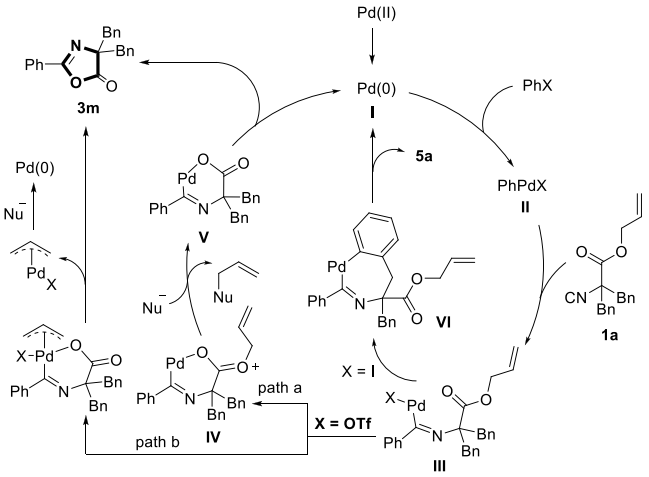
Scheme 7. Mechanistic Studies



Scheme 8. Proposed Mechanism



benzyl(or allyl)-2-isocyanoacetates were used in the reaction with aryl triflates as electrophiles. Mechanistic studies suggested that the allyl eater group may play the role of an intramolecular nucleophile to trap the imidoyl-Pd(II) intermediate. Cyclic ketoimines were generated in the presence of aryl iodides with the allyl ester group remaining unreacted. Furthermore, tandem annulation reactions were realized, offering an efficient approach to oxindole-oxazolone biheterocyclic systems.

EXPERIMENTAL SECTION

General Information. Reactions were monitored by using thin-layer chromatography (TLC) on commercial silica gel plates (GF 254). Visualization of the developed plates was performed under UV lights (GF 254 nm). Flash column chromatography was performed on silica gel (200−300 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a 400 or 500 MHz spectrometer. Chemical shifts were reported in units (ppm) by assigning TMS resonance in the ^{1}H spectrum as 0.00 ppm, $CDCl_3$ resonance in the ^{13}C spectrum as 77.16 ppm. All coupling constants (J values) were reported in Hertz (Hz). NMR analysis was carried out at 298 K unless noted otherwise. High-resolution mass spectrometry (HRMS) was obtained on an ESI-LC−MS/MS or APCI-LC−MS/MS spectrometer.

General Procedure for the Synthesis of Multisubstituted Oxazol-5(4*H*)-ones. *Synthesis of **3a**−**3l**.* An oven-dried 25 mL Schlenk tube charged with $Pd(OAc)_2$ (0.01 mmol, 2.24 mg, 10 mol %), PPh_3 (0.02 mmol, 10.8 mg, 20 mol %), and Cs_2CO_3 (0.1 mmol, 32.6 mg, 1.0 equiv) was refilled with Ar three times. Then, a solution of **2** (0.15 mmol, 1.5 equiv), PivOH (0.06 mmol, 6.1 mg, 0.6 equiv) in 0.5 mL of toluene was added by syringe and the tube was placed in an 80 °C oil-bath. A solution of **1** (0.1 mmol, 1.0 equiv) in 1.0 mL of toluene was added dropwise with a syringe pump to the reaction mixture within 1 h. The crude reaction mixture was extracted with EA (20 mL × 3) and washed with brine (20 mL). The organic phase was concentrated in *vacuo* and the residue was purified by silica gel flash column chromatography to afford the corresponding products.

*Synthesis of **3m**−**3t**.* An oven-dried 25 mL Schlenk tube charged with $Pd(OAc)_2$ (0.01 mmol, 2.24 mg, 10 mol %), PPh_3 (0.02 mmol, 10.8 mg, 20 mol %), and Cs_2CO_3 (0.1 mmol, 32.6 mg, 1.0 equiv) was refilled with Ar three times. Then, a solution of **2** (0.3 mmol, 1.5 equiv), PivOH (0.06 mmol, 6.1 mg, 0.6 equiv) in 0.5 mL of toluene was added by syringe and the tube was placed in an 80 °C oil-bath. A solution of **1** (0.1 mmol, 1.0 equiv) in 1.0 mL of toluene was added dropwise with a syringe pump to the reaction mixture within 1 h. The crude reaction mixture was extracted with EA (20 mL × 3) and washed with brine (20 mL). The organic phase was concentrated in *vacuo* and the residue was purified by silica gel flash column chromatography to afford the corresponding products.

*Gram-Scale Preparation of **3a**.* An oven-dried round-bottom flask charged with $Pd(OAc)_2$ (0.98 mmol, 220 mg, 10 mol %), PPh_3 (1.96 mmol, 1.06 g, 20 mol %), and Cs_2CO_3 (9.8 mmol, 3.2 g, 1.0 equiv) was refilled with Ar three times. Then, a solution of **2a** (14.7 mmol, 4.06 g, 1.5 equiv), PivOH (5.88 mmol, 598 mg, 0.6 equiv) in 49 mL of toluene was added by syringe and the tube was placed in an 80 °C

https://dx.doi.org/10.1021/acs.joc.0c00672
J. Org. Chem. XXXX, XXX, XXX−XXX

oil-bath. A solution of **1a** (9.8 mmol, 3.0 g, 1.0 equiv) in 98 mL of toluene was added dropwise with a syringe pump to the reaction mixture within 1 h. The crude reaction mixture was extracted with EA (200 mL × 3) and washed with brine (200 mL). The organic phase was concentrated in *vacuo* and the residue was purified by silica gel flash column chromatography to afford the compound **3a** in 54% yield (2.06 g).

Substrates 1a−1i Were Prepared by the Following Procedures. Compound **1a** was prepared according to the similar route of literature-reported methods.[18,20,21]

(i)To a solution of ethyl isocyanoacetate **A** (4.0 g, 35 mmol) in tetrahydrofuran (THF) (20 mL) was added a solution of KOH (85%, 2.0 g, 35 mmol) in H_2O (5.0 mL) at room temperature. The mixture was stirred for 5 h and concentrated in *vacuo* to give a crude. The crude was pulverized in a mortar, washed with Et_2O (50 mL), and dried in *vacuo* to give **B** (4.29 g, 99%) as pale yellow solids.

(ii)To a suspension of potassium isocyanoacetate **B** (2.46 g, 20 mmol) in 15 mL of dimethylformamide (DMF), allyl bromide (2.42 g, 20 mmol) were added and stirred at 55−60 °C for 3 h. DMF was evaporated and the residue was diluted in 40 mL of ethyl acetate and washed with water (3 × 15 mL). The organic layer was separated and dried over Mg_2SO_4 and concentrated. The product was purified by column chromatography to give 1.482 g (60%) of a colorless oil.

(iii)To a solution of allyl 2-isocyanoacetate **C** (5 mmol) in acetonitrile (20 mL) were added K_2CO_3 (3.0 g, 22 mmol), TBAHS (1.0 mmol), and (bromomethyl)benzene (10 mmol). The mixture was heated at 70 °C until the reaction was completed, monitoring with TLC. Then, the mixture was cooled and the solvent was removed under reduced pressure. H_2O (20 mL) and ethyl acetate (20 mL) were added into the mixture. The organic phase was separated and the aqueous phase was extracted with ethyl acetate (20.0 mL × 3). The combined organic phase was washed with H_2O and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography to afford the product **1a** as a colorless oil in 80% yield (new compound).

*Allyl 2-Benzyl-2-isocyano-3-phenylpropanoate (**1a**).* Eluent: petroleum ether/ethyl acetate (8:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.24 (m, 10H), 5.68−5.60 (m, 1H), 5.14−5.09 (m, 2H), 4.47 (dt, J = 5.5, 1.5 Hz, 2H), 3.36 (d, J = 13.5 Hz, 2H), 3.07 (d, J = 13.5 Hz, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.7, 161.5, 133.5, 130.7, 130.4, 128.6, 128.0, 119.3, 70.4, 67.0, 45.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{20}H_{20}NO_2$, 306.1489; found, 306.1482.

*Allyl 2-Isocyano-2-(4-methylbenzyl)-3-(p-tolyl)propanoate (**1b**).* This compound was prepared similarly to **1a**. Eluent: petroleum ether/ethyl acetate (8:1). Colorless oil, 79% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16−7.10 (m, 8H), 5.74−5.64 (m, 1H), 5.17−5.11 (m, 2H), 4.49 (dt, J = 5.6, 1.2 Hz, 2H), 3.31 (d, J = 13.6 Hz, 2H), 3.03 (d, J = 13.6 Hz, 2H), 2.32 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.9, 161.2, 137.7, 130.9, 130.6, 130.3, 129.3, 119.3, 70.7, 67.0, 44.6, 21.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{22}H_{23}NO_2$, 342.1802; found, 342.1810.

*Allyl 2-(4-Fluorobenzyl)-3-(4-fluorophenyl)-2-isocyanopropanoate (**1c**).* This compound was prepared similarly to **1a**. Eluent: petroleum ether/ethyl acetate (8:1). Colorless oil, 84% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26−7.22 (m, 4H), 7.04−6.99 (m, 4H), 5.69−5.61 (m, 1H), 5.18−5.10 (m, 2H), 4.47 (dt, J = 6.0, 1.5 Hz, 2H), 3.34 (d, J = 14.0 Hz, 2H), 3.04 (d, J = 13.5 Hz, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.5 162.8 (d, J = 245.4 Hz) 161.9 132.0 (d, J = 8.1 Hz) 130.5 129.2 (d, J = 3.0 Hz) 119.6 115.6 (d, J = 21.3 Hz) 70.5 67.1 44.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{20}H_{18}F_2NO_2$, 342.1300; found, 342.1307.

*Allyl 2-(4-Chlorobenzyl)-3-(4-chlorophenyl)-2-isocyanopropanoate (**1d**).* This compound was prepared similarly to **1a**. Eluent: petroleum ether/ethyl acetate (8:1). Colorless oil, 85% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32−7.28 (m, 4H), 7.22−7.18 (m, 4H), 5.70−5.62 (m, 1H), 5.20−5.11 (m, 2H), 4.48 (dt, J = 6.0, 1.5 Hz, 2H), 3.32 (d, J = 13.5 Hz, 2H), 3.03 (d, J = 14.0 Hz, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.3, 162.1, 134.2, 131.8, 131.7, 130.4, 128.9, 119.7, 70.1, 67.2, 44.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{20}H_{18}Cl_2NO_2$, 374.0709; found, 374.0705.

*Allyl 2-(4-Bromobenzyl)-3-(4-bromophenyl)-2-isocyanopropanoate (**1e**).* This compound was prepared similarly to **1a**. Eluent: petroleum ether/ethyl acetate (8:1). White solid, 82% yield. mp = 61−63 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.32 (m, 4H), 7.06−7.03 (m, 4H), 5.62−5.52 (m, 1H), 5.11−5.01 (m, 2H), 4.40 (dt, J = 5.6, 1.2 Hz, 2H), 3.22 (d, J = 13.6 Hz, 2H), 2.92 (d, J = 13.6 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.2, 162.0, 132.2, 131.9, 131.7, 130.3, 122.3, 119.7, 69.9, 67.1, 44.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{20}H_{18}Br_2NO_2$, 461.9699; found, 461.9696.

*Allyl 2-Isocyano-2-(4-(trifluoromethyl)benzyl)-3-(4-(trifluoromethyl)phenyl)propanoate (**1f**).* This compound was prepared similarly to **1a**. Eluent: petroleum ether/ethyl acetate (8:1). White solid, 68% yield. mp = 67−68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 8.0 Hz, 4H), 7.40 (d, J = 8.0 Hz, 4H), 5.65−5.55 (m, 1H), 5.15−5.04 (m, 2H), 4.47 (dt, J = 5.6, 1.2 Hz, 2H), 3.45 (d, J = 13.6 Hz, 2H), 3.14 (d, J = 13.6 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) 167.1, 162.8, 137.2, 130.8, 130.6 (q, J = 32.5) 130.2, 125.7 (q, J = 3.7 Hz), 124.1 (q, J = 270.5 Hz), 119.9, 69.8, 67.4, 44.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{22}H_{18}F_6NO_2$, 442.1236; found, 442.1239.

*Dimethyl 4,4′-(2-((Allyloxy)carbonyl)-2-isocyanopropane-1,3-diyl)dibenzoate (**1g**).* This compound was prepared similarly to **1a**. Eluent: petroleum ether/ethyl acetate (6:1). White solid, 78% yield. mp = 138−139 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 8.4 Hz, 4H), 7.34 (d, J = 8.0 Hz, 4H),5.69−5.59 (m, 1H), 5.17−5.11 (m, 2H), 4.47 (dt, J = 6.0, 1.2 Hz, 2H), 3.91 (s, 6H), 3.44 (d, J = 13.6 Hz, 2H), 3.13 (d, J = 13.6 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.3, 166.9, 162.6, 138.4, 130.5, 130.4, 130.1, 129.9, 119.9, 69.8, 67.3, 52.3, 44.8. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{24}NO_6$, 442.1598; found, 442.1601.

*Allyl 2-(2,6-Difluorobenzyl)-3-(2,6-difluorophenyl)-2-isocyanopropanoate (**1h**).* This compound was prepared similarly to **1a**. Eluent: petroleum ether/ethyl acetate (8:1). White solid, 72% yield. mp = 93−95 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26−7.18 (m, 2H), 6.89−6.82 (m, 4H), 5.87−5.77 (m, 1H), 5.27−5.17 (m, 2H), 4.61 (dt, J = 6.0, 1.2 Hz, 2H), 3.44−3.34 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.2, 162.6, 162.0 (dd, J = 247.8, 7.4 Hz), 130.9, 130.2 (t, J = 10.2 Hz), 119.6, 111.6 (dd, J = 19.4, 6.0 Hz) 110.1 (t, J = 19.4 Hz), 67.9, 67.0, 31.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{20}H_{16}F_4NO_2$, 378.1112; found, 378.1120.

*Allyl 2-(2-Chlorobenzyl)-3-(2-chlorophenyl)-2-isocyanopropanoate (**1i**).* This compound was prepared similarly to **1a**. Eluent: petroleum ether/ethyl acetate (8:1). Colorless oil, 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40−7.37 (m, 4H), 7.24−7.22 (m, 4H), 5.81−5.73 (m, 1H), 5.26−5.19 (m, 2H), 4.62 (dt, J = 6.0, 1.5 Hz, 2H), 3.55−3.48 (m, 4H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.67 163.0, 135.4, 131.9, 131.8, 130.6, 130.0, 129.3, 127.0, 119.5, 68.5, 67.5, 40.3. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{20}H_{18}Cl_2NO_2$, 374.0709; found, 374.0710.

Substrates 1j−1l & 6 Were Prepared by the Following Procedures. Compound **1j** was prepared according to a route similar to the methods reported in literature:[19]

(i) A 100 mL round bottom flask charged with 30 mL of $CH(OMe)_3$ (solvent) and **D** (10 mmol, 1.95 g) was heated at 110 °C for 5 h. The solvent was removed under reduced pressure to afford the crude product **E** for the next step without further purification.

(ii)To a solution of crude **E** (10 mmol, 1.0 equiv) and Et_3N (4 equiv) in 30 mL of dry DCM was added $POCl_3$ (1.2 equiv) dropwise in 30 min at −20 °C. The reaction mixture was stirred for 4 h. Then, 10 mL of H_2O was added slowly to the reaction mixture at −20 °C. The crude reaction mixture was extracted with DCM (100 mL × 3) and washed with brine (100 mL). The organic phase was concentrated in *vacuo* and the residue was purified by silica gel flash column

https://dx.doi.org/10.1021/acs.joc.0c00672
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chromatography (petroleum ether/EtOAc = 6:1) to afford the product **F** as a yellow oil in 90% yield for two steps.

(iii)To a solution of ethyl isocyanoacetate **F** (7.10 g, 35 mmol) in THF (20 mL) was added a solution of KOH (85%, 2.0 g, 35 mmol) in H_2O (5.0 mL) at room temperature. The mixture was stirred for 5 h and concentrated in *vacuo* to give a crude. The crude was pulverized in a mortar, washed with Et_2O (50 mL), and dried in *vacuo* to give **G** (6.70 g, 90%) as a white solid.

(iv) To a suspension of potassium isocyanoacetate **G** (4.26 g, 20 mmol) in 15 mL of DMF, allyl bromide (2.42 g, 20 mmol) were added and stirred at 55−60 °C for 3 h. DMF was evaporated and the residue was diluted in 40 mL of ethyl acetate and washed with water (3 × 15 mL). The organic layer was separated and dried over Mg_2SO_4 and concentrated. The product was purified by distillation (p:1,2 mbar, *T*(oil bath) 91 °C, *T* 58−60 °C) to give **H** (2.67 g,62%) as a colorless oil.

(v) An oven-dried 100 mL round bottom flask charged with a stir-bar and NaH (60%) (15 mmol, 1.5 equiv) was vacuumed and refilled with Ar three times. A mixture solution of DMSO (2 mL) and Et_2O (50 mL) was added to the flask using a syringe. Then, 10 mmol of **H** with a syringe and the reaction mixture was stirred for 30 min. Two equivalents of bromoethane was added with a syringe and the reaction mixture was stirred for 30 min. Then, 2 mL of H_2O was added dropwise to the reaction mixture carefully at room temperature. The crude reaction mixture was extracted with DCM (20 mL × 3) and washed with brine (20 mL). The organic phase was concentrated in *vacuo* and the residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 16:1) to afford the product **1j** as a colorless liquid in 70% yield (new compound).

*Allyl 2-Isocyano-3-phenylpropanoate (**H**).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.22 (m, 5H), 5.89−5.79 (m, 1H), 5.33−5.23 (m, 2H), 4.63 (dt, *J* = 6.0, 1.6 Hz, 2H), 4.48−4.42 (m, 1H), 3.23 (dd, *J* = 14.0, 5.2 Hz, 1H), 3.11 (dd, *J* = 14.0, 8.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 165.6, 160.8, 134.3, 130.6, 129.2, 128.6, 127.7, 119.5, 66.9, 57.9, 38.6. HRMS (APCI) *m*/*z*: [M + H]$^+$ calcd for $C_{13}H_{14}NO_2$, 216.1019; found, 216.1023.

*Allyl 2-Benzyl-2-isocyanobutanoate (**1j**).* Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.28 (m, 3H),7.26−7.23 (m, 2H), 5.86−5.76 (m, 1H), 5.30−5.21 (m, 2H), 4.61−4.58 (m, 2H), 3.22 (d, *J* = 13.6 Hz, 1H), 3.04 (d, *J* = 13.6 Hz, 1H),2.14−2.05 (m, 1H), 1.91−1.82 (m, 1H), 1.05 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.1, 160.2, 133.7, 130.9, 130.3, 128.5, 127.9, 119.5, 70.2, 66.9, 44.6, 32.5, 8.6. HRMS (APCI) *m*/*z*: [M + H]$^+$ calcd for $C_{15}H_{18}NO_2$, 244.1332; found, 244.1338.

*Allyl 2-Benzyl-2-isocyanobutanoate (**1k**).* This compound was prepared similarly to **1j**. Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil, 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.27 (m, 3H), 7.25−7.22 (m, 2H), 5.84−5.74 (m, 1H), 5.29−5.27 (m, 2H), 4.58−4.56 (m, 2H), 3.21 (d, *J* = 13.6 Hz, 1H), 3.02 (d, *J* = 13.6 Hz, 1H), 2.07−1.93 (m, 1H), 1.82−1.75 (m, 1H), 1.69−1.57 (m, 1H), 1.38−1.25 (m, 1H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.1, 160.2, 133.6, 130.8, 130.2, 128.4, 127.8, 119.3, 69.3, 66.7, 44.8, 41.0, 17.5, 13.5. HRMS (APCI) *m*/*z*: [M + H]$^+$ calcd for $C_{16}H_{20}NO_2$, 258.1489; found, 258.1492.

*Allyl 2-Benzyl-2-isocyano-4-methylpentanoate (**1l**).* This compound was prepared similarly to **1j**. Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil, 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.28 (m, 3H), 7.24−7.21 (m, 2H), 5.81−5.72 (m, 1H), 5.29−5.17 (m, 2H),4.56−4.49 (m, 2H), 3.18 (d, *J* = 13.6 Hz, 1H), 2.98 (d, *J* = 13.6 Hz, 1H), 2.04−1.87 (m, 2H), 1.81 (dd, *J* = 13.6, 4.8 Hz, 1H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.87 (d, *J* = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.4, 160.8, 133.4, 130.7, 130.2, 128.3, 127.8, 119.4, 68.5, 66.8, 46.9, 46.3, 25.0, 23.6, 22.1. HRMS (APCI) *m*/*z*: [M + H]$^+$ calcd for $C_{17}H_{22}NO_2$, 272.1645; found, 272.1647.

Substrates 1m & 1n Were Prepared by the Following Procedure.[18a]

(i)Compound **1m** was prepared according to the route of methods reported in the literature.[18a]

(ii) To a solution of **1m** (2.93 g, 10 mmol) in THF (6 mL) was added a solution of KOH (85%, 0.56 g, 10 mmol) in H_2O (1.4 mL) at room temperature. The mixture was stirred for 5 h and concentrated in *vacuo* to give a crude. The crude was pulverized in a mortar, washed with Et_2O (50 mL), and dried in *vacuo* to give **I** (2.73 g, 90%) as a white solid.

(iii) To a suspension of **I** (3.03 g, 10 mmol) in 5 mL of MeCN, BnBr (1.71 g, 10 mmol) was added and stirred at 80 °C for 4 h. MeCN was evaporated, the residue was diluted in 40 mL of ethyl acetate, and washed with water (3 × 15 mL). The organic layer was separated and dried over Mg_2SO_4 and concentrated. The product was purified by column chromatography [eluent: petroleum ether/ethyl acetate (8:1)]. to give **1n** (2.87 g,78%) as a colorless oil.

*Benzyl 2-Benzyl-2-isocyano-3-phenylpropanoate (**1n**).* ^{1}H NMR (500 MHz): δ 7.30−7.25 (m, 9H), 7.23−7.20 (m, 4H), 7.09−7.07 (m, 2H), 5.02 (s, 2H), 3.37 (d, *J* = 13.5 Hz), 3.08 (d, *J* = 14.0 Hz); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.9, 161.6, 134.5, 133.5, 130.4, 128.7, 128.6, 128.6, 128.4, 128.0, 70.5, 68.2, 45.0. HRMS (ESI) *m*/*z*: [M + H]$^+$ calcd for $C_{16}H_{18}NO_2$, 356.1645; found, 356.1637.

*Allyl 2-Benzyl-2-isocyanopent-4-enoate (**6**).* This compound was prepared similarly to **1j**. Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.23 (m, 5H), 5.87−5.74 (m, 2H), 5.29−5.21 (m, 4H), 4.58 (dt, *J* = 6.0, 1.6 Hz, 2H), 3.23 (d, *J* = 13.6 Hz, 1H), 3.05 (d, *J* = 13.6 Hz, 1H), 2.77 (dd, *J* = 13.6, 7.2 Hz, 1H), 2.57 (dd, *J* = 13.6, 7.2 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.6, 160.7, 133.5, 130.8, 130.3, 123.0, 128.5, 127.9, 121.4, 119.5, 69.0, 67.0, 44.3, 43.2. HRMS (APCI) *m*/*z*: [M + H]$^+$ calcd for $C_{16}H_{18}NO_2$, 256.1332; found, 256.1329.

Substrates 8 Was Prepared by the Following Procedure.[17]

An oven-dried 100 mL round bottom flask charged with a stir-bar and NaH (60%) (15 mmol, 3 equiv) was vacuumed and refilled with Ar three times. A mixture solution of DMSO (2 mL) and Et_2O (50 mL) was added to the flask using a syringe. Then, 5 mmol of **C** (1.0 equiv) was added to the mixture dropwise in 10 min at room temperature and the reaction mixture was stirred for 30 min. Three equivalents of bromoethane was added with a syringe and the reaction mixture was stirred for 30 min. Then, 2 mL of H_2O was added dropwise to the reaction mixture carefully at room temperature. The crude reaction mixture was extracted with DCM (20 mL × 3) and washed with brine (20 mL). The organic phase was concentrated in *vacuo* and the residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 16:1) to afford the product **8** as a colorless liquid in 86% yield (new compound).

*Allyl 2-Ethyl-2-isocyanobutanoate (**8**).* Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.98−5.88 (m, 1H), 5.43−5.29 (m, 2H), 4.70 (dt, *J* = 5.6, 1.6 Hz, 2H), 2.02−1.93 (m, 2H), 1.89−1.80 (m, 2H), 1.03 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 159.0, 131.2, 119.6, 70.1, 66.9, 32.3, 8.6. HRMS (APCI) *m*/*z*: [M + H]$^+$ calcd for $C_{10}H_{16}NO_2$, 182.1176; found, 182.1174.

*4,4-Dibenzyl-2-(naphthalen-2-yl)oxazol-5(4H)-one (**3a**).* Eluent: petroleum ether/ethyl acetate (16:1). White solid (35 mg, 89% yield.). mp = 100−102 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.88−7.86 (m, 1H), 7.83−7.78 (m, 3H),7.55−7.47 (m, 2H), 7.24−7.22 (m, 4H), 7.17−7.14 (m, 4H), 7.11−7.09 (m, 2H), 3.37−3.31 (m, 4H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 179.1, 159.9, 135.2, 134.5, 132.5, 130.3, 129.2, 129.1, 128.6, 128.3, 128.3, 127.9, 127.4, 127.0, 123.5, 122.9, 76.2, 43.8. HRMS (ESI) *m*/*z*: [M + H]$^+$ calcd for $C_{27}H_{22}NO_2$, 392.1645; found, 392.1642.

*4,4-Bis(4-methylbenzyl)-2-(naphthalen-2-yl)oxazol-5(4H)-one (**3b**).* Eluent: petroleum ether/ethyl acetate (16:1). Colorless oil. (37 mg, 89% yield.). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.85−7.82 (m, 1H), 7.79−7.73 (m, 3H), 7.50−7.41 (m, 2H), 7.04−7.02

https://dx.doi.org/10.1021/acs.joc.0c00672
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(m, 4H), 6.89−6.88 (m, 4H), 3.26−3.18 (m, 4H). 2.11 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 179.1, 159.8, 136.8, 135.2, 132.5, 131.4, 130.2, 129.2, 129.0, 128.6, 128.3, 127.9, 127.0, 123.6, 123.0, 76.4, 43.3, 21.1. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{29}H_{26}NO_2$, 420.1958; found, 420.1955.

4-(3-Fluorobenzyl)-4-(4-fluorobenzyl)-2-(naphthalen-2-yl)-oxazol-5(4H)-one (**3c**). Eluent: petroleum ether/ethyl acetate (16:1). White solid (22 mg, 52% yield.) mp = 116−118 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.79−7.82 (m, 4H), 7.58−7.50 (m, 2H), 7.21−7.16 (m, 4H), 6.87−6.83 (m, 4H), 3.32−3.26 (m, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 178.9, 162.2 (d, *J* = 244.4 Hz), 160.2, 135.4, 132.6, 131.9 (d, *J* = 7.9 Hz), 130.2, 130.1, 129.2(d, *J* = 7.3 Hz), 128.8, 128.5, 128.0, 127.1, 123.3, 122.5, 115.3(d, *J* = 21.1 Hz), 76.2, 42.8. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{20}F_2NO_2$, 428.1457; found, 428.1452.

4,4-Bis(4-chlorobenzyl)-2-(naphthalen-2-yl)oxazol-5(4H)-one (**3d**). Eluent: petroleum ether/ethyl acetate (16:1). White solid (42 mg, 91% yield.) mp = 149−151 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.83−7.76 (m, 4H), 7.53−7.44 (m, 2H), 7.10−7.05 (m, 8H), 3.25−3.17 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 178.7, 160.4, 135.4, 133.5, 132.8, 132.5, 131.6, 129.4, 129.3, 128.9, 128.6, 128.0, 127.1, 123.3, 122.4, 75.9, 42.9. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{20}Cl_2NO_2$, 460.0866; found, 460.0859.

4,4-Bis(4-bromobenzyl)-2-(naphthalen-2-yl)oxazol-5(4H)-one (**3e**). Eluent: petroleum ether/ethyl acetate (16:1). White solid (40 mg, 73% yield.) mp = 149−151 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.82−7.78 (m, 4H), 7.53−7.45 (m, 2H), 7.24−7.19 (m, 4H), 7.03−7.01 (m, 4H), 3.23−3.16 (m, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 178.6, 160.4, 135.5, 133.3, 132.6, 132.0, 131.5, 129.5, 129.3, 128.9, 128.6, 128.0, 127.2, 123.3, 121.7, 75.6, 43.0. HRMS (APCI) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{20}Br_2NO_2$, 547.9855; found, 547.9850.

2-(Naphthalen-2-yl)-4,4-bis(4-(trifluoromethyl)benzyl)oxazol-5(4H)-one (**3f**). Eluent: petroleum ether/ethyl acetate (16:1). White solid (35 mg, 66% yield.) mp = 116−118 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.80−7.75 (m, 4H), 7.53−7.42 (m, 2H), 7.39−7.37 (m, 4H), 7.29−7.27 (m, 4H), 3.35−3.27 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 178.5, 160.6, 138.3, 135.5, 132.5, 130.7, 129.8 (q, *J* = 32.4 Hz), 129.5, 129.3, 128.9, 128.7, 128.0, 127.2, 125.4 (q, *J* = 3.7 Hz), 124.1 (q, *J* = 270.4 Hz), 123.2, 122.2, 75.4, 43.3. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{29}H_{20}F_6NO_2$, 528.1393; found, 528.1399.

Methyl 3-((4-(4-(Methoxycarbonyl)benzyl)-2-(naphthalen-2-yl)-5-oxo-4,5-dihydrooxazol-4-yl)methyl)benzoate (**3g**). Eluent: petroleum ether/ethyl acetate (12:1). White solid (33 mg, 65% yield.) mp = 149−151 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.86−7.80 (m, 8H), 7.58−7.55 (m, 1H), 7.53−7.51 (m, 1H), 7.31−7.29 (m, 4H), 3.81 (s, 6H), 3.41−3.56 (m, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 178.6, 166.9, 160.4, 139.6, 135.5, 132.5, 130.4, 129.7, 129.4, 129.4, 128.9, 128.5, 128.0, 127.1, 123.3, 122.3, 75.6, 52.1, 43.6. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{31}H_{26}NO_6$, 508.1755; found, 508.1759.

4,4-Bis(2,6-difluorobenzyl)-2-(naphthalen-2-yl)oxazol-5(4H)-one (**3h**). Eluent: petroleum ether/ethyl acetate (16:1). White solid (31 mg, 66% yield.) mp = 165−167 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.85 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.80−7.76 (m, 3H), 7.51−7.43 (m, 2H), 7.09−7.03 (m, 2H), 6.76−6.71 (m, 4H), 3.43−3.36 (m, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 178.1, 161.9 (dd, *J* = 248.1, 7.9 Hz), 160.4, 135.4, 132.6, 129.50 (t, *J* = 10.3 Hz), 129.4, 129.2, 128.7, 128.4, 128.0, 127.0, 123.7, 123.0, 111.3 (dd, *J* = 206.3, 4.8 Hz), 110.8,(t, *J* = 19.9 Hz), 73.2, 30.2. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{18}F_4NO_2$, 464.1268; found, 464.1271.

4,4-Bis(2-chlorobenzyl)-2-(naphthalen-2-yl)oxazol-5(4H)-one (**3i**). Eluent: petroleum ether/ethyl acetate (16:1). White solid (37 mg, 81% yield.) mp = 105−107 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.11−8.10 (m, 1H), 7.89−7.87 (m, 1H), 7.79−7.76 (m, 3H), 7.51−7.43 (m, 2H), 7.30−7.26 (m, 2H), 7.24−7.19 (m, 2H), 7.04−6.99 (m, 4H), 3.57 (d, *J* = 13.5 Hz, 2H), 3.45 (d, *J* = 14.0 Hz, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 179.1, 159.7, 135.4, 135.3, 132.7, 132.6, 132.1, 129.9, 129.3, 129.2, 128.8, 128.7, 128.4, 128.0, 127.0, 126.7, 123.7, 122.9, 75.6, 39.5. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{20}Cl_2NO_2$, 460.0866; found, 460.0862.

4-Benzyl-4-ethyl-2-(naphthalen-2-yl)oxazol-5(4H)-one (**3j**). Eluent: petroleum ether/ethyl acetate (16:1). Colorless oil (23 mg, 70% yield.). ^1H NMR (400 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.98 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.90−7.86 (m, 3H), 7.60−7.52 (m, 2H), 7.22−7.10 (m, 5H), 3.26 (d, *J* = 13.4 Hz, 1H), 3.18 (d, *J* = 13.4 Hz, 1H), 2.15−2.05 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 179.9, 160.2, 135.3, 134.7, 132.6, 130.3, 129.3, 129.2, 128.8, 128.4, 128.3, 128.0, 127.3, 127.1, 123.6, 123.0, 75.7, 43.7, 30.8, 8.6. HRMS (APCI) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{20}NO_2$, 330.1489; found, 330.1485.

5-4-Benzyl-2-(naphthalen-2-yl)-4-propyloxazol-5(4H)-one (**3k**). Eluent: petroleum ether/ethyl acetate (16:1). Colorless oil (25 mg, 72% yield.). ^1H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.97 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.90−7.85 (m, 3H), 7.60−7.51 (m, 2H), 7.21−7.11 (m, 5H), 3.27−3.16 (m, 2H), 2.06−2.01 (m, 2H), 1.41−1.30 (m, 1H), 0.93 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 180.0, 160.1, 135.3, 134.6, 132.6, 130.3, 129.3, 129.2, 128.8, 128.4, 128.3, 128.0, 127.3, 127.1, 123.5, 123.0, 75.2, 44.0, 39.7, 17.7, 14.1. HRMS (APCI) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{22}NO_2$, 344.1645; found, 344.1639.

4-Benzyl-4-isobutyl-2-(naphthalen-2-yl)oxazol-5(4H)-one (**3l**). Eluent: petroleum ether/ethyl acetate (16:1). Colorless oil (31 mg, 86% yield.). ^1H NMR (400 MHz, $CDCl_3$): δ 8.28 (s, 1H), 7.97 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.90−7.85 (m, 3H), 7.60−7.51 (m, 2H), 7.28−7.09 (m, 5H), 3.25−3.14 (m, 2H), 2.14−1.98 (m, 2H), 1.76−1.66 (m 1H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 180.4, 159.8, 135.3, 134.2, 132.7, 130.4, 129.2, 128.8, 128.4, 128.2, 128.0, 127.4, 127.1, 123.5, 123.1, 74.7, 46.4, 45.2, 25.4, 24.2, 23.2. HRMS (APCI) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{24}NO_2$, 358.1802; found, 358.1806.

4,4-Dibenzyl-2-phenyloxazol-5(4H)-one (**3m**). Eluent: petroleum ether/ethyl acetate (16:1). Colorless oil (25 mg, 72% yield.) ^1H NMR (400 MHz, $CDCl_3$): δ 7.69−7.67 (m, 2H), 7.49−7.45 (m, 1H), 7.38−7.33 (m, 2H), 7.22−7.12 (m, 10H), 3.33−3.26 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 179.2, 159.9, 134.5, 132.5, 130.4, 128.7, 128.3, 127.8, 127.3, 125.8, 76.1, 43.7. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{20}NO_2$, 342.1489; found, 342.1486.

4,4-Dibenzyl-2-(p-tolyl)oxazol-5(4H)-one (**3n**). Eluent: petroleum ether/ethyl acetate (16:1). White solid (29 mg, 81% yield.) mp = 64−65 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.23−7.10 (m, 12H), 3.32−3.25 (m, 4H), 2.35 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 179.3, 159.9, 143.2, 134.6, 130.3, 129.4, 128.3, 127.8, 127.3, 123.0, 76.0, 43.7, 21.8. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{22}NO_2$, 356.1645; found, 356.1652.

4,4-Dibenzyl-2-(4-methoxyphenyl)oxazol-5(4H)-one (**3o**). Eluent: petroleum ether/ethyl acetate (16:1). White solid (27 mg, 74% yield.) mp = 75−76 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58−7.54 (m, 2H), 7.14−7.04 (m, 10H), 6.79−6.75 (m, 2H), 3.74 (s, 3H), 3.24−3.17 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 179.3, 163.0, 159.5, 134.7, 130.4, 129.6, 128.3, 127.3, 118.1, 114.1, 75.9, 55.5, 43.7. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{22}NO_3$, 372.1594; found, 372.1603.

4,4-Dibenzyl-2-(4-fluorophenyl)oxazol-5(4H)-one (**3p**). Eluent: petroleum ether/ethyl acetate (16:1). Colorless oil (26 mg, 72% yield.) ^1H NMR (400 MHz, $CDCl_3$): δ 7.70−7.67 (m, 2H), 7.20−7.12 (m, 10H), 7.05−7.01 (m, 2H), 3.32−3.25 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 178.9, 165.4 (d, *J* = 252.6 Hz), 158.9, 134.5, 130.3, 130.1 (d, *J* = 8.8 Hz), 128.3, 127.3, 121.9 (d, *J* = 2.9 Hz), 116.0 (d, *J* = 22.3 Hz). 76.1, 43.7. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{19}FNO_2$, 360.1394; found, 360.1390.

4,4-Dibenzyl-2-(4-chlorophenyl)oxazol-5(4H)-one (**3q**). Eluent: petroleum ether/ethyl acetate (16:1). Yellow oil (29 mg, 78% yield.). ^1H NMR (400 MHz, $CDCl_3$): δ 7.63−7.59 (m, 2H), 7.34−7.31 (m, 2H), 7.19−7.13 (m, 10H), 3.29 (s, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 178.8, 159.0, 138.9, 134.4, 130.3, 129.1, 129.0, 128.3, 127.4, 124.2, 76.2, 43.6. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{19}ClNO_2$, 376.1099; found, 376.1106.

https://dx.doi.org/10.1021/acs.joc.0c00672
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*4,4-Dibenzyl-2-(4-bromophenyl)oxazol-5(4H)-one (**3r**).* Eluent: petroleum ether/ethyl acetate (16:1). White solid (31 mg, 74% yield.) mp = 91−92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79−7.76 (m, 2H), 7.27−7.25 (m, 2H), 7.19−7.16 (m, 10H), 3.31 (s, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 178.5, 158.3, 152.1, 134.3, 130.3, 129.9, 128.4, 127.5, 126.0, 121.9, 76.4, 43.6. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{23}H_{19}BrNO_2$, 420.0594; found, 420.0590.

*4,4-Dibenzyl-2-(4-(trifluoromethyl)phenyl)oxazol-5(4H)-one (**3s**).* Eluent: petroleum ether/ethyl acetate (16:1). White solid (27 mg, 67% yield.) mp = 96−98 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.20−7.13 (m, 10H), 3.35−3.28 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 178.6, 158.7, 134.3, 134.0 (q, *J* = 32.5 Hz), 130.3, 129.0, 128.4, 128.1, 127.5, 125.8 (q, *J* = 38.0 Hz), 123.6 (q, *J* = 271.0 Hz), 76.4, 43.6. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{24}H_{19}F_3NO_2$, 410.1362; found, 410.1363.

*4,4-Dibenzyl-2-(m-tolyl)oxazol-5(4H)-one (**3t**).* Eluent: petroleum ether/ethyl acetate (16:1). Pale yellow solid (30 mg, 83% yield.) mp = 57−59 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.47 (m, 2H), 7.28−7.12 (m, 12H), 3.33−3.27 (m, 4H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 179.1, 160.0, 138.5, 134.5, 133.4, 130.3, 128.6, 128.3, 128.2, 127.3, 125.6, 125.0, 76.0, 43.7, 21.3. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{24}H_{22}NO_2$, 356.1645; found, 356.1652.

*Ethyl 3-Benzyl-1-(naphthalen-2-yl)-3,4-dihydroisoquinoline-3-carboxylate (**3u**).*[18a] (Known compound) eluent: petroleum ether/ethyl acetate (12:1). Colorless oil (33 mg, 78% yield.). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (s, 1H), 7.92−7.88 (m, 3H), 7.80 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.53−7.50 (m, 2H), 7.43−7.39 (m, 1H), 7.33−7.21 (m, 8H), 4.07 (q, *J* = 7.2 Hz, 2H), 3.37 (d, *J* = 13.2 Hz, 1H), 3.28 (d, *J* = 16.0 Hz, 1H), 3.10 (d, *J* = 13.2 Hz, 1H), 2.97 (d, *J* = 16.0 Hz, 1H), 1.11 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.5, 167.1, 136.8, 136.8, 136.2, 134.1, 133.0, 131.3, 130.6, 129.1, 128.8, 128.7, 128.5, 128.4, 128.1, 127.9, 127.8, 127.0, 126.9, 126.8, 126.8, 126.4, 67.2, 61.2, 42.9, 33.0, 14.1.

*Ethyl 3-Benzyl-1-phenyl-3,4-dihydroisoquinoline-3-carboxylate (**3v**).*[18a] (Known compound) eluent: petroleum ether/ethyl acetate (12:1). Colorless oil (30 mg, 81% yield.). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66−7.63 (m, 2H), 7.47−7.38 (m, 4H), 7.28−7.19 (m, 8H), 4.05 (q, *J* = 7.2 Hz, 2H), 3.33 (d, *J* = 13.2 Hz, 1H), 3.25 (d, *J* = 16.0 Hz, 1H), 3.04 (d, *J* = 13.2 Hz, 1H), 2.94 (d, *J* = 16.0 Hz, 1H), 1.09 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.5, 167.1, 138.9, 136.8, 136.7, 131.3, 130.6, 129.6, 129.4, 128.6, 128.5, 128.4, 128.3, 128.1, 127.0, 126.8, 67.1, 61.2, 42.9, 33.0, 14.1.

*Ethyl 3-Benzyl-1-(p-tolyl)-3,4-dihydroisoquinoline-3-carboxylate (**3w**).* Eluent: petroleum ether/ethyl acetate (12:1). Colorless oil (33 mg, 86% yield.). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.0 Hz, 2H), 7.40−7.37 (m, 1H), 7.29−7.19 (m, 10H), 4.06−4.01 (m, 2H), 3.32 (d, *J* = 13.0 Hz, 1H), 3.23 (d, *J* = 16.0 Hz, 1H), 3.02 (d, *J* = 13.5 Hz, 1H), 2.92 (d, *J* = 16.0 Hz, 1H), 2.42 (s, 3H), 1.08 (t, *J* = 7.5 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 173.6, 166.9, 139.7, 136.8, 136.8, 136.0, 131.2, 130.6, 129.3, 128.9, 128.6, 128.4, 128.4, 128.1, 126.9, 126.6, 67.0, 61.1, 42.8, 32.9, 21.5, 14.1. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{26}H_{26}NO_2$, 384.1958; found, 384.1964.

*Ethyl 3-Benzyl-1-(4-methoxyphenyl)-3,4-dihydroisoquinoline-3-carboxylate (**3x**).* Eluent: petroleum ether/ethyl acetate (8:1). Colorless oil (26 mg, 65% yield.). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.5 Hz, 2H), 7.41−7.38 (m, 1H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.27−7.19 (m, 7H), 6.96 (d, *J* = 8.5 Hz, 2H), 4.05−4.01 (m, 2H), 3.86 (s, 3H), 3.31 (d, *J* = 13.0 Hz, 1H), 3.22 (d, *J* = 16.0 Hz, 1H), 3.01 (d, *J* = 13.5 Hz, 1H), 2.92 (d, *J* = 16.0 Hz, 1H), 1.08 (t, *J* = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 173.6, 166.3, 161.0, 136.9, 136.8, 131.3, 131.1, 130.9, 130.5, 128.7, 128.5, 128.3, 128.1, 126.9, 126.7, 113.6, 67.0, 61.1, 55.5, 42.8, 33.1, 14.1. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{26}H_{26}NO_3$, 400.1907; found, 400.1912.

*Ethyl 3-Benzyl-1-(4-bromophenyl)-3,4-dihydroisoquinoline-3-carboxylate (**3y**).*[18a] (Known compound) eluent: petroleum ether/ethyl acetate (12:1). Colorless oil (37 mg, 81% yield.) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.4Hz, 2H), 7.38−7.34 (m, 1H), 7.30−7.27 (m, 2H), 7.23−7.09 (m, 8H), 4.01−3.95 (m, 2H), 3.20 (m, 2H), 2.98 (d, *J* = 13.2 Hz, 1H), 2.88 (d, *J* = 16.0 Hz, 1H), 1.02 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.2, 165.5, 150.5, 139.1, 136.7, 136.5, 131.8, 131.4, 130.5, 128.7, 128.2, 127.9, 127.9, 127.2, 126.9, 121.3, 67.2, 61.3, 42.7, 33.0, 14.1.

*Benzyl 3-Benzyl-1-(naphthalen-2-yl)-3,4-dihydroisoquinoline-3-carboxylate (**3z**).* Eluent: petroleum ether/ethyl acetate (12:1). Colorless oil (38 mg, 78% yield.) ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (s, 1H), 7.91−7.86 (m, 3H), 7.77 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.53−7.51 (m, 2H), 7.41−7.38 (m, 1H), 7.31−7.29 (m, 1H), 7.27−7.25 (m, 4H), 7.24−7.19 (m, 4H), 7.17−7.12 (m, 4H), 5.05 (s, 2H), 3.40 (d, *J* = 13.0 Hz, 1H), 3.29 (d, *J* = 16.0 Hz, 1H), 3.12 (d, *J* = 13.0 Hz, 1H), 2.98 (d, *J* = 16.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 173.4, 167.2, 136.7, 136.6, 136.1, 135.8, 134.1, 133.0, 131.4, 130.6, 129.2, 128.8, 128.6, 128.5, 128.5, 128.5, 128.2, 128.2, 128.1, 127.9, 127.8, 127.1, 126.9, 126.8, 126.8, 126.4, 67.4, 66.9, 43.2, 33.0. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{34}H_{27}NO_2$, 482.2115; found, 482.2110.

*Allyl 3-Benzyl-1-phenyl-3,4-dihydroisoquinoline-3-carboxylate (**5a**).* Eluent: petroleum ether/ethyl acetate (14:1). Colorless oil (28 mg, 72% yield.). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59−7.56 (m, 2H), 7.39−7.31 (m, 4H), 7.21−7.10 (m, 8H), 5.72−5.63 (m, 1H), 5.11−5.03 (m, 2H), 4.43 (dt, *J* = 5.6, 1.6 Hz, 2H), 3.27 (d, *J* = 13.2 Hz, 1H), 3.19 (d, *J* = 16.0 Hz, 1H), 2.96 (d, *J* = 13.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.2, 167.1, 138.7, 136.6, 136.6, 132.0, 131.4, 130.5, 129.7, 129.3, 128.5, 128.5, 128.4, 128.3, 128.2, 127.0, 126.8, 118.2, 67.3, 65.8, 42.7, 32.8. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{26}H_{24}NO_2$, 382.1802; found, 382.1801.

*Allyl 1-([1,1′-Biphenyl]-4-yl)-3-benzyl-3,4-dihydroisoquinoline-3-carboxylate (**5b**).* Eluent: petroleum ether/ethyl acetate (14:1). Colorless oil (42 mg, 92% yield.). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77−7.74 (m, 2H), 7.69−7.64 (m, 4H), 7.49−7.44 (m, 3H), 7.44−7.35 (m, 3H), 7.30−7.27 (m, 2H),7.23−7.19 (m, 4H), 5.81−5.71 (m, 1H), 5.19−5.11 (m, 2H), 4.51 (dt, *J* = 5.6, 1.6 Hz, 2H), 3.36 (d, *J* = 13.3 Hz, 1H), 3.28 (d, *J* = 16.0 Hz, 1H), 3.06 (d, *J* = 13.4 Hz, 1H), 2.97 (d, *J* = 16.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.2, 166.8, 142.6, 140.9, 137.7, 136.7, 136.7, 132.0, 131.4, 130.6, 130.6, 129.9, 129.0, 128.6, 128.5, 128.4, 128.2, 127.7, 127.3, 127.1, 126.9, 118.2, 67.4, 65.8, 42.8, 33.0. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{32}H_{28}NO_2$, 458.2115; found, 458.2112.

*Allyl 3-Benzyl-1-(3-methoxyphenyl)-3,4-dihydroisoquinoline-3-carboxylate (**5c**).* Eluent: petroleum ether/ethyl acetate (14:1). Colorless oil (27 mg, 65% yield.). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.11 (m, 12H), 6.96−6.93 (m, 1H), 5.73−5.63 (m, 1H), 5.11−5.03 (m, 2H), 4.43 (dt, *J* = 5.6, 1.6 Hz, 2H), 3.78 (s, 3H), 3.26 (d, *J* = 13.2 Hz, 1H), 3.20 (d, *J* = 15.6 Hz, 1H), 2.97 (d, *J* = 13.6 Hz, 1H), 2.88 (d, *J* = 16.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) 173.2, 166.9, 159.6, 140.1, 136.6, 136.6, 132.0, 131.4, 130.6, 129.3, 128.5, 128.4, 128.3, 128.1, 127.1, 126.9, 121.9, 118.2, 115.8, 114.4, 67.3, 65.8, 55.5, 42.7, 32.8. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{27}H_{26}NO_3$, 412.1907; found, 412.1904.

*Allyl 3-Benzyl-1-(4-fluorophenyl)-3,4-dihydroisoquinoline-3-carboxylate (**5d**).* Eluent: petroleum ether/ethyl acetate (14:1). Yellow oil (32 mg, 81% yield.) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61−7.57 (m, 2H), 7.37−7.32 (m, 1H), 7.22−7.14 (m, 6H), 7.12−7.04 (m, 4H), 5.71−5.64 (m, 1H), 5.10−5.04 (m, 2H), 4.43 (dt, *J* = 5.6, 1.6 Hz, 2H), 3.24 (d, *J* = 13.3 Hz, 1H), 3.19 (d, *J* = 16.0 Hz, 1H), 2.95 (d, *J* = 13.3 Hz, 1H), 2.88 (d, *J* = 16.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.1, 166.1, 163.9 (d, *J* = 247.6 Hz) 136.7, 136.5, 134.8, 131.9, 131.5, 131.4, 131.3, 130.5, 128.6, 128.3, 128.2 (d, *J* = 2.9 Hz), 127.1, 126.9, 118.3, 115.3(d, *J* = 21.2 Hz), 67.3, 65.8, 42.7, 32.9. HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{26}H_{23}FNO_2$, 400.1707; found, 400.1699.

*Allyl 3-Benzyl-1-(4-chlorophenyl)-3,4-dihydroisoquinoline-3-carboxylate (**5e**).* Eluent: petroleum ether/ethyl acetate (14:1). Yellow oil (31 mg, 76% yield.). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55−7.52 (m, 2H), 7.36−7.32 (m, 3H), 7.21−7.13 (m, 6H), 7.11−7.08 (m, 2H), 5.70−5.61 (m, 1H), 5.09−5.03 (m, 2H), 4.42 (dt, *J* = 5.6, 1.6 Hz, 2H), 3.23 (d, *J* = 13.2 Hz, 1H),.3.18 (d, *J* = 16.0 Hz) 2.96 (d, *J* = 13.2 Hz, 1H), 2.87 (d, *J* = 16.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.0, 166.1, 137.1, 136.6, 136.4, 135.8, 131.9, 131.6, 130.7, 130.5, 128.6, 128.5, 128.2, 128.1, 128.1, 127.1, 126.9, 118.3,

https://dx.doi.org/10.1021/acs.joc.0c00672
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67.3, 65.8, 42.7, 32.8. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{26}H_{23}ClNO_2$, 416.1412; found, 416.1403.

*Allyl 3-Benzyl-1-(naphthalen-2-yl)-3,4-dihydroisoquinoline-3-carboxylate (**5f**).* Eluent: petroleum ether/ethyl acetate (14:1). Colorless oil (34 mg, 79% yield.). ^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (s, 1H), 7.93−7.89 (m, 3H), 7.80 (dd, J = 8.4, 1.6 Hz, 1H), 7.55−7.52 (m, 2H), 7.43−7.41 (m, 1H), 7.34−7.28 (m, 3H), 7.25−7.20 (m, 5H), 5.81−5.72 (m, 1H), 5.20−5.11 (m, 2H), 4.53 (dt, J = 5.6, 1.6 Hz, 2H), 3.38 (d, J = 13.2 Hz, 1H), 3.30 (d, J = 16.0 Hz, 1H), 3.10 (d, J = 13.2 Hz, 1H), 2.98 (d, J = 16.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.3, 167.1, 136.8, 136.7, 136.2, 134.1, 133.1, 132.0, 131.4, 130.7, 129.2, 128.8, 128.7, 128.6, 128.5, 128.2, 128.0, 127.9, 127.1, 126.9, 126.8, 126.4, 118.2, 67.4, 65.8, 42.9, 32.9. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{26}NO_2$, 432.1958; found, 432.1957.

*Allyl 5-Chloro-3-(2-chlorobenzyl)-1-phenyl-3,4-dihydroisoquinoline-3-carboxylate (**5g**).* Eluent: petroleum ether/ethyl acetate (14:1). Colorless oil (35 mg, 77% yield.). ^1H NMR (400 MHz, $CDCl_3$): δ 7.61−7.59 (m, 2H), 7.47−7.40 (m, 5H), 7.31−7.29 (m, 1H), 7.14−7.11 (m, 4H), 5.81−5.71 (m, 1H), 5.20−5.11 (m, 2H), 4.55−4.53 (m, 2H), 3.63 (d, J = 14.0 Hz, 1H), 3.52 (d, J = 16.4 Hz, 1H), 3.47 (d, J = 14.0 Hz, 1H), 3.06 (d, J = 16.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 172.8, 167.1, 138.4, 135.3, 134.6, 133.9, 132.7, 132.0, 131.8, 130.1, 129.8, 129.5, 129.3, 128.3, 128.2, 127.5, 126.8, 126.5, 118.3, 66.9, 66.0, 40.2, 30.4. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{26}H_{22}Cl_2NO_2$, 450.1022; found, 450.1020.

*Allyl 2-Benzyl-4-methylene-5-phenyl-3,4-dihydro-2H-pyrrole-2-carboxylate (**7a**).* Eluent: petroleum ether/ethyl acetate (12:1). Yellow oil (23 mg, 72% yield.) ^1H NMR (400 MHz, $CDCl_3$): δ 7.60−7.57 (m, 2H), 7.45−7.39 (m, 3H), 7.23−7.19 (m, 5H), 5.99−5.89 (m, 1H), 5.36−5.30 (m, 1H), 5.25−5.19 (m, 3H), 4.70−4.68 (m, 2H), 3.38−3.30 (m, 2H), 3.20−3.15 (m, 1H), 2.88−2.82 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.7, 173.2, 147.8, 135.9, 133.2, 132.1, 131.0, 130.2, 128.8, 128.5, 128.1, 126.8, 118.7, 112.8, 79.8, 66.2, 43.8, 38.4. HRMS (APCI) m/z: $[M + H]^+$ calcd for $C_{22}H_{22}NO_2$, 332.1645; found, 322.1646.

*4-Allyl-4-Benzyl-2-(naphthalen-2-yl)oxazol-5(4H)-one (**7b**).* Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil (25 mg, 74% yield.). ^1H NMR (400 MHz, $CDCl_3$): δ 8.29 (s, 1H), 7.97 (dd, J = 8.4, 1.6 Hz, 1H), 7.89−7.85 (m, 3H), 7.60−7.51 (m, 2H), 7.22−7.10 (m, 5H), 5.77−5.67 (m, 1H), 5.26−5.21 (m, 1H), 5.15−5.12 (m, 1H), 3.29−3.18 (m, 2H), 2.83−2.72 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 179.2, 160.2, 135.3, 134.4, 132.6, 130.92, 130.3, 129.4, 129.2, 128.7, 128.4, 128.3, 128.0, 127.4, 127.1, 123.6, 122.9, 120.8, 75.1, 43.4, 41.7. HRMS (APCI) m/z: $[M + H]^+$ calcd for $C_{23}H_{20}NO_2$, 342.1489; found, 342.1496.

*2-((1,3-Dimethyl-2-oxoindolin-3-yl)methyl)-4,4-diethyloxazol-5(4H)-one (**9a**).* Eluent: petroleum ether/ethyl acetate (5:1). White solid (25 mg, 81% yield.) mp = 94−96 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.27−7.23 (m, 2H), 7.03 (t, J = 7.6 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 3.26−3.22 (m, 4H), 2.96 (d, J = 15.6 Hz, 1H), 1.53−1.51 (m, 4H), 1.47 (s, 3H), 0.46 (t, J = 7.2 Hz, 3H), 0.37 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 180.2, 179.2, 160.3, 143.9, 131.9, 128.6, 123.0, 122.7, 108.4, 73.8, 46.0, 36.9, 29.8, 29.6, 26.6, 24.6, 7.7, 7.6. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{23}N_2O_3$, 315.1703; found, 315.1703.

*4,4-Diethyl-2-((1-methyl-2-oxoindolin-3-ylidene) (phenyl)-methyl)oxazol-5(4H)-one (**9b**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid (22 mg, 58% yield.) mp = 89−91 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.56−7.52 (m, 2H), 7.51−7.49 (m, 3H), 7.28−7.23 (m, 1H), 6.78−6.66 (m, 3H), 3.23 (s, 3H), 1.93 (q, J = 7.6 Hz, 4H), 0.91 (t, J = 7.6 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 180.5, 165.6, 160.4, 145.0, 135.3, 134.3, 131.4, 131.1, 130.2, 129.4, 128.6, 124.3, 122.1, 120.8, 108.4, 74.1, 29.4, 26.2, 8.3. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{23}H_{23}N_2O_3$, 375.1703; found, 375.1709.

Compounds 10a and 10b Were Prepared by the Following Procedure.[22] To a solution of **3a** (0.1 mmol) in MeOH (0.5 mL, 5 mL/mmol), two drops of triflic acid were added and the solution was stirred at room temperature until completion of reaction (1 h). After that the solvent was removed under reduced pressure, and the crude material was purified by flash column chromatography on silica gel to afford the product **10a**.

*Methyl 2-(2-naphthamido)-2-benzyl-3-phenylpropanoate (**10a**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid (42 mg, 99% yield.) mp = 110−112 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.08−8.07 (m, 1H), 7.87−7.85 (m, 3H), 7.70−7.67 (m, 1H), 7.58−7.50 (m, 2H), 7.22−7.09 (m, 10H), 6.98 (s, 1H), 4.24 (d, J = 13.6 Hz, 2H), 3.87 (s, 1H),3.35 (d, J = 13.2 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.2, 167.7, 136.4, 134.9, 132.8, 129.8, 129.1, 128.7, 128.5, 127.9, 127.8, 127.4, 127.2, 126.9, 123.6, 68.3, 52.8, 40.9. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{28}H_{26}NO_3$, 424.1907; found, 424.1908.

*Allyl 2-(2-Naphthamido)-2-benzyl-3-phenylpropanoate (**10b**).* This compound was prepared similarly to **13a**. Eluent: petroleum ether/ethyl acetate (10:1). White solid (20 mg, 44% yield.) mp = 130−132 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.86 (d, J = 9.2 Hz, 3H),7.71−7.69 (m, 1H), 7.56−7.52 (m, 2H), 7.31−7.28 (m, 1H), 7.18−7.11 (m, 10H), 6.98 (s, 1H), 6.11−6.01 (m, 1H), 5.52−5.41 (m, 2H), 4.70−4.68 (m, 2H), 4.27 (d, J = 13.6 Hz, 2H), 3.37 (d, J = 13.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 172.5, 167.6, 136.4, 134.9, 132.9, 132.8, 131.3, 129.9, 129.1, 128.7, 128.4, 127.9, 127.8, 127.4, 127.2, 126.9, 123.6, 120.3, 68.2, 67.0, 41.0. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{28}NO_3$, 450.2064; found, 450.2067.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c00672.

^1H and $^{13}C\{^1H\}$ NMR spectra of starting materials and products (PDF)

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https://dx.doi.org/10.1021/acs.joc.0c00672
J. Org. Chem. XXXX, XXX, XXX−XXX

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (21702003, 21772001) and the Natural Science Foundation of Anhui Province (1808085QB31)

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