JOC The Journal of Organic Chemistry

pubs.acs.org/joc Article

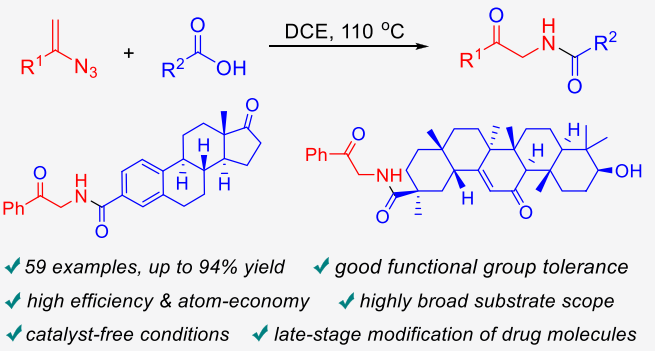
Synthesis of α-Amidoketones through the Cascade Reaction of Carboxylic Acids with Vinyl Azides under Catalyst-Free Conditions

Cai Gao, Qianting Zhou, Li Yang, Xinying Zhang,* and Xuesen Fan*

Cite This: https://dx.doi.org/10.1021/acs.joc.0c01871 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: An efficient synthesis of α-amidoketone derivatives through the cascade reactions of carboxylic acids with vinyl azides is presented. Compared with literature protocols, notable features of this new method include catalyst-free conditions, broad substrate scope, good tolerance of a wide range of functional groups, and high efficiency. In addition, the synthetic potential of this method as a tool for late-stage modification was convincingly manifested by its application in the structural elaborations of a number of carboxylic acid drug molecules.

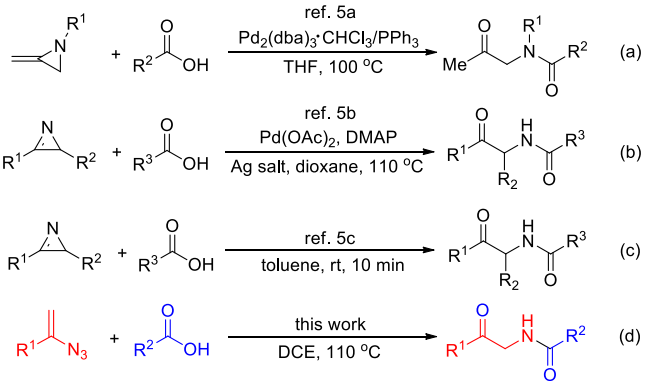


INTRODUCTION

α-Amidoketone derivatives have attracted considerable attention because they are not only the essential motifs of a plethora of pharmaceutically active compounds but also the indispensable intermediates that are widely used in organic synthesis.[1,2] Due to their importance, a number of methods for the preparation of α-amidoketone derivatives have been developed, which mainly include condensation of ketone-derived nitrones with *N*-methyl carboximidoyl chloride followed by hydrolytic workup,[3a] aza-benzoin condensation of aldehydes with *N*-acylimines promoted by organocatalysts,[3b−d] Rh-catalyzed denitrogenative hydration of *N*-sulfonyl-1,2,3-triazoles,[3e] the radical cascade reaction of alkynes with *N*-fluoroarylsulfonimides and alcohols,[3f] the Dakin−West reaction of α-aminoacids with acid anhydrides, Rh-catalyzed hydroformylation of vinyl ester followed by condensation with primary amines and rearrangement, the Ru-catalyzed cascade reaction of 1,2-azidoalcohols, and Cu-catalyzed condensation of *N*-alkoxylbenzamids with 2*H*-azirines. Although these literature methods are generally efficient and reliable, some of them still suffer from the use of expensive transition-metal catalysts, harsh reaction conditions, poor atom economy, and/or limited substrate scope. Therefore, the search for more general, efficient, and sustainable methods for the preparation of α-amidoketone derivatives is highly desirable.

Meanwhile, carboxylic acids are among the most abundant naturally occurring compounds. In addition, they are relatively cheap, easy-to-handle, and versatile in terms of reaction patterns. Therefore, carboxylic acids are ideal starting materials for the preparation of various classes of fine chemicals.[4] In this regard, Yamamoto et al. have developed an efficient preparation method of α-amidoketone derivatives via a Pd-catalyzed ring-opening reaction of methylene aziridines using carboxylic acids as an efficient coupling partner (Scheme 1a).[5a] In addition, Xu et al. reported an alternative method for this purpose via a Pd-catalyzed coupling reaction of 2*H*-azirines with carboxylic acids (Scheme 1b).[5b] Very recently, Majee et al. reported an elegant self-catalyzed rapid synthesis of α-amidoketones from the reaction of 3-aryl-2*H*-azirines with

Scheme 1. Synthesis of α-Amidoketones Starting from Carboxylic Acids



Received: August 3, 2020

https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX−XXX

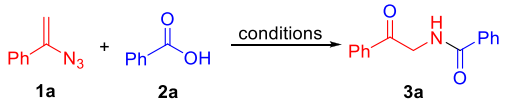
carboxylic acids (Scheme 1c).[5c] Inspired by these elegant pioneering studies and as a continuation of our own interest in the economical construction of nitrogen-containing biologically attractive compounds,[6] especially using vinyl azides as convenient three-atom synthons,[7,8] we have studied the reaction of vinyl azides with carboxylic acids. From this reaction, we successfully developed a highly efficient and general synthesis of α-amidoketones under catalyst-free conditions (Scheme 1d). Herein, we wish to report our results in this regard.

RESULTS AND DISCUSSION

Initially, (1-azidovinyl)benzene (**1a**) was treated with benzoic acid (**2a**) in methanol at 90 °C for 6 h. From this reaction, the desired *N*-(2-oxo-2-phenylethyl)benzamide (**3a**) was obtained in a yield of 12% (Table 1, entry 1). Encouraged by this preliminary result, we then tried different solvents such as toluene, dichloromethane (DCM), 1,2-dichloroethane (DCE), acetone, 2,2,2-trifluoroethanol (THF), dioxane, CH_3CN, and tetrafluoroethylene (TFE) to improve the reaction efficiency (entries 2−9). Gratifyingly, the reaction carried out in DCE afforded **3a** in an enhanced yield of 49% (entry 4). This study showed that the reaction temperature also played an important role. To be specific, reducing the reaction temperature from 90 to 80 °C resulted in an obvious decline in the yield of **3a** (entry 10 vs 4). On the other hand, when the reaction temperature was increased from 90 to 100, 110, or 120 °C, the yield of **3a** could be improved from 49 to 61, 71, or 70% (entries 11−13 vs 4). Subsequent optimization in terms of reaction time showed that prolonging the reaction period from 6 to 8 or 10 h could increase the yield from 71 to 74 or 76% (entries 14 and 15 vs 12). It was also demonstrated that raising the molar ratio of **1a** to **2a** from 1.2:1 to 1.5:1 did not lead to a substantial improvement in the yield of **3a** (entry 16).

With the establishment of the optimal reaction conditions, the substrate generality of this novel synthesis of α-amidoketones was explored. First, the scope of vinyl azides (**1**) was tested using **2a** as a model substrate. The results included in Table 2 demonstrated that 1-phenyl-substituted vinyl azides with either an electron-donating group (EDG) such as methyl, *tert*-butyl, or methoxy, or an electron-withdrawing group (EWG) such as fluoro, chloro, bromo, trifluoromethyl, or phenyl attached on the *para*-site of the 1-phenyl ring took part in this reaction smoothly to give the corresponding products **3b**−**3i** in yields ranging from 66 to 82%. It is worth noting herein that this reaction was compatible with substrates bearing a reactive formyl or acetoxy unit to give **3j** and **3k** in reasonably good yields. For substrates bearing a *meta*-methyl, *ortho*-methyl, or 3,4-dimethoxy-substituted phenyl moiety, the corresponding reactions took place to give **3l**, **3m**, and **3n**. Furthermore, 2-naphthyl-substituted vinyl azide reacted with **2a** to afford **3o**. Interestingly, vinyl azides bearing a heterocyclic unit such as 2-thienyl or 3-pyridinyl could also participate in this reaction to give **3p** and **3q**. In addition to aromatic moieties, an alkyl unit-substituted vinyl azide, 2-azidodec-1-ene, was found to be also suitable for this reaction to afford **3r** in 66% yield.

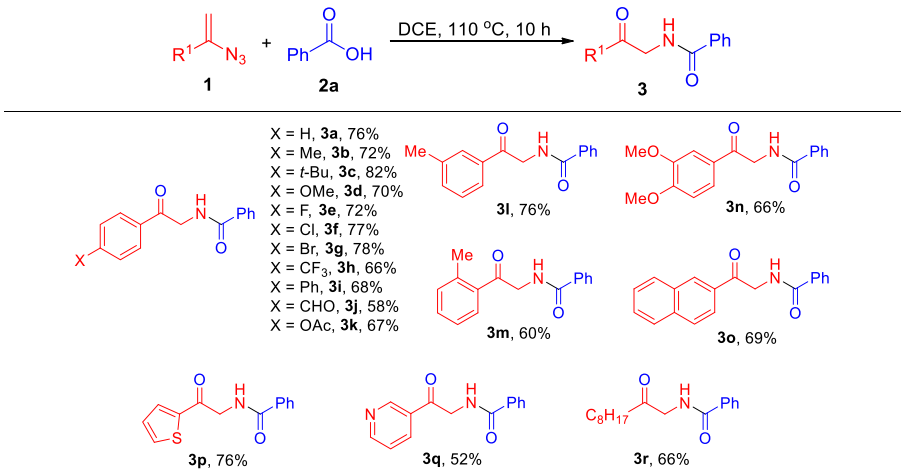
Table 1. Optimization Study for the Formation of 3a[a]



entry	solvent	T (°C)	time (h)	yield (%)[b]
1	MeOH	90	6	12
2	toluene	90	6	18
3	DCM	90	6	35
4	DCE	90	6	49
5	acetone	90	6	25
6	THF	90	6	12
7	dioxane	90	6	trace
8	CH_3CN	90	6	40
9	TFE	90	6	trace
10	DCE	80	6	33
11	DCE	100	6	61
12	DCE	110	6	71
13	DCE	120	6	70
14	DCE	110	8	74
15	DCE	110	10	76
16[c]	DCE	110	10	77

[a]Conditions: **1a** (0.36 mmol), **2a** (0.3 mmol), solvent (2 mL), sealed tube. [b]Isolated yield. [c]Conditions: **1a** (0.45 mmol), **2a** (0.3 mmol).

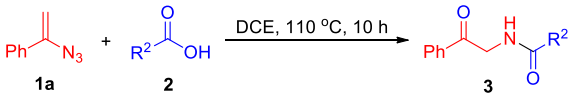
Table 2. Scope of Substrate 1[a,b]

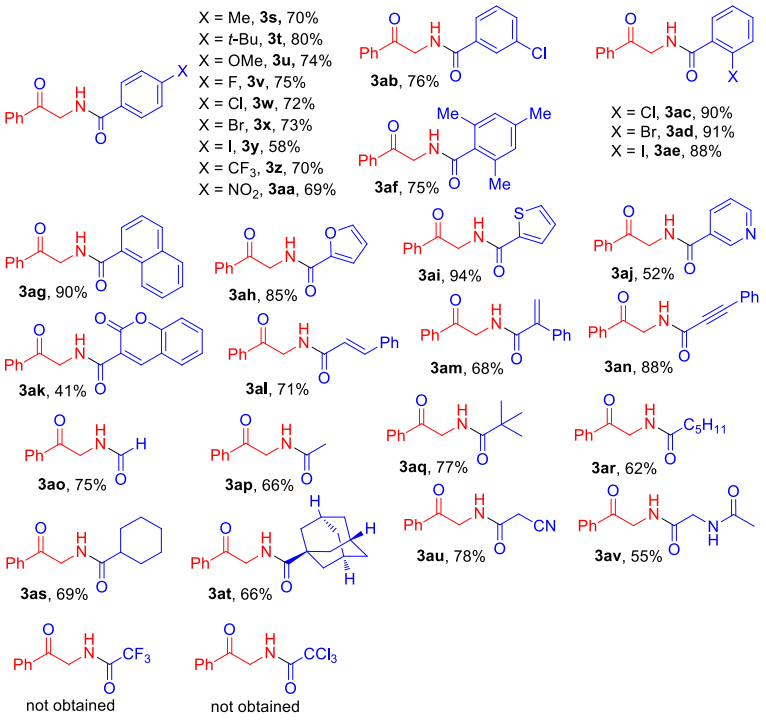


[a]Conditions: **1** (0.36 mmol), **2a** (0.3 mmol), DCE (2 mL), 110 °C, sealed tube, 10 h. [b]Isolated yield.

https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX−XXX

Table 3. Scope of Substrate 2[a,b]





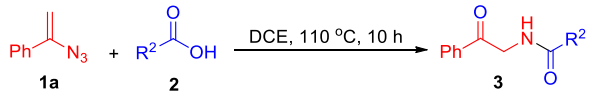
[a]Conditions: **1a** (0.36 mmol), **2** (0.3 mmol), DCE (2 mL), 110 °C, sealed tube, 10 h. [b]Isolated yield.

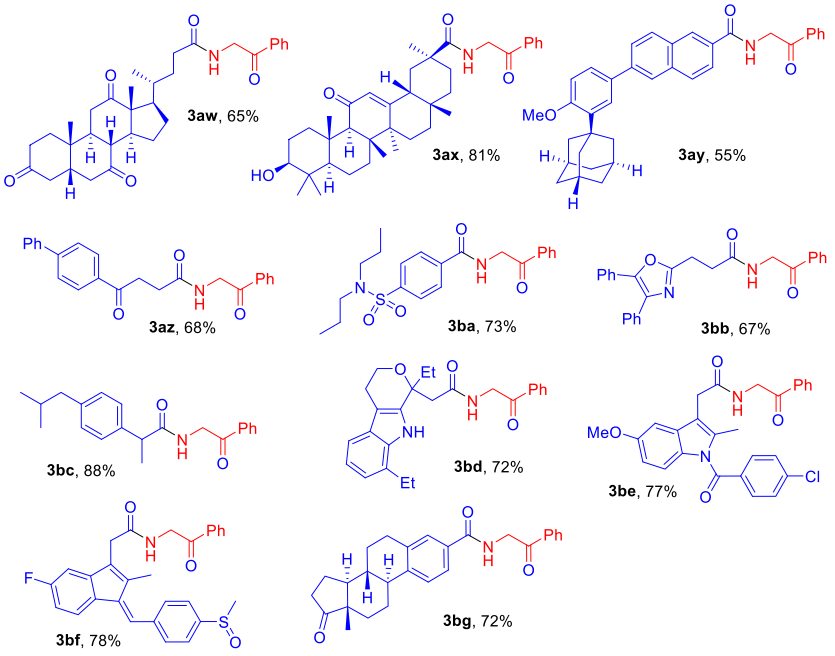
Next, the generality of carboxylic acids (**2**) was explored using **1a** as a model substrate, and the results were listed in Table 3. First, a number of aromatic carboxylic acids were tried. It was thus observed that **2** bearing a 4-methyl, 4-*tert*-butyl, 4-methoxy, 4-fluoro, 4-chloro, 4-bromo, 4-iodo, 4-trifluoromethyl, 4-nitro, or 3-chloro-substituted phenyl ring as the R^2 moiety reacted with **1a** smoothly to give **3s**−**3ab** in moderate to good yields. It is worth noting herein that even the iodo unit could remain intact under the reaction conditions, demonstrating remarkable advantages of this novel method and allowing for versatile structural elaborations of the products. Surprisingly, **2** bearing an *ortho*-halide-substituted phenyl ring gave the corresponding products in higher efficiency than their *para*- or *meta*-substituted counterparts, most likely due to the stronger acidity of *ortho*-substituted benzoic acids. In addition, 2,4,6-trimethylbenzoic acid and 1-naphthoic acid reacted with **1a** smoothly to give **3af** and **3ag**. Gratifyingly, furan-2-carboxylic acid and thiophene-2-carboxylic acid showed excellent efficiency to afford **3ah** and **3ai**, while nicotinic acid and coumarin-3-carboxylic acid gave their products **3aj** and **3ak** in moderate yields. Interestingly, some alkenyl and alkynyl acids such as cinnamic acid, 2-phenylacrylic acid, and 3-phenylpropiolic acid were found to be also viable substrates to give **3al**, **3am**, and **3an**. In addition, the suitability of aliphatic carboxylic acids such as formic acid, acetic acid, pivalic acid, hexanoic acid, cyclohexanecarboxylic acid, and adamantane-1-carboxylic acid was also tested. It turned out that the reactions of these aliphatic carboxylic acids with **1a** took place as efficiently as those of their aromatic counterparts to afford **3ao**−**3at**. Interestingly, aliphatic carboxylic acids containing an EWG or an EDG on the α-position of the carboxyl group, such as 2-cyanoacetic acid and acetylglycine, showed moderate to good efficiency to give **3au** and **3av**. On the other hand, trifluoroacetic acid and trichloroacetic acid failed to give the corresponding α-amidoketone products. In these cases, **1a** underwent a rearrangement to afford *N*-phenylacetamide. As described in the Introduction section, Majee et al. developed a self-catalyzed rapid synthesis of α-amidoketones from the reaction of 3-aryl-2*H*-azirines with carboxylic acids.[5c] Despite being highly facile, convenient, and catalyst-free, Majee's method is viable to formic acid, difluoroacetic acid, trichloroacetic acid, bromoacetic acid, propiolic acid, and phenylpropiolic acid but not applicable for more common carboxylic acids such as acetic acid, benzoic acid, propionic acid, and pivalic acid. Therefore, it might be reasonable to suggest that our method could be considered as complementary to Majee's method in terms of the scope of acid substrates. By the way, the structure of **3w** was unambiguously established by single-crystal X-ray crystallography (see the Supporting Information).

To further explore the generality of this α-amidoketone-forming reaction and investigate its synthetic potential as a tool for late-stage modifications, some carboxylic acid drug molecules such as dehydrocholic acid, 18β-glycyrrhetinic acid, adapalene, fenbufen, probenecid, oxaprozin, ibuprofen, etodolac, indometacin, and sulindac were tried to react with **1a**. It was thus found that all of them were compatible with the reaction conditions to give the corresponding products **3aw**−

https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX−XXX

Table 4. Structural Elaboration of Carboxylic Acid Drug Molecules[a,b]





[a]Conditions: **1a** (0.36 mmol), **2** (0.3 mmol), DCE (2 mL), 110 °C, sealed tube, 10 h. [b]Isolated yield.

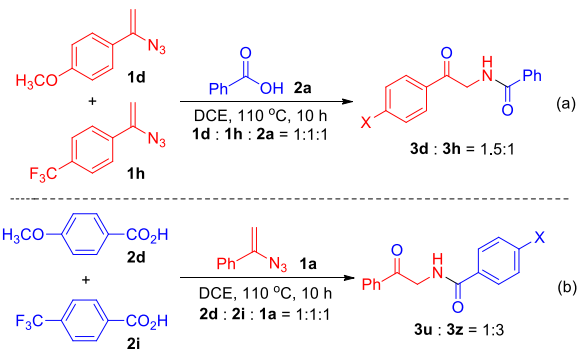
3bf in moderate to good yields. Interestingly, an estrone-derived carboxylic acid substrate was found to be also suitable for this reaction to give **3bg**. Notably, the presence of a free hydroxyl group in glycyrrhetinic acid did not affect the reaction efficiency in the formation of **3ax** (Table 4). These results demonstrated that this newly found transformation is a highly general and versatile synthetic approach toward α-amidoketone derivatives under catalyst- and metal-free conditions.

To gain some insight into the mechanism of this reaction, a set of competition experiments were performed. First, 1-phenylvinyl azide bearing an EDG or an EWG on the phenyl ring was reacted with **2a** (Scheme 2a). It turned out that the *para*-OMe-substituted substrate **1d** reacted with **2a** slightly faster than its CF_3-substituted analogue **1h**. Second, the benzoic acid derivative (**2**) bearing an EDG or an EWG on the phenyl ring was reacted with **1a** (Scheme 2b). It was thus found that the *para*-CF_3-substituted substrate **2i** reacted with **1a** three times faster than its OMe-substituted analogue **2d**.

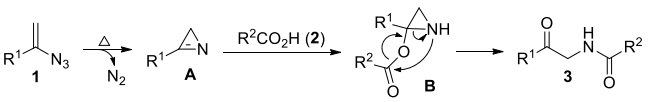
Based on the above described experimental results and literature reports,[5] a plausible mechanism accounting for the formation of **3** is proposed in Scheme 3. Initially, the vinyl azide (**1**) is decomposed under the reaction conditions to give an azirine intermediate **A**. **A** then reacts with the carboxylic acid (**2**) to give an aziridine species **B**. Finally, the unstable aziridine **B** undergoes a thermal rearrangement to give the α-amidoketone product **3**.

To illustrate the usefulness of the products obtained above, the following transformations were conducted. First, **3a** was treated with H_2SO_4 in Ac_2O.[1c] From this reaction, 2,5-diphenyloxazole (**4**) was obtained in 88% yield (Scheme 4).

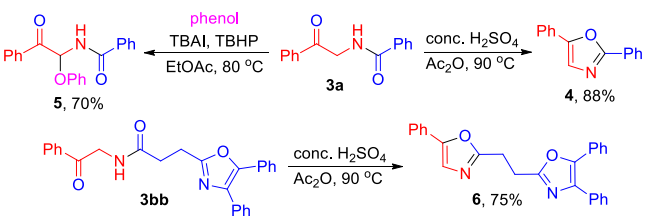
Scheme 2. Mechanistic Studies



Scheme 3. Plausible Mechanism Accounting for the Formation of 3



Scheme 4. Structural Elaborations of 3

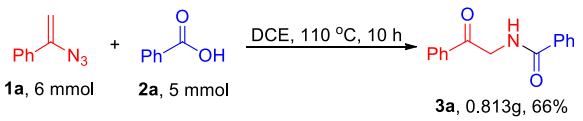


https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX−XXX

Second, **3a** was treated with phenol under the promotion of tetrabutyl ammonium iodide (TBAI) and *tert*-butyl hydroperoxide (TBHP) to afford α-phenoxylated amidoketone (**5**) in 70% yield.[9] Third, **3bb**, the α-amidoketone derivative of oxaprozin, was treated with H_2SO_4 in Ac_2O to afford a structurally and biologically attractive bisoxazole derivative (**6**) with good efficiency.[10]

Finally, to check the suitability of this protocol for large-scale synthetic missions, 6 mmol of **1a** was treated with 5 mmol of **2a** under the standard reaction conditions (Scheme 5). It turned out that the corresponding reaction proceeded smoothly to afford **3a** in 66% yield.

Scheme 5. Gram-Scale Synthesis of 3a



CONCLUSIONS

To conclude, we have developed a convenient and efficient method for the synthesis of α-amidoketones through an unprecedented cascade reaction of vinyl azides with carboxylic acids. Using this method, a library of diversely substituted α-amidoketone derivatives was obtained in good to excellent yields. In addition, the synthetic potential of this method as a tool for late-stage modification was well showcased by its application on a number of complex carboxylic acid drug molecules. With notable advantages such as catalyst-free conditions, good tolerance of sensitive functional groups, broad scope of both coupling partners, simple operation, and high efficiency, this method is expected to find wide applications in related areas.

EXPERIMENTAL SECTION

General Experimental Information. Commercial reagents were used without further purification. Vinyl azides (**1**)[11] were prepared based on literature procedures. Melting points were recorded with a micro melting point apparatus and uncorrected. The ^{1}H nuclear magnetic resonance (NMR) spectra were recorded at 400 or 600 MHz. The ^{13}C NMR spectra were recorded at 100 or 150 MHz. The ^{19}F NMR spectra were recorded at 376 MHz or 565 MHz. Chemical shifts were expressed in parts per million (δ) and were reported as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), m (multiplet), br s (broad singlet), etc. The coupling constant J was given in Hz. High-resolution mass spectra (HRMS) were obtained via electrospray ionization (ESI) mode using a micrOTOF mass spectrometer. The conversion of starting materials was monitored by thin-layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm), and components were visualized by observation under UV light (254 and 365 nm).

Experimental Procedures and Spectroscopic Data. *General Synthetic Procedure for the Preparation of **3** and Spectroscopic Data of **3a–3bg**.* To a reaction tube equipped with a stir bar were charged with vinyl azides (**1**, 0.36 mmol), carboxylic acids (**2**, 0.3 mmol), and DCE (2 mL). The tube was then sealed and stirred at 110 °C (oil bath) under air for 10 h. Upon completion, it was cooled to room temperature and concentrated under a reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate as an eluent to afford product **3**.

*N-(2-Oxo-2-Phenylethyl)Benzamide (**3a**).* Eluent: petroleum ether/ethyl acetate (5:1).[12] White solid (54.5 mg, 76%), mp: 123–124 °C (lit.[12] 124–125 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.6 Hz, 2H), 7.88 (d, J = 7.2 Hz, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.40–7.51 (m, 6H), 4.92 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.4, 167.4, 134.4, 134.2, 133.9, 131.7, 128.9, 128.6, 128.0, 127.2, 46.9. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{15}H_{13}NNaO_2^+$ 262.0838; found, 262.0832.

*N-(2-Oxo-2-(p-Tolyl)Ethyl)Benzamide (**3b**).* Eluent: petroleum ether/ethyl acetate (5:1). Yellowish solid (54.7 mg, 72%), mp: 107–109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87–7.91 (m, 4H), 7.48–7.53 (m, 1H), 7.39–7.45 (m, 3H), 7.28 (d, J = 8.0 Hz, 2H), 4.90 (d, J = 4.4 Hz, 2H), 2.41 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 193.9, 167.4, 145.2, 134.0, 131.9, 131.7, 129.6, 128.6, 128.1, 127.2, 46.8, 21.8. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{16}H_{15}NNaO_2^+$ 276.0995; found, 276.0991.

*N-(2-(4-(tert-Butyl)Phenyl)-2-Oxoethyl)Benzamide (**3c**).* Eluent: petroleum ether/ethyl acetate (5:1). White solid (72.6 mg, 82%), mp: 138–139 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.4 Hz, 2H), 7.88–7.90 (m, 2H), 7.49–7.52 (m, 3H), 7.42–7.46 (m, 3H), 4.93 (d, J = 4.0 Hz, 2H), 1.35 (s, 9H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 193.9, 167.4, 158.2, 134.0, 131.9, 131.7, 128.6, 128.0, 127.2, 125.9, 46.8, 35.3, 31.0. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{19}H_{21}NNaO_2^+$ 318.1465; found, 318.1448.

*N-(2-(4-Methoxyphenyl)-2-Oxoethyl)Benzamide (**3d**).* Eluent: petroleum ether/ethyl acetate (5:1). White solid (56.5 mg, 70%), mp: 106–107 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–8.03 (m, 2H), 7.87–7.90 (m, 2H), 7.51–7.55 (m, 1H), 7.44–7.48 (m, 2H), 7.36 (br s, 1H), 6.97–7.00 (m, 2H), 4.90 (d, J = 4.0 Hz, 2H), 3.89 (s, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 192.6, 167.4, 164.4, 134.0, 131.7, 130.4, 128.6, 127.4, 127.2, 114.2, 55.6, 46.5. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{16}H_{15}NNaO_3^+$ 292.0944; found, 292.0940.

*N-(2-(4-Fluorophenyl)-2-Oxoethyl)Benzamide (**3e**).* Eluent: petroleum ether/ethyl acetate (5:1). White solid (55.5 mg, 72%), mp: 154–156 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03–8.08 (m, 2H), 7.87–7.90 (m, 2H), 7.53 (tt, J_1 = 7.2 Hz, J_2 = 2.0 Hz, 1H), 7.44–7.48 (m, 2H), 7.33 (br s, 1H), 7.16–7.21 (m, 2H), 4.92 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 192.8, 167.4, 166.4 (d,$^1J_{C\text{-}F}$ = 254.9 Hz), 133.8, 131.8, 130.9 (d,$^4J_{C\text{-}F}$ = 3.3 Hz), 130.8 (d,$^3J_{C\text{-}F}$ = 8.9 Hz), 128.7, 127.2, 116.2 (d,$^2J_{C\text{-}F}$ = 21.8 Hz), 46.8. ^{19}F NMR (565 MHz, $CDCl_3$) δ −102.78. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{15}H_{12}FNNaO_2^+$ 280.0744; found, 280.0735.

*N-(2-(4-Chlorophenyl)-2-Oxoethyl)Benzamide (**3f**).* Eluent: petroleum ether/ethyl acetate (5:1). White solid (63.1 mg, 77%), mp: 150–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.97 (m, 2H), 7.86–7.88 (m, 2H), 7.43–7.55 (m, 5H), 7.31 (br s, 1H), 4.92 (d, J = 4.0 Hz, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 193.3, 167.4, 140.8, 133.8, 132.7, 131.9, 129.40, 129.37, 128.7, 127.2, 46.9. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{15}H_{12}ClNNaO_2^+$ 296.0449; found, 296.0444.

*N-(2-(4-Bromophenyl)-2-Oxoethyl)Benzamide (**3g**).* Eluent: petroleum ether/ethyl acetate (5:1). White solid (74.2 mg, 78%), mp: 149–150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 4H), 7.65 (d, J = 8.4 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.2 Hz, 2H), 7.31 (br s, 1H), 4.91 (d, J = 4.0 Hz, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 193.5, 167.4, 133.8, 133.1, 132.4, 131.9, 129.6, 129.5, 128.7, 127.2, 46.8. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{15}H_{12}BrNNaO_2^+$ 339.9944; found, 339.9926.

*N-(2-Oxo-2-(4-(Trifluoromethyl)Phenyl)Ethyl)Benzamide (**3h**).* Eluent: petroleum ether/ethyl acetate (5:1). White solid (60.8 mg, 66%), mp: 167–168 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.0 Hz, 2H), 7.87–7.89 (m, 2H), 7.79 (d, J = 8.4 Hz, 2H), 7.53–7.56 (m, 1H), 7.47 (t, J = 6.8 Hz, 2H), 7.27 (s, 1H), 4.99 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 193.6, 167.5, 137.0, 135.5 (q,$^2J_{C\text{-}F}$ = 32.7 Hz), 133.7, 131.9, 128.7, 128.4, 127.2, 126.1 (q,$^3J_{C\text{-}F}$ = 3.3 Hz), 123.4 (q,$^1J_{C\text{-}F}$ = 271.2 Hz), 47.2. ^{19}F NMR (376 MHz,$CDCl_3$) δ −63.27. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{16}H_{12}F_3NNaO_2^+$ 330.0712; found, 330.0709.

*N-(2-([1,1′-Biphenyl]-4-yl)-2-Oxoethyl)Benzamide (**3i**).* Eluent: petroleum ether/ethyl acetate (3:1). Yellow solid (64.3 mg, 68%), mp: 168–170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07–8.09 (m, 2H), 8.88–8.91 (m, 2H), 7.71 (m, 2H), 7.60–7.63 (m, 2H), 7.50–7.54 (m, 1H), 7.37–7.49 (m, 6H), 4.97 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 193.9, 167.5, 146.9, 139.5, 133.9, 133.1,

https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX–XXX

131.8, 129.1, 128.7, 128.64, 128.57, 127.6, 127.3, 127.2, 47.0. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{21}H_{17}NNaO_2^+$ 338.1151; found, 338.1138.

*N-(2-(4-Formylphenyl)-2-Oxoethyl)Benzamide (**3j**)*. Eluent: petroleum ether/ethyl acetate (1:1). Orange solid (46.4 mg, 58%), mp: 120−122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.13 (s, 1H), 8.18 (d, J = 8.4 Hz, 2H), 8.02−8.04 (m, 2H), 7.87−7.89 (m, 2H), 7.54 (tt, J_1 = 7.2 Hz, J_2 = 2.0 Hz, 1H), 7.45−7.49 (m, 2H), 7.29 (br s, 1H), 5.00 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.0, 191.4, 167.5, 139.8, 138.5, 133.7, 132.0, 130.1, 128.7, 128.6, 127.2, 47.3. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{13}NNaO_3^+$ 290.0788; found, 290.0777.

*4-(Benzoylglycyl)Phenyl Acetate (**3k**)*. Eluent: petroleum ether/ethyl acetate (1:1). White solid (59.7 mg, 67%), mp: 145−147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−8.05 (m, 2H), 7.86−7.89 (m, 2H), 7.49−7.53 (m, 1H), 7.42−7.46 (m, 2H), 7.36 (br s, 1H), 7.22−7.26 (m, 2H), 4.91 (d, J = 4.4 Hz, 2H), 2.32 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 193.1, 168.7, 167.4, 155.2, 133.9, 131.9, 131.8, 129.7, 128.6, 127.2, 122.3, 46.8, 21.1. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{15}NNaO_4^+$ 320.0893; found, 320.0884.

*N-(2-Oxo-2-(m-Tolyl)Ethyl)Benzamide (**3l**)*. Eluent: petroleum ether/ethyl acetate (5:1). White solid (57.7 mg, 76%), mp: 105−106 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87−7.90 (m, 2H), 7.80−7.83 (m, 2H), 7.50−7.54 (m, 1H), 7.43−7.47 (m, 3H), 7.36−7.41 (m, 2H), 4.93 (d, J = 4.0 Hz, 2H), 2.42 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.5, 167.4, 138.9, 135.0, 134.4, 134.0, 131.8, 128.9, 128.6, 128.5, 127.2, 125.2, 46.9, 21.3. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{15}NNaO_2^+$ 276.0995; found, 276.0994.

*N-(2-Oxo-2-(o-Tolyl)Ethyl)Benzamide (**3m**)*. Eluent: petroleum ether/ethyl acetate (5:1). White solid (45.6 mg, 60%), mp: 107−108 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88−7.91 (m, 2H), 7.80 (d, J = 8.0 Hz, 2H), 7.52 (tt, J_1 = 7.2 Hz, J_2 = 2.4 Hz, 1H), 7.44−7.47 (m, 3H), 7.29−7.34 (m, 3H), 4.86 (d, J = 4.4 Hz, 2H), 2.58 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 197.0, 167.4, 139.7, 134.1, 134.0, 132.8, 132.5, 131.8, 128.9, 128.6, 127.2, 126.2, 48.3, 21.8. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{15}NNaO_2^+$ 276.0995; found, 276.0996.

*N-(2-(3,4-Dimethoxyphenyl)-2-Oxoethyl)Benzamide (**3n**)*. Eluent: petroleum ether/ethyl acetate (3:1). Yellowish solid (59.2 mg, 66%), mp: 151−152 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, J = 7.2 Hz, 2H), 7.66 (d, J = 8.4 Hz, 1H), 7.51−7.54 (m, 2H), 7.46 (t, J = 7.2 Hz, 2H), 7.38 (br s, 1H), 6.93 (d, J = 8.4 Hz, 1H), 4.91 (d, J = 3.6 Hz, 2H), 3.95 (d, J = 8.4 Hz, 6H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 192.7, 167.4, 154.2, 149.3, 134.0, 131.7, 128.6, 127.5, 127.1, 122.8, 110.4, 109.9, 56.2, 56.1, 46.5. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{17}NNaO_4^+$ 322.1050; found, 322.1039.

*N-(2-(Naphthalen-2-yl)-2-Oxoethyl)Benzamide (**3o**)*. Eluent: petroleum ether/ethyl acetate (3:1). Brown solid (59.8 mg, 69%), mp: 117−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.04 (dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.87−7.93 (m, 4H), 7.51−7.65 (m, 3H), 7.44−7.48 (m, 2H), 7.39 (br s, 1H), 5.08 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.2, 167.5, 136.1, 134.0, 132.5, 131.8, 131.7, 130.1, 129.8, 129.1, 128.9, 128.7, 127.9, 127.2, 123.2, 47.0. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{19}H_{15}NNaO_2^+$ 312.0995; found, 312.0987.

*N-(2-Oxo-2-(Thiophen-2-yl)Ethyl)Benzamide (**3p**)*. Eluent: petroleum ether/ethyl acetate (3:1). White solid (55.9 mg, 76%), mp: 149−150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.88 (m, 3H), 7.72 (dd, J_1 = 5.2 Hz, J_2 = 0.8 Hz, 1H), 7.50−7.53 (m, 1H), 7.44 (t, J = 6.8 Hz, 2H), 7.29 (br s, 1H), 7.17−7.19 (m, 1H), 4.88 (d, J = 4.8 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 187.4, 167.4, 140.9, 134.7, 133.8, 132.7, 131.8, 128.65, 128.57, 127.2, 46.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{11}NNaO_2S^+$ 268.0403; found, 268.0396.

*N-(2-Oxo-2-(Pyridin-3-yl)Ethyl)Benzamide (**3q**)*. Eluent: petroleum ether/ethyl acetate (1:2). White solid (37.5 mg, 52%), mp: 127−128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (d, J = 1.6 Hz, 1H), 8.84 (dd, J_1 = 4.8 Hz, J_2 = 2.0 Hz, 1H), 8.28 (dt, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 7.87−7.89 (m, 2H), 7.53 (tt, J_1 = 7.2 Hz, J_2 = 2.0 Hz, 1H), 7.43−7.49 (m, 3H), 7.37 (br s, 1H), 4.97 (d, J = 4.8 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 193.7, 167.5, 154.5, 149.4, 135.3, 133.7, 131.9, 130.0, 128.7, 127.2, 123.9, 47.0. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{13}N_2O_2^+$ 241.0972; found, 241.0972.

*N-(2-Oxodecyl)Benzamide (**3r**)*. Eluent: petroleum ether/ethyl acetate (5:1). White solid (54.5 mg, 66%), mp: 89−90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81−7.83 (m, 2H), 7.49−7.53 (m, 1H), 7.41−7.45 (m, 2H), 7.08 (br s, 1H), 4.33 (d, J = 4.4 Hz, 2H), 2.50 (t, J = 7.6 Hz, 2H), 1.61−1.66 (m, 2H), 1.28 (d, J = 6.8 Hz, 10H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 205.8, 167.3, 133.8, 131.7, 128.6, 127.1, 49.6, 40.4, 31.8, 29.3, 29.2, 29.1, 23.8, 22.6, 14.1. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{25}NNaO_2^+$ 298.1778; found, 298.1767.

*4-Methyl-N-(2-Oxo-2-Phenylethyl)Benzamide (**3s**)*. Eluent: petroleum ether/ethyl acetate (5:1). White solid (53.2 mg, 70%), mp: 122−124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.64 (t, J = 7.2 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H), 7.25−7.29 (m, 3H), 4.95 (d, J = 4.4 Hz, 2H), 2.41 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.4, 167.4, 142.2, 134.4, 134.3, 131.1, 129.3, 129.0, 128.0, 127.2, 46.9, 21.5. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{15}NNaO_2^+$ 276.0995; found, 276.0988.

*4-(tert-Butyl)-N-(2-Oxo-2-Phenylethyl)Benzamide (**3t**)*. Eluent: petroleum ether/ethyl acetate (5:1). Yellowish solid (70.8 mg, 80%), mp: 136−137 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 7.64 (t, J = 7.6 Hz, 1H), 7.47−7.54 (m, 4H), 7.30 (br s, 1H), 4.97 (d, J = 4.0 Hz, 2H), 1.35 (s, 9H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.4, 167.4, 155.3, 134.4, 134.3, 131.1, 129.0, 128.0, 127.0, 125.6, 46.9, 35.0, 31.2. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{19}H_{21}NNaO_2^+$ 318.1465; found, 318.1454.

*4-Methoxy-N-(2-Oxo-2-Phenylethyl)Benzamide (**3u**)*. Eluent: petroleum ether/ethyl acetate (3:1).[12] Yellowish solid (59.7 mg, 74%), mp: 133−135 °C (lit.[12] 133−134 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, J = 7.2 Hz, 2H), 7.85−7.87 (m, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.8 Hz, 2H), 7.21 (br s, 1H), 6.95−6.97 (m, 2H), 4.96 (d, J = 4.2 Hz, 2H), 3.87 (s, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 194.5, 166.9, 162.4, 134.4, 134.3, 129.0, 128.0, 126.2, 113.8, 55.4, 46.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{15}NNaO_3^+$ 292.0944; found, 292.0935.

*4-Fluoro-N-(2-Oxo-2-Phenylethyl)Benzamide (**3v**)*. Eluent: petroleum ether/ethyl acetate (5:1). White solid (57.8 mg, 75%), mp: 124−126 °C (lit.[13] 122−126 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.0 Hz, 2H), 7.90 (dd, J_1 = 8.4 Hz, J_2 = 5.6 Hz, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 8.0 Hz, 2H), 7.29 (br s, 1H), 7.14 (t, J = 8.4 Hz, 2H), 4.95 (d, J = 4.0 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.3, 166.3, 164.9 (d, $^1J_{C-F}$ = 250.7 Hz), 134.34, 134.32, 130.1 (d, $^4J_{C-F}$ = 2.8 Hz), 129.5 (d, $^3J_{C-F}$ = 8.6 Hz), 129.0, 128.0, 115.7 (d, $^2J_{C-F}$ = 21.7 Hz), 46.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ −107.76. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{12}FNNaO_2^+$ 280.0744; Found 280.0743.

*4-Chloro-N-(2-Oxo-2-Phenylethyl)Benzamide (**3w**)*. Eluent: petroleum ether/ethyl acetate (5:1). White solid (59.0 mg, 72%), mp: 139−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 7.6 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 7.66 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 7.29 (br s, 1H), 4.95 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.2, 166.3, 138.1, 134.4, 134.3, 132.3, 129.1, 128.9, 128.6, 128.0, 46.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{12}ClNNaO_2^+$ 296.0449; found, 296.0442.

*4-Bromo-N-(2-Oxo-2-Phenylethyl)Benzamide (**3x**)*. Eluent: petroleum ether/ethyl acetate (5:1). White solid (69.4 mg, 73%), mp: 150−151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.0 Hz, 2H), 7.76 (d, J = 8.4 Hz, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.53 (t, J = 7.6 Hz, 2H), 7.31 (br s, 1H), 4.95 (d, J = 4.0 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.1, 166.4, 134.4, 134.3, 132.7, 131.9, 129.1, 128.8, 128.0, 126.6, 46.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{12}BrNNaO_2^+$ 339.9944; found, 339.9929.

*4-Iodo-N-(2-Oxo-2-Phenylethyl)Benzamide (**3y**)*. Eluent: petroleum ether/ethyl acetate (3:1). White solid (63.5 mg, 58%), mp: 171−173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01−8.03 (m, 2H), 7.80−7.82 (m, 2H), 7.60−7.67 (m, 3H), 7.52 (t, J = 7.6 Hz, 2H), 7.31 (br s, 1H), 4.94 (d, J = 4.0 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.2, 166.6, 137.9, 134.4, 134.3, 133.3, 129.0, 128.8, 128.0,

https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX−XXX

98.9, 46.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{12}INNaO_2^+$ 387.9805; found, 387.9806.

N-(2-Oxo-2-Phenylethyl)-4-(Trifluoromethyl)Benzamide (**3z**). Eluent: petroleum ether/ethyl acetate (2:1). White solid (64.5 mg, 70%), mp: 171−173 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, J = 7.2 Hz, 2H), 8.00 (d, J = 7.2 Hz, 2H), 7.74 (d, J = 7.8 Hz, 2H), 7.66−7.67 (m, 1H), 7.55−7.56 (m, 2H), 7.36 (br s, 1H), 4.98 (d, J = 3.0 Hz, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 194.0, 166.1, 137.2, 134.5, 134.2, 133.5 (q, $^2J_{C\text{-}F}$ = 32.9 Hz), 129.1, 128.0, 127.7, 125.7 (q, $^3J_{C\text{-}F}$ = 4.5 Hz), 123.7 (q, $^1J_{C\text{-}F}$ = 271.4 Hz), 46.9. ^{19}F NMR (565 MHz, $CDCl_3$) δ −62.95. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{12}F_3NNaO_2^+$ 330.0712; found, 330.0701.

4-Nitro-N-(2-Oxo-2-Phenylethyl)Benzamide (**3aa**). Eluent: petroleum ether/ethyl acetate (2:1). White solid (58.8 mg, 69%), mp: 170−172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 8.4 Hz, 2H), 8.05 (t, J = 7.0 Hz, 4H), 7.68 (t, J = 7.2 Hz, 1H), 7.55 (t, J = 7.6 Hz, 2H), 7.39 (br s, 1H), 4.98 (d, J = 3.6 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 193.8, 165.3, 149.9, 139.4, 134.6, 134.1, 129.1, 128.4, 128.1, 123.9, 47.0. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{12}N_2NaO_4^+$ 307.0689; found, 307.0685.

3-Chloro-N-(2-Oxo-2-Phenylethyl)Benzamide (**3ab**). Eluent: petroleum ether/ethyl acetate (5:1). White solid (62.3 mg, 76%), mp: 134−135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.0 Hz, 2H), 7.88 (s, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.52 (q, J = 7.6 Hz, 3H), 7.40 (t, J = 7.6 Hz, 1H), 7.31 (br s, 1H), 4.95 (d, J = 4.0 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.1, 166.1, 135.7, 134.9, 134.4, 134.3, 131.8, 130.0, 129.0, 128.0, 127.6, 125.2, 46.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{12}ClNNaO_2^+$ 296.0449; found, 296.0441.

2-Chloro-N-(2-Oxo-2-Phenylethyl)Benzamide (**3ac**). Eluent: petroleum ether/ethyl acetate (5:1). White solid (73.7 mg, 90%), mp: 100−102 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 2H), 7.73 (d, J = 7.2 Hz, 1H), 7.64 (t, J = 7.2 Hz, 1H), 7.52 (t, J = 8.0 Hz, 2H), 7.42−7.44 (m, 2H), 7.32−7.40 (m, 2H), 4.99 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 193.8, 166.5, 134.5, 134.3, 131.6, 131.1, 130.4, 130.3, 129.00, 128.0, 127.1, 47.1. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{12}ClNNaO_2^+$ 296.0449; found, 296.0439.

2-Bromo-N-(2-Oxo-2-Phenylethyl)Benzamide (**3ad**). Eluent: petroleum ether/ethyl acetate (5:1). White solid (86.5 mg, 91%), mp: 104−106 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (d, J = 7.2 Hz, 2H), 7.59−7.65 (m, 3H), 7.51 (t, J = 7.8 Hz, 2H), 7.36 (t, J = 7.2 Hz, 1H), 7.27−7.30 (m, 1H), 7.24 (br s, 1H), 4.97 (d, J = 4.2 Hz, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 193.7, 167.6, 137.2, 134.3, 133.5, 131.5, 129.7, 129.0, 128.0, 127.6, 119.6, 47.0. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{12}BrNNaO_2^+$ 339.9944; found, 339.9936.

2-Iodo-N-(2-Oxo-2-Phenylethyl)Benzamide (**3ae**). Eluent: petroleum ether/ethyl acetate (4:1). White solid (96.4 mg, 88%), mp: 107−108 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.6 Hz, 2H), 7.85 (d, J = 7.6 Hz, 1H), 7.62 (t, J = 7.2 Hz, 1H), 7.45−7.52 (m, 3H), 7.36 (t, J = 7.6 Hz, 1H), 7.08 (td, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 2H), 4.94 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 193.8, 169.3, 141.6, 140.0, 134.3, 131.3, 129.0, 128.5, 128.2, 128.0, 92.7, 46.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{12}INNaO_2^+$ 387.9805; found, 387.9805.

2,4,6-Trimethyl-N-(2-Oxo-2-Phenylethyl)Benzamide (**3af**). Eluent: petroleum ether/ethyl acetate (5:1). White solid (63.3 mg, 75%), mp: 148−150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.6 Hz, 2H), 7.64 (t, J = 7.2 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H), 6.86 (s, 2H), 6.74 (br s, 1H), 4.98 (d, J = 4.4 Hz, 2H), 2.31 (s, 6H), 2.29 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.0, 170.9, 138.7, 134.41, 134.38, 134.3, 129.0, 128.3, 128.0, 46.4, 21.1, 19.2. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{18}H_{19}NNaO_2^+$ 304.1308; found, 304.1300.

N-(2-Oxo-2-Phenylethyl)-1-Naphthamide (**3ag**). Eluent: petroleum ether/ethyl acetate (5:1). Yellowish solid (78.0 mg, 90%), mp: 124−126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 8.0 Hz, 2H), 7.93 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 6.8 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.45−7.58 (m, 5H), 7.14 (br s, 1H), 5.04 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.1, 169.6, 134.4, 134.3, 133.8, 133.7, 131.0, 130.2, 129.0, 128.4, 128.0, 127.3, 126.5, 125.52, 125.47, 124.8, 46.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{19}H_{15}NNaO_2^+$ 312.0995; found, 312.0985.

N-(2-Oxo-2-Phenylethyl)Furan-2-Carboxamide (**3ah**). Eluent: petroleum ether/ethyl acetate (5:1). Yellowish solid (58.4 mg, 85%), mp: 138−139 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, J = 7.2 Hz, 2H), 7.62 (t, J = 7.8 Hz, 1H), 7.46−7.51 (m, 4H), 7.15 (d, J = 3.6 Hz, 1H), 6.51 (q, J = 1.8 Hz, 1H), 4.92 (d, J = 4.8 Hz, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 193.9, 158.4, 147.7, 144.3, 134.4, 134.2, 128.9, 128.0, 114.5, 112.1, 46.1. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{11}NNaO_3^+$ 252.0631; found, 252.0628.

N-(2-Oxo-2-Phenylethyl)Thiophene-2-Carboxamide (**3ai**). Eluent: petroleum ether/ethyl acetate (5:1). Yellowish solid (69.1 mg, 94%), mp: 140−141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.0 Hz, 2H), 7.62−7.66 (m, 2H), 7.50−7.53 (m, 3H), 7.19 (br s, 1H), 7.10 (t, J = 4.4 Hz, 1H), 4.94 (d, J = 4.0 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.1, 161.9, 138.3, 134.3, 130.4, 129.0, 128.6, 128.0, 127.8, 46.8. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{11}NNaO_2S^+$ 268.0403; found, 268.0403.

N-(2-Oxo-2-Phenylethyl)Nicotinamide (**3aj**). Eluent: petroleum ether/ethyl acetate (1:1). Brown solid (37.5 mg, 52%), mp: 129−130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (d, J = 1.6 Hz, 1H), 8.76 (dd, J_1 = 4.4 Hz, J_2 = 1.2 Hz, 1H), 8.19 (dt, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 1H), 8.02−8.05 (m, 2H), 7.66 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.6 Hz, 2H), 7.40−7.43 (m, 2H), 4.98 (d, J = 4.0 Hz, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 194.0, 165.6, 152.5, 148.3, 135.1, 134.4, 134.2, 129.6, 129.1, 128.0, 123.5, 46.8. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{13}N_2O_2^+$ 241.0972; found, 241.0980.

2-Oxo-N-(2-Oxo-2-Phenylethyl)-2H-Chromene-3-Carboxamide (**3ak**). Eluent: petroleum ether/ethyl acetate (1:1). Brown solid (37.8 mg, 41%), mp: 192−193 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (br s, 1H), 8.93 (s, 1H), 8.03−8.05 (m, 2H), 7.62−7.71 (m, 3H), 7.52 (t, J = 7.2 Hz, 2H), 7.43 (d, J = 8.4 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 4.98 (d, J = 4.8 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 193.4, 161.8, 161.1, 154.6, 148.5, 134.7, 134.2, 134.0, 129.9, 128.9, 128.0, 125.3, 118.6, 118.3, 116.8, 47.0. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{18}H_{13}NNaO_4^+$ 330.0737; found, 330.0730.

N-(2-Oxo-2-Phenylethyl)Cinnamamide (**3al**). Eluent: petroleum ether/ethyl acetate (5:1). Yellowish solid (56.5 mg, 71%), mp: 133−134 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, J = 7.8 Hz, 2H), 7.69 (d, J = 16.2 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.47−7.52 (m, 4H), 7.34−7.36 (m, 3H), 6.98 (br s, 1H), 6.62 (d, J = 15.6 Hz, 1H), 4.92 (d, J = 4.2 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.4, 166.0, 141.6, 134.8, 134.4, 134.2, 129.8, 129.0, 128.8, 128.0, 127.9, 120.2, 46.8. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{15}NNaO_2^+$ 288.0995; found, 288.0983.

N-(2-Oxo-2-Phenylethyl)-2-Phenylacrylamide (**3am**). Eluent: petroleum ether/ethyl acetate (5:1). Orange solid (54.1 mg, 68%), mp: 77−79 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.97 (m, 2H), 7.59−7.63 (m, 1H), 7.36−7.50 (m, 7H), 6.84 (br s, 1H), 6.20 (d, J = 0.8 Hz, 1H), 5.69 (d, J = 0.8 Hz, 1H), 4.85 (d, J = 4.4 Hz, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 194.0, 167.4, 144.4, 136.8, 134.4, 134.2, 129.0, 128.8, 128.7, 128.2, 128.0, 122.6, 46.8. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{15}NNaO_2^+$ 288.0995; found, 288.0989.

N-(2-Oxo-2-Phenylethyl)-3-Phenylpropiolamide (**3an**). Eluent: petroleum ether/ethyl acetate (3:1). Yellow solid (69.5 mg, 88%), mp: 147−149 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 2H), 7.62 (t, J = 7.2 Hz, 1H), 7.54−7.55 (m, 2H), 7.49 (t, J = 7.8 Hz, 2H), 7.40−7.42 (m, 1H), 7.34 (t, J = 7.2 Hz, 2H), 7.21 (br s, 1H), 4.86 (d, J = 4.2 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 193.3, 153.4, 134.3, 134.2, 132.6, 130.2, 129.0, 128.6, 128.0, 120.1, 85.5, 82.7, 46.7. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{13}NNaO_2^+$ 286.0838; found, 286.0835.

N-(2-Oxo-2-Phenylethyl)Formamide (**3ao**). Eluent: petroleum ether/ethyl acetate (1:1). Yellowish solid (36.7 mg, 75%), mp: 74−75 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.98 (d, J = 7.2 Hz, 2H), 7.64 (t, J = 7.8 Hz, 1H), 7.51 (t, J = 7.8 Hz, 2H), 6.92 (br s, 1H), 4.82 (d, J = 4.2 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ

https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX−XXX

193.6, 161.3, 134.3, 134.2, 129.0, 128.0, 45.0. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_9H_9NNaO_2^+$ 186.0525; found, 186.0527.

*N-(2-Oxo-2-Phenylethyl)Acetamide (**3ap**).* Eluent: petroleum ether/ethyl acetate (1:1). Yellowish solid (35.1 mg, 66%), mp: 85−86 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.99 (m, 2H), 7.62 (tt, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 6.75 (br s, 1H), 4.78 (d, J = 4.4 Hz, 2H), 2.11 (s, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 194.3, 170.4, 134.4, 134.2, 128.9, 127.9, 46.6, 23.0. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{10}H_{11}NNaO_2^+$ 200.0682; found, 200.0680.

*N-(2-Oxo-2-Phenylethyl)Pivalamide (**3aq**).* Eluent: petroleum ether/ethyl acetate (3:1). Brown oil (50.6 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.99 (m, 2H), 7.60−7.64 (m, 1H), 7.50 (t, J = 7.6 Hz, 2H), 6.82 (br s, 1H), 4.74 (d, J = 4.4 Hz, 2H), 1.28 (s, 9H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 194.5, 178.7, 134.5, 134.1, 128.9, 127.9, 46.5, 38.8, 27.6. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{17}NNaO_2^+$ 242.1151; found 242.1152.

*N-(2-Oxo-2-Phenylethyl)Hexanamide (**3ar**).* Eluent: petroleum ether/ethyl acetate (3:1). Yellowish solid (43.4 mg, 62%), mp: 69−71 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−8.00 (m, 2H), 7.60−7.64 (m, 1H), 7.50 (t, J = 7.6 Hz, 2H), 6.65 (br s, 1H), 4.78 (d, J = 4.0 Hz, 2H), 2.31 (t, J = 8.0 Hz, 2H), 1.66−1.73 (m, 2H), 1.32−1.37 (m, 4H), 0.89−0.92 (m, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 194.5, 173.4, 134.4, 134.1, 128.9, 127.9, 46.4, 36.5, 31.5, 25.4, 22.4, 13.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{19}NNaO_2^+$ 256.1308; found, 256.1306.

*N-(2-Oxo-2-Phenylethyl)Cyclohexanecarboxamide (**3as**).* Eluent: petroleum ether/ethyl acetate (3:1). Yellowish solid (50.7 mg, 69%), mp: 111−113 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.99 (m, 2H), 7.62 (tt, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 6.63 (br s, 1H), 4.76 (d, J = 4.4 Hz, 2H), 2.25 (tt, J_1 = 12.0 Hz, J_2 = 3.6 Hz, 1H), 1.93 (dd, J_1 = 13.2 Hz, J_2 = 1.6 Hz, 2H), 1.80−1.84 (m, 2H), 1.67−1.71 (m, 1H), 1.50 (qd, J_1 = 12.0 Hz,J_2 = 3.2 Hz, 2H), 1.21−1.36 (m, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 194.6, 176.3, 134.5, 134.1, 128.9, 127.9, 46.3, 45.3, 29.7, 25.75, 25.72. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{19}NNaO_2^+$ 268.1308; found, 268.1303.

*(3R,5R,7R)-N-(2-Oxo-2-Phenylethyl)Adamantane-1-Carboxamide (**3at**).* Eluent: petroleum ether/ethyl acetate (3:1). Yellowish solid (58.8 mg, 66%), mp: 127−128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−8.00 (m, 2H), 7.60−7.64 (m, 1H), 7.50 (t, J = 7.2 Hz, 2H), 6.78 (br s, 1H), 4.74 (d, J = 4.4 Hz, 2H), 2.07 (s, 3H), 1.94 (d, J = 2.8 Hz, 6H), 1.71−1.79 (m, 6H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 194.7, 178.2, 134.5, 134.1, 128.9, 127.9, 46.3, 40.8, 39.2, 36.5, 28.1. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{19}H_{23}NNaO_2^+$ 320.1621; found 320.1612.

*2-Cyano-N-(2-Oxo-2-Phenylethyl)Acetamide (**3au**).* Eluent: petroleum ether/ethyl acetate (5:1). Yellowish solid (47.3 mg, 78%), mp: 156−157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.99 (m, 2H), 7.66 (t, J = 7.6 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 7.14 (br s, 1H), 4.80 (d, J = 4.4 Hz, 2H), 3.50 (s, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 193.0, 161.1, 134.6, 134.0, 129.1, 128.0, 114.2, 46.8, 25.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{11}H_{10}N_2NaO_2^+$ 225.0634; found 225.0634.

*2-Acetamido-N-(2-Oxo-2-Phenylethyl)Acetamide (**3av**).* Eluent: petroleum ether/ethyl acetate (1:2). White solid (38.6 mg, 55%), mp: 177−178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96−7.98 (m, 2H), 7.63 (tt, J_1 = 7.6 Hz, J_2 = 2.0 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.15 (br s, 1H), 6.56 (br s, 1H), 4.78 (d, J = 4.4 Hz, 2H), 4.08 (d, J = 5.2 Hz, 2H), 2.08 (s, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 193.8, 170.8, 169.2, 134.30, 134.27, 129.0, 128.0, 46.4, 43.1, 23.0. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{12}H_{14}N_2NaO_3^+$ 257.0897; found 257.0893.

*(R)-4-((5S,8R,9S,10S,13R,14S,17R)-10,13-Dimethyl-3,7,12-Trioxohexadecahydro-1H-Cyclopenta[a]Phenanthren-17-yl)-N-(2-Oxo-2-Phenylethyl)Pentanamide (**3aw**).* Eluent: petroleum ether/ethyl acetate (1:1). White solid (101.3 mg, 65%), mp: 189−190 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.99 (m, 2H), 7.62 (t, J = 7.2 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 6.67 (t, J = 4.0 Hz, 1H), 4.77 (d, J = 4.4 Hz, 2H), 2.82−2.95 (m, 3H), 2.11−2.46 (m, 10H), 1.81−2.04 (m, 6H), 1.62 (td, J_1 = 14.4 Hz, J_2 = 4.4 Hz, 1H), 1.21−1.50 (m, 7H), 1.08 (s, 3H), 0.88 (d, J = 6.4 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 212.0, 209.2, 208.8, 194.4, 173.6, 134.4, 134.1, 128.9, 127.9, 56.9, 51.7, 49.0, 46.8, 46.4, 45.6, 45.5, 45.0, 42.8, 38.6, 36.5, 36.0, 35.6, 35.2, 33.5, 31.1, 27.6, 25.1, 21.9, 18.8, 11.9. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{32}H_{41}NNaO_5^+$ 542.2877; found, 542.2869.

*(2S,4aS,6aS,6bR,8aR,10S,12aS,12bR,14bR)-10-Hydroxy-2,4a,6a,6b,9,9,12a-Heptamethyl-13-Oxo-N-(2-Oxo-2-Phenylethyl)-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-Icosahydropicene-2-Carboxamide (**3ax**).* Eluent: petroleum ether/ethyl acetate (1:1). Yellowish solid (142.6 mg, 81%), mp: 143−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−8.00 (m, 2H), 7.61 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 8.0 Hz, 2H), 6.86 (t, J = 4.4 Hz, 1H), 5.78 (s, 1H), 4.77 (qd, J_1 = 12.8 Hz, J_2 = 4.0 Hz, 2H), 3.23 (dd, J_1 = 11.2 Hz, J_2 = 5.2 Hz, 1H), 2.77−2.81 (m, 1H), 2.35 (s. 1H), 2.26 (dd, J_1 = 13.2 Hz, J_2 = 3.2 Hz, 1H), 1.58−2.08 (m, 10H), 1.40−1.46 (m, 8H), 1.18−1.25 (m, 4H), 1.12 (d. J = 5.2 Hz, 6H), 0.96−1.05 (m, 5H), 0.81 (d, J = 0.4 Hz, 6H), 0.70 (d, J = 11.2 Hz, 1H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 200.1, 194.6, 176.2, 169.0, 134.5, 134.1, 128.9, 128.6, 128.0, 78.6, 61.8, 54.9, 47.9, 46.3, 45.4, 43.8, 43.2, 41.6, 39.2, 39.1, 37.5, 37.1, 32.8, 31.9, 31.5, 29.6, 28.4, 28.2, 27.3, 26.5, 26.4, 23.4, 18.7, 17.5, 16.4, 15.7. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{38}H_{54}NO_4^+$ 588.4047; found, 588.4030.

*6-(3-((3r,5r,7r)-Adamantan-1-yl)-4-Methoxyphenyl)-N-(2-Oxo-2-Phenylethyl)-2-Naphthamide (**3ay**).* Eluent: petroleum ether/ethyl acetate (3:1). Brown solid (87.3 mg, 55%), mp: 200−202 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.00−8.05 (m, 3H), 7.93−7.98 (m, 3H), 7.79 (dd, J_1 = 8.8 Hz, J_2 = 1.6 Hz, 1H), 7.60−7.63 (m, 2H), 7.47−7.54 (m, 4H), 6.98 (d, J = 8.4 Hz, 1H), 5.00 (d, J = 4.4 Hz, 2H), 3.88 (s, 3H), 2.19 (s, 6H), 2.11 (s, 3H), 1.80 (s, 6H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.4, 167.5, 158.9, 140.9, 139.0, 135.4, 134.4, 134.3, 132.6, 131.4, 130.6, 129.4, 129.0, 128.6, 128.1, 127.6, 126.6, 126.0, 125.7, 124.7, 124.0, 112.1, 55.2, 47.1, 40.7, 37.24, 37.17, 29.2. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{36}H_{35}NNaO_3^+$ 552.2509; found, 552.2503.

*4-([1,1′-Biphenyl]-4-yl)-4-Oxo-N-(2-Oxo-2-Phenylethyl)-Butanamide (**3az**).* Eluent: petroleum ether/ethyl acetate (3:1). Pink solid (75.7 mg, 68%), mp: 169−171 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.4 Hz, 2H), 7.96−7.98 (m, 2H), 7.67 (d, J = 8.4 Hz, 2H), 7.59−7.63 (m, 3H), 7.47 (q, J = 8.4 Hz, 4H), 7.37−7.41 (m, 1H), 6.88 (br s, 1H), 4.79 (d, J = 4.4 Hz, 2H), 3.43 (t, J = 6.4 Hz, 2H), 2.80 (t, J = 6.8 Hz, 2H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$) δ 198.4, 194.2, 172.3, 145.9, 139.9, 135.3, 134.5, 134.1, 128.98, 128.95, 128.7, 128.3, 128.0, 127.30, 127.27, 46.6, 33.9, 30.1. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{24}H_{21}NNaO_3^+$ 394.1414; found, 394.1403.

*4-(N,N-Dipropylsulfamoyl)-N-(2-Oxo-2-Phenylethyl)Benzamide (**3ba**).* Eluent: petroleum ether/ethyl acetate (1:1). Yellowish solid (88.1 mg, 73%), mp: 108−109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−8.01 (m, 4H), 7.87 (d, J = 8.4 Hz, 2H), 7.64 (t, J = 7.2 Hz, 1H), 7.51 (t, J = 8.0 Hz, 3H), 4.95 (d, J = 4.8 Hz, 2H), 3.09 (t, J = 7.6 Hz, 4H), 1.50−1.59 (m, 4H), 0.87 (t, J = 7.6 Hz, 6H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.0, 166.0, 143.0, 137.3, 134.32, 134.26, 129.0, 127.98, 127.95, 127.2, 49.9, 46.9, 21.9, 11.1. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{21}H_{26}N_2NaO_4S^+$ 425.1505; found, 425.1496.

*3-(4,5-Diphenyloxazol-2-yl)-N-(2-Oxo-2-Phenylethyl)-Propanamide (**3bb**).* Eluent: petroleum ether/ethyl acetate (1:1). White solid (82.4 mg, 67%), mp: 105−106 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.2 Hz, 2H), 7.63−7.65 (m, 2H), 7.54−7.59 (m, 3H), 7.45 (d, J = 7.6 Hz, 2H), 7.28−7.36 (m, 6H), 7.08 (br s, 1H), 4.78 (d, J = 4.4 Hz, 2H), 3.24 (t, J = 7.6 Hz, 2H), 2.91 (t, J = 7.6 Hz, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 194.2, 171.5, 162.3, 145.5, 135.1, 134.4, 134.1, 132.5, 129.0, 128.9, 128.7, 128.6, 128.5, 128.1, 127.98, 127.97, 126.5, 46.6, 32.8, 24.0. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{23}N_2O_3^+$ 411.1703; found, 411.1690.

*2-(4-Isobutylphenyl)-N-(2-Oxo-2-Phenylethyl)Propanamide (**3bc**).* Eluent: petroleum ether/ethyl acetate (5:1). White solid (85.3 mg, 88%), mp: 81−82 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92−7.93 (m, 2H), 7.59 (t, J = 7.8 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 7.8 Hz, 2H), 6.51 (br s, 1H), 4.64−4.77 (m, 2H), 3.67 (q, J = 7.2 Hz, 1H), 2.46 (d, J = 6.6 Hz, 2H), 1.83−1.89 (m, 1H), 1.56 (d, J = 7.2 Hz, 3H), 0.91 (d, J = 6.6 Hz, 6H).

https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX−XXX

$^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ 194.2, 174.6, 140.8, 138.2, 134.4, 134.1, 129.7, 128.9, 127.9, 127.4, 46.7, 46.5, 45.1, 30.2, 22.4, 18.5. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{21}H_{25}NNaO_2^+$ 346.1778; found, 346.1766.

*2-(1,8-Diethyl-1,3,4,9-Tetrahydropyrano[3,4-b]Indol-1-yl)-N-(2-Oxo-2-Phenylethyl)Acetamide (**3bd**).* Eluent: petroleum ether/ethyl acetate (3:1). White solid (87.3 mg, 72%), mp: 195−196 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.97 (d, J = 7.8 Hz, 2H), 7.62 (t, J = 7.8 Hz, 1H), 7.49 (t, J = 7.8 Hz, 3H), 7.34 (d, J = 7.8 Hz, 1H), 7.03 (t, J = 7.2 Hz, 1H), 6.97 (d, J = 7.2 Hz, 1H), 4.74 (qd, J_1 = 19.2 Hz, J_2 = 4.8 Hz, 2H), 4.11 (t, J = 5.4 Hz, 2H), 3.06 (d, J = 15.6 Hz, 1H), 2.97 (d, J = 15.6 Hz, 1H), 2.79−2.92 (m, 4H), 2.11−2.17 (m, 1H), 2.00−2.06 (m, 1H), 1.30 (t, J = 7.8 Hz, 3H), 0.89 (t, J = 7.8 Hz, 3H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ 194.0, 171.4, 136.0, 134.8, 134.4, 134.2, 129.0, 128.0, 126.9, 126.3, 120.2, 119.5, 115.9, 108.1, 75.6, 60.8, 46.5, 44.6, 31.0, 24.1, 22.3, 13.9, 7.8. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{25}H_{28}N_2NaO_3^+$ 427.1992; found, 427.1977.

*2-(1-(4-Chlorobenzoyl)-5-Methoxy-2-Methyl-1H-Indol-3-yl)-N-(2-Oxo-2-Phenylethyl)Acetamide (**3be**).* Eluent: petroleum ether/ethyl acetate (1:1). Yellowish solid (109.5 mg, 77%), mp: 108−109 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, J = 7.8 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.44−7.48 (m, 4H), 6.99−6.71 (m, 2H), 6.81 (t, J = 4.2 Hz, 1H), 6.71 (dd, J_1 = 9.0 Hz, J_2 = 2.4 Hz, 1H), 4.70 (d, J = 4.2 Hz, 2H), 3.83 (s, 3H), 3.72 (s, 2H), 2.38 (s, 3H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ 193.9, 170.2, 168.3, 156.3, 139.4, 136.1, 134.3, 134.1, 133.8, 131.3, 131.1, 130.4, 129.2, 128.9, 127.9, 115.2, 112.9, 112.4, 100.9, 55.7, 46.4, 32.1, 13.5. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{27}H_{23}ClN_2NaO_4^+$ 497.1239; found, 497.1230.

*(E)-2-(5-Fluoro-2-Methyl-1-(4-(Methylsulfinyl)Benzylidene)-1H-Inden-3-yl)-N-(2-Oxo-2-Phenylethyl)Acetamide (**3bf**).* Eluent: petroleum ether/ethyl acetate (1:3). Yellow solid (110.7 mg, 78%), mp: 169−170 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.81 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.57 (d, J = 7.8 Hz, 2H), 7.48 (t, J = 7.8 Hz, 1H), 7.35 (t, J = 8.4 Hz, 2H), 7.07−7.10 (m, 2H), 6.83−6.86 (m, 2H), 6.46 (td, J_1 = 9.0 Hz, J_2 = 2.4 Hz, 1H), 4.63 (d, J = 4.8 Hz, 2H), 3.52 (s, 2H), 2.71 (s, 3H), 2.17 (s, 3H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ 194.1, 169.5, 163.4 (d, $^1J_{C-F}$ = 245.1 Hz), 146.6 (d, $^3J_{C-F}$ = 8.7 Hz), 145.5, 141.6, 139.5, 138.7, 134.3, 134.1, 132.5 (d, $^4J_{C-F}$ = 2.1 Hz), 130.3, 129.6 (d, $^4J_{C-F}$ = 2.1 Hz), 128.9, 128.6, 127.9, 123.85, 123.77 (d, $^3J_{C-F}$ = 8.9 Hz), 111.0 (d, $^2J_{C-F}$ = 23.0 Hz), 106.2 (d, $^2J_{C-F}$ = 23.0 Hz), 46.5, 43.8, 33.5, 10.6. ^{19}F NMR (565 MHz,$CDCl_3$) δ −112.45. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{28}H_{24}FNNaO_3S^+$ 496.1353; found, 496.1346.

*(8R,9S,13S,14S)-13-Methyl-17-Oxo-N-(2-Oxo-2-Phenylethyl)-7,8,9,11,12,13,14,15,16,17-Decahydro-6H-Cyclopenta[a]-Phenanthrene-3-Carboxamide (**3bg**).* Eluent: petroleum ether/ethyl acetate (1:1). White solid (89.7 mg, 72%), mp: 177−178 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.03−8.06 (m, 2H), 7.64−7.67 (m, 3H), 7.54 (t, J = 7.6 Hz, 2H), 7.39 (d, J = 8.0 Hz, 1H), 7.26 (br s, 1H), 4.97 (d, J = 4.0 Hz, 2H), 2.97−3.01 (m, 2H), 2.45−2.56 (m, 2H), 2.36 (td, J_1 = 10.8 Hz, J_2 = 3.6 Hz, 1H), 1.98−2.21 (m, 4H), 1.62−1.68 (m, 2H), 1.47−1.58 (m, 4H), 0.93 (s, 3H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ 194.4, 167.4, 143.9, 137.1, 134.4, 134.3, 131.3, 129.0, 128.0, 127.9, 125.7, 124.4, 50.5, 47.9, 46.9, 44.6, 37.9, 35.8, 31.6, 29.3, 26.3, 25.6, 21.6, 13.8. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{27}H_{29}NNaO_3^+$ 438.2040; found, 438.2026.

Structural Elaborations of 3. *Synthesis of 2,5-Diphenyloxazole (**4**) from **3a**.* To a round-bottom flask equipped with a stir bar were added *N*-(2-oxo-2-phenylethyl) benzamide (**3a**, 478 mg, 2 mmol) and acetic anhydride (5 mL) followed by dropwise addition of conc. H_2SO_4 (50 μL, 0.9 mmol) with stirring.[1c] It was then stirred at 90 °C (oil bath) under air and monitored by TLC. Upon completion, it was cooled to room temperature and diluted with water and DCM. The organic layer was separated and washed with saturated sodium bicarbonate, brine, and then dried over sodium sulfate, filtered, and concentrated under a reduced pressure. The crude mixture was purified on a silica gel column, eluting with petroleum ether/ethyl acetate (5:1) to yield **4**.

*2,5-Diphenyloxazole (**4**).* Eluent: petroleum ether/ethyl acetate (5:1). Yellowish solid (389.1 mg, 88%), mp: 73−74 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.08−8.11 (m, 2H), 7.69−7.72 (m, 2H), 7.40−7.49 (m, 6H), 7.32 (tt, J_1 = 7.2 Hz, J_2 = 2.0 Hz, 1H). $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.2, 151.3, 130.3, 129.0, 128.9, 128.5, 128.1, 127.5, 126.3, 124.2, 123.5. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{12}NO^+$ 222.0913; found, 222.0914.

*Synthesis of N-(2-Oxo-1-Phenoxy-2-Phenylethyl)Benzamide (**5**) from **3a**.* To a solution of *N*-(2-oxo-2-phenylethyl)benzamide (**3a**, 120 mg, 0.5 mmol) in ethyl acetate (3 mL) were added with phenol (236 mg, 2.5 mmol), TBAI (37 mg, 0.1 mmol), and TBHP (0.23 mL, 1.75 mmol, 70% aqueous solution).[9] The resulting mixture was stirred at 80 °C (oil bath) for 20 min. Upon completion, it was cooled to room temperature, quenched with a saturated aqueous solution of $Na_2S_2O_3$ (10 mL), and extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under a reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20:1) to give **5**.

*N-(2-Oxo-1-Phenoxy-2-Phenylethyl)Benzamide (**5**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (115.9 mg, 70%), mp: 150−151 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, J = 7.8 Hz, 2H), 7.87 (d, J = 7.8 Hz, 2H), 7.67 (d, J = 9.0 Hz, 1H), 7.62 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.43−7.49 (m, 4H), 7.30−7.34 (m, 3H), 7.23 (d, J = 8.4 Hz, 2H), 7.05 (t, J = 7.2 Hz, 1H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ 191.3, 167.3, 155.7, 134.5, 133.5, 133.2, 132.4, 129.9, 129.5, 129.0, 128.8, 127.4, 122.9, 116.7, 76.1. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{21}H_{17}NNaO_3^+$ 354.1101; found, 354.1110.

*Synthesis of 4,5-Diphenyl-2-(2-(5-Phenyloxazol-2-yl)Ethyl)-Oxazole (**6**) from **3bb**.* To a round-bottom flask equipped with a stir bar were added 3-(4,5-diphenyloxazol-2-yl) -*N*-(2-oxo-2-phenylethyl)propanamide (**3bb**, 205 mg, 0.5 mmol) and acetic anhydride (1 mL) followed by dropwise addition of conc. H_2SO_4 (10 μL, 0.18 mmol) with stirring.[1c] It was then stirred at 90 °C (oil bath) under air and monitored by TLC. Upon completion, it was cooled to room temperature and diluted with water and DCM. The organic layer was separated and washed with saturated sodium bicarbonate, brine, and then dried over sodium sulfate, filtered, and concentrated under a reduced pressure. The crude mixture was purified on a silica gel column, eluting with petroleum ether/ethyl acetate (5:1) to yield **6**.

*4,5-Diphenyl-2-(2-(5-Phenyloxazol-2-yl)Ethyl)Oxazole (**6**).* Eluent: petroleum ether/ethyl acetate (5:1). Yellowish solid (147.0 mg, 75%), mp: 108−110 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.64 (d, J = 7.2 Hz, 2H), 7.57 (m, 4H), 7.27−7.37 (m, 9H), 7.25 (s, 1H), 3.41 (t, J = 13.2 Hz, 4H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ 162.4, 161.5, 151.4, 145.6, 135.3, 132.5, 129.0, 128.9, 128.7, 128.6, 128.5, 128.3, 128.14, 128.05, 128.0, 126.5, 124.1, 122.0, 25.8, 25.7. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{21}N_2O_2^+$ 393.1598; found, 393.1601.

*Gram-Scale Preparation of **3a**.* To a reaction tube equipped with a stir bar were charged (1-azidovinyl)benzene (**1a**, 0.87 g, 6 mmol), benzoic acid (**2a**, 0.61 g, 5 mmol), and DCE (20 mL). The tube was then sealed and stirred at 110 °C (oil bath) under air for 10 h. Upon completion, it was cooled to room temperature and concentrated under a reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (5:1) as an eluent to afford product **3a** (0.813 g, 66%).

Mechanism Studies. To a reaction tube equipped with a stir bar were charged 1-(1-azidovinyl)-4-methoxybenzene (**1d**, 52.5 mg, 0.3 mmol), 1-(1-azidovinyl)-4-(trifluoromethy)benzene (**1h**, 64.0 mg, 0.3 mmol), benzoic acid (**2a**, 36.6 mg, 0.3 mmol), and DCE (3 mL). The tube was then sealed and stirred at 110 °C (oil bath) under air for 10 h. Upon completion, it was cooled to room temperature and concentrated under a reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (5:1) as an eluent to afford *N*-(2-(4-methoxyphenyl)-2-oxoethyl)- benzamide (**3d**, 29.9 mg, 37%) and *N*-(2-oxo-2-(4-(trifluoromethyl)-phenyl)ethyl)benzamide (**3h**, 22.1 mg, 24%). Thus, the ratio of **3d** to **3h** was calculated as about 1.5:1.

https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX−XXX

To a reaction tube equipped with a stir bar were charged 4-methoxybenzoic acid (**2d**, 45.6 mg, 0.3 mmol), 4-(trifluoromethyl)-benzoic acid (**2i**, 57.0 mg, 0.3 mmol), (1-azidovinyl)benzene (**1a**, 43.5 mg, 0.3 mmol), and DCE (3 mL). The tube was sealed and stirred at 110 °C (oil bath) under air for 10 h. Upon completion, it was cooled to room temperature and concentrated under a reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (5:1) as an eluent to afford 4-methoxy-*N*-(2-oxo-2-phenylethyl)benzamide (**3u**, 13.7 mg, 17%) and *N*-(2-oxo-2- phenylethyl)-4-(trifluoromethyl)benzamide (**3z**, 48.8 mg, 53%). Thus, the ratio of **3u** to **3z** was calculated as about 1:3.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c01871.

Copies of the NMR spectra of all products and the X-ray crystal structure and data of **3w** (CCDC 2010162) (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

Xinying Zhang − *Henan Key Laboratory of Organic Functional Molecules and Drug Innovation, Collaborative Innovation Center of Henan Province for Green Manufacturing of Fine Chemicals, Key Laboratory of Green Chemical Media and Reactions, Ministry of Education, School of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang, Henan 453007, China;* orcid.org/0000-0002-3416-4623; Email: xinyingzhang@htu.cn

Xuesen Fan − *Henan Key Laboratory of Organic Functional Molecules and Drug Innovation, Collaborative Innovation Center of Henan Province for Green Manufacturing of Fine Chemicals, Key Laboratory of Green Chemical Media and Reactions, Ministry of Education, School of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang, Henan 453007, China;* orcid.org/0000-0002-2040-6919; Email: xuesen.fan@htu.cn

Authors

Cai Gao − *Henan Key Laboratory of Organic Functional Molecules and Drug Innovation, Collaborative Innovation Center of Henan Province for Green Manufacturing of Fine Chemicals, Key Laboratory of Green Chemical Media and Reactions, Ministry of Education, School of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang, Henan 453007, China*

Qianting Zhou − *Henan Key Laboratory of Organic Functional Molecules and Drug Innovation, Collaborative Innovation Center of Henan Province for Green Manufacturing of Fine Chemicals, Key Laboratory of Green Chemical Media and Reactions, Ministry of Education, School of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang, Henan 453007, China*

Li Yang − *Henan Key Laboratory of Organic Functional Molecules and Drug Innovation, Collaborative Innovation Center of Henan Province for Green Manufacturing of Fine Chemicals, Key Laboratory of Green Chemical Media and Reactions, Ministry of Education, School of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang, Henan 453007, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.0c01871

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors are grateful to the National Natural Science Foundation of China (NSFC) (21572047), Program for Innovative Research Team in Science and Technology in Universities of Henan Province (20IRTSTHN005), Key Project of Science and Technology of Henan Province (192102310412), and 111 Project (D17007) for financial support.

■ REFERENCES

(1) (a) Białas, A.; Grembecka, J.; Krowarsch, D.; Otlewski, J.; Potempa, J.; Mucha, A. Exploring the S*n* Binding Pockets in Gingipains by Newly Developed Inhibitors: Structure-Based Design, Chemistry, and Activity. *J. Med. Chem.* **2006**, *49*, 1744−1753. (b) El-Dahshan, A.; Al-Gharabli, S. I.; Radetzki, S.; Al-Tel, T. H.; Kumar, P.; Rademann, J. Flexible, Polymer-Supported Synthesis of Sphingosine Derivatives Provides Ceramides with Enhanced Biological Activity. *Bioorg. Med. Chem.* **2014**, *22*, 5506−5512. (c) Robles, A. J.; McCowen, S.; Cai, S.; Glassman, M.; Ruiz, F., II; Cichewicz, R. H.; McHardy, S. F.; Mooberry, S. L. Structure−Activity Relationships of New Natural Product-Based Diaryloxazoles with Selective Activity against Androgen Receptor-Positive Breast Cancer Cells. *J. Med. Chem.* **2017**, *60*, 9275−9289.

(2) (a) Griesbeck, A. G.; Heckroth, H. Stereoselective Synthesis of 2-Aminocyclobutanols via Photocyclization of α-Amido Alkylaryl Ketones: Mechanistic Implications for the Norrish/Y ang Reaction. *J. Am. Chem. Soc.* **2002**, *124*, 396−403. (b) Nicolaou, K. C.; Hao, J.; Reddy, M. V.; Rao, P. B.; Rassias, G.; Snyder, S. A.; Huang, X.; Chen, D. Y. K.; Brenzovich, W. E.; Giuseppone, N.; Giannakakou, P.; O'Brate, A. Chemistry and Biology of Diazonamide A: Second Total Synthesis and Biological Investigations. *J. Am. Chem. Soc.* **2004**, *126*, 12897−12906. (c) Frantz, D. E.; Morency, L.; Soheili, A.; Murry, J. A.; Grabowski, E. J. J.; Tillyer, R. D. Synthesis of Substituted Imidazoles via Organocatalysis. *Org. Lett.* **2004**, *6*, 843−846. (d) Chen, W.; Cui, J.; Zhu, Y.; Hu, X.; Mo, W. DBU-Promoted Cyclization of *ortho*-(3-Hydroxy-1- alkynyl)benzamide: Synthesis of *trans*-3,4-Dihydroisoquinolin-1(2*H*)-ones and (*E*)-4-(1- Alkenyl)-isoquinolin-1(2*H*)-ones. *J. Org. Chem.* **2012**, *77*, 1585−1591. (e) Viviano, M.; Milite, C.; Rescigno, D.; Castellano, S.; Sbardella, G. A Continuous-flow Synthesis of 1,4-Benzo- diazepin-5-ones, Privileged Scaffolds for Drug Discovery. *RSC Adv.* **2015**, *5*, 1268−1273. (f) Zhou, R.-R.; Cai, Q.; Li, D.-K.; Zhuang, S.-Y.; Wu, Y.-D.; Wu, A.-X. Acid-Promoted Multicomponent Tandem Cyclization to Synthesize Fully Substituted Oxazoles via Robinson−Gabriel-Type Reaction. *J. Org. Chem.* **2017**, *82*, 6450−6456. (g) Dowling, M. S.; Jiao, W.; Hou, J.; Jiang, Y.; Gong, S. Modular Synthesis of 3,6-Disubstituted-1,2,4-triazines via the Cyclodehydration of β-Keto-*N*-acylsulfonamides with Hydrazine Salts. *J. Org. Chem.* **2018**, *83*, 4229−4238.

(3) (a) Wilde, M. M. D.; Gravel, M. Bis(amino)cyclopropenylidene (BAC) Catalyzed Aza-Benzoin Reaction. *Org. Lett.* **2014**, *16*, 5308−5311. (b) Zheng, G.; Li, Y.; Han, J.; Xiong, T.; Zhang, Q. Radical Cascade Reaction of Alkynes with *N*-Fluoroarylsulfonimides and Alcohols. *Nat. Commun.* **2015**, *6*, 7011−7042. (c) Wende, R. C.; Seitz, A.; Niedek, D.; Schuler, S. M. M.; Hofmann, C.; Becker, J.; Schreiner, P. R. T. The Enantioselective Dakin−West Reaction. *Angew. Chem., Int. Ed.* **2016**, *55*, 2719−2723. (d) Holthusen, K.; Leitner, W.; Franciò, G. Synthesis of α-Amidoketones from Vinyl Esters via a Catalytic/Thermal Cascade Reaction. *J. Org. Chem.* **2016**, *81*, 4823−4828. (e) Kim, Y.; Pak, H. K.; Rhee, Y. H.; Park, J. Catalytic Transformation of Esters of 1,2-Azido Alcohols into α-Amido Ketones. *Chem. Commun.* **2016**, *52*, 6549−6552. (f) Wu, F.; Zhang, M.; Zhou, W.; Chen, W.; Liu, M.; Wu, H. Copper(I)- Catalyzed N−O Bond Formation through Vinyl Nitrene Mediated Pathway under Mild Conditions. *J. Org. Chem.* **2018**, *83*, 5999−6005.

https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX−XXX

(4) (a) Zhang, M.; Xie, J.; Zhu, C. A General Deoxygenation Approach for Synthesis of Ketones from Aromatic Carboxylic Acids and Alkenes. *Nat. Commun.* **2018**, *9*, 3517−3527. (b) Shi, X.; Chen, X.; Wang, M.; Zhang, X.; Fan, X. Regioselective Synthesis of Acylated N-Heterocycles via the Cascade Reactions of Saturated Cyclic Amines with 2-Oxo-2-arylacetic Acids. *J. Org. Chem.* **2018**, *83*, 6524−6533. (c) Shi, X.; He, Y.; Zhang, X.; Fan, X. $FeCl_3$−Catalyzed Cascade Reactions of Cyclic Amines with 2-Oxo-2-arylacetic Acids toward Furan-2(5*H*)-one Fused *N*,*O*-Bicyclic Compounds. *Adv. Synth. Catal.* **2018**, *360*, 261−266. (d) Zhao, Y.- L.; Tang, Y.-Q.; Fei, X.-H.; Yang, F.-F.; Cao, Z.-X.; Duan, D.-Z.; Zhao, Q.-J.; Yang, Y.-Y.; Zhou, M.; He, B. Direct C(sp^3)−H Acyloxylation of Indolin-3-ones with Carboxylic Acids Catalysed by KI. *Green Chem.* **2020**, *22*, 2354−2358. (e) Cianfanelli, M.; Olivo, G.; Milan, M.; Gebbink, R. J. M. K.; Ribas, X.; Bietti, M.; Costas, M. Enantioselective C−H Lactonization of Unactivated Methylenes Directed by Carboxylic Acids. *J. Am. Chem. Soc.* **2020**, *142*, 1584−1593. (f) Uttry, A.; van Gemmeren, M. Direct C(sp^3)−H Activation of Carboxylic Acids. *Synthesis* **2020**, *52*, 479−488.

(5) (a) Oh, B. H.; Nakamura, I.; Yamamoto, Y. Palladium-Catalyzed Ring-Opening Reaction of Methyleneaziridines with Carboxylic Acids: Synthesis of α-Amidoketones. *J. Org. Chem.* **2004**, *69*, 2856−2858. (b) Xu, F.; Si, X.-J.; Song, Y.-Y.; Wang, X.-D.; Liu, C.-S.; Geng, P.-F.; Du, M. Palladium-Catalyzed C−N Bond Cleavage of 2*H*-Azirines for the Synthesis of Functionalized α-Amido Ketones. *J. Org. Chem.* **2019**, *84*, 2200−2208. (c) De, A.; Santra, S.; Zyryanov, G. V.; Majee, A. Self-Catalyzed Rapid Synthesis of N-Acylated/*N*-Formylated α-Aminoketones and *N*-Hydroxymethylated Formamides from 3-Aryl-2*H*-Azirines and 2-Me/Ph-3-Aryl-2*H*- Azirines. *Org. Lett.* **2020**, *22*, 3926−3930.

(6) (a) Wang, Z.; Chen, G.; Zhang, X.; Fan, X. Synthesis of 3-Acylquinolines Through Cu-catalyzed Double C(sp^3)−H Bond Functionalization of Saturated Ketones. *Org. Chem. Front.* **2017**, *4*, 612−616. (b) Li, B.; Zhang, B.; Zhang, X.; Fan, X. Regio-Selective Synthesis of Diversely Substituted Benzo[*a*]carbazoles Through Rh(III)-Catalyzed Annulation of 2-Arylindoles with α-Diazo Carbonyl Compounds. *Chem. Commun.* **2017**, *53*, 1297−1300. (c) Xu, Y.; Li, B.; Zhang, X.; Zhang, X.; Fan, X. One-Pot Synthesis of Fused *N*,*O*-Heterocycles through Rh(III) Catalyzed Cascade Reactions of Aromatic/Vinylic *N*-Alkoxy-Amides with 4-Hydroxy-2- Alkynoates. *Adv. Synth. Catal.* **2018**, *360*, 2613−2620. (d) Xu, Y.; Zhang, L.; Liu, M.; Zhang, X.; Fan, X. Synthesis of Benzoazepine Derivatives *via* Rh(III)-Catalyzed Inert C(sp^2)−H Functionalization and [4 + 3] Annulation. *Org. Biomol. Chem.* **2019**, *17*, 8706−8710. (e) Gao, C.; Ben Li; Geng, X.; Zhou, Q.; Zhang, X.; Fan, X. Two Birds With One Stone: One-pot Simultaneous Synthesis of 2,2,2-Trifluoroethylphenanthridines and Benzochromenones Featuring the Utilization of the Byproduct of Togni's Reagent. *Green Chem.* **2019**, *21*, 5113−5117. (f) Guo, C.; Li, Bin.; Liu, H.; Zhang, X.; Zhang, X.; Fan, X. Synthesis of Fused or Spiro Polyheterocyclic Compounds via the Dehydrogenative Annulation Reactions of 2-Arylindazoles with Maleimides. *Org. Lett.* **2019**, *21*, 7189−7193. (g) Xu, Y.; Shen, M.; Zhang, X.; Fan, X. Selective Synthesis of Pyrazolo[1,2-*a*]pyrazolones and 2-Acylindoles via Rh(III)-Catalyzed Tunable Redox-Neutral Coupling of 1-Phenylpyrazolidinones with Alkynyl Cyclobutanols. *Org. Lett.* **2020**, *22*, 4697−4702, DOI: 10.1021/acs.orglett.0c01475.

(7) (a) Ni, H.; Zhang, G.; Yu, Y. Vinyl Azides as Versatile Synthons for the Synthesis of Nitrogen-containing Heterocycles. *Curr. Org. Chem.* **2015**, *19*, 776−789. (b) Fu, J.; Zanoni, G.; Anderson, E. A.; Bi, X. α-Substituted Vinyl Azides: an Emerging Functionalized Alkene. *Chem. Soc. Rev.* **2017**, *46*, 7208−7228. (c) Hayashi, H.; Kaga, A.; Chiba, S. Application of Vinyl Azides in Chemical Synthesis: A Recent Update. *J. Org. Chem.* **2017**, *82*, 11981−11989. (d) Yan, J.; Ji, X.; Hua, S.; Wang, J. Recent Advances of α-Aryl Vinyl Azides in Nitrogen Heterocycle Synthesis. *Chin. J. Org. Chem.* **2018**, *38*, 791−801.

(8) (a) Jie, L.; Wang, L.; Xiong, D.; Yang, Z.; Zhao, D.; Cui, X. Synthesis of 2-Arylindoles through Pd(II)-Catalyzed Cyclization of Anilines with Vinyl Azides. *J. Org. Chem.* **2018**, *83*, 10974−10984. (b) Zhou, B.; Zheng, L.; Xu, Z.; Jin, H.; Wu, Q.; Li, T.; Liu, Y. Synthesis of Functionalized Phenathridine-6-carbonitriles via Copper-catalyzed Annulation of Vinyl Azides and NaN_3 in the Presence of $PhI(OAc)_2$. *ChemistrySelect* **2018**, *3*, 7354−7357. (c) Wang, X.; Li, Y.; Qiu, G.; Wu, J. Synthesis of 6-(Sulfonylmethyl)phenanthridines Through a Reaction of Aryldiazonium Tetrafluoroborates, Sulfur Dioxide, and Vinyl Azides. *Org. Chem. Front.* **2018**, *5*, 2555−2559. (d) Ning, Y.; Mekareeya, A.; Babu, K. R.; Anderson, E. A.; Bi, X. Silver- Catalyzed *C*- to *N*-Center Remote Arene Migration. *ACS Catal.* **2019**, *9*, 4203−4210. (e) Mulina, O. M.; Zhironkina, N. V.; Paveliev, S. A.; Demchuk, D. V.; Terent'ev, A. O. Electrochemically Induced Synthesis of Sulfonylated *N*-Unsubstituted Enamines from Vinyl Azides and Sulfonyl Hydrazides. *Org. Lett.* **2020**, *22*, 1818−1824. (f) More, A. A.; Szpilman, A. M. Indium(III) Catalyzed Reactions of Vinyl Azides and Indoles. *Org. Lett.* **2020**, *22*, 3759−3764. (g) Qin, C.; Feng, P.; Ou, Y.; Shen, T.; Wang, T.; Jiao, N. Selective C_{sp2}-C_{sp} Bond Cleavage: The Nitrogenation of Alkynes to Amides. *Angew. Chem., Int. Ed.* **2013**, *52*, 7850−7854.

(9) Xu, W.; Nachtsheim, B. J. TBAI-Catalyzed Oxidative Cross-Coupling of Phenols and 2-Amino- acetophenones. *Org. Lett.* **2015**, *17*, 1585−1588.

(10) (a) Allred, T. K.; Manoni, F.; Harran, P. G. Exploring the Boundaries of "Practical": De Novo Syntheses of Complex Natural Product- Based Drug Candidates. *Chem. Rev.* **2017**, *117*, 11994−12051. For some interesting bisoxazole derivatives, see: (b) Anderson, Z. J.; Fox, D. J. Total Synthesis of the Azolemycins. *Org. Biomol. Chem.* **2016**, *14*, 1450−1454. (c) Knowles, R. R.; Carpenter, J.; Blakey, S. B.; Kayano, A.; Mangion, I. K.; Sinz, C. J.; MacMillan, D. W. C. Total Synthesis of Diazonamide A. *Chem. Sci.* **2011**, *2*, 308−311.

(11) Qin, H.-T.; Wu, S.-W.; Liu, J.-L.; Liu, F. Photoredox-Catalysed Redox-Neutral Trifluoromethylation of Vinyl Azides for the Synthesis of α-Trifluoromethylated Ketones. *Chem. Commun.* **2017**, *53*, 1696−1699.

(12) Moriya, T.; Takabe, S.; Maeda, S.; Matsumoto, K.; Takashima, K.; Mori, T.; Takeyama, S. Synthesis and Hypolipidemic Activities of 5-Thienyl-4-oxazoleacetic Acid Derivatives. *J. Med. Chem.* **1986**, *29*, 333−341.

(13) Gálvez, A. O.; Schaack, C. P.; Noda, H.; Bode, J. W. Chemoselective Acylation of Primary Amines and Amides with Potassium Acyltrifluoroborates under Acidic Conditions. *J. Am. Chem. Soc.* **2017**, *139*, 1826−1829.

https://dx.doi.org/10.1021/acs.joc.0c01871
J. Org. Chem. XXXX, XXX, XXX−XXX