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Copper-Catalyzed *N*-Arylation of Azoles and Mannich-Type Coupling of Ketones and Azoles under Metal-Free Conditions

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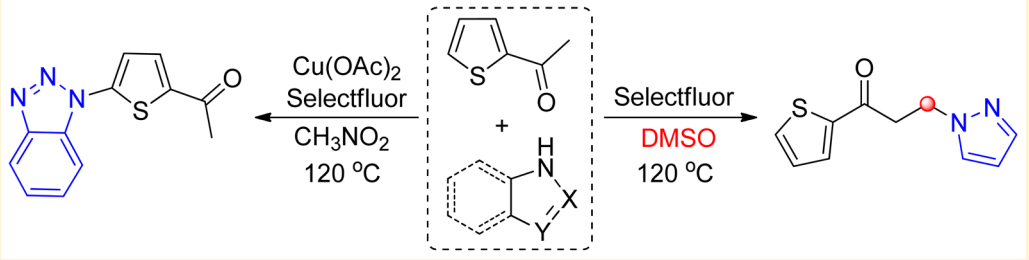
Supporting Information



ABSTRACT: A new process has been developed for the copper-catalyzed direct *N*-arylation of five-membered heterocycles with azoles. Five-membered heterocycles bearing an acetyl group also underwent a Mannich-type reaction with activated azoles to give the corresponding *β*-amino ketones under metal-free conditions. These reactions exhibited wide substrate scope, high functional group tolerance, and ease of operation, making them useful tools with numerous potential applications in synthetic chemistry.

INTRODUCTION

The importance of nitrogen-containing compounds stems from their wide occurrence in nature, as well as their broad range of applications in chemistry, biology, and materials science.[1] Five-membered heterocycles bearing an amine substituent are commonly used in medicinal chemistry. For example, several 2-aminothiophene derivatives are currently used as inhibitors of APE 1 and tubulin polymerization.[2] Furthermore, Zyprexa (Olanzapine), which is based on a 2-aminothiophene core, is ranked as one of the world's top 200 drugs in terms of its sales. On the basis of their importance, considerable research efforts have been directed toward the development of direct and convenient methods for the synthesis of five-membered heterocycles bearing an amine substituent. Compared with the cyclocondensation reaction of two functionalized precursors,[3] the convinent coupling of the N−H bond with 2-halogenated precursors is commonly used in the industry.[4] Recently, the direct C−H activation and C−N formation reaction became an additional powerful methodology for the construction of C−N bonds, which could avoid prefunctionalization of the substrates and minimize environmental impact.[5] The successful reports of Mori et al., Schreiber et al., and Chang et al. concerning the Cu-catalyzed direct C−H amination of azoles have inspired an impressive series of achievements in the transition-metal-catalyzed amination of azoles.[6] Despite these achievements, further research is still required in several areas, including (1) the suppression of the homodimerization pathway of five-membered heterocycles, and (2) improving the substrate scope of the nitrogen source, especially nitrogen-containing heterocyclic compounds.[7]

Azoles are one of the most widely used and extensively studied heterocyclic compounds, which have been reported to play important roles in medicinal and pesticide chemistry with a wide range of bioactivities.[8] The direct coupling of a five-membered heteroaromatic compound to another type of heteroarene (e.g., azole) represents an attractive, but challenging, transformation.[1f] As part of our ongoing interest in the development of new methods for C−X (X = N, S, I) bond construction,[9] more recently, using the copper salt and Selectfluor (1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetra-fluoroborate)) combination, we developed the direct amination of arenes and azines.[9f,g] Herein, is our most recent research toward the copper-catalyzed *N*-arylation of five-membered pyrrole, furan, and thiophene derivatives with azoles. Notably, under metal-free conditions, this reaction also provides access to the corresponding *β*-amino ketones for heterocyclic substrates bearing an acetyl substituent via a Mannich-type reaction. It is noteworthy that the methylene derived from poisonous formaldehyde analogues in the Mannich reaction could be replaced with DMF, DMSO, or NMP.

RESULTS AND DISCUSSION

The reaction of 2-acetylthiophene (**1a**) with 1*H*-benzotriazole (**2a**) was selected as a model reaction to identify the optimum conditions for this transformation (Table 1). We initially tested a variety of different copper salts instead of the palladium catalyst to avoid the occurrence of unwanted side reaction such as homocoupling (for detailed condition screenings, please see the SI). A variety of copper salts were tested, and only $Cu(OTf)_2$ provided the higher 56% yield of **2a** (Table 1, entry 1). When the loading of the catalyst was reduced from 10 to 2.5 mol %,

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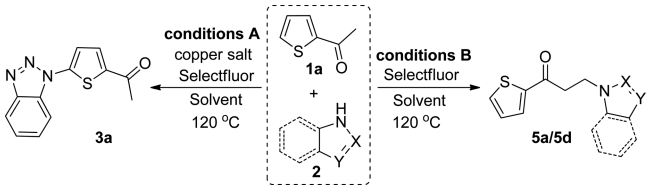
Table 1. Survey of the Reaction Conditions[a]



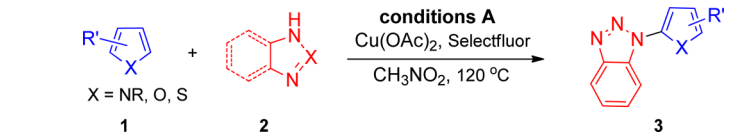
entry	cat (10 mol %)	base	solvent	yield of **3a** (%)[b]	yield of **5a**/**5d** (%)[b]
1	$Cu(OAc)_2$	no	CH_3NO_2	56	0
2	$Cu(OAc)_2$ (2.5 mol %)	no	CH_3NO_2	27	0
3	$Cu(OAc)_2$	K_2CO_3	CH_3NO_2	61	0
4	$Cu(OAc)_2$	K_2CO_3	DMF	0	0
5	$Cu(OAc)_2$	K_2CO_3	DCE	46	0
6	$Cu(OAc)_2$	K_2CO_3	CH_3CN	22	0
7	no	K_2CO_3	CH_3NO_2	0	21
8	no	no	CH_3NO_2	0	23
9	no	no	DMF	0	45
10	no	no	DMSO	0	53
11	no	no	NMP	0	52
12	no	no	DMF	0	91[c]
13	no	no	DMSO	0	95[c]
14	no	no	NMP	0	94[c]

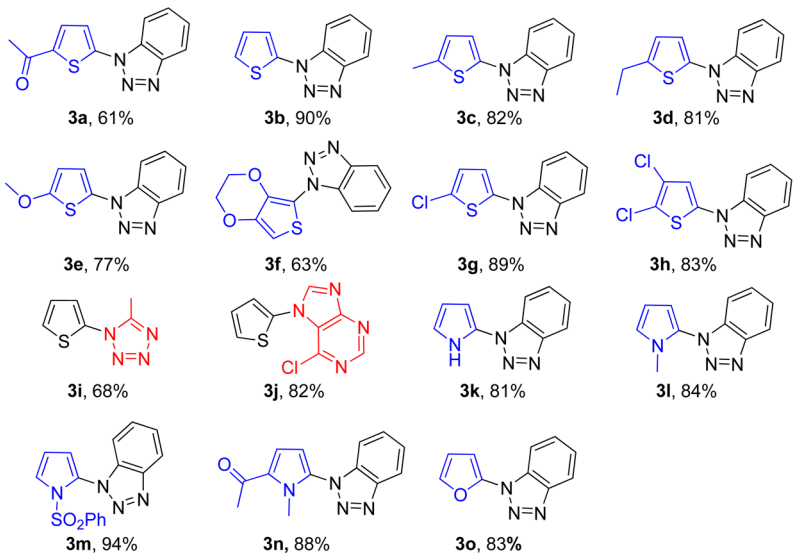
[a]Reactions were carried out with 2-acetylthiophene (**1a**) (0.5 mmol), 1*H*-benzotriazole (**2a**) (1.0 mmol), Cu catalyst (10 mol %), base (2.0 equiv), and Selectfluor (2.0 equiv) in solvent (2 mL) at 120 °C. [b]Yield of the isolated product. [c]Imidazole was used instead of 1*H*-benzotriazole.

we observed a significant decrease in the yield (Table 1, entry 2). Several bases were also investigated, and only K_2CO_3 gave a slight increase in the yield (Table 1, entry 3). We also evaluated various other solvents, including toluene, DMF, DCE, and CH_3CN, but failed to provide a substantial increase in the yield (Table 1, entries 4–6). It is noteworthy that none of the desired amination product **3a** was observed in the absence of a copper salt (Table 1, entry 7). Interestingly, however, this reaction led to the formation of the *β*-amino ketone **5a** via a Mannich-type reaction in 21% yield. Intrigued by this result, we screened this reaction against a variety of different solvents and managed to increase the yield of the *β*-amino ketone to 53% (Table 1, entries 8–11). A variety of different azoles were then screened under these conditions. Pleasingly, imidazole proved to be the best coupling partner and gave much higher yields of **5d** in the range of 91–95% using DMF, DMSO, or NMP as the solvent (Table 1, entries 12–14).

With the optimized conditions in hand (i.e., conditions A), we proceeded to investigate the scope of the reaction using a series of five-membered heterocycles (Table 2). In all 15 examples, the product was obtained as a single regioisomer with selectivity toward the C2 position. Thiophenes containing an electron-donating group such as Me, Et, or OMe reacted smoothly under the optimized conditions to give the corresponding C–N bond formation products **3c**, **3d**, **3e**, and **3f** in moderate yields (63–82%). Chloride substituents were well tolerated on the thiophene ring, as exemplified by 2-chlorothiophene (**1g**) and 2,3-dichlorothiophene (**1h**), which afforded **3g** and **3h** in 89% and 83% yields, respectively, and provided a handle for further synthetic manipulations. Several other heterocyclic partners were also briefly investigated, including 5-methyl-1*H*-tetrazole and 6-chloro-7*H*-purine, which all reacted effectively to give the desired *N*-arylation products **3i** and **3j** in 68% and 82% yields. 1*H*-Pyrrole (**1k**), 1-methyl-1*H*-pyrrole (**1l**), 1-(phenylsulfonyl)-1*H*-pyrrole (**1m**), and 1-(1-methyl-1*H*-pyrrol-2-yl)ethanone

Table 2. Scope of Heterocyclic Compounds and Azoles[a,b]





[a]Reactions were carried out with a five-membered heterocycle **1** (0.5 mmol), azole **2** (1.0 mmol), $Cu(OAc)_2$ (10 mol %), and Selectfluor (2.0 equiv) in CH_3NO_2 (2 mL) at 120 °C. [b]Yield of the isolated product.

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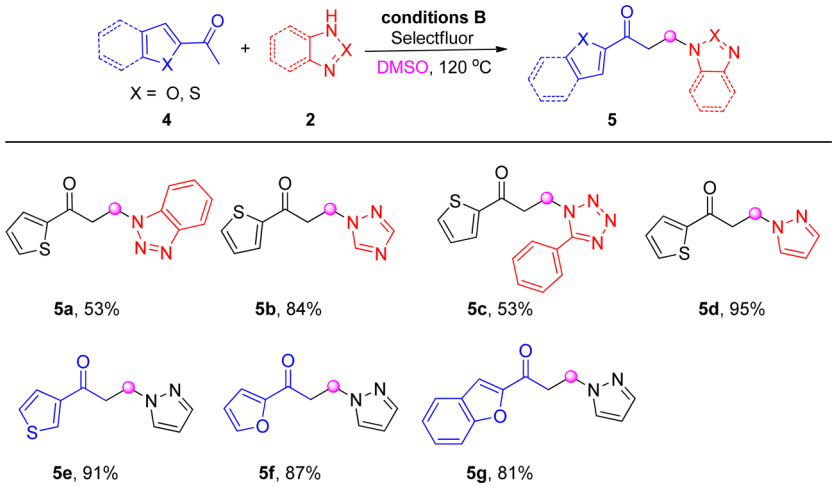
Table 3. Scope of Heterocyclic Compounds and Azoles[a,b]



[a]Reactions were carried out with **4** (0.5 mmol), azole **2** (1.0 mmol), and Selectfluor (2.0 equiv) in DMSO (2 mL) at 120 °C. [b]Yield of the isolated product.

(**1n**) were also suitable for this method and afforded **3k**, **3l**, **3m**, and **3n** in 81, 84, 94, and 88% yields, respectively.

The optimized conditions for the Michael-type reaction (i.e., conditions B) were applied to 1-(thiophen-3-yl)ethanone (**4e**), 1-(furan-2-yl)ethanone (**4f**), and 1-(benzofuran-2-yl)ethanone (**4g**), which reacted smoothly to give the corresponding *β*-amino ketones **5e**, **5f**, and **5g** in 81−91% yields (Table 3). *β*-Amino ketones are an important class of compounds with a wide range of biological activities that can also be used as synthetic intermediates for the preparation of pharmaceutical agents and natural products.[10] On the basis of their importance, numerous approaches have been developed for the synthesis of *β*-amino ketones.[11] The classic three-component Mannich reaction is a well established approach for the synthesis of *β*-amino ketones which has achieved a great deal of success.[12] However, the application of this reaction to the preparation of pharmaceutical agents has been limited by its requirement for the use of poisonous formaldehyde analogues. The common polar solvents dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and methyl-2-pyrrolidinone (NMP) have attracted considerable attention as multipurpose building blocks,[13] with particular emphasis on C−N bond forming reactions involving N−H bond-containing substrates and the C(sp^3)−H bonds of these solvent molecules.[14] On the basis of these developments, the scope of this Mannich-type reaction has been broadened to acetophenone derivatives.

As shown in Table 4, acetophenones bearing a methyl substituent at the *ortho*-, *meta*-, or *para*-position of the phenyl ring, including 1-(*o*-tolyl)ethanone (**6b**), 1-(*m*-tolyl)ethanone (**6d**), and 1-(*p*-tolyl)ethanone (**6f**), reacted smoothly with 1*H*-pyrazole to give the corresponding Mannich-type products **7b**, **7d**, and **7f**, respectively, in excellent yields (91−96%). Acetophenone derivatives containing an electron-donating (e.g., Me, OMe, Ph) or electron-withdrawing (F, Cl, Br, NO_2, CO_2Et, and CF_3) group at the *para*-position of their aromatic ring were well tolerated under the optimized reaction conditions (i.e., conditions B) to afford the corresponding products **7b**−**p** (87−97%). The multisubstituted substrate **6q** and fused bicyclic acetylnaphthalene **6r** also reacted efficiently to provide the desired products **7q** and **7r** in high yield (85% and 94%). Furthermore, the substrate scope of this reaction was extended to several propiophenone derivatives, including propiophenone (**6s**), 1-(4-chlorophenyl)propan-1-one (**6t**), and 1-(*p*-tolyl)propan-1-one (**6u**), to give the desired products **7s**−**u** in 96, 94, and 95% yields, respectively.

From a mechanistic point of view, the C(sp^2)−N bond formation observed in the *N*-arylation reaction most likely proceeds via an electrophilic mechanism. Indeed, our methodology furnished the C2 functionalized products exclusively, which, therefore, supports this kind of mechanism. When the reaction was conducted in the absence of a copper salt, the mode of reactivity switched to the Mannich-type reaction. We supposed that the methylene adjacent to the nitrogen atom of the *β*-amino ketone product derives from the decomposition of DMSO and that this would be the initial step in the C(sp^3)−N bond formation between DMSO and the azole. To obtain some mechanistic evidence for this transformation, we reacted DMSO with 1*H*-benzo[*d*][1,2,3]triazole (**2a**), which gave the 1-((methylsulfinyl)methyl)-1*H*-benzo[*d*][1,2,3]triazole **A** in reasonable yield (eq 1).[15] The structure of this addition product was confirmed by ^1H and ^{13}C NMR spectroscopy (see the SI). As expected, the desired *β*-amino ketone **5a** was obtained in 74% yield when **4a** was reacted with **A** under the optimized conditions (i.e., conditions B) (eq 2). Furthermore, the reaction of **4a** with 1-methyl-1*H*-benzo[*d*][1,2,3]triazole (**B**) instead of 1*H*-benzo-[*d*][1,2,3]triazole (**2a**) under the optimized conditions gave **5a** in a lower isolated yield of 17% (eq 3). On the basis of these results, we have proposed a mechanism for this reaction, which is shown in Scheme 1.

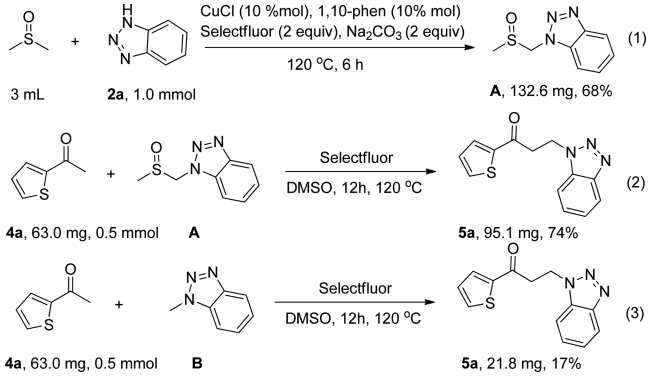


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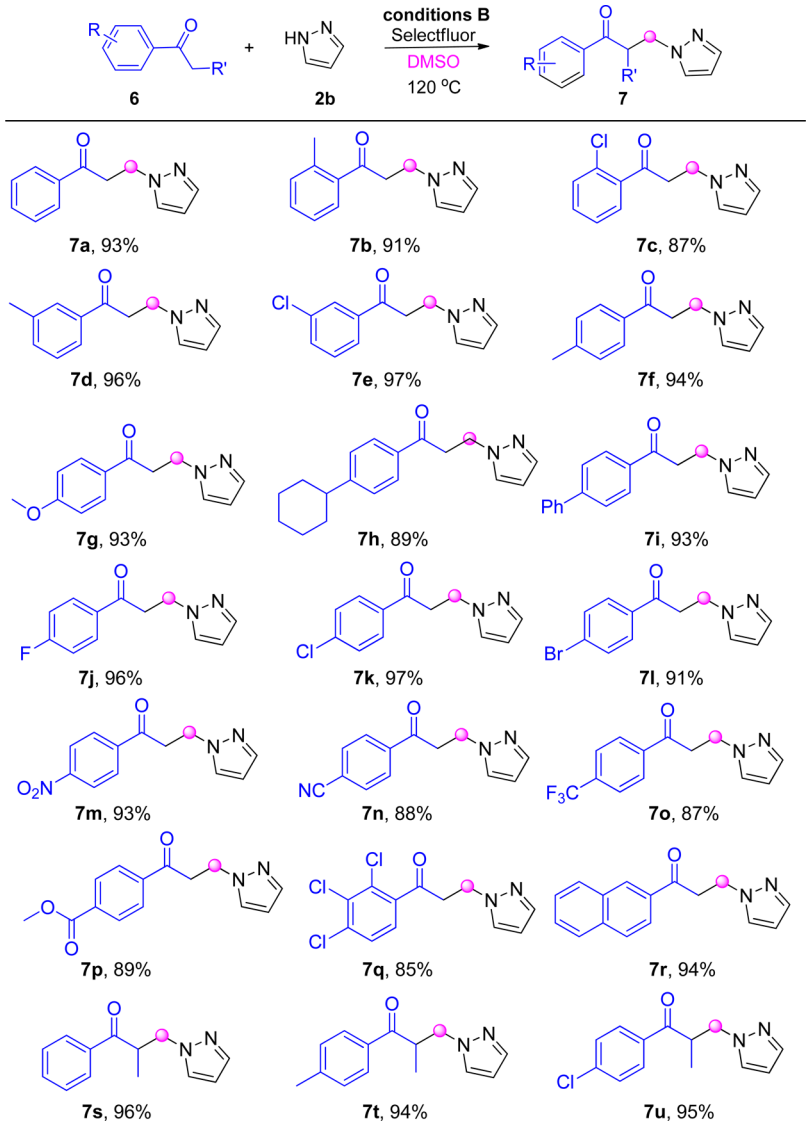
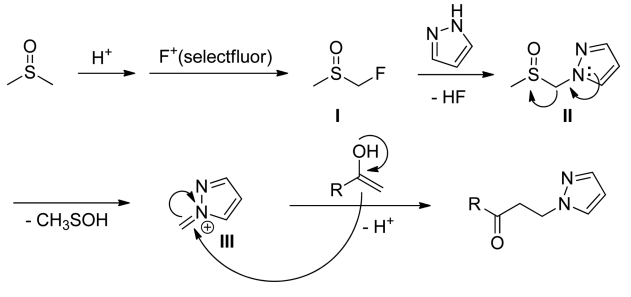
Table 4. Scope of Heterocyclic Compounds and Azoles[a,b]



[a]Reactions were carried out with **6** (0.5 mmol), azole **2** (1.0 mmol), and Selectfluor (2.0 equiv) in DMSO (2 mL) at 120 °C. [b]Yield of the isolated product.

Scheme 1. Proposed Mechanism



The initial substitution of 1*H*-pyrazole to an electrophilic fluoro(methylsulfinyl)methane **I** delivers the 1-((methylsulfinyl)methyl)-1H-imidazole **II**, which then undergoes a C−S bond cleavage reaction mediated by Selectfluor to afford the key iminium ion **III** and CH_3SOH. The final nucleophilic addition between **III** and the enol tautomer of the ketone affords the desired product.

In conclusion, we have successfully developed a copper-catalyzed process for the direct *N*-arylation of the C(sp^2)−H bonds of five-membered heterocycles with azoles, which are well-known to be crucial precursors for the synthesis of numerous biologically active compounds. In addition, we have developed a new Mannich-type reaction for the synthesis of *β*-amino ketones under metal-free conditions from five-membered heterocycles bearing an acetyl group, including acetophenone derivatives. Notably, this reaction exhibited broad substrate scope and wide functional group compatibility, as well as being easy to operate, making it an attractive supplement to the traditional Mannich reaction. Further research toward the application of this protocol to the synthesis of bioactive molecules and a detailed mechanistic investigation are currently in progress.

EXPERIMENTAL SECTION

General Information. All of the reagents were purchased from commercial sources and used without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 spectrometer in

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deuterated solvents containing TMS as an internal reference standard. High-resolution mass spectrometry (HRMS) analyses were measured at 70 eV using a double focusing magnetic sector mass analyzer with an EI source. Melting points were measured on a melting point apparatus equipped with a thermometer and were uncorrected. All of the reactions were monitored by thin-layer chromatography (TLC) using GF254 silica gel-coated TLC plates. Purifications by flash column chromatography were carried out over SiO_2 (silica gel 200−300 mesh).

General Procedure (Conditions A) for the *N*-Arylation Reactions of the Heterocyclic Compounds and the Azoles To Generate Compounds 3a−r. 1*H*-Benzo[*d*][1,2,3]triazole **2a** (1.0 mmol, 119.0 mg), $Cu(OAc)_2$ (10 mol %, 9.5 mg), and Selectfluor (2.0 equiv, 354.2 mg) were added to a sealable reactor vial containing a five-membered heterocycle **1a** (0.5 mmol, 62.5 mg) in CH_3NO_2 (2 mL). The tube was then sealed, and the mixture was stirred at 120 °C for 8−14 h. Upon completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and quenched with water before being extracted with dichloromethane (5 × 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a residue, which was purified by flash column chromatography over silica gel (EtOAc/petroleum ether = 1:6, v/v) to give compound **3a** (74.1 mg) in 61% yield.

General Procedure (Conditions B) for the Mannich-Type Reaction between Ketones and Azoles (5a−5h, 7a−7u). 1*H*-Pyrazole **2b** (1.0 mmol, 68.0 mg) and Selectfluor (2.0 equiv, 354.2 mg) were added to a sealable reactor vial containing a five-membered heterocycle **4d** (0.5 mmol, 63.0 mg) in 2 mL of DMSO. The tube was then sealed, and the mixture was stirred at 120 °C for 2−6 h. Upon completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and quenched with water before being extracted with dichloromethane (5 × 3 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a residue, which was purified by flash column chromatography over silica gel (EtOAc/petro ether = 1:5, v/v) to give compound **5d** (97.9 mg) in 95% yield.

*1-(5-(1H-Benzo[d][1,2,3]triazol-1-yl)thiophen-2-yl)ethanone (**3a**).* White solid (61%, 74.1 mg), melting point: 94−95 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.69 (s, 3H), 7.01 (d, J = 4.4, 1H), 7.17 (d, J = 4.0, 1H), 7.45 (t, J = 6.8, 1H), 7.58 (t, J = 8.0, 1H), 7.73 (d, J = 8.4, 1H), 8.13 (d, J = 8.8, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 33.5, 105.9, 107.5, 110.2, 120.0, 122.4, 123.5, 124.4, 128.5, 134.9, 145.2, 190.2. HRMS (ESI-TOF) Calcd for $C_{12}H_{10}N_3SO$, $[M + H]^+$ 244.0541; Found 244.0537.

*1-(Thiophen-2-yl)-1H-benzo[d][1,2,3]triazole (**3b**).* White solid (90%, 90.5 mg), melting point: 74−76 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.17−7.47 (m, 4H), 7.60 (t, J = 7.6, 1H), 7.77 (d, J = 8.4, 1H), 8.15 (d, J = 8.4, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 108.4, 118.0, 118.6, 121.5, 122.9, 124.5, 129.9, 130.9, 135.7, 144.3. HRMS (ESI-TOF) Calcd for $C_{10}H_8N_3S$, $[M + H]^+$ 202.0435; Found 202.0439.

*1-(5-Methylthiophen-2-yl)-1H-benzo[d][1,2,3]triazole (**3c**).* White oil (82%, 68.2 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 2.58 (s, 3H), 6.81 (d, J = 2.0, 1H), 7.17 (d, J = 3.6, 1H), 7.45 (t, J = 6.8, 1H), 7.58 (t, J = 7.6, 1H), 7.73 (d, J = 8.4, 1H), 8.13 (d, J = 8.4, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 15.5, 110.3, 120.3, 120.4, 124.6, 128.5, 132.9, 134.4, 138.5, 145.9. HRMS (ESI-TOF) Calcd for $C_{11}H_{10}N_3S$, $[M + H]^+$ 216.0594; Found 216.0599.

*1-(5-Ethylthiophen-2-yl)-1H-benzo[d][1,2,3]triazole (**3d**).* White solid (81%, 62.8 mg), melting point: 66−67 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 1.39 (t, J = 7.6, 3H), 2.93 (d, J = 7.6, 2H), 6.84 (t, J = 7.2, 1H), 7.20 (d, J = 7.6, 1H), 7.45 (t, J = 8.0, 1H), 7.58 (d, J = 7.6, 1H), 7.74 (d, J = 8.4, 1H), 8.13 (d, J = 8.0, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 15.7, 23.6, 110.3, 120.1, 120.3, 122.3, 124.5, 128.5, 132.9, 134.3, 146.0, 146.1. HRMS (ESI-TOF) Calcd for $C_{12}H_{12}N_3S$, $[M + H]^+$ 230.0752; Found 230.0746.

*1-(5-Methoxythiophen-2-yl)-1H-benzo[d][1,2,3]triazole (**3e**).* White oil (77%, 88.9 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.90 (s, 3H), 6.24 (d, J = 2.0, 1H), 7.10 (d, J = 2.0, 1H), 7.47 (d, J = 8.4, 1H), 7.60 (t, J = 8.0, 1H), 7.79 (d, J = 8.4, 1H), 8.14 (d, J = 8.4, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 57.2, 93.9, 110.3, 112.0, 120.5, 124.8, 128.8, 132.4, 146.2, 155.6. HRMS (ESI-TOF) Calcd for $C_{11}H_{10}N_3OS$, $[M + H]^+$ 232.0541; Found 232.0536.

*1-(2,3-Dihydrothieno[3,4-b][1,4]dioxin-5-yl)-1H-benzo[d][1,2,3]-triazole (**3f**).* White solid (63%, 81.6 mg), melting point: 93−94 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 4.24−4.26 (m, 4H), 6.43 (d, J = 9.6, 1H), 7.37−7.42 (m, 1H), 7.50−7.59 (m, 2H), 8.07 (t, J = 8.8, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 64.6, 65.1, 98.3, 110.7, 120.0, 124.5, 128.3, 134.1, 136.1, 140.5, 145.4. HRMS (ESI-TOF) Calcd for $C_{12}H_{10}N_3O_2S$, $[M + H]^+$ 260.0494; Found 260.0498.

*1-(5-Chlorothiophen-2-yl)-1H-benzo[d][1,2,3]triazole (**3g**).* White solid (89%, 106.6 mg), melting point: 94−95 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.00 (d, J = 2.0, 1H), 7.17 (d, J = 3.6, 1H), 7.49 (d, J = 8.4, 1H), 7.61 (t, J = 8.0, 1H) 7.72 (d, J = 8.4, 1H), 8.15 (d, J = 8.4, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 109.9, 110.0, 113.5, 119.3, 120.5, 120.6, 121.4, 124.6, 125.3, 128.7, 129.0, 132.0, 132.6, 134.9, 146.1. HRMS (ESI-TOF) Calcd for $C_{10}H_7ClN_3S$, $[M + H]^+$ 236.0049; Found 236.0043.

*1-(4,5-Dichlorothiophen-2-yl)-1H-benzo[d][1,2,3]triazole (**3h**).* White solid (83%, 112.0 mg), melting point: 160−162 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.20 (s, 1H), 7.51 (d, J = 8.0, 1H), 7.66 (d, J = 6.8, 1H), 7.74 (d, J = 8.4, 1H), 8.15 (d, J = 8.4, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 106.0, 109.8, 118.1, 120.1, 124.7, 129.1, 130.3, 130.6, 134.5, 145.3. HRMS (ESI-TOF) Calcd for $C_{10}H_6Cl_2N_3S$, $[M + H]^+$ 269.9653; Found 269.9658.

*5-Methyl-1-(thiophen-2-yl)-1H-tetrazole (**3i**).* White solid (68%, 56.5 mg), melting point: 72−73 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 2.65 (s, 3H), 7.15 (q, J = 4.0, 1H), 7.24 (t, J = 2.4, 1H), 7.45 (q, J = 1.2, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 9.63, 124.0, 126.1, 126.5, 133.2, 152.4. HRMS (ESI-TOF) Calcd for $C_6H_7N_4S$, $[M + H]^+$ 167.0388; Found 167.0393.

*6-Chloro-7-(thiophen-2-yl)-7H-purine (**3j**).* White solid (82%, 96.7 mg), melting point: 153−154 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.14 (t, J = 3.6, 1H), 7.28 (q, J = 4.4, 1H), 7.17 (q, J = 2.4, 1H), 7.49 (d, J = 8.4, 1H), 8.35 (s, 1H) 8.97 (s, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 121.9, 124.1, 126.1, 126.5, 128.1, 144.4, 149.9, 152.9, 153.2. HRMS (ESI-TOF) Calcd for $C_9H_6ClN_4S$, $[M + H]^+$ 237.0004; Found 237.0012.

*1-(1H-Pyrrol-2-yl)-1H-benzo[d][1,2,3]triazole (**3k**).* White solid (81%, 74.5 mg), melting point: 119−121 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 6.40 (d, J = 3.2, 1H), 6.48 (d, J = 1.2, 1H), 6.90 (d, J = 1.2, 1H), 7.45 (d, J = 3.6, 1H), 7.55 (d, J = 8.0, 1H), 7.74 (d, J = 8.4, 1H), 8.10 (d, J = 8.4, 1H), 9.40 (s, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 99.4, 109.1, 110.5, 116.8, 120.1, 124.6, 125.0, 128.5, 131.9, 145.8. HRMS (ESI-TOF) Calcd for $C_{10}H_9N_4$, $[M + H]^+$ 185.0821; Found 185.0816.

*1-(1-Methyl-1H-pyrrol-2-yl)-1H-benzo[d][1,2,3]triazole (**3l**).* White solid (84%, 63.2 mg), melting point: 104−106 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.47 (s, 3H), 6.31 (d, J = 3.6, 1H), 6.40 (t, J = 2.0, 1H), 6.79 (t, J = 2.4, 1H), 7.40−7.54 (m, 3H), 8.13 (d, J = 8.4, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 33.5, 105.9, 107.5, 110.2, 120.0, 122.4, 123.5, 124.4, 128.5, 134.9, 145.2. HRMS (ESI-TOF) Calcd for $C_{11}H_{11}N_4$, $[M + H]^+$ 199.0987; Found 199.0982.

*1-(1-(Phenylsulfonyl)-1H-pyrrol-2-yl)-1H-benzo[d][1,2,3]triazole (**3m**).* Yellow solid (94%, 152.3 mg), melting point: 98−100 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 6.48 (d, J = 3.6, 1H), 6.54 (t, J = 2.0, 1H), 7.30 (t, J = 8.4, 1H), 7.41−7.58 (m, 8H), 8.11 (d, J = 8.4, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 110.4, 111.1, 114.7, 119.1, 123.5, 124.5, 127.6, 128.7, 129.3, 134.5, 134.7, 144.8. HRMS (ESI-TOF) Calcd for $C_{16}H_{13}N_4O_2S$, $[M + H]^+$ 325.0754; Found 325.0759.

*1-(5-(1H-Benzo[d][1,2,3]triazol-1-yl)-1-methyl-1H-pyrrol-2-yl)-ethanone (**3n**).* White solid (88%, 105.6 mg), melting point: 134−136 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 2.51 (s, 3H), 3.69 (s, 3H), 6.41 (d, J = 4.0, 1H), 7.10 (d, J = 4.4, 1H), 7.43 (q, J = 7.6, 2H), 7.54 (d, J = 7.6, 1H), 8.12 (d, J = 8.0, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 27.3, 33.4, 106.1, 109.8, 118.1, 120.4, 124.8, 129.1, 130.4, 130.7, 134.5, 145.3, 189.1. HRMS (ESI-TOF) Calcd for $C_{13}H_{13}N_4O$, $[M + H]^+$ 241.1084; Found 241.1080.

*1-(Furan-2-yl)-1H-benzo[d][1,2,3]triazole (**3o**).* Yellow oil (83%, 76.8 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 6.65 (d, J = 2.0, 1H) 6.71

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(q, J = 2.8, 1H), 7.44−7.61 (m, 3H), 7.81 (d, J = 8.4, 1H), 8.13 (d, J = 8.4, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 100.5, 110.7, 111.9, 120.2, 124.0, 128.8, 140.4, 145.5. HRMS (ESI-TOF) Calcd for $C_{10}H_8N_3O$, $[M + H]^+$ 186.0664; Found 186.0669.

3-(1H-Benzo[d][1,2,3]triazol-1-yl)-1-(thiophen-2-yl)propan-1-one (**5a**). White solid (53%, 68.1 mg), melting point: 74−76 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.77 (t, J = 7.2, 2H), 5.11 (t, J = 6.8, 2H), 6.41 (d, J = 1.6, 1H), 6.94 (d, J = 1.6, 1H), 7.10 (d, J = 4.4, 1H), 7.41−7.45 (m, 2H), 7.54 (d, J = 7.6, 1H), 8.12 (d, J = 8.0, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 39.9, 46.5, 110.3, 120.1, 120.3, 122.3, 124.5, 128.5, 132.9, 134.3, 146.0, 146.1, 191.1. HRMS (ESI-TOF) Calcd for $C_{13}H_{12}N_3OS$, $[M + H]^+$ 258.0702; Found 258.0706.

1-(Thiophen-2-yl)-3-(1H-1,2,4-triazol-1-yl)propan-1-one (**5b**). White solid (84%, 86.9 mg), melting point: 68−70 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.52 (d, J = 6.4, 2H), 4.62 (t, J = 6.4, 2H), 7.11 (t, J = 4.8, 1H), 7.65−7.69 (m, 2H), 7.91 (s, 1H), 8.21 (s, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 38.5, 44.0, 128.3, 132.5, 134.5, 143.1, 152.0, 189.3. HRMS (ESI-TOF) Calcd for $C_9H_{10}N_3OS$, $[M + H]^+$ 208.0544; Found 208.0540.

3-(5-Phenyl-1H-tetrazol-1-yl)-1-(thiophen-2-yl)propan-1-one (**5c**). White solid (53%, 75.2 mg), melting point: 53−55 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.77 (d, J = 6.8, 2H), 5.11 (t, J = 6.8, 2H), 7.16 (t, J = 4.4, 1H), 7.48 (q, J_1 = 1.6, J_2 = 5.2, 3H), 7.70 (d, J = 3.6, 1H), 7.77 (d, J = 3.6, 1H), 8.13(J_1 = 2.8, J_2 = 7.6, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 37.9, 47.9, 126.8, 127.3, 128.3, 128.9, 130.3, 132.5, 134.6, 143.0, 165.2, 188.4. HRMS (ESI-TOF) Calcd for $C_{14}H_{13}N_4OS$, $[M + H]^+$ 285.0810; Found 285.0815.

3-(1H-Pyrazol-1-yl)-1-(thiophen-2-yl)propan-1-one (**5d**). White solid (95%, 97.8 mg), melting point: 58−59 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.51 (t, J = 6.4, 2H), 4.57 (t, J = 6.8, 2H), 6.19 (t, J = 2.0, 1H), 7.10 (J = 4.0, 1H), 7.49 (dd, J_1 = 1.2, J_2 = 7.2, 2H), 7.63−7.69 (m, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 39.4, 45.6, 105.3, 128.2, 130.1, 132.4, 134.2, 139.7, 143.5, 190.2. HRMS (ESI-TOF) Calcd for $C_{10}H_{11}N_2OS$, $[M + H]^+$ 207.0591; Found 207.0587.

3-(1H-Pyrazol-1-yl)-1-(thiophen-3-yl)propan-1-one (**5e**). White solid (91%, 93.8 mg), melting point: 63−64 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.51 (t, J = 6.4, 2H), 4.58 (t, J = 6.8, 2H), 7.31 (q, J = 3.2, 1H), 7.48−7.51 (m, 3H), 8.05 (q = 1.2, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 39.9, 46.5, 105.3, 126.6, 126.7, 130.1, 132.5, 139.6, 141.7, 191.7. HRMS (ESI-TOF) Calcd for $C_{10}H_{11}N_2OS$, $[M + H]^+$ 207.0591; Found 207.0586.

1-(Furan-2-yl)-3-(1H-pyrazol-1-yl)propan-1-one (**5f**). White solid (87%, 62.7 mg), melting point: 55−57 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.44 (t, J = 6.4, 2H), 4.57 (t, J = 6.8, 2H), 6.19 (t, J = 2.0, 1H), 6.52 (q, J = 2.0, 1H), 7.18 (d, J = 3.6, 1H), 7.49 (dd, J_1 = 2.0, J_2 = 7.2, 2H), 7.57 (d, J = 1.6, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 38.6, 46.2, 105.3, 112.4, 117.7, 130.0, 139.6, 146.8, 152.2, 188.2. HRMS (ESI-TOF) Calcd for $C_{10}H_{11}N_2O_2$, $[M + H]^+$ 191.0821; Found 191.0824.

1-(Benzofuran-2-yl)-3-(1H-pyrazol-1-yl)propan-1-one (**5g**). White solid (81%, 97.2 mg) melting point: 64−65 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.59 (t, J = 6.4, 2H), 4.62 (t, J = 6.8, 2H), 6.20 (t, J = 2.0, 1H), 7.31 (s, 1H), 7.48−7.57 (m, 5H), 7.70 (d, J = 8.0, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 39.1, 46.2, 105.4, 112.5, 113.5, 123.4, 124.0, 126.9, 128.6, 130.1, 139.7, 152.0, 155.7, 188.3. HRMS (ESI-TOF) Calcd for $C_{14}H_{12}N_2O_2$, $[M + H]^+$ 241.0977; Found 241.0970.

1-Phenyl-3-(1H-pyrazol-1-yl)propan-1-one (**7a**). White solid (93%, 93.0 mg), melting point: 66−67 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.60 (t, J = 6.4, 2H), 4.62 (t, J = 6.8, 2H), 6.21 (t, J = 2.0, 1H), 7.44−7.52 (m, 4H), 7.57 (t, J = 7.6, 1H), 7.94 (t, J = 7.2, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 38.8, 46.6, 105.3, 128.0, 128.7, 130.1, 133.5, 136.4, 139.6, 197.4. HRMS (ESI-TOF) Calcd for $C_{12}H_{13}N_2O$, $[M + H]^+$ 201.1028; Found 201.1023.

3-(1H-Pyrazol-1-yl)-1-(o-tolyl)propan-1-one (**7b**). White oil (91%, 97.4 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 2.46 (s, 3H), 3.51 (t, J = 6.4, 2H), 4.58 (t, J = 6.4, 2H), 6.21 (t, J = 2.4, 1H), 7.23 (t, J = 6.8, 2H), 7.35 (t, J = 2.0, 1H), 7.49 (t, J = 3.2, 2H), 7.61 (d, J = 1.6, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 21.4, 41.4, 46.8, 105.3, 125.8, 128.7, 130.1, 131.8, 132.1, 137.0, 138.5, 139.6, 201.1. HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2O$, $[M + H]^+$ 215.1184; Found 215.1181.

1-(2-Chlorophenyl)-3-(1H-pyrazol-1-yl)propan-1-one (**7c**). White oil (87%, 101.8 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.56 (dd, J_1 = 1.2, J_2 = 6.4, 2H), 4.59 (dd, J_1 = 1.2, J_2 = 6.4, 2H), 6.21 (t, J = 1.6, 1H), 7.29−7.49 (m, 6H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 42.9, 46.6, 105.4, 126.9, 129.2, 130.0, 131.1, 132.2, 138.4, 139.6, 200.2. HRMS (ESI-TOF) Calcd for $C_{12}H_{12}ClN_2O$, $[M + H]^+$ 235.0634; Found 235.0630.

3-(1H-Pyrazol-1-yl)-1-(m-tolyl)propan-1-one (**7d**). White oil (96%, 102.7 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 2.36 (s, 3H), 3.55 (t, J = 6.4, 2H), 4.58 (t, J = 6.4, 2H), 6.18 (t, J = 2.0, 1H), 7.32 (t, J = 6.8, 2H), 7.49 (t, J = 2.4, 2H), 7.71 (d, J = 8.8, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 21.3, 38.4, 46.6, 105.3, 125.3, 128.5, 128.6, 130.1, 134.2, 138.5, 139.5, 197.6. HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2O$, $[M + H]^+$ 215.1184; Found 215.1188.

1-(3-Chlorophenyl)-3-(1H-pyrazol-1-yl)propan-1-one (**7e**). White oil (97%, 113.5 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.56 (m, 2H), 4.58 (t, J = 6.4, 2H), 6.21 (t, J = 2.0, 1H), 7.38−7.55 (m, 4H), 7.79−7.91 (m, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 38.9, 46.5, 105.4, 126.1, 128.2, 129.5, 130.0, 130.1, 133.4, 135.1, 137.8, 139.7, 196.2. HRMS (ESI-TOF) Calcd for $C_{12}H_{12}ClN_2O$, $[M + H]^+$ 235.0634; Found 235.0639.

3-(1H-Pyrazol-1-yl)-1-(p-tolyl)propan-1-one (**7f**). White oil (94%, 100.6 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 2.38 (s, 3H), 3.55 (t, J = 6.4, 2H), 4.58 (t, J = 6.4, 2H), 6.19 (t, J = 2.0, 1H), 7.23 (d, J = 8.0, 2H), 7.49 (d, J = 2.0, 2H), 7.82 (d, J = 8.0, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 21.7, 38.7, 46.7, 105.3, 128.2, 129.4, 130.1, 133.9, 139.5, 144.4, 197.1. HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2O$, $[M + H]^+$ 215.1184; Found 215.1189.

1-(4-Methoxyphenyl)-3-(1H-pyrazol-1-yl)propan-1-one (**7g**). White oil (93%, 107.0 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.55 (t, J = 6.4, 2H), 3.87 (s, 3H), 4.58 (t, J = 6.4, 2H), 6.20 (t, J = 2.0, 1H), 6.92 (d, J = 9.2, 2H), 7.50 (d, J = 2.0, 2H), 7.92 (dd, J_1 = 2.0, J_2 = 7.6, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 21.7, 38.7, 46.7, 105.3, 128.2, 129.4, 130.1, 133.9, 139.5, 144.4, 197.1. HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2O_2$, $[M + H]^+$ 231.1134; Found 231.1130.

1-(4-Cyclohexylphenyl)-3-(1H-pyrazol-1-yl)propan-1-one (**7h**). White oil (89%, 125.5 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 1.23−1.46 (m, 5H), 1.74−1.86 (m, 5H), 2.55 (d, J = 10.0, 1H), 3.56 (t, J = 6.4, 2H), 4.59 (t, J = 6.4, 2H), 6.19 (s, 1H), 7.28 (d, J = 8.4, 2H), 7.49 (d, J = 2.0, 2H), 7.86 (d, J = 8.0, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 25.9, 28.7, 34.1, 38.8, 44.6, 46.6, 109.2, 127.2, 128.3, 130.1, 134.2, 139.5, 156.2, 197.0. HRMS (ESI-TOF) Calcd for $C_{18}H_{23}N_2O$, $[M + H]^+$ 283.1807; Found 283.1810.

1-([1,1′-Biphenyl]-4-yl)-3-(1H-pyrazol-1-yl)propan-1-one (**7i**). White solid (93%, 128.3 mg), melting point: 119−120 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.63 (t, J = 6.4, 2H), 4.63 (t, J = 6.4, 2H), 6.23 (t, J = 2.0, 1H), 7.40−7.53 (m, 5H), 7.61−8.02 (m, 6H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 38.8, 46.7, 109.3, 127.3, 128.4, 128.7, 128.9, 130.1, 135.1, 139.6, 146.1, 196.9. HRMS (ESI-TOF) Calcd for $C_{18}H_{17}N_2O$, $[M + H]^+$ 277.1341; Found 277.1346.

1-(4-Fluorophenyl)-3-(1H-pyrazol-1-yl)propan-1-one (**7j**). White oil (96%, 104.6 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.57 (t, J = 6.4, 2H), 4.60 (t, J = 6.4, 2H), 6.21 (s, 1H), 7.12 (t, J = 8.4, 2H), 7.60 (t, J = 6.4, 2H), 7.97 (q, J = 5.6, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 38.7, 46.6, 105.3, 115.7, 115.9, 130.1, 130.7, 130.8, 132.8, 139.6, 164.7, 167.2 (d, ^{1}JC-F = 254 Hz), 195.8. HRMS (ESI-TOF) Calcd for $C_{12}H_{12}FN_2O$, $[M + H]^+$ 219.0934; Found 219.0936.

1-(4-Chlorophenyl)-3-(1H-pyrazol-1-yl)propan-1-one (**7k**). White solid (97%, 113.9 mg), melting point: 72−73 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.57 (t, J = 6.4, 2H), 4.60 (t, J = 6.4, 2H), 6.21 (t, J = 2.0, 1H), 7.44 (t, J = 2.0, 2H), 7.50 (q, J = 2.4, 2H), 7.89 (d, J = 8.8, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 38.8, 46.6, 105.3, 129.0, 129.4, 130.1, 134.7, 139.7, 140.0, 196.3. HRMS (ESI-TOF) Calcd for $C_{12}H_{12}ClN_2O$, $[M + H]^+$ 235.0634; Found 235.0638.

1-(4-Bromophenyl)-3-(1H-pyrazol-1-yl)propan-1-one (**7l**). White solid (91%, 126.5 mg), melting point: 95−97 °C (91%, 126.5 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.55 (t, J = 6.4, 2H), 4.58 (t, J = 6.4, 2H), 6.21 (t, J = 2.0, 1H), 7.49 (q, J = 2.4, 2H), 7.58 (t, J = 7.2, 2H), 7.78 (d, J = 8.4, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 38.7, 46.5,

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105.3, 128.7, 129.5, 130.0, 132.0, 135.1, 139.7, 196.5. HRMS (ESI-TOF) Calcd for $C_{12}H_{12}BrN_2O$, $[M + H]^+$ 279.0134; Found 279.0137.

*1-(4-Nitrophenyl)-3-(1H-pyrazol-1-yl)propan-1-one (**7m**).* White solid (93%, 113.9 mg), melting point: 106−107 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.65 (t, J = 6.4, 2H), 4.62 (t, J = 6.4, 2H), 6.22 (t, J = 2.0, 1H), 7.50 (d, J = 8.8, 2H), 8.10 (d, J = 8.8, 2H), 8.30 (d, J = 8.4, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 39.2, 46.3, 105.5, 123.9, 129.1, 130.2, 139.8, 140.7, 196.1. HRMS (ESI-TOF) Calcd for $C_{12}H_{12}N_3O_3$, $[M + H]^+$ 246.0877; Found 246.0871.

*4-(3-(1H-Pyrazol-1-yl)propanoyl)benzonitrile (**7n**).* White oil (88%, 100.3 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.60 (t, J = 6.4, 2H), 4.59 (t, J = 6.4, 2H), 6.20 (t, J = 2.0, 1H), 7.48 (d, J = 2.0, 2H), 7.75 (d, J = 6.4, 2H), 8.01 (dd, J_1 = 1.6, J_2 = 6.8, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 38.9, 46.3, 105.4, 116.7, 117.6, 128.5, 130.2, 132.6, 139.2, 139.8, 196.3. HRMS (ESI-TOF) Calcd for $C_{13}H_{12}N_3O$, $[M + H]^+$ 226.0980; Found 226.0975.

*3-(1H-Pyrazol-1-yl)-1-(4-(trifluoromethyl)phenyl)propan-1-one (**7o**).* White solid (87%, 116.6 mg), melting point: 51−52 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.61 (t, J = 6.4, 2H), 4.60 (t, J = 6.4, 2H), 6.20 (t, J = 2.0, 1H), 7.50 (d, J = 1.6, 2H), 7.71 (d, J = 8.4, 2H), 8.02 (d, J = 8.0, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 39.0, 46.3, 105.9, 122.1, 125.7, 125.8, 128.4 (d, ^{1}JC-F = 258 Hz), 130.1, 134.5, 134.8, 138.9, 139.7, 196.6. HRMS (ESI-TOF) Calcd for $C_{13}H_{12}F_3N_2O$, $[M + H]^+$ 269.0904; Found 269.0909.

*Methyl 4-(3-(1H-Pyrazol-1-yl)propanoyl)benzoate (**7p**).* White oil (89%, 114.8 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.63 (t, J = 6.4, 2H), 3.96 (s, 1H), 4.62 (t, J = 6.4, 2H), 6.22 (t, J = 2.0, 1H), 7.52 (s, 2H), 8.00 (d, J = 8.8, 2H), 8.12 (d, J = 8.4, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 39.1, 46.5, 52.5, 105.4, 127.9, 129.8, 130.1, 134.2, 139.5, 139.7, 166.1, 197.0. HRMS (ESI-TOF) Calcd for $C_{14}H_{15}N_2O_3$, $[M + H]^+$ 259.1083; Found 259.1080.

*3-(1H-Pyrazol-1-yl)-1-(2,3,4-trichlorophenyl)propan-1-one (**7q**).* White oil (85%, 128.4 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.51 (t, J = 6.4, 2H), 4.57 (t, J = 6.4, 2H), 6.21 (t, J = 2.0, 1H), 7.20 (d, J = 8.4, 1H), 7.40−7.48 (m, 3H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 42.9, 46.5, 105.5, 126.6, 128.6, 130.1, 130.9, 133.1, 136.8, 139.0, 139.7, 199.2. HRMS (ESI-TOF) Calcd for $C_{12}H_{10}Cl_3N_2O$, $[M + H]^+$ 302.9859; Found 302.9853.

*1-(Naphthalen-2-yl)-3-(1H-pyrazol-1-yl)propan-1-one (**7r**).* White solid (94%,117.5 mg), melting point: 98−100 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.74 (t, J = 6.4, 2H), 4.63 (t, J = 6.4, 2H), 6.23 (t, J = 2.0, 1H), 7.54−7.61 (m, 4H), 7.86−8.02 (m, 4H), 8.45 (s, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 38.3, 46.8, 105.3, 123.5, 126.9, 127.8, 128.6, 128.7, 129.6, 130.0, 130.1, 132.4, 133.7, 135.7, 139.7, 197.4. HRMS (ESI-TOF) Calcd for $C_{16}H_{15}N_2O$, $[M + H]^+$ 251.1184; Found 251.1180.

*2-Methyl-1-phenyl-3-(1H-pyrazol-1-yl)propan-1-one (**7s**).* White oil (96%, 102.7 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 1.21 (d, J = 6.4, 3H), 4.19−4.26 (m, 2H), 4.62 (t, J = 9.36, 1H), 6.15 (s, 1H), 7.39−7.56 (m, 5H), 7.91 (d, J = 8.0, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 16.1, 41.9, 54.0, 105.1, 128.4, 128.7, 130.4, 133.4, 135.8, 139.8, 202.2. HRMS (ESI-TOF) Calcd for $C_{13}H_{15}N_2O$, $[M + H]^+$ 215.1183; Found 215.1179.

*2-Methyl-3-(1H-pyrazol-1-yl)-1-(p-tolyl)propan-1-one (**7t**).* White oil (94%, 107.2 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 1.20 (d, J = 7.2, 3H), 2.39 (s, 3H), 4.22 (q, J = 6.4, 2H), 4.57 (d, J = 6.4, 1H), 6.15 (t, J = 2.0, 1H), 7.22−7.51 (m, 5H), 7.84 (d, J = 8.8, 2H), 8.01 (d, J = 8.0, 1H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 15.9, 21.6, 41.8, 54.0, 105.2, 129.0, 129.8, 130.4, 134.1, 139.9, 201.8. HRMS (ESI-TOF) Calcd for $C_{14}H_{17}N_2O$, $[M + H]^+$ 229.1338; Found 229.1341.

*1-(4-Chlorophenyl)-2-methyl-3-(1H-pyrazol-1-yl)propan-1-one (**7u**).* White oil (95%, 117.8 mg); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 1.20 (d, J = 7.2, 3H), 4.22 (q, J = 6.4, 2H), 4.57 (d, J = 6.4, 1H), 6.15 (t, J = 2.0, 1H), 7.36−7.49 (m, 4H), 7.84 (d, J = 8.8, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ = 16.2, 21.6, 41.7, 54.0, 105.1, 128.5, 129.1, 129.4, 130.1, 130.6, 133.3, 139.7, 144.3, 201.6. HRMS (ESI-TOF) Calcd for $C_{13}H_{14}ClN_2O$, $[M + H]^+$ 249.0791; Found 249.0794.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02593.

Optimization details, X-ray data for compounds **3k** and **7r**, and copies of ^{1}H and ^{13}C NMR spectra for **3**, **5**, **7**, and **A** (PDF)

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

Crystallographic data for **7r** (CIF)

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Notes

The authors declare no competing financial interest.

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