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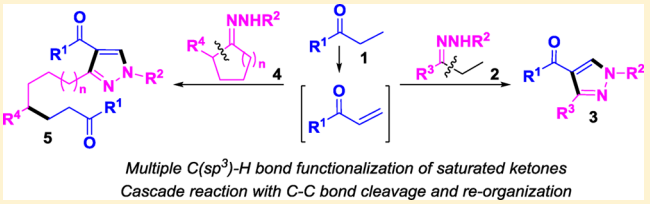
Synthesis of 4-Acylpyrazoles from Saturated Ketones and Hydrazones Featured with Multiple C(sp^3)−H Bond Functionalization and C−C Bond Cleavage and Reorganization

Miaomiao Tian, Xiaonan Shi, Xinying Zhang,* and Xuesen Fan*

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

Supporting Information

ABSTRACT: In this paper, an efficient and convenient one-pot synthesis of diversely substituted 4-acylpyrazole derivatives via copper-catalyzed one-pot cascade reactions of saturated ketones with hydrazones is reported. Mechanistically, the formation of the title compounds involves the in situ formation of an enone intermediate through the dehydrogenation of a saturated ketone and the [2 + 3] cyclization of the enone with hydrazone followed by an aromatization-driven C−C bond cleavage and reorganization. To our knowledge, this is the first example in which the biologically and pharmaceutically important yet otherwise difficult-to-obtain 4-acylpyrazole derivatives are directly prepared from saturated ketones and hydrazones featured with multiple aliphatic C−H bond functionalization and C−C bond cleavage and reorganization. Compared with literature methods, this novel process has advantages such as simple and economical starting materials, a sustainable oxidant, excellent regioselectivity, and good efficiency.



Multiple C(sp^3)-H bond functionalization of saturated ketones
Cascade reaction with C-C bond cleavage and re-organization

INTRODUCTION

The pyrazole unit is an essential building block embedded in compounds routinely used as pharmaceuticals, agrochemicals, and functional materials, etc.[1−4] Due to its importance, numerous methods for the construction of the pyrazole scaffold have been developed.[1−8] While these literature protocols are generally reliable, some of them still suffer from limitations such as the difficulty in obtaining the prefunctionalized substrates, poor regioselectivity, and harsh reaction conditions. Therefore, the development of a more selective and general method to prepare pyrazoles with diverse substitution patterns starting from simple and/or easily obtainable substrates remains a highly desirable yet still challenging topic.

In recent years, direct functionalization of the inert C(sp^3)−H bonds has attracted much attention. Among various versions of C(sp^3)−H bond functionalization, the oxidative dehydrogenation of saturated ketones without preactivation, affording the corresponding enone derivatives, is of significant importance as enones are highly valuable in organic synthesis.[9,10] Moreover, some elegantly designed one-pot cascade reactions combining the oxidative dehydrogenation of saturated ketones with other kinds of transformations, leading to the formation of advanced molecular scaffolds, have also been successfully realized.[11−15] Inspired by those pioneering studies and as a continuation of our own interest in this aspect,[16] we have designed an alternative synthesis of 1,5-disubstituted pyrazoles from the reaction of saturated ketones with hydrazine by taking advantage of the C(sp^3)−H bond functionalization strategy. During our study on this proposal, we serendipitously found a novel synthesis of the otherwise difficult-to-obtain 1,3,4-trisubstituted pyrazoles with an acyl unit attached on the 4-position of the pyrazole scaffold. Herein, we report the results we obtained in this regard.

RESULTS AND DISCUSSION

Our study was commenced by treating propiophenone (**1a**; 0.6 mmol) with phenylhydrazine (**I**; 0.5 mmol) in the presence of $Cu(OAc)_2$ (0.1 mmol), TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxyl; 0.5 mmol), and bpy (2,2′-bipyridine; 0.05 mmol) in toluene at 120 °C for 10 h under N_2.[16] From this reaction, the proposed 1,5-diphenylpyrazole (**II**) was not obtained. An unexpected product, 1,3-diphenyl-4-benzoylpyrazole (**3a**), was isolated in a yield of 15% (Scheme 1).

Notwithstanding the proposed 1,5-diphenylpyrazole (**II**) was not obtained, it occurred to us that the unexpected formation of **3a** might be more interesting owing to the following reasons: (1) 4-acyl-substituted pyrazole derivatives are well-known for their biological activities and rich reactivity;[17] (2) in spite of their importance, synthetic methods for the preparation of 4-acylpyrazoles are only scarcely available.[17,18] On the basis of these facts, we decided to thoroughly study this newly found reaction with the aim to establish it into a novel and practical synthesis of 4-acylpyrazole derivatives.

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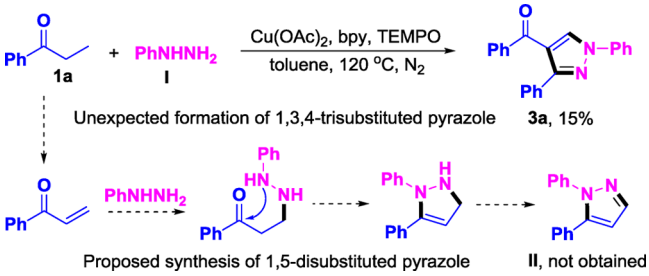
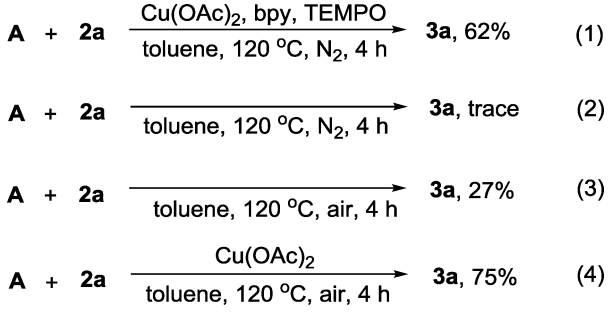
Scheme 1. Unexpected Formation of 3a from the Reaction of 1a with I



Scheme 3. Control Experiments I



First, we need to clarify how **3a** is formed from the reaction of **1a** with **I**. On the basis of the structure of **3a**, we postulate that **1a** should first condense with **I** to give hydrazone **2a**. Meanwhile, an oxidative dehydrogenation occurs with **1a** to give enone **A**,[10] which then undergoes a conjugate addition with **2a** to afford adduct **B**. Next, an intramolecular nucleophilic addition occurs with **B** to afford tetrahydropyrazole **C**. Through an oxidative dehydrogenation of **C**, dihydropyrazole **D** is formed. Finally, an aromatization-driven C−C bond cleavage occurs with **D** to afford **3a** as the final product (Scheme 2).

To verify the reaction mechanism as shown in Scheme 2, some control experiments were carried out. First, the proposed enone **A**[10] and hydrazone **2a** were synthesized separately from **1a** and **I**. Then 0.5 mmol of **A** was treated with 0.5 mmol of **2a** in the presence of $Cu(OAc)_2$ (0.1 mmol), TEMPO (0.5 mmol), and bpy (0.05 mmol). From this reaction, **3a** was obtained in a yield of 62% (Scheme 3, reaction 1). This result indicated that **A** and **2a** should be the key intermediates in the formation of **3a**. Another control experiment showed that, in the absence of any oxidant, **3a** was formed only in a trace amount (Scheme 3, reaction 2). When the reaction was carried out under air, **3a** was obtained in a yield of 27% (Scheme 3, reaction 3). In the presence of 0.2 equiv of $Cu(OAc)_2$ under air, on the other hand, the yield of **3a** increased to 75% (Scheme 3, reaction 4). These results revealed that an oxidant is indispensable for the formation of **3a** from the reaction of **A** with **2a** and a combination of Cu(II) with air can act as an efficient oxidant for this transformation.

Moreover, it should be noted herein that violent gas bubbling was observed in the initial stage of the reaction shown in Scheme 1, most likely due to the generation of nitrogen through the oxidation and decomposition of **I** under the promotion of $Cu(OAc)_2$ and TEMPO.[19] In other words, when the mixture of **1a** and **I** was directly treated with $Cu(OAc)_2$ and TEMPO, **I** could be consumed by the oxidant and decomposed rapidly before it had the chance to react with **1a** to afford **2a**. That is why the yield of **3a** was only 15% in that case.

On the basis of the results as described above, we tried to realize the preparation of **3a** in a more efficient manner by directly using **1a** and **2a**, instead of **1a** and **I**, as the substrates to prevent the oxidation and decomposition of **I**. To be specific, 0.5 mmol of **1a** was treated with 0.1 mmol of $Cu(OAc)_2$, 0.5 mmol of TEMPO, and 0.05 mmol of bpy in toluene at 120 °C under N_2 for 10 h. The resulting mixture was then treated with 0.5 mmol of **2a** at 120 °C under air for 4 h. From this reaction, **3a** was obtained in a yield of 60%. To further improve the yield of **3a**, a series of solvents, various temperatures and periods, and different amounts of **1a**, **2a**, and the oxidants were screened. After some trials and errors, we found that a yield of 72% could be realized through treatment of 0.6 mmol of **1a** with 0.1 mmol of $Cu(OAc)_2$, 0.5 mmol of TEMPO, and 0.05 mmo1 of bpy in chlorobenzene (PhCl) under N_2 at 120 °C for 10 h and then with 0.5 mmol of **2a** under air at 120 °C for 4 h.

With the optimized reaction conditions in hand, the scope and generality of this 4-acylpyrazole-forming reaction was studied, and the results are listed in Table 1. First, a range of ketones **1** were screened by using **2a** as a model substrate. It turned out that propiophenones with various substituents on the phenyl ring reacted with **2a** smoothly to give **3a**−**3h** in good yields. Various functional groups, from the electron-donating methoxy to the electron-withdrawing trifluoromethyl, were very compatible with the reaction conditions. Meanwhile, it was also noted that the electronic nature of the phenyl unit of **1** had some effect on the outcome of this reaction in that substrates bearing electron-withdrawing groups (EWGs) on the phenyl ring generally showed higher efficiency than those with electron-donating groups (EDGs) (**3b**−**3d**, **3g** vs **3e**, **3f**). Moreover, heteroaromatic ketones such as 2-propionylthiophene and 3-propionylpyridine took part in this cascade process to give **3i** and **3j** with equally good efficiency. Interestingly, an aliphatic ketone, 1-cyclohexylpropan-1-one,

Scheme 2. Plausible Reaction Pathway Accounting for the Formation of 3a

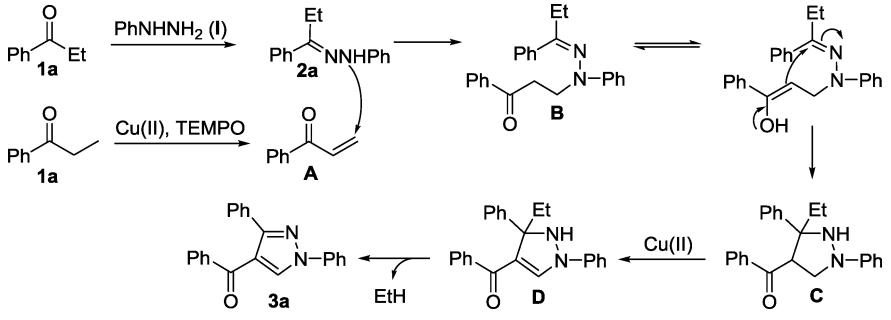


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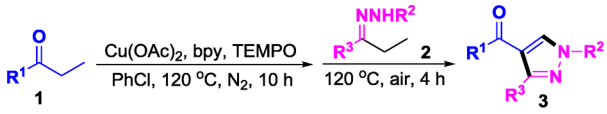
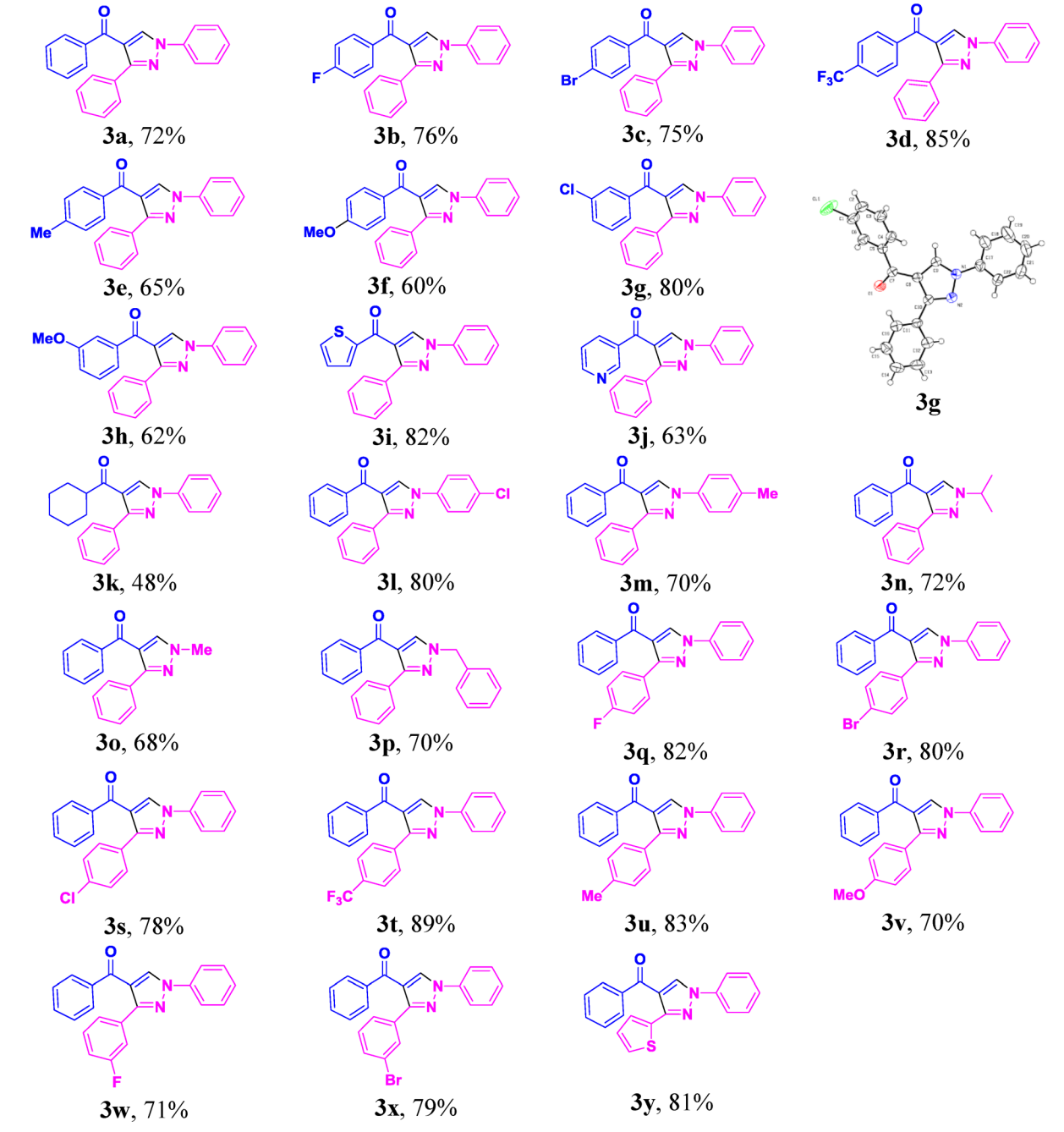
Table 1. Substrate Scope for the Preparation of 3[a,b]





[a]Reaction conditions: **1** (0.6 mmol), **2** (0.5 mmol), $Cu(OAc)_2$ (0.1 mmol), TEMPO (0.5 mmol), bpy (0.05 mmol), PhCl (3 mL). [b]Isolated yields.

was also found to be compatible, although the yield of the corresponding product **3k** was lower. Next, the scope of hydrazones **2** was studied. It was first found that hydrazones derived from 4-chlorophenylhydrazine, 4-methylphenylhydrazine, isopropylhydrazine, methylhydrazine, or benzylhydrazine could take part in this cascade reaction as smoothly as **2a** to give **3l**−**3p** in moderate to good yields. Promisingly, hydrazones **2** derived from diversely substituted propiophenones and 2-propionylthiophene were also found to be suitable substrates for this reaction to give **3q**−**3y** in reasonably good yields.

Next, the scope of the hydrazone substrates was extended from acyclic ketone hydrazones **2** to cyclic ketone hydrazones **4**. Thus, **1a** was allowed to react with 1-cyclopentylidene-2-phenylhydrazine (**4a**) following the procedure employed in the preparation of **3**. To our surprise, the expected (3-butyl-1-phenyl-1*H*-pyrazol-4-yl)phenylmethanone (**III**) was not obtained from this reaction. Instead, 7-(4-benzoyl-1-phenyl-1*H*-

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Scheme 4. Unexpected Formation of 5a from the Reaction of 1a and 4a

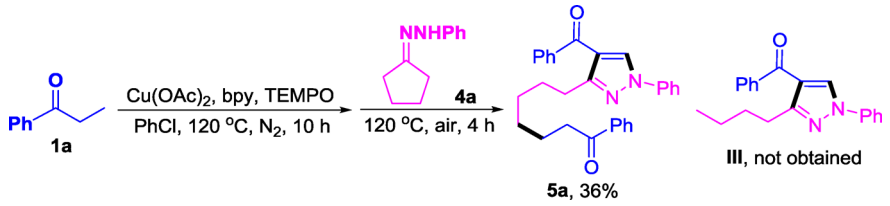
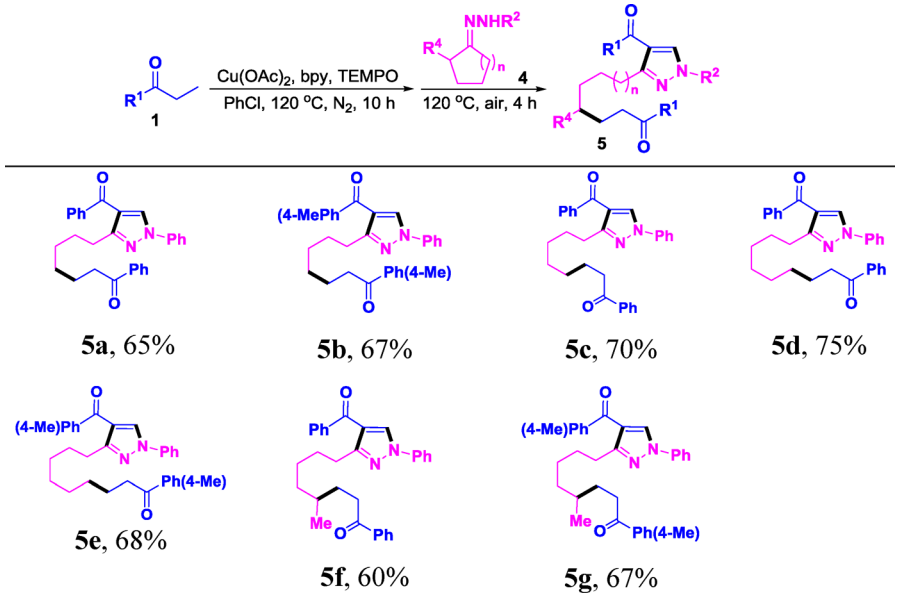
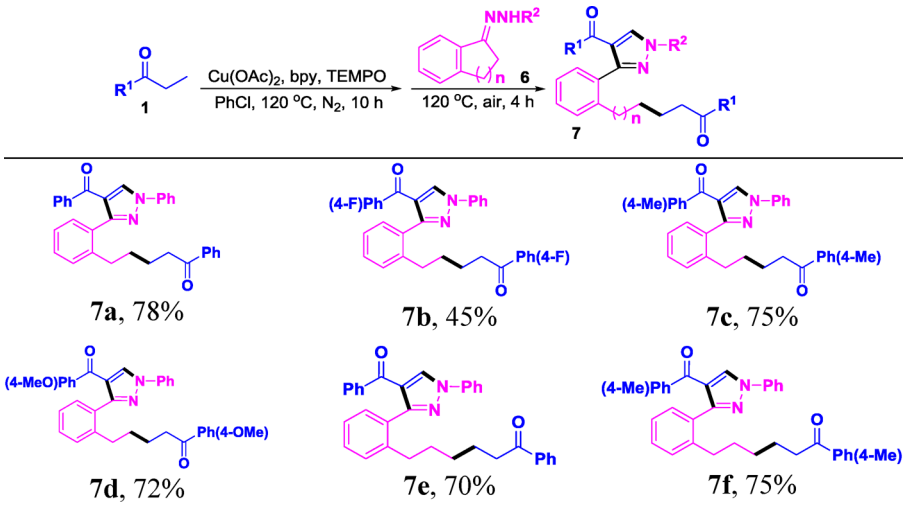


Table 2. Substrate Scope for the Preparation of 5[a,b]



[a]Reaction conditions: **1** (1.2 mmol), **4** (0.5 mmol), $Cu(OAc)_2$ (0.2 mmol), TEMPO (1 mmol), bpy (0.1 mmol), PhCl (3 mL). [b]Isolated yields.

Table 3. Substrate Scope for the Preparation of 7[a,b]



[a]Reaction conditions: **1** (1.2 mmol), **6** (0.5 mmol), $Cu(OAc)_2$ (0.2 mmol), TEMPO (1 mmol), bpy (0.1 mmol), PhCl (3 mL). [b]Isolated yields.

pyrazol-3-yl)-1-phenylheptan-1-one (**5a**) was formed in a yield of 36% (Scheme 4).

We realized that this should be a synthetically promising and mechanistically intriguing transformation as it led to a novel pyrazole derivative (**5a**) with a considerable increase in its molecular complexity compared with that of **3a**. Meanwhile, the structure of **5a** indicated that 2 equiv of **1a** should have been involved by acting as the required enone intermediate, in situ formed via the oxidative dehydrogenation. Under this circumstance, we tried to improve the yield of **5a** by increasing the amounts of **1a** and the oxidants. Thus, 1.2 mmol of **1a** was treated with 0.2 mmol of $Cu(OAc)_2$, 1 mmol of TEMPO, and 0.1 mmo1 of bpy in PhCl at 120 °C under N_2 for 10 h, and the resulting mixture was then treated with 0.5 mmol of **4a** under air at 120 °C for 4 h. From this one-pot cascade process, **5a** was obtained in a yield of 65% (Table 2).

To explore the substrate scope of this novel reaction, attempts were made to react several cyclic ketone hydrazones **4**

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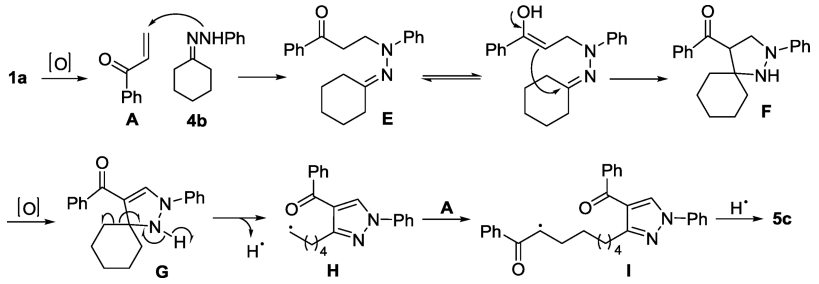
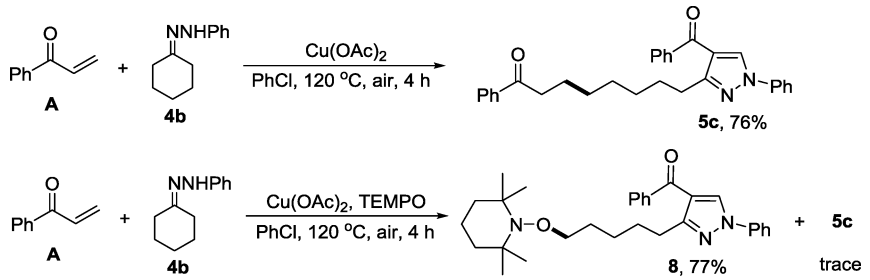
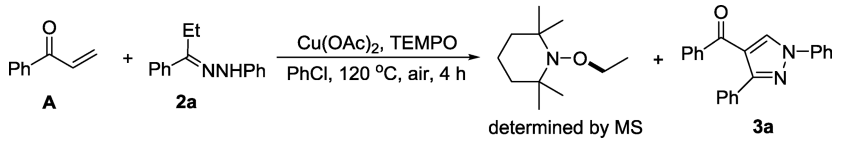
Scheme 5. Proposed Mechanism Accounting for the Formation of 5c



Scheme 6. Control Experiments II



Scheme 7. Control Experiments III



with propiophenone (R^1 = Ph) or 1-(*p*-tolyl)propan-1-one (R^1 = 4-CH_3Ph). The results listed in Table 2 showed that, in addition to hydrazone derived from cyclopentanone, from which **5a** and **5b** were obtained, those derived from cyclohexanone or cycloheptanone could also take part in this reaction to afford **5c**, **5d**, and **5e** in good yields. Promisingly, the reactions of the hydrazones derived from 2-methylcyclohexanone not only took place smoothly but also showed an excellent regioselectivity in that only the more substituted α-C−C bond of the hydrazone was broken to afford **5f** and **5g** in 60% and 67% yields, respectively.[20]

Next, the substrate scope was extended from hydrazones derived from simple cyclic ketones (**4**) to those derived from 2,3-dihydro-1*H*-inden-1-one and 3,4-dihydronaphthalen-1(2*H*)-one (**6**). To our pleasure, the corresponding reactions proceeded smoothly to give 4-acylpyrazole derivatives with a phenyl group bearing an *ortho*-functionalized side chain attached on the 3-position of the pyrazole scaffold in moderate to good yields (**7a**−**7f**, Table 3).

On the basis of the above results, a plausible mechanism for the formation of 8-(4-benzoyl-1-phenyl-1*H*-pyrazol-3-yl)-1-phenyloctan-1-one (**5c**) from the reaction of **1a** with 1-cyclohexylidene-2-phenylhydrazine (**4b**) was proposed in Scheme 5. Initially, **1a** is transformed into enone **A** through an oxidative dehydrogenation. Next, conjugate addition of **4b** onto **A** affords intermediate **E**, which then undergoes an intramolecular nucleophilic addition to give a spirocyclic tetrahydropyrazole (**F**). Through the dehydrogenation of **F**, dihydropyrazole **G** is formed, which then undergoes an aromatization-driven ring opening through C−C bond cleavage to form 4-acylpyrazole attached to an alkyl chain radical (**H**). The alkyl chain radical is then trapped by enone **A** to afford a radical intermediate (**I**). Finally, **I** couples with a hydrogen radical to give the final product **5c**.

To verify the reaction mechanism as described in Scheme 5, the following control experiments were carried out. First, the preprepared enone **A** (1 mmol) was treated with **4b** (0.5 mmol) in the presence of $Cu(OAc)_2$ (0.1 mmol) under air. From this reaction, **5c** was obtained in a yield of 76%. When **A** (1 mmol) was treated with **4b** (0.5 mmol) in the presence of $Cu(OAc)_2$ (0.1 mmol) and TEMPO (0.5 mmol) under air, phenyl(1-phenyl-3-(5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-pentyl)-1*H*-pyrazol-4-yl)methanone (**8**) was isolated in a yield of 77%, and the formation of **5c** was almost completely inhibited (Scheme 6). This study suggests that the formation of **5c** should involve a single electron transfer (SET) process, and the proposed C-radical **H** (Scheme 5) must be a key intermediate leading to the formation of **5c**.

Furthermore, it is reasonable to deduce that the formation of **3a** from the reaction of **1a** with **2a** might involve an elimination of an ethyl radical (Et•) from the in situ formed dihydropyrazole intermediate **D** as shown in Scheme 2. To verify this proposal, **A** was treated with **2a** in the presence of $Cu(OAc)_2$ and TEMPO. From this reaction, 1-ethoxy-2,2,6,6-tetramethylpiperidine, the proposed radical-trapping product, was identified by a GC−MS study (Scheme 7).

Finally, to showcase the utility of this new synthetic method, we have tried to prepare **3a** on a 5 mmol scale. As a result, **3a** was obtained in a total yield of 61%. Moreover, we have also tried to prepare **5a** on an enlarged scale of 5 mmol, and **5a** was obtained in a yield of 55% (Scheme 8).

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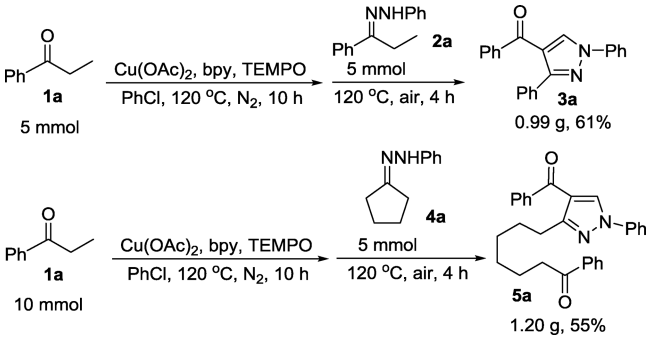
Scheme 8. Gram-Scale Synthesis of 3a and 5a



In summary, we have developed a novel and efficient one-pot synthesis of diversely substituted 4-acylpyrazole derivatives directly from saturated ketones and hydrazones through multiple aliphatic C−H bond functionalization and C−C bond cleavage and reorganization. With advantages such as simple and economical starting materials, a sustainable oxidant, excellent regioselectivity, and high efficiency, this new synthetic strategy is expected to find wide applications in both heterocyclic and medicinal chemistry.

EXPERIMENTAL SECTION

General Methods. Commercial reagents were used without further purification, and solvents were dried before use. Melting points were recorded with a micro melting point apparatus and are uncorrected. The ^{1}H NMR spectra were recorded at 400 or 600 MHz. The ^{13}C NMR spectra were recorded at 100 or 150 MHz. Chemical shifts are expressed in parts per million (δ) downfield from the internal standard tetramethylsilane and are reported as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), dt (doublet of triplets), m (multiplet), br s (broad singlet), etc. The coupling constants J are given in hertz. High-resolution mass spectrometry (HRMS) was performed in ESI mode by 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 the components were visualized by observation under UV light (254 and 365 nm).

Experimental Procedures. *Typical Procedure for the Synthesis of 3a.* To a reaction tube equipped with a stir bar were added propiophenone (**1a**; 81 mg, 0.6 mmol), PhCl (3 mL), $Cu(OAc)_2$ (18 mg, 0.1 mmol), bpy (8 mg, 0.05 mmol), and TEMPO (78 mg, 0.5 mmol). The mixture was stirred at 120 °C under N_2 for 10 h. In another reaction tube, propiophenone (67 mg, 0.5 mmol) was treated with phenylhydrazine (54 mg, 0.5 mmol) in ethanol (2 mL) at ambient temperature for 0.5 h to give 1-phenyl-2-(1-phenylpropylidene)hydrazine (**2a**), which was then transferred into the first reaction tube after the mixture had been concentrated under reduced pressure to remove ethanol and diluted with PhCl. The resulting mixture was then stirred under air at 120 °C for 4 h. Upon completion, it was diluted with DCM (15 mL) and washed with water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20:1) as the eluent to give **3a**. **3b**−**3w** were obtained in a similar manner.

*(1,3-Diphenyl-1H-pyrazol-4-yl)phenylmethanone (**3a**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (117 mg, 72%). Mp: 143−145 °C (lit.[18b] 138−141 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.42 (m, 6H), 7.47−7.54 (m, 3H), 7.72−7.74 (m, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 7.6 Hz, 2H), 8.28 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 119.6, 121.2, 127.6, 128.2, 128.4, 128.6, 128.9, 129.5, 129.7, 132.1, 132.3, 132.6, 138.9, 139.3, 154.0, 190.1. HRMS: calcd for $C_{22}H_{16}N_2ONa$ 347.1155 $[M + Na]^+$, found 347.1157.

*(1,3-Diphenyl-1H-pyrazol-4-yl)(4-fluorophenyl)methanone (**3b**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (130 mg, 76%). Mp: 146−147 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.03 (t, J = 8.4 Hz, 2H), 7.30−7.32 (m, 3H), 7.34 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 7.66−7.68 (m, 2H), 7.77−7.80 (m, 2H), 7.82−7.84 (m, 2H), 8.27 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 115.5 (d, $^2J_{C-F}$ = 21.9 Hz), 119.6, 121.1, 127.6, 128.2, 128.7, 128.9, 129.7, 132.0, 132.1 (d, $^3J_{C-F}$ = 9.9 Hz), 135.0 (d, $^4J_{C-F}$ = 3.3 Hz), 139.2, 153.8, 165.5 (d, $^1J_{C-F}$ = 252.6 Hz), 188.6. HRMS: calcd for $C_{22}H_{15}FN_2ONa$ 365.1061 $[M + Na]^+$, found 365.1031.

*(4-Bromophenyl)(1,3-diphenyl-1H-pyrazol-4-yl)methanone (**3c**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (150 mg, 75%). Mp: 153−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.34 (m, 3H), 7.37 (t, J = 7.6 Hz, 1H), 7.48−7.53 (m, 4H), 7.67−7.70 (m, 4H), 7.78 (dd, J_1 = 8.8 Hz, J_2 = 1.2 Hz, 2H), 8.28 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 119.6, 121.0, 127.6, 127.7, 128.2, 128.8, 128.9, 129.7, 131.0, 131.6, 131.9, 132.2, 137.6, 139.2, 153.9, 188.9. HRMS: calcd for $C_{22}H_{16}BrN_2O$ 403.0441 $[M + H]^+$, found 403.0452.

*(1,3-Diphenyl-1H-pyrazol-4-yl)(4-(trifluoromethyl)phenyl)-methanone (**3d**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (167 mg, 85%). Mp: 163−165 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.38 (m, 4H), 7.46−7.50 (m, 2H), 7.62 (d, J = 8.0 Hz, 2H), 7.66−7.69 (m, 2H), 7.76−7.78 (m, 2H), 7.87 (d, J = 8.0 Hz, 2H), 8.29 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 119.6, 120.9, 123.6 (q, $^1J_{C-F}$ = 271.3 Hz), 125.4 (q, $^3J_{C-F}$ = 3.7 Hz), 127.8, 128.2, 128.8, 129.0, 129.6, 129.7, 131.8, 132.6, 133.8 (q, $^2J_{C-F}$ = 32.8 Hz), 139.1, 141.9, 154.2, 188.8. HRMS calcd for $C_{23}H_{16}F_3N_2O$: 393.1209 $[M + H]^+$, found 393.1210.

*(1,3-Diphenyl-1H-pyrazol-4-yl)-p-tolylmethanone (**3e**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (110 mg, 65%). Mp: 159−161 °C (lit.[18b] 151−155 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H), 7.19 (d, J = 8.0 Hz, 2H), 7.32−7.35 (m, 4H), 7.47 (t, J = 8.0 Hz, 2H), 7.74−7.78 (m, 6H), 8.24 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7, 119.5, 121.4, 127.4, 128.2, 128.6, 128.9, 129.1, 129.6, 129.7, 132.0, 132.2, 136.3, 139.3, 143.5, 153.8, 189.8. HRMS: calcd for $C_{23}H_{19}N_2O$ 339.1492 $[M + H]^+$, found 339.1474.

*(1,3-Diphenyl-1H-pyrazol-4-yl)(4-methoxyphenyl)methanone (**3f**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid (106 mg, 60%). Mp: 132−134 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.85 (s, 3H), 6.87 (dd, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 2H), 7.32−7.34 (m, 3H), 7.37 (d, J = 7.2 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 7.71−7.73 (m, 2H), 7.79 (d, J = 7.6 Hz, 2H), 7.85 (dd, J_1 = 6.8 Hz, J_2 = 2.0 Hz, 2H), 8.26 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 55.5, 113.6, 119.5, 121.5, 127.4, 128.2, 128.5, 128.8, 129.6, 131.4, 131.6, 132.0, 132.2, 139.4, 153.6, 163.4, 188.9. HRMS: calcd for $C_{23}H_{18}N_2O_2Na$ 377.1260 $[M + Na]^+$, found 377.1228.

*(3-Chlorophenyl)(1,3-diphenyl-1H-pyrazol-4-yl)methanone (**3g**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (143 mg, 80%). Mp: 154−156 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (t, J = 7.8 Hz, 1H), 7.33−7.35 (m, 3H), 7.38 (t, J = 7.8 Hz, 1H), 7.47 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 7.66−7.69 (m, 3H), 7.78−7.80 (m, 3H), 8.31 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 119.7, 120.9, 127.6, 127.7, 128.2, 128.8, 129.0, 129.4, 129.6, 129.7, 131.9, 132.3, 132.5, 134.6, 139.2, 140.4, 154.1, 188.6. HRMS: calcd for $C_{22}H_{15}ClN_2ONa$ 381.0765 $[M + Na]^+$, found 381.0769.

*(1,3-Diphenyl-1H-pyrazol-4-yl)(3-methoxyphenyl)methanone (**3h**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid (110 mg, 62%). Mp: 131−133 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.66 (s, 3H), 6.94−6.97 (m, 1H), 7.16−7.27 (m, 6H), 7.31 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 8.0 Hz, 2H), 7.62−7.68 (m, 4H), 8.18 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 55.4, 113.7, 119.3, 119.6, 121.2, 122.3, 127.6, 128.2, 128.7, 128.9, 129.4, 129.7, 132.2, 132.4, 139.3, 140.2, 154.0, 159.7, 189.7. HRMS: calcd for $C_{23}H_{19}N_2O_2$ 355.1441 $[M + H]^+$, found 355.1434.

*(1,3-Diphenyl-1H-pyrazol-4-yl)thiophene-2-ylmethanone (**3i**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (135 mg, 82%). Mp: 154−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06−7.09 (m, 1H), 7.35−7.40 (m, 4H), 7.52 (t, J = 8.0 Hz, 2H), 7.62 (dd, J_1 = 4.0 Hz, J_2 = 0.8 Hz, 1H), 7.66 (dd, J_1 = 4.8 Hz, J_2 = 0.8 Hz, 1H), 7.78−7.82 (m, 4H), 8.40 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 119.6,

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121.1, 127.6, 128.0, 128.3, 128.7, 128.8, 129.7, 131.2, 132.0, 133.9, 134.0, 139.3, 145.0, 153.4, 181.4. HRMS: calcd for $C_{20}H_{14}N_2OSNa$ 353.0719 $[M + Na]^+$, found 353.0707.

*(1,3-Diphenyl-1H-pyrazol-4-yl)pyridin-3-ylmethanone (**3j**).* Eluent: dichloromethane/methanol (20:1). White solid (102 mg, 63%). Mp: 130−132 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.38 (m, 5H), 7.48 (t, J = 8.0 Hz, 2H), 7.67−7.69 (m, 2H), 7.78 (d, J = 8.0 Hz, 2H), 8.05 (d, J = 7.6 Hz, 1H), 8.35 (s, 1H), 8.71 (s, 1H), 9.02 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 119.6, 120.9, 123.4, 127.8, 128.3, 128.9, 129.1, 129.7, 131.8, 132.5, 134.4, 136.6, 139.1, 150.3, 152.8, 154.1, 188.1. HRMS: calcd for $C_{21}H_{16}N_3O$ 326.1288 $[M + H]^+$, found 326.1276.

*Cyclohexyl(1,3-diphenyl-1H-pyrazol-4-yl)methanone (**3k**).* petroleum ether/ethyl acetate (20:1). White solid (79 mg, 48%). Mp: 113−114 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.13−1.24 (m, 3H), 1.45−1.51 (m, 2H), 1.64−1.66 (m, 1H), 1.76−1.79 (m, 2H), 1.83−1.85 (m, 2H), 2.78−2.82 (m, 1H), 7.36 (t, J = 7.8 Hz, 1H), 7.42−7.46 (m, 3H), 7.49 (t, J = 7.8 Hz, 2H), 7.73 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 2H), 7.78 (d, J = 7.2 Hz, 2H), 8.42 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 25.7, 25.8, 29.4, 48.9, 119.7, 121.7, 127.6, 128.1, 128.8, 129.3, 129.6, 130.9, 132.7, 139.3, 153.9, 199.0. HRMS: calcd for $C_{22}H_{23}N_2O$ 331.1805 $[M + H]^+$, found 331.1789.

*(1-(4-Chlorophenyl)-3-phenyl-1H-pyrazol-4-yl)phenylmethanone (**3l**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (143 mg, 80%). Mp: 165−167 °C (lit.[18b] 171−172 °C). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32−7.34 (m, 3H), 7.39 (t, J = 7.2 Hz, 2H), 7.45 (d, J = 7.8 Hz, 2H), 7.52 (t, J = 6.6 Hz, 1H), 7.70−7.74 (m, 4H), 7.82 (d, J = 7.2 Hz, 2H), 8.25 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 120.7, 121.6, 128.2, 128.4, 128.7, 128.9, 129.5, 129.8, 131.9, 132.1, 132.7, 133.1, 137.8, 138.7, 154.2, 189.9. HRMS: calcd for $C_{22}H_{15}ClN_2ONa$ 381.0765 $[M + Na]^+$, found 381.0747.

*Phenyl(3-phenyl-1-(p-tolyl)-1H-pyrazol-4-yl)methanone (**3m**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (118 mg, 70%). Mp: 148−150 °C (lit.[18b] 149−151 °C). ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.41 (s, 3H), 7.29 (d, J = 7.8 Hz, 2H), 7.32−7.34 (m, 3H), 7.40 (t, J = 7.2 Hz, 2H), 7.52 (t, J = 7.2 Hz, 1H), 7.66 (d, J = 7.8 Hz, 2H), 7.73 (d, J = 6.0 Hz, 2H), 7.83 (d, J = 7.2 Hz, 2H), 8.24 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.0, 119.5, 121.0, 128.1, 128.3, 128.5, 128.9, 129.5, 130.1, 132.2, 132.3, 132.6, 137.0, 137.5, 139.0, 153.8, 190.1. HRMS: calcd for $C_{23}H_{19}N_2O$ 339.1492 $[M + H]^+$, found 339.1475.

*(1-Isopropyl-3-phenyl-1H-pyrazol-4-yl)phenylmethanone (**3n**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (104 mg, 72%). Mp: 98−99 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.51 (d, J = 6.6 Hz, 6H), 4.48−4.50 (m, 1H), 7.19−7.21 (m, 3H), 7.28 (t, J = 7.2 Hz, 2H), 7.40 (t, J = 6.6 Hz, 1H), 7.55 (d, J = 6.6 Hz, 2H), 7.68 (d, J = 7.2 Hz, 2H), 7.74 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.8, 53.4, 118.0, 127.0, 127.1, 127.2, 127.9, 128.3, 131.2, 131.5, 131.7, 138.2, 151.6, 189.2. HRMS: calcd for $C_{19}H_{19}N_2O$ 291.1492 $[M + H]^+$, found 291.1468.

*(1-Methyl-3-phenyl-1H-pyrazol-4-yl)phenylmethanone (**3o**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (89 mg, 68%). Mp: 88−90 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.95 (s, 3H), 7.28−7.37 (m, 5H), 7.47 (t, J = 7.2 Hz, 1H), 7.62−7.64 (m, 2H), 7.73−7.76 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 39.3, 119.5, 128.1, 128.2, 128.3, 128.8, 129.4, 132.3, 132.4, 136.2, 139.2, 153.2, 189.9. HRMS: calcd for $C_{17}H_{14}N_2NaO$ 285.0998 $[M + Na]^+$, found 285.0999.

*(1-Benzyl-3-phenyl-1H-pyrazol-4-yl)phenylmethanone (**3p**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (118 mg, 70%). Mp: 102−103 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.34 (s, 2H), 7.27−7.37 (m, 10H), 7.44 (t, J = 7.2 Hz, 1H), 7.63−7.65 (m, 2H), 7.73 (d, J = 8.0 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 56.5, 119.9, 128.0, 128.1, 128.2, 128.3, 128.6, 128.9, 129.1, 129.4, 132.3, 132.4, 135.3, 135.4, 139.1, 153.2, 190.0. HRMS: calcd for $C_{23}H_{19}N_2O$ 339.1492 $[M + H]^+$, found 339.1498.

*(3-(4-Fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)phenylmethanone (**3q**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (140 mg, 82%). Mp: 135−136 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00−7.06 (m, 2H), 7.35 (t, J = 7.2 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.46−7.50 (m, 2H), 7.52−7.56 (m, 1H), 7.74−7.79 (m, 4H), 7.82−7.84 (m, 2H), 8.25 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 115.2 (d, $^2J_{C-F}$ = 21.9 Hz), 119.6, 121.0, 127.7, 128.3 (d, $^4J_{C-F}$ = 3.3 Hz), 128.5, 129.4, 129.7, 130.8 (d, $^3J_{C-F}$ = 8.7 Hz), 132.6, 132.7, 139.0, 139.2, 153.1, 163.1 (d, $^1J_{C-F}$ = 246.0 Hz), 189.9. HRMS: calcd for $C_{22}H_{16}FN_2O$ 343.1241 $[M + H]^+$, found 343.1214.

*(3-(4-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl)phenylmethanone (**3r**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (161 mg, 80%). Mp: 159−161 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 7.2 Hz, 2H), 7.45−7.48 (m, 4H), 7.54 (t, J = 7.2 Hz, 1H), 7.66 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 7.8 Hz, 2H), 7.83 (d, J = 7.8 Hz, 2H), 8.23 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 119.6, 121.1, 123.0, 127.7, 128.5, 129.5, 129.7, 130.5, 131.1, 131.3, 132.6, 132.8, 138.9, 139.1, 152.9, 189.7. HRMS: calcd for $C_{22}H_{16}BrN_2O$ 403.0441 $[M + H]^+$, found 403.0464.

*(3-(4-Chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)phenylmethanone (**3s**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (140 mg, 78%). Mp: 147−149 °C (lit.[18c] 142−145 °C). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (d, J = 8.4 Hz, 2H), 7.35 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 7.2 Hz, 2H), 7.47 (t, J = 7.8 Hz, 2H), 7.54 (d, J = 7.2 Hz, 1H), 7.72−7.75 (m, 4H), 7.83 (d, J = 7.2 Hz, 2H), 8.24 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 119.6, 121.1, 127.7, 128.4, 128.5, 129.5, 129.7, 130.3, 130.7, 132.6, 132.8, 134.7, 138.9, 139.1, 152.9, 189.8. HRMS: calcd for $C_{22}H_{16}ClN_2O$ 359.0946 $[M + H]^+$, found 359.0924.

*Phenyl(1-phenyl-3-(4-(trifluoromethyl)phenyl)-1H-pyrazol-4-yl)-methanone (**3t**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (174 mg, 89%). Mp: 141−143 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.2 Hz, 2H), 7.50 (t, J = 7.2 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.61 (d, J = 7.8 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H), 7.85 (d, J = 7.8 Hz, 2H), 7.91 (d, J = 7.8 Hz, 2H), 8.28 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 119.6, 121.3, 124.2 (q, $^1J_{C-F}$ = 270.6 Hz), 125.1 (q, $^3J_{C-F}$ = 4.4 Hz), 127.9, 128.6, 129.2, 129.4, 129.7, 130.4 (q, $^2J_{C-F}$ = 32 Hz), 132.7, 132.9, 135.7 (q, $^4J_{C-F}$ = 1.5 Hz), 138.8, 139.1, 152.6, 189.6. HRMS: calcd for $C_{23}H_{16}F_3N_2O$ 393.1209 $[M + H]^+$, found 393.1218.

*Phenyl(1-phenyl-3-(p-tolyl)-1H-pyrazol-4-yl)methanone (**3u**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (140 mg, 83%). Mp: 146−148 °C (lit.[18c] 137−140 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 3H), 7.14 (d, J = 7.8 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 7.39 (t, J = 7.8 Hz, 2H), 7.46 (t, J = 7.8 Hz, 2H), 7.51 (t, J = 7.8 Hz, 1H), 7.64 (d, J = 7.8 Hz, 2H), 7.76 (d, J = 7.8 Hz, 2H), 7.84 (d, J = 7.2 Hz, 2H), 8.23 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.4, 119.6, 121.1, 127.4, 128.4, 128.8, 128.9, 129.2, 129.5, 129.6, 132.3, 132.6, 138.5, 139.1, 139.3, 154.1, 190.0. HRMS: calcd for $C_{23}H_{19}N_2O$ 339.1492 $[M + H]^+$, found 339.1506.

*(3-(4-Methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)-phenylmethanone (**3v**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid (124 mg, 70%). Mp: 132−134 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3H), 6.88 (d, J = 9.2 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.48 (t, J = 8.0 Hz, 2H), 7.53 (t, J = 7.6 Hz, 1H), 7.72 (d, J = 8.8 Hz, 2H), 7.76 (d, J = 7.6 Hz, 2H), 7.84 (d, J = 7.2 Hz, 2H), 8.24 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 55.3, 113.6, 119.5, 120.9, 124.6, 127.4, 128.4, 129.5, 129.6, 130.3, 132.4, 132.6, 139.1, 139.3, 153.8, 160.0, 190.1. HRMS: calcd for $C_{23}H_{19}N_2O_2$ 355.1441 $[M + H]^+$, found 355.1442.

*(3-(3-Fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)phenylmethanone (**3w**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (121 mg, 71%). Mp: 129−131 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.90−6.94 (m, 1H), 7.17−7.20 (m, 1H), 7.25 (t, J = 7.2 Hz, 1H), 7.32 (t, J = 7.8 Hz, 2H), 7.38 (t, J = 7.8 Hz, 2H), 7.43−7.45 (m, 3H), 7.66 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 7.2 Hz, 2H), 8.16 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 115.5 (d, $^2J_{C-F}$ = 20.7 Hz), 115.8 (d, $^2J_{C-F}$ = 23.0 Hz), 119.6, 121.2, 124.8 (d, $^4J_{C-F}$ = 3.3 Hz), 127.7, 128.5, 129.5, 129.6 (d, $^3J_{C-F}$ = 8.7 Hz), 129.7, 132.5, 132.8, 134.3 (d, $^3J_{C-F}$ = 8.7 Hz), 138.9, 139.1, 152.7 (d, $^4J_{C-F}$ = 2.2 Hz), 162.6 (d, $^1J_{C-F}$ = 242.7 Hz), 189.8. HRMS: calcd for $C_{22}H_{16}FN_2O$ 343.1241 $[M + H]^+$, found 343.1242.

*(3-(3-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl)phenylmethanone (**3x**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (159 mg, 79%). Mp: 145−147 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.20 (t, J = 7.8 Hz, 1H), 7.37 (t, J = 7.8 Hz, 1H), 7.40−7.46 (m, 3H), 7.50 (t, J

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= 7.2 Hz, 2H), 7.55 (t, J = 7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.77 (d, J = 7.8 Hz, 2H), 7.83 (d, J = 7.8 Hz, 2H), 7.96 (s, 1H), 8.27 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 119.6, 121.3, 122.2, 127.7, 127.8, 128.5, 129.4, 129.6, 129.7, 131.6, 131.7, 132.6, 132.8, 134.1, 138.9, 139.1, 152.5, 189.8. HRMS: calcd for $C_{22}H_{16}BrN_2O$ 403.0441 $[M + H]^+$, found 403.0440.

*Phenyl(1-phenyl-3-thiophene-2-yl-1H-pyrazol-4-yl)methanone (**3y**).* Eluent: petroleum ether/ethyl acetate (20:1). White solid (133 mg, 81%). Mp: 137−139 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.04−7.05 (m, 1H), 7.33−7.34 (m, 2H), 7.45−7.47 (m, 4H), 7.57 (t, J = 7.2 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.85 (d, J = 7.8 Hz, 2H), 7.93−7.94 (m, 1H), 8.17 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 119.6, 120.4, 126.8, 127.5, 127.7, 128.6, 128.9, 129.4, 129.7, 132.6, 132.9, 134.2, 139.0, 139.5, 148.3, 189.5. HRMS: calcd for $C_{20}H_{14}N_2OSNa$ 353.0719 $[M + Na]^+$, found 353.0706.

*Typical Procedure for the Synthesis of **5a**.* To a reaction tube equipped with a stir bar were added propiophenone (**1a**; 161 mg, 1.2 mmol), PhCl (5 mL), $Cu(OAc)_2$ (36 mg, 0.2 mmol), 2,2′-bipyridine (16 mg, 0.1 mmol), and TEMPO (156 mg, 1 mmol). The mixture was stirred under N_2 at 120 °C for 10 h. Afterward, 1-cyclopentylidene-2-phenylhydrazine (**4a**; 87 mg, 0.5 mmol) was added, and the resulting mixture was stirred under air at 120 °C for 4 h. Upon completion, it was diluted with DCM (15 mL) and washed with water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (10:1) as the eluent to give **5a**. **5b**−**5g** and **7a**−**7f** were obtained in a similar manner.

*7-(4-Benzoyl-1-phenyl-1H-pyrazol-3-yl)-1-phenylheptan-1-one (**5a**).* Eluent: petroleum ether/ethyl acetate (10:1). Syrup (141 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42−1.52 (m, 4H), 1.72−1.84 (m, 4H), 2.96 (t, J = 7.6 Hz, 2H), 3.04 (t, J = 7.6 Hz, 2H), 7.31 (t, J = 7.6 Hz, 1H), 7.41−7.59 (m, 8H), 7.67 (d, J = 8.0 Hz, 2H), 7.82 (d, J = 8.0 Hz, 2H), 7.94 (d, J = 8.4 Hz, 2H), 8.11 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.4, 28.0, 28.8, 29.1, 29.4, 38.6, 119.6, 120.7, 127.3, 128.1, 128.5, 128.8, 129.6, 132.1, 132.2, 132.8, 137.1, 139.3, 140.1, 157.4, 190.0, 200.6. HRMS: calcd for $C_{29}H_{29}N_2O_2$ 437.2224 $[M + H]^+$, found 437.2224.

*7-(4-(4-Methylbenzoyl)-1-phenyl-1H-pyrazol-3-yl)-1-(p-tolyl)-heptan-1-one (**5b**).* Eluent: petroleum ether/ethyl acetate (10:1). Syrup (155 mg, 67%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.42−1.51 (m, 4H), 1.71−1.76 (m, 2H), 1.77−1.82 (m, 2H), 2.39 (s, 3H), 2.43 (s, 3H), 2.92 (t, J = 7.2 Hz, 2H), 3.03 (t, J = 7.2 Hz, 2H), 7.23 (d, J = 7.8 Hz, 2H), 7.25−7.32 (m, 3H), 7.44 (t, J = 7.8 Hz, 2H), 7.68 (d, J = 7.8 Hz, 2H), 7.74 (d, J = 7.8 Hz, 2H), 7.84 (d, J = 7.8 Hz, 2H), 8.11 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.6, 24.5, 27.9, 28.9, 29.2, 29.4, 38.5, 119.5, 120.8, 127.2, 128.2, 129.0, 129.2, 129.3, 129.6, 131.9, 134.7, 137.4, 139.4, 142.8, 143.5, 157.3, 189.8, 200.3. HRMS: calcd for $C_{31}H_{32}N_2O_2Na$ 487.2356 $[M + Na]^+$, found 487.2366.

*8-(4-Benzoyl-1-phenyl-1H-pyrazol-3-yl)-1-phenyloctan-1-one (**5c**).* Eluent: petroleum ether/ethyl acetate (10:1). Syrup (157 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40−1.47 (m, 6H), 1.70−1.82 (m, 4H), 2.95 (t, J = 7.6 Hz, 2H), 3.03 (t, J = 7.6 Hz, 2H), 7.32 (t, J = 7.6 Hz, 1H), 7.42−7.47 (m, 4H), 7.49−7.52 (m, 2H), 7.54−7.60 (m, 2H), 7.68 (d, J = 7.6 Hz, 2H), 7.83 (d, J = 7.2 Hz, 2H), 7.95 (d, J = 7.6 Hz, 2H), 8.11 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.4, 28.0, 28.9, 29.2, 29.3, 29.5, 38.7, 119.6, 120.7, 127.3, 128.1, 128.5, 128.6, 128.8, 129.6, 132.1, 132.2, 132.8, 137.1, 139.4, 140.1, 157.5, 190.0, 200.7. HRMS: calcd for $C_{30}H_{30}N_2O_2Na$ 473.2199 $[M + Na]^+$, found 473.2179.

*9-(4-Benzoyl-1-phenyl-1H-pyrazol-3-yl)-1-phenylnonan-1-one (**5d**).* Eluent: petroleum ether/ethyl acetate (10:1). Syrup (174 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (s, 6H), 1.42−1.46 (m, 2H), 1.68−1.81 (m, 4H), 2.94 (t, J = 7.6 Hz, 2H), 3.03 (t, J = 7.6 Hz, 2H), 7.31 (t, J = 7.6 Hz, 1H), 7.42−7.51 (m, 6H), 7.53−7.59 (m, 2H), 7.68 (d, J = 7.6 Hz, 2H), 7.82 (d, J = 6.8 Hz, 2H), 7.95 (d, J = 7.6 Hz, 2H), 8.11 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.4, 28.0, 28.9, 29.2, 29.3, 29.4, 29.6, 38.7, 119.6, 120.7, 127.3, 128.1, 128.5, 128.6, 128.8, 129.6, 132.1, 132.2, 132.9, 137.1, 139.3, 140.1, 157.5, 190.0, 200.7. HRMS: calcd for $C_{31}H_{32}N_2O_2Na$ 487.2356 $[M + Na]^+$, found 487.2330.

*9-(4-(4-Methylbenzoyl)-1-phenyl-1H-pyrazol-3-yl)-1-(p-tolyl)-nonan-1-one (**5e**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid (167 mg, 68%). Mp 94−95 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (s, 6H), 1.40−1.45 (m, 2H), 1.68−1.72 (m, 2H), 1.73−1.81 (m, 2H), 2.38 (s, 3H), 2.42 (s, 3H), 2.90 (t, J = 7.6 Hz, 2H), 3.01 (t, J = 7.6 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.27−7.31 (m, 3H), 7.43 (t, J = 8.0 Hz, 2H), 7.67 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H), 7.83 (d, J = 8.0 Hz, 2H), 8.11 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.6, 24.5, 28.0, 29.0, 29.3, 29.4, 29.6, 38.5, 119.5, 120.8, 127.2, 128.2, 129.0, 129.2, 129.3, 129.6, 131.9, 134.7, 137.4, 139.4, 142.8, 143.5, 157.4, 189.7, 200.3. HRMS: calcd for $C_{33}H_{36}N_2O_2Na$ 515.2669 $[M + Na]^+$, found 515.2623.

*8-(4-Benzoyl-1-phenyl-1H-pyrazol-3-yl)-4-methyl-1-phenyloctan-1-one (**5f**).* Eluent: petroleum ether/ethyl acetate (10:1). Syrup (139 mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.93 (d, J = 7.2 Hz, 3H), 1.22−1.27 (m, 1H), 1.41−1.47 (m, 2H), 1.49−1.59 (m, 3H), 1.72−1.82 (m, 3H), 2.94−2.98 (m, 2H), 3.04 (t, J = 7.2 Hz, 2H), 7.32 (t, J = 7.2 Hz, 1H), 7.43−7.46 (m, 4H), 7.49 (t, J = 7.2 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.58 (t, J = 7.2 Hz, 1H), 7.68 (d, J = 7.8 Hz, 2H), 7.82 (d, J = 7.8 Hz, 2H), 7.95 (d, J = 7.8 Hz, 2H), 8.11 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 19.3, 27.0, 28.0, 29.2, 31.5, 32.6, 36.4, 36.5, 119.6, 120.7, 127.3, 128.1, 128.5, 128.6, 128.8, 129.6, 132.1, 132.2, 132.8, 137.1, 139.3, 140.1, 157.4, 190.0, 200.9. HRMS: calcd for $C_{31}H_{32}N_2O_2Na$ 487.2356 $[M + Na]^+$, found 487.2347.

*4-Methyl-8-(4-(4-methylbenzoyl)-1-phenyl-1H-pyrazol-3-yl)-1-(p-tolyl)octan-1-one (**5g**).* Eluent: petroleum ether/ethyl acetate (10:1). Syrup (164 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (d, J = 6.0 Hz, 3H), 1.21−1.28 (m, 1H), 1.39−1.45 (m, 2H), 1.47−1.57 (m, 3H), 1.71−1.78 (m, 3H), 2.40 (s, 3H), 2.44 (s, 3H), 2.90−2.96 (m, 2H), 3.02 (t, J = 7.6 Hz, 2H), 7.23−7.34 (m, 5H), 7.46 (t, J = 8.0 Hz, 2H), 7.68 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.4 Hz, 2H), 8.12 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 19.6, 21.6, 27.0, 28.0, 29.3, 31.6, 32.6, 36.3, 36.5, 119.5, 120.8, 127.2, 128.2, 129.0, 129.1, 129.2, 129.6, 131.9, 134.7, 137.4, 139.4, 142.8, 143.5, 157.3, 189.8, 200.6. HRMS: calcd for $C_{33}H_{36}N_2O_2Na$ 515.2669 $[M + Na]^+$, found 515.2652.

*5-(2-(4-Benzoyl-1-phenyl-1H-pyrazol-3-yl)phenyl)-1-phenylpentan-1-one (**7a**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid (188 mg, 78%). Mp: 116−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.65−1.70 (m, 4H), 2.69 (t, J = 6.8 Hz, 2H), 2.84 (t, J = 6.8 Hz, 2H), 7.14−7.18 (m, 1H), 7.24−7.31 (m, 2H), 7.33−7.38 (m, 6H), 7.45−7.49 (m, 4H), 7.75−7.78 (m, 4H), 7.82 (d, J = 7.6 Hz, 2H), 8.34 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.1, 30.7, 33.4, 38.3, 119.4, 122.3, 125.6, 127.5, 128.0, 128.3, 128.5, 128.7, 129.1, 129.2, 129.7, 130.8, 131.3, 132.4, 132.8, 137.0, 138.8, 139.3, 141.1, 154.3, 189.3, 200.3. HRMS: calcd for $C_{33}H_{29}N_2O_2$ 485.2224 $[M + H]^+$, found 485.2224.

*5-(2-(4-(4-Fluorobenzoyl)-1-phenyl-1H-pyrazol-3-yl)phenyl)-1-(4-fluorophenyl)pentan-1-one (**7b**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid (117 mg, 45%). Mp: 109−111 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.63−1.69 (m, 4H), 2.67 (t, J = 7.2 Hz, 2H), 2.81 (t, J = 7.2 Hz, 2H), 7.00−7.04 (m, 4H), 7.16 (t, J = 7.2 Hz, 1H), 7.22 (d, J = 7.2 Hz, 1H), 7.26−7.29 (m, 2H), 7.37 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 7.2 Hz, 2H), 7.75−7.79 (m, 4H), 7.83−7.85 (m, 2H), 8.37 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.0, 30.6, 33.3, 38.1, 115.3 (d, $^2J_{C-F}$ = 21.9 Hz), 115.5 (d, $^2J_{C-F}$ = 21.8 Hz), 119.4, 122.3, 125.7, 127.6, 128.8, 129.2, 129.7, 130.6 (d, $^3J_{C-F}$ = 8.7 Hz), 130.8, 130.9, 131.1, 131.7 (d, $^3J_{C-F}$ = 8.7 Hz), 133.4 (d, $^4J_{C-F}$ = 2.3 Hz), 134.9 (d, $^4J_{C-F}$ = 3.3 Hz), 139.2, 141.0, 154.0, 165.3 (d, $^1J_{C-F}$ = 252.8 Hz), 165.6 (d, $^1J_{C-F}$ = 252.6 Hz), 188.0, 198.6. HRMS: calcd for $C_{33}H_{26}F_2N_2O_2Na$ 543.1855 $[M + Na]^+$, found 543.1825.

*5-(2-(4-(4-Methylbenzoyl)-1-phenyl-1H-pyrazol-3-yl)phenyl)-1-(p-tolyl)pentan-1-one (**7c**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid (192 mg, 75%). Mp: 114−116 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.63−1.69 (m, 4H), 2.35 (s, 3H), 2.36 (s, 3H), 2.71 (t, J = 7.2 Hz, 2H), 2.79 (t, J = 7.2 Hz, 2H), 7.16 (t, J = 7.6 Hz, 5H), 7.22−7.27 (m, 2H), 7.34 (t, J = 7.2 Hz, 2H), 7.47 (t, J = 8.0 Hz, 2H), 7.68−7.73 (m, 4H), 7.77 (d, J = 7.6 Hz, 2H), 8.32 (s, 1H). ^{13}C NMR

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(100 MHz, $CDCl_3$): δ 21.6, 24.3, 30.7, 33.4, 38.2, 119.4, 122.5, 125.6, 127.4, 128.1, 128.6, 129.0, 129.2, 129.4, 129.6, 130.8, 131.0, 131.9, 134.6, 136.2, 139.3, 141.1, 143.2, 143.5, 154.2, 189.0, 200.0. HRMS: calcd for $C_{35}H_{32}N_2O_2Na$ 535.2356 $[M + Na]^+$, found 535.2317.

*5-(2-(4-(4-Methoxybenzoyl)-1-phenyl-1H-pyrazol-3-yl)phenyl)-1-(4-methoxyphenyl)pentan-1-one (**7d**).* Eluent: petroleum ether/ethyl acetate (5:1). White solid (195 mg, 72%). Mp: 127−129 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 1.64−1.68 (m, 4H), 2.69 (t, *J* = 7.2 Hz, 2H), 2.77 (t, *J* = 7.2 Hz, 2H), 3.81 (s, 3H), 3.83 (s, 3H), 6.84 (d, *J* = 8.4 Hz, 4H), 7.16 (t, *J* = 7.2 Hz, 1H), 7.23−7.27 (m, 2H), 7.32−7.36 (m, 2H), 7.48 (t, *J* = 7.2 Hz, 2H), 7.77−7.81 (m, 6H), 8.33 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.4, 30.7, 33.4, 37.9, 55.4, 55.5, 113.5, 113.6, 119.4, 122.6, 125.6, 127.3, 128.6, 129.2, 129.6, 130.1, 130.2, 130.7, 130.8, 131.4, 131.6, 131.9, 139.4, 141.1, 154.0, 163.1, 163.2, 188.1, 198.9. HRMS: calcd for $C_{35}H_{33}N_2O_4$ 545.2435 $[M + H]^+$, found 545.2397.

*6-(2-(4-Benzoyl-1-phenyl-1H-pyrazol-3-yl)phenyl)-1-phenylhexan-1-one (**7e**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid (174 mg, 70%). Mp: 129−130 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 1.30−1.34 (m, 2H), 1.59−1.66 (m, 4H), 2.65 (t, *J* = 7.6 Hz, 2H), 2.83 (t, *J* = 7.2 Hz, 2H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.21−7.27 (m, 2H), 7.31−7.42 (m, 6H), 7.44−7.53 (m, 4H), 7.77 (d, *J* = 8.0 Hz, 4H), 7.86 (d, *J* = 7.6 Hz, 2H), 8.35 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.0, 29.1, 30.9, 33.3, 38.4, 119.5, 122.3, 125.5, 127.5, 128.0, 128.3, 128.5, 128.7, 129.1, 129.2, 129.6, 130.7, 131.3, 131.8, 132.3, 132.8, 137.0, 138.8, 139.3, 141.4, 154.4, 189.3, 200.4. HRMS: calcd for $C_{34}H_{31}N_2O_2$ 499.2380 $[M + H]^+$, found 499.2340.

*6-(2-(4-(4-Methylbenzoyl)-1-phenyl-1H-pyrazol-3-yl)phenyl)-1-(p-tolyl)hexan-1-one (**7f**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid (197 mg, 75%). Mp: 125−127 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 1.29−1.33 (m, 2H), 1.57−1.63 (m, 4H), 2.36 (s, 3H), 2.37 (s, 3H), 2.65 (t, *J* = 7.8 Hz, 2H), 2.78 (t, *J* = 7.2 Hz, 2H), 7.17 (t, *J* = 9.0 Hz, 5H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.70 (d, *J* = 7.2 Hz, 2H), 7.76 (d, *J* = 7.2 Hz, 4H), 8.31 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.6, 24.2, 29.1, 30.9, 33.4, 38.3, 119.4, 122.4, 125.5, 127.4, 128.2, 128.6, 129.0, 129.1, 129.2, 129.4, 129.6, 130.7, 131.1, 131.9, 134.6, 136.2, 139.3, 141.4, 143.1, 143.5, 154.3, 188.9, 200.1. HRMS: calcd for $C_{36}H_{35}N_2O_2$ 527.2693 $[M + H]^+$, found 527.2670.

Control Experiments I. Experiment 1. To a reaction tube equipped with a stir bar were added **A** (66 mg, 0.5 mmol), **2a** (in situ formed from the reaction of 0.5 mmol of propiophenone with 0.5 mmol of phenylhydrazine), toluene (3 mL), $Cu(OAc)_2$ (18 mg, 0.1 mmol), bpy (8 mg, 0.05 mmol), and TEMPO (78 mg, 0.5 mmol). The resulting mixture was stirred at 120 °C under N_2 for 4 h. Then it was diluted with DCM (15 mL) and washed with water (10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20:1) as the eluent to give **3a** in a yield of 62%.

Experiment 2. To a reaction tube equipped with a stir bar were added **A** (66 mg, 0.5 mmol), **2a** (in situ formed from the reaction of 0.5 mmol of propiophenone with 0.5 mmol of phenylhydrazine), and toluene (3 mL). The resulting mixture was stirred at 120 °C under N_2 for 4 h to give **3a** in a trace amount.

Experiment 3. To a reaction tube equipped with a stir bar were added **A** (66 mg, 0.5 mmol), **2a** (in situ formed from the reaction of 0.5 mmol of propiophenone with 0.5 mmol of phenylhydrazine), and toluene (3 mL). The resulting mixture was stirred at 120 °C under air for 4 h. Then it was diluted with DCM (15 mL) and washed with water (10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20:1) as the eluent to give **3a** in a yield of 27%.

Experiment 4. To a reaction tube equipped with a stir bar were added **A** (66 mg, 0.5 mmol), **2a** (in situ formed from the reaction of 0.5 mmol of propiophenone with 0.5 mmol of phenylhydrazine), toluene (3 mL) and $Cu(OAc)_2$ (18 mg, 0.1 mmol) with stirring. The resulting mixture was stirred at 120 °C under air for 4 h. Then it was diluted with DCM (15 mL) and washed with water (10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20:1) as the eluent to give **3a** in a yield of 75%.

Control Experiments II. Experiment 1. To a reaction tube equipped with a stir bar were added **A** (132 mg, 1.0 mmol), **4b** (94 mg, 0.5 mmol), PhCl (5 mL), and $Cu(OAc)_2$ (18 mg, 0.1 mmol) with stirring. The resulting mixture was stirred at 120 °C under air for 4 h. Then it was diluted with DCM (15 mL) and washed with water (10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (10:1) as the eluent to give **5c** in a yield of 76%.

Experiment 2. To a reaction tube equipped with a stir bar were added **A** (132 mg, 1 mmol), **4b** (94 mg, 0.5 mmol), PhCl (5 mL), $Cu(OAc)_2$ (18 mg, 0.1 mmol), and TEMPO (78 mg, 0.5 mmol) with stirring. The resulting mixture was stirred at 120 °C under air for 4 h. Then it was diluted with DCM (15 mL) and washed with water (10 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (10:1) as the eluent to give **8**.

*Phenyl(1-phenyl-3-(5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-pentyl)-1H-pyrazol-4-yl)methanone (**8**).* Eluent: petroleum ether/ethyl acetate (10:1). Syrup (182 mg, 77%). ^1H NMR (600 MHz, $CDCl_3$): δ 0.99 (s, 6H), 1.06 (s, 6H), 1.17−1.23 (m, 1H), 1.33−1.34 (m, 4H), 1.42−1.54 (m, 5H), 1.68−1.76 (m, 2H), 2.97 (t, *J* = 7.6 Hz, 2H), 3.66 (t, *J* = 6.4 Hz, 2H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.35−7.43 (m, 4H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.73−7.75 (m, 2H), 8.03 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.2, 20.1, 26.5, 28.0, 28.6, 29.1, 33.1, 39.6, 59.6, 76.8, 119.6, 120.6, 127.3, 128.5, 128.8, 129.6, 132.1, 132.2, 139.3, 140.1, 157.4, 190.0. HRMS: calcd for $C_{30}H_{40}N_3O_2$ 474.3115 $[M + H]^+$, found 474.3091.

Control Experiments III. To a reaction tube equipped with a stir bar were added **A** (66 mg, 0.5 mmol), **2a** (112 mg, 0.5 mmol), PhCl (5 mL), $Cu(OAc)_2$ (18 mg, 0.1 mmol), and TEMPO (78 mg, 0.5 mmol) with stirring. The resulting mixture was stirred at 120 °C under air for 4 h. Afterward, it was cooled to room temperature and filtered. A GC−MS study of the resulting mixture thus obtained showed that 1-ethoxy-2,2,6,6-tetramethylpiperidine was formed.

*Scale-Up Synthesis of **3a** and **5a**.* To a reaction tube equipped with a stir bar were added propiophenone (**1a**, 0.67 g, 5 mmol), PhCl (20 mL), $Cu(OAc)_2$ (181 mg, 1 mmol), bpy (78 mg, 0.5 mmol), and TEMPO (781 mg, 5 mmol). The mixture was stirred at 120 °C under N_2 for 10 h. In another reaction tube, propiophenone (670 mg, 5 mmol) was treated with phenylhydrazine (540 mg, 5 mmol) in ethanol (10 mL) at ambient temperature for 0.5 h to give 1-phenyl-2-(1-phenylpropylidene)hydrazine (**2a**), which was then transferred into the first reaction tube after the mixture had been concentrated under reduced pressure to remove ethanol and diluted with PhCl. The resulting mixture was then stirred under air at 120 °C for 4 h. Upon completion, it was diluted with DCM (80 mL) and washed with water (30 mL) and brine (30 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20:1) as the eluent to give **3a** (0.99 g, 61%).

To a reaction tube equipped with a stir bar were added propiophenone (**1a**, 1.34 g, 10 mmol), PhCl (30 mL), $Cu(OAc)_2$ (362 mg, 2 mmol), 2,2′-bipyridine (156 mg, 1 mmol), and TEMPO (1.56 g, 10 mmol). The mixture was stirred under N_2 at 120 °C for 10 h. Afterward, 1-cyclopentylidene-2-phenylhydrazine (**4a**; 870 mg, 5 mmol) was added, and the resulting mixture was stirred under air at 120 °C for 4 h. Upon completion, it was diluted with DCM (100 mL) and washed with water (40 mL) and brine (40 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (10:1) as the eluent to give **5a** (1.20 g, 55%).

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01013.

^{1}H and ^{13}C NMR spectra of all products, X-ray crystal structure and data of **3g**, H−H COSY 2D NMR spectrum of **5f**, and identification of 1-ethoxy-2,2,6,6-tetramethylpiperidine by a GC−MS study (PDF)

X-ray crystallographic data for **3g** (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: xinyingzhang@htu.cn.

*E-mail: xuesen.fan@htu.cn.

ORCID

Xuesen Fan: 0000-0002-2040-6919

Notes

The authors declare no competing financial interest.

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(20) The structure of **5f** was confirmed by its ^{1}H and H−H COSY NMR study (please see the Supporting Information for the details).

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