The Journal of Organic Chemistry

Subscriber access provided by - Access paid by the | UCSB Libraries

Article

Radical Addition of Hydrazones by alpha-Bromo Ketones to Prepare 1,3,5-Trisubstituted Pyrazoles via Visible Light Catalysis

Xiu-Wei Fan, Tao Lei, Chao Zhou, Qing-yuan Meng, Bin Chen, Chen-Ho Tung, and Li-Zhu Wu

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.6b00992 • Publication Date (Web): 30 Jun 2016

Downloaded from http://pubs.acs.org on July 1, 2016

Just Accepted

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a free service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are accessible to all readers and citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Published by American Chemical Society. Copyright © American Chemical Society. However, no copyright claim is made to original U.S. Government works, or works produced by employees of any Commonwealth realm Crown government in the course of their duties.

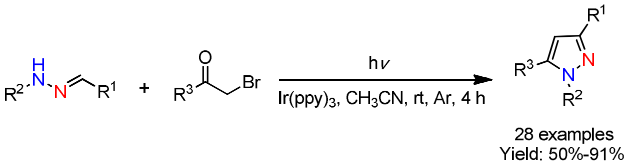
Radical Addition of Hydrazones by α-Bromo Ketones to Prepare 1,3,5-Trisubstituted Pyrazoles via Visible Light Catalysis

Xiu-Wei Fan[†], Tao Lei[†], Chao Zhou, Qing-Yuan Meng, Bin Chen, Chen-Ho Tung, and Li-Zhu Wu*

Key Laboratory of Photochemical Conversion and Optoelectronic Materials,
Technical Institute of Physics and Chemistry & University of Chinese Academy of
Sciences, the Chinese Academy of Sciences, Beijing 100190, P. R. China

[†]These authors contributed equally to this work.

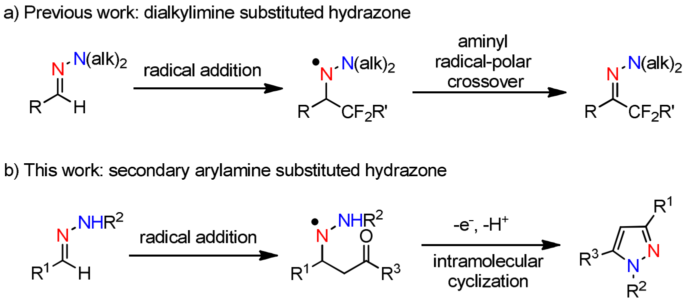
*E-mail: lzwu@mail.ipc.ac.cn



ABSTRACT: A novel efficient tandem reaction of hydrazones and α-bromo ketones is reported to prepare 1,3,5-trisubstituted pyrazoles by visible light catalysis. In this system, the monosubstituted hydrazones show wonderful reaction activity with alkyl radicals, generated from α-bromo ketones. A radical addition followed by intramolecular cyclization affords the important pyrazole skeleton in good to excellent yields. This efficient strategy with mild condition and wide group tolerance provides a potential approach to the 1,3,5-trisubstituted pyrazoles.

INTRODUCTION

Visible light photoredox catalysis has attracted wide attention in organic synthesis due to its low cost, easy availability and environmental friendliness.[1] Particularly, it features a unique ability to facilitate radical/polar crossover reactions via single electron transfer. Following this strategy, many kinds of covalent bonds such as C=O, C=C, C-X even C-H have been activated into relative radical intermediates by photocatalysis,[2] and numerous significant chemical conversions have been realized including radical addition, dehydrogen cross coupling and cyclic reaction.[3] Recently, Zhu and Hashni independently reported visible-light photoredox catalyzed aminyl radical/polar crossover reaction to C-H difluoroalkylation of aldehyde-derived hydrazones.[4] They proposed that the generated CF_2 radical addition to the C=N bond leads to the aminyl radical intermediate and then proceeds singlet-electron oxidation and deprotonation to obtain the product (Scheme 1a). In their work, the disubstituted groups on nitrogen are essential for the successful conversion, or complex byproducts would be obtained if there was only one substitution. Herein, we report that the hydrazones that own monosubstituted group can react with α-bromo ketones to construct pyrazoles in an efficient way (Scheme 1b).



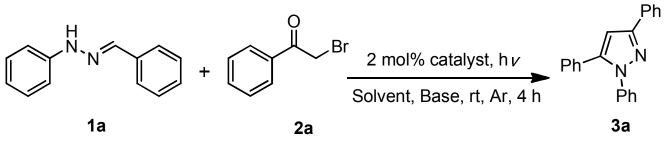
Scheme 1. Radical addition to carbon-nitrogen π bonds

Pyrazoles, with a wide range of biological activities and pharmacological properties,[5] are important structural motifs widely existing in nature products[6] and synthetic biologically active compounds such as Celebrex, [7,5f] Viagra.[8] In addition, pyrazoles can be used as ligands of metallic complexes for carbon-carbon coupling reaction.[9] Traditional strategies for 1,3,5-trisubstituted pyrazoles synthesis include: oxidative aromatization of 1,3,5-triaryl pyrazolines,[10] cyclocondensation of hydrazines with 1,3-dicarbonyl compounds,[11] intramolecular C-N coupling of acetylenic and alkenyl hydrazones.[12] Despite these great advances, the synthetic processes suffer from the use of toxic, expensive reagents and harsh reaction conditions. The strategy presented here is very attractive, because it shows the good to excellent yields of 1,3,5-trisubstituted pyrazole in mild condition, short reaction time and good function group tolerance.

RESULTS AND DICUSSION

We started our investigation by using (*E*)-1-benzylidene-2-phenylhydrazine (**1a**) and α-bromoacetophenone (**2a**) as substrates (Table 1). Upon irradiation of **1a** (0.1 mmol), **2a** (0.15 mmol), $NaHCO_3$ (0.1 mmol) and $Ir(ppy)_3$ (2 mol %) in 2 mL DMSO with blue LEDs (λ_{max} = 450 nm) under Ar atmosphere for 2 h, 80% yield of **3a** was obtained (Table 1, entry 1). The good yield stimulated us to explore and optimize the reaction conditions. Considering that DMSO is inconvenient in workup, we screened other different solvents and found CH_3CN as the best medium for this conversion, which provide the target compound **3a** in a 75% yield (Table 1, entries 2-4). When $NaHCO_3$ was replaced by K_2CO_3 and Na_2CO_3, the yield became 71% and 80%, respectively (Table 1, entries 5-6). When the reaction occurred in DMSO and Na_2CO_3, the product was achieved in 81% yield (Table 1, entry 7). Furthermore, the dosage of Na_2CO_3 and **2a** were examined and found that 1 equivalent of Na_2CO_3 and 1.5 equivalent of **2a** in the reaction could get the highest yield (Table 1, entries 8-11). However, Eosine and $Ru(bpy)_3Cl_2{\cdot}6H_2O$ were inappropriate for this photoreaction (Table 1, entries 12-13), possibly due to unfavorable redox potential[1,13] of the two photocatalysts relative to substrate **2a**. Then different reaction concentrations were screened and found that 0.05 M of **1a** in the reaction is the best (Table 1, entries 14-15). Therefore, the optimized reaction conditions were confirmed to be 0.1 mmol **1a**, 0.15 mmol **2a**, 1 equiv. Na_2CO_3, and 2 mol% $Ir(ppy)_3$ in 2 mL CH_3CN with the irradiation of blue LEDs under Ar atmosphere for 4 h.

Table 1. Optimization of the reaction condition[a]



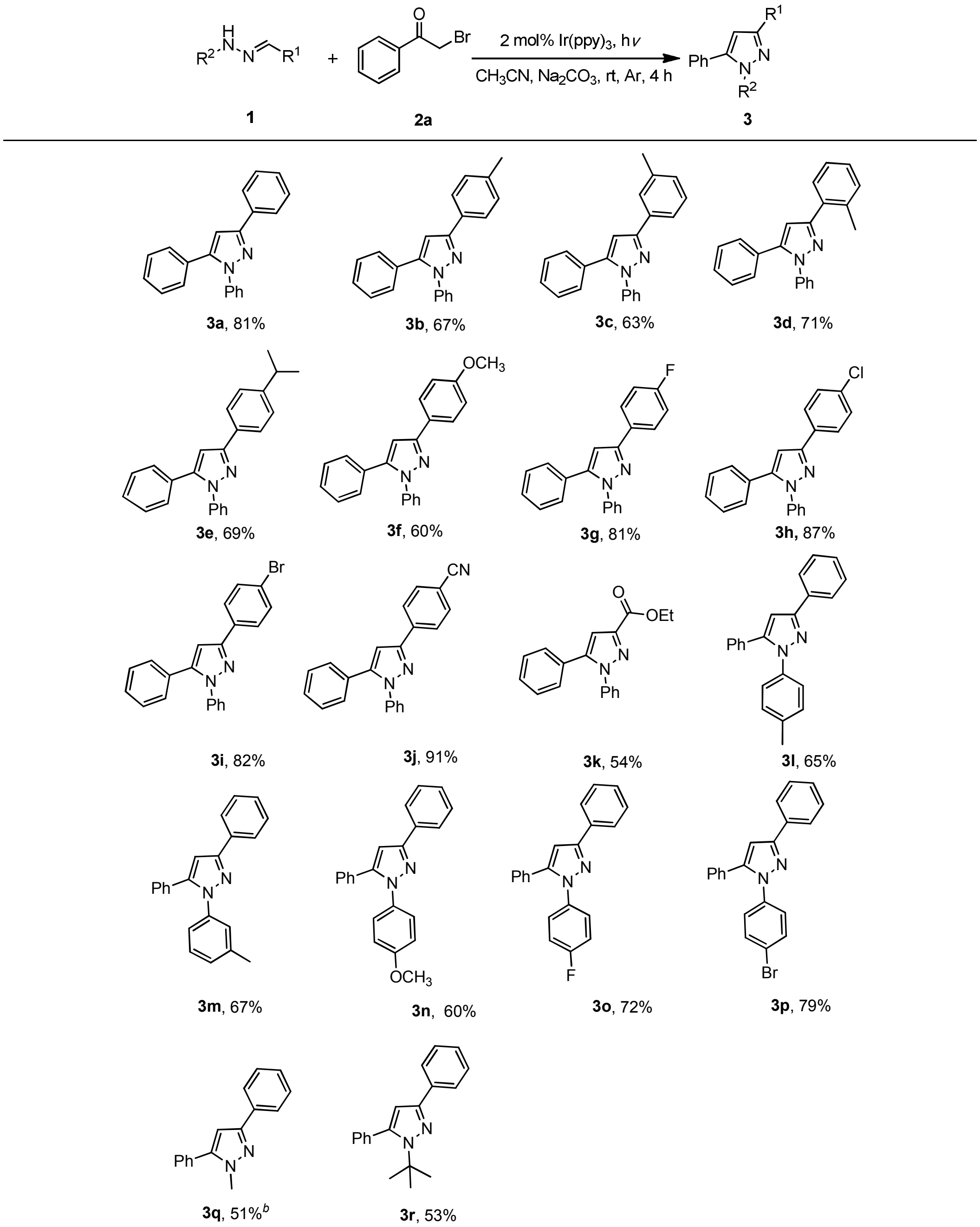
Entry	Solvent	Catalyst	Base (1eq)	Yield (%)[b]
1[c]	DMSO	$Ir(ppy)_3$	$NaHCO_3$	80
2	Dioxane	$Ir(ppy)_3$	$NaHCO_3$	51
3	$ClCH_2CH_2Cl$	$Ir(ppy)_3$	$NaHCO_3$	<5
4	CH_3CN	$Ir(ppy)_3$	$NaHCO_3$	75
5	CH_3CN	$Ir(ppy)_3$	K_2CO_3	71
6	CH_3CN	$Ir(ppy)_3$	Na_2CO_3	80
7[c]	DMSO	$Ir(ppy)_3$	Na_2CO_3	81
8[d]	CH_3CN	$Ir(ppy)_3$	Na_2CO_3	66
9[e]	CH_3CN	$Ir(ppy)_3$	Na_2CO_3	76
10[f]	CH_3CN	$Ir(ppy)_3$	Na_2CO_3	66
11[g]	CH_3CN	$Ir(ppy)_3$	Na_2CO_3	67
12	CH_3CN	Eosine	Na_2CO_3	< 5
13	CH_3CN	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	Na_2CO_3	17

14[h]	CH_3CN	Ir(ppy)$_3$	Na_2CO_3	70
15[i]	CH_3CN	Ir(ppy)$_3$	Na_2CO_3	77
16[j]	CH_3CN	Ir(ppy)$_3$	Na_2CO_3	0
17	CH_3CN	---	Na_2CO_3	0

[a]Reaction conditions: 0.1 mmol (*E*)-1-benzylidene-2-phenylhydrazine, 0.15 mmol α-bromoacetophenone, 2 mol% catalyst, and 1 equiv. base in 2 mL solvent irradiated by blue LEDs under Ar for 4 h. [b]Yields determined by ^{1}H NMR using diphenylacetonitrile as an internal standard. [c]reaction time is 2 h. [d]0.5 equiv. of Na_2CO_3 was used. [e]2 equiv. of Na_2CO_3 was used. [f]1 equiv. of **2a** was used. [g]2 equiv. of **2a** was used. [h]the reaction concentration is 0.025 M. [i] the reaction concentration is 0.1 M. [k]in dark.

With the optimized reaction conditions in hand, we explored the scope of hydrazones with α-bromoacetophenone as reaction partner, and the results were summarized in Table 2. Various substituted benzylidene phenylhydrazones were converted into the corresponding products in moderate to good yields. Comparison of the yields of **3b**, **3c** and **3d** indicated the slightly steric effect in phenyl group of R_1 (Table 2, **3b-3d**). The different functional groups of *p*-substituted benzylidene showed the electronic properties of the benzylidene phenylhydrazone substituents affected the efficiency of the reaction (Table 2, **3e-3j**). The electron-withdrawing substrates like F, Cl and Br in phenyl group of R_1 showed a higher reactivity than the electron-donating ones. Introducing CN group promoted the yield of relative product to 91%. When R_1 was replaced by ester group, the reaction also has a good yield (Table 2, **3k**). However, the substitution of R_2 decreased the reaction efficiency. The hydrazone with different groups in phenyl group of R_2 could generate corresponding products in a moderate yields (Table 2, **3l-3p**). Satisfyingly, the *N*-alkyl substituted hydrazine could get the corresponding products in moderate yields as well (Table 2, **3q-3r**).

Table 2. Scope of substituted phenylhydrazone[a]

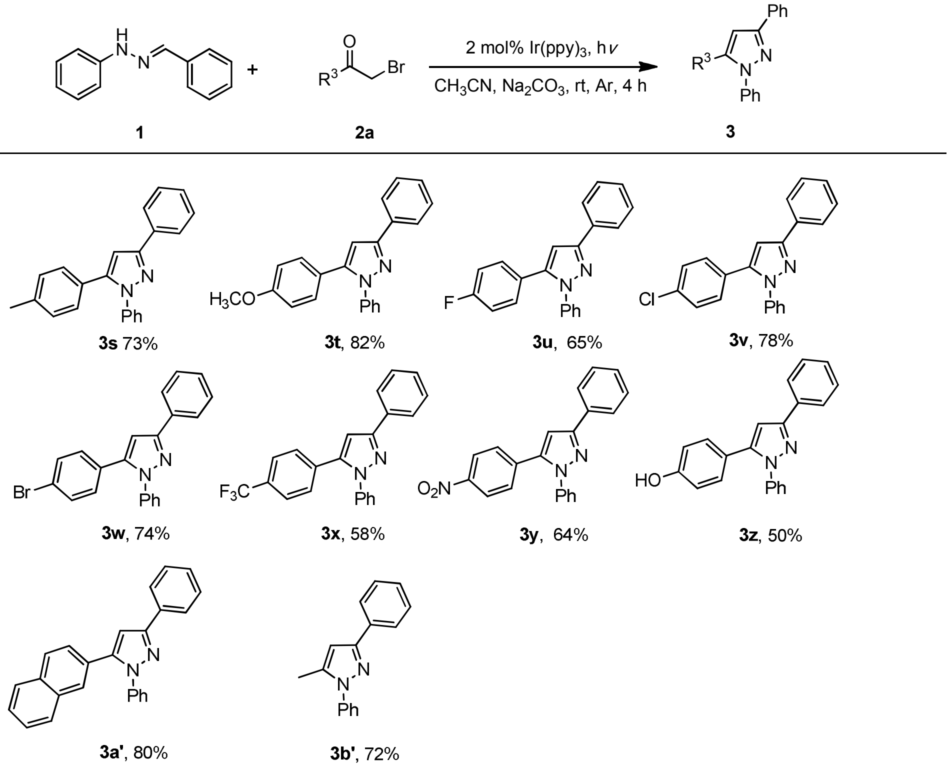


3a, 81%
3b, 67%
3c, 63%
3d, 71%
3e, 69%
3f, 60%
3g, 81%
3h, 87%
3i, 82%
3j, 91%
3k, 54%
3l, 65%
3m, 67%
3n, 60%
3o, 72%
3p, 79%
3q, 51%[b]
3r, 53%

[a]Reaction conditions: 0.1 mmol (*E*)-1-benzylidene-2-phenylhydrazine, 0.15 mmol α-bromoacetophenone, 2 mol% Ir(ppy)$_3$, and 1 equiv. Na$_2$CO$_3$ in 2 mL CH$_3$CN irradiated by blue LEDs under Ar for 4 h. [b]One pot reaction of methyldrazine sulphate, benzaldehyde and α-bromoacetophenone. More details see Experimental Section.

Further experiments were performed to understand the reaction efficiency of various α-bromo ketone derivatives (Table 3). A wide range of functional groups were tolerated in this system. *P*-CH$_3$, *p*-OCH$_3$, *p*-F, *p*-Cl, *p*-Br substituted α-bromoacetophenone and 2-(bromoacetyl) naphthalene could react with (*E*)-1-benzylidene-2-phenylhydrazine to yield the products in moderate yields (Table 3, **3s-3w**, **3a'**). Strong electron-withdrawing group like *p*-CF_3Ph and *p*-NO_2Ph were tolerated in this system (Table 3, **3v-3y**). To our surprise, the *p*-hydroxyl α-bromoacetophenone could also react smoothly under the optimized condition to yield the hydroxyl product in 50% yield (Table 3, **3z**).

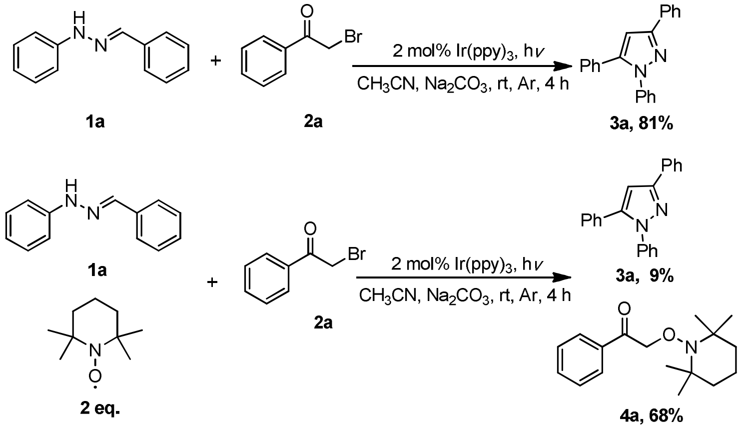
Table 3. Scope of substituted α-bromo ketone[a]



[a] Reaction conditions: 0.1 mmol (*E*)-1-benzylidene-2-phenylhydrazine, 0.15 mmol α-bromo ketone, 2 mol% Ir(ppy)$_3$, and 1 equiv. Na_2CO_3 in 2 mL CH_3CN irradiated by blue LEDs under Ar for 4 h.

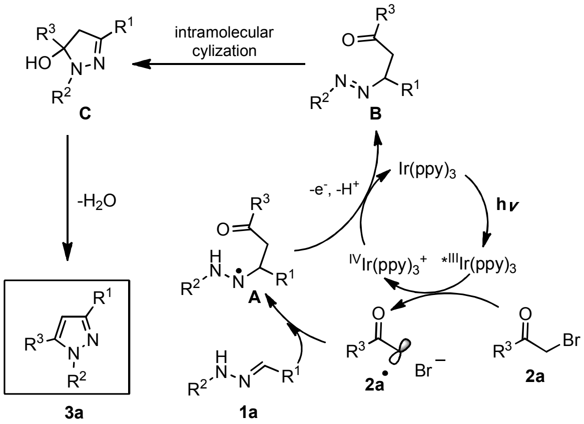
Under optimized condition, the template reaction could get the product with isolated yield of 81% at room temperature. When 2 equivalent 2,2,6,6-tetramethyl piperidin-1-oxyl (TEMPO) was added, only 9% yield of target compound was obtained (Scheme 2). Furthermore, an addition product **4a** of acetophenone radical and TEMPO was observed, with an isolated yield of 68%. This result demonstrated that a radical procedure was involved in this system and the acetophenone radical from **2a** is the key intermediate.

In order to elucidate more details about the reaction mechanism, the spectroscopic experiments were carried out. UV-vis absorption spectra of these three compounds showed only $\mathrm{Ir^{III}(ppy)_3}$ could absorb visible light. When the photocatalyst $\mathrm{Ir^{III}(ppy)_3}$ was irradiated by the light of 405 nm, a strong emission in 529 nm was observed. Progressive addition of **1a** or **2a** into the solution of excited $\mathrm{{}^*Ir^{III}(ppy)_3}$ demonstrated the quenching degree caused by **2a** was much stronger than **1a** (more details see in SI). These results directly indicated the efficient interaction between **2a** and excited $\mathrm{Ir^{III}(ppy)_3}$. According to the redox potential of **1a** ($E_{red} < -2.0$ V *vs.* SCE and $E_{ox} = 0.94$ V *vs.* SCE), the electron transfer process between **1a** and $\mathrm{{}^*Ir(ppy)_3}$ ($E^{IV/III*} = -1.84$ V *vs.* SCE, $E^{III*/II} = 0.26$ V)[14] was less likely than that of **2a** ($E_{ox} > 1.6$ V *vs.* SCE, $E_{red} = -1.2$ V *vs.* SCE).



Scheme 2. Control experiments

On the basis of above results, a plausible mechanism was proposed in Scheme 3. Under the irradiation of visible light, the photocatalyst Ir$^{\square}$(ppy)$_3$ is pumped to its excited state *Ir$^{\square}$(ppy)$_3$. Then this excited species transfers one electron to **2a**, which leads to the generation of alkyl radical **2a•** and Ir$^{\mathrm{IV}}$(ppy)$_3^+$. As a high electrophilic specie, radical **2a•** tends to react with the electron-rich hydrazine and produces the aminyl radical **A**. Further oxidation of **A** by Ir$^{\mathrm{IV}}$(ppy)$_3^+$ affords intermediate **B** and regenerates Ir$^{\mathrm{III}}$(ppy)$_3$. To our delight, this intermediate **B** could further cyclize to construct the pyrazole skeleton with mono *N*-substituted hydrazone.



Scheme 3. Proposed mechanism

In conclusion, a novel one-pot visible light-promoted singlet electron transfer process has been developed for the facile synthesis of 1,3,5-trisubstituted pyrazoles from easily accessible starting materials. The reaction has been demonstrated general for a wide range of functional groups with electron-withdrawing and electron-donating, such as nitro, nitrile and hydroxyl etc. in hydrazones and α-bromo ketones. The good to excellent yields indicate the reaction potential of monosubstituted hydrazones in photocatalyzed radical addition. Such an approach enriches photoredox reaction and represents a lower cost, milder, and greener process for the synthesis of 1,3,5-trisubstituted pyrazoles.

EXPERIMENTAL SECTION

General experimental procedure

^{1}H and ^{13}C NMR spectra were recorded with 400 MHz and 100 MHz NMR instruments. Chemical shifts (δ, ppm) are given with tetramethylsilane (TMS) as an internal standard. The coupling constants (*J*) were reported in hertz. Flash column chromatography was performed over silica gel 200-300 mesh, and the eluent was a mixture of ethyl acetate (EA) and petroleum ether (PE). High–resolution mass spectra (HRMS-ESI) were obtained on a Q-TOF mass spectrometer. All the substituted α-bromo ketones, benzaldehydes and phenylhydrazines hydrochloride salts were purchased from commercial and used without further purification. All the substituted phenylhydrazines obtained from neutralization reaction of corresponding hydrochloride salts with sodium hydroxide in water and diethyl ether two-phase solution.

General Procedure for the Synthesis of Substituted Benzylidene Phenylhydrazones 1. To a stirred solution of substituted phenylhydrazine (5.5 mmol) in methanol (5 mL), benzaldehyde derivatives (5 mmol) were added dropwise. Then stirring at room temperature until the conversion was complete (disappearance of benzaldehydes, monitored by TLC). The solid was collected by filtration and washed with cooled MeOH. Then dried to afford the product **1**.

General Procedure for the Synthesis of Pyrazoles. benzylidene phenylhydrazone (0.1 mmol, 1 equiv.), α-bromo ketone (0.15 mmol, 1.5 equiv.), Na_2CO_3 (0.1 mmol, 1 equiv.) and $Ir(ppy)_3$ (2 μmol, 0.02 equiv.) were dissolved in CH_3CN (2 mL) in a 10 mL pyrex tube equipped with a rubber septum and magnetic stir bar, and then the argon-purged solution was irradiated by blue LEDs (λ_{max} = 450nm) at room temperature for 4 h. The solvent was removed under reduced pressure after the reaction was finished. Then the residue was purified by column chromatography on silica gel eluting with ethyl acetate/petroleum ether to give the corresponding product. **The one pot synthesis of 3q:** 0.1 mmol Methylhydrazine sulphate, 0.15 mmol benzaldehyde, 2 equiv. Na_2CO_3 was dissolved in 1.5 mL CH_3CN 10 mL in a pyrex tube equipped with a rubber septum and magnetic stir bar. After the solution was purged with argon and stirred for 1 h, the reaction solution was injected with 0.15 mmol α-bromoacetophenone in 0.5 mL CH_3CN, and then irradiated by blue LEDs for 4 h.

*1,3,5-Triphenyl-1H-pyrazole (**3a**).* Yield: 23.9 mg, 81%. White solid, m.p. 138-140 ℃. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.96 (d, J = 7.7 Hz, 2H), 7.45 (t, J = 7.4 Hz, 2H), 7.42-7.29 (m, 11H), 6.85 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.0, 144.4, 140.2, 133.1, 130.6, 128.9, 128.8, 128.7, 128.5, 128.3, 128.0, 127.5, 125.9, 125.3, 105.2; HRMS (ESI) calcd. for $C_{21}H_{17}N_2$ $[M + H]^+$ 297.1386, found 297.1386.

*1,5-Diphenyl-3-(p-tolyl)-1H-pyrazole (**3b**).* Yield: 20.8 mg, 67%. White solid, m.p. 127-128 ℃. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.82 (d, J = 7.6 Hz, 2H), 7.30 (m, 12H), 6.79 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.0, 144.3, 140.2, 137.8, 130.7, 130.2, 129.4, 128.9, 128.8, 128.5, 128.3, 127.4, 125.8, 125.3, 105.1, 21.3.

HRMS (ESI) calcd. for $C_{22}H_{19}N_2$ $[M + H]^+$ 311.1543, found 311.1543.

1,5-Diphenyl-3-(m-tolyl)-1H-pyrazole (3c). Yield: 19.5 mg, 63%. White solid, m.p. 88-90 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.80 (s, 1H), 7.72 (d, J = 7.6 Hz, 1H), 7.40-7.26 (m, 11H), 7.17 (d, J = 7.5 Hz, 1H) 6.83 (s, 1H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 144.4, 140.2, 138.3, 132.9, 130.64, 128.9, 128.84, 128.78, 128.6, 128.5, 128.3, 127.5, 126.5, 125.4, 123.1, 105.3, 21.5. HRMS (ESI) calcd. for $C_{22}H_{19}N_2$ $[M + H]^+$ 311.1543, found 311.1542.

*1,5-Diphenyl-3-(o-tolyl)-1H-pyrazole (**3d**).* Yield: 21.9 mg, 71%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.71 (t, J = 3.8 Hz, 1H), 7.42-7.27 (m, 13H), 6.69 (s, 1H), 2.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.4, 143.4, 140.1, 136.2, 132.8, 130.9, 130.7, 129.4, 128.9, 128.8, 128.5, 128.3, 127.9, 127.3, 125.9, 125.2, 108.3, 21.4. HRMS (ESI) calcd. for $C_{22}H_{19}N_2$ $[M + H]^+$ 311.1543, found 311.1543.

*3-(4-Isopropylphenyl)-1,5-diphenyl-1H-pyrazole (**3e**).* Yield: 23.3 mg, 69%. White solid. m.p. 101-102 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.85 (d, J = 7.4 Hz, 2H), 7.43-7.27 (m, 12H), 6.80 (s, 1H), 2.95 (m, 1H), 1.30 (s, 3H), 1.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 148.8, 144.3, 140.2, 130.7, 130.6, 128.9, 128.8, 128.5, 128.3, 127.4, 126.7, 125.9, 125.3, 105.1, 34.0, 24.0. HRMS (ESI) calcd. for $C_{24}H_{23}N_2$ $[M + H]^+$ 339.1856, found 339.1856.

*3-(4-Methoxyphenyl)-1,5-diphenyl-1H-pyrazole (**3f**).* Yield: 19.7 mg, 60%. White solid, m.p. 143-144 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.86 (d, J = 8.0 Hz, 2H), 7.39–7.26 (m, 10H), 6.97 (d, J = 8.0 Hz, 2H), 6.76 (s, 1H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.7, 151.8, 144.4, 140.1, 130.6, 128.9, 128.8, 128.5, 128.3, 127.4, 127.2, 125.7, 125.3, 114.1, 104.8, 55.3. HRMS (ESI) calcd. for $C_{22}H_{19}N_2O$ $[M + H]^+$ 327.1492, found 327.1491.

*3-(4-Fluorophenyl)-1,5-diphenyl-1H-pyrazole (**3g**).* Yield: 25.4 mg, 81%. White solid, m.p. 143-144 ℃. ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.90 (t, J = 6.72 Hz, 2H), 7.40-7.27 (m, 10H), 7.12 (t, J = 8.2 Hz, 2H), 6.78 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ = 162. 8 (d, J = 246.6 Hz), 151.1, 144.6, 140.1, 130.5, 129.3 (d, J = 3.2 Hz), 129.0, 128.7, 128.5, 128.4, 127.5 (d, J = 8.0 Hz), 127.5, 125.3, 115.6 (d, J = 21.6 Hz), 105.0. HRMS (ESI) calcd. for $C_{21}H_{16}FN_2$ [M + H]$^+$ 315.1292, found 315.1292.

*3-(4-Chlorophenyl)-1,5-diphenyl-1H-pyrazole (**3h**).* Yield: 28.9 mg, 87%. White solid, m.p. 138-139 ℃. ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.86 (d, J = 7.6 Hz, 2H), 7.42-7.24 (m, 12H), 6.79 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ = 150.9, 144.6, 140.0, 133.8, 131.6, 130.4, 129.0, 128.8, 128.7, 128.5, 128.4, 127.6, 127.1, 125.3, 105.1. HRMS (ESI) calcd. for $C_{21}H_{16}ClN_2$ [M + H]$^+$ 331.0997, found 331.0996.

*3-(4-Bromophenyl)-1,5-diphenyl-1H-pyrazole (**3i**).* Yield: 30.8 mg, 82%. White solid, m.p. 152-154 ℃. ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.79 (d, J = 8.1 Hz, 2H), 7.54 (d, J = 8.1 Hz, 2H), 7.37-7.24 (m, 10H), 6.79 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ = 150.9, 144.7, 140.0, 132.1, 131.8, 130.4, 129.0, 128.8, 128.54, 128.45, 127.6, 127.4, 125.3, 122.0, 105.1. HRMS (ESI) calcd. for $C_{21}H_{16}BrN_2$ [M + H]$^+$ 375.0491, found 375.0490.

*4-(1,5-Diphenyl-1H-pyrazol-3-yl)benzonitrile (**3j**).* Yield: 29.1 mg, 91%. Light yellow solid, m.p. 168-170 ℃. ^{1}H NMR (400 MHz, CDCl$_3$) δ = 8.02 (d, J = 7.7 Hz, 2H), 7.70 (d, J = 7.7 Hz, 2H), 7.39-7.31 (m, 8H), 7.28-7.24 (m, 2H), 6.86 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ = 150.0, 145.0, 139.8, 137.5, 132.6, 130.1, 129.1, 128.8, 128.7, 128.6, 127.9, 126.2, 125.3, 119.1, 111.2, 105.6. HRMS (ESI) calcd. for $C_{22}H_{16}N_3$ [M + H]$^+$ 322.1339, found 322.1337.

*Ethyl 1,5-diphenyl-1H-pyrazole-3-carboxylate (**3k**).* Yield: 15.8 mg, 54%. Yellow oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.38-7.27 (m, 8H), 7.21 (d, J = 7.4 Hz, 2H), 7.05 (s, 1H), 4.46 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ = 162.5, 144.7, 144.4 139.6, 129.6, 129.0, 128.8, 128.7, 128.6, 128.3, 125.8, 109.9, 61.1, 14.4. HRMS (ESI) calcd. for $C_{18}H_{17}N_2O_2$ $[M + H]^+$ 293.1285, found 293.1285.

*3,5-Diphenyl-1-(p-tolyl)-1H-pyrazole (**3l**).* Yield: 20.3 mg, 65%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (d, J = 7.5 Hz, 2H), 7.42 (t, J = 7.4 Hz, 2H), 7.36-7.23 (m, 8H), 7.14 (d, J = 7.7 Hz, 2H), 6.81 (s, 1H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.7, 144.3, 137.7, 137.4, 133.1, 130.7, 129.5, 128.7, 128.6, 128.5, 128.2, 128.0, 125.8, 125.2, 104.9, 21.1. HRMS (ESI) calcd. for $C_{22}H_{19}N_2$ $[M + H]^+$ 311.1543, found 311.1543.

*3,5-Diphenyl-1-(m-tolyl)-1H-pyrazole (**3m**).* Yield: 20.9 mg, 67%. White solid, m.p. 72-73 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.94 (d, J = 7.6 Hz, 2H), 7.44 (t, J = 7.4 Hz, 2H), 7.34 (m, 7H), 7.20 (t, J = 7.7 Hz, 1H), 7.13 (d, J = 7.4 Hz, 1H), 7.05 (d, J = 7.8 Hz, 1H), 6.83 (s, 1H), 2.34 (d, J = 11.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.9, 144.4, 140.1, 139.1, 133.1, 130.7, 128.7, 128.64, 128.55, 128.4, 128.27, 128.25, 128.0, 126.0, 125.9, 122.5, 105.1, 21.4. HRMS (ESI) calcd. for $C_{22}H_{19}N_2$ $[M + H]^+$ 311.1543, found 311.1543.

*1-(4-Methoxyphenyl)-3,5-diphenyl-1H-pyrazole (**3n**)*. Yield: 19.6 mg, 60%. White solid, m.p. 109-111 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.4 Hz, 2H), 7.37-7.27 (m, 8H), 6.87 (d, J = 7.6 Hz, 2H), 6.82 (s, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.9, 151.6, 144.4, 133.4, 133.1, 130.6, 128.7, 128.6, 128.5, 128.2, 127.9, 126.8, 125.8, 114.1, 104.7, 55.5. HRMS (ESI) calcd. for $C_{22}H_{19}N_2O$ $[M + H]^+$ 327.1492, found 327.1492.

*1-(4-Fluorophenyl)-3,5-diphenyl-1H-pyrazole (**3o**).* Yield: 22.3 mg, 72%. Light yellow solid, m.p. 107-108 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.91 (d, J = 7.7 Hz, 2H), 7.43 (t, J = 7.4 Hz, 2H), 7.34 (m, 6H), 7.29-7.23 (m, 2H), 7.04 (t, J = 7.9 Hz, 2H), 6.82 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 161.7 (d, J = 247.5 Hz), 152.1, 144.5, 136.3 (d, J = 3.0 Hz), 132.9, 130.4, 128.8, 128.7, 128.6, 128.5, 128.1, 127.1 (d, J = 8.6 Hz), 125.8, 115.8 (d, J = 22.9 Hz), 105.2. HRMS (ESI) calcd. for $C_{21}H_{16}FN_2$

$[M + H]^+$ 315.1292, found 315.1291.

*1-(4-Bromophenyl)-3,5-diphenyl-1H-pyrazole (**3p**).* Yield: 29.5 mg, 79%. White solid, m.p. 100-101 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.83 (d, J = 7.6 Hz, 2H), 7.36 (m, 4H), 7.27 (m, 4H), 7.18 (m, 4H), 6.73 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.3, 144.5, 139.2, 132.8, 132.0, 130.3, 128.8, 128.72, 128.69, 128.6, 128.2, 126.6, 125.9, 121.0, 105.7. HRMS (ESI) calcd. for $C_{21}H_{16}BrN_2$ $[M + H]^+$ 375.0491, found 375.0490.

1-methyl-3,5-diphenyl-1H-pyrazole (**3q**). Yield: 11.9 mg, 51%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.83 (d, J = 7.7 Hz, 2H), 7.51 – 7.43 (m, 5H), 7.41 (t, J = 7.5 Hz, 2H), 7.31 (t, J = 7.3 Hz, 1H), 6.61 (s, 1H), 3.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.5, 145.1, 133.3, 130.6, 128.8, 128.7, 128.63, 128.59, 127.7, 125.6, 103.3, 37.6. HRMS (ESI) calcd. for $C_{16}H_{15}N_2$ $[M + H]^+$ 235.1230, found 235.1226.

1-(Tert-butyl)-3,5-diphenyl-1H-pyrazole (**3r**). Yield: 14.7 mg, 53%. White solid, m.p. 110-112 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 (d, J = 7.8 Hz, 2H), 7.45 – 7.33 (m, 8H), 7.27 (t, J = 6.4 Hz, 1H), 6.45 (s, 1H), 1.51 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 147.8, 144.0, 134.4, 134.0, 130.5, 128.5, 128.4, 127.8, 127.2, 125.5, 106.5, 61.5, 31.2. HRMS (ESI) calcd. for $C_{19}H_{21}N_2$ $[M + H]^+$ 277.1700, found 277.1700.

*1,3-Diphenyl-5-(p-tolyl)-1H-pyrazole (**3s**).* Yield: 22.8 mg, 73%. Yellow solid, m.p. 113-115 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.94 (d, J = 7.5 Hz, 2H), 7.38 (m, 8H), 7.19 (d, J = 7.8 Hz, 2H), 7.14 (d, J = 7.8 Hz, 2H), 6.81 (s, 1H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.9, 144.5, 140.3, 138.3, 133.1, 129.2, 128.9, 128.7, 128.0, 127.7, 127.4, 125.9, 125.4, 105.0, 21.3. HRMS (ESI) calcd. for $C_{22}H_{19}N_2$ $[M + H]^+$ 311.1542, found 311.1543.

*5-(4-Methoxyphenyl)-1,3-diphenyl-1H-pyrazole (**3t**).* Yield: 26.8 mg, 82%. White solid, m.p. 77-78 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 (d, J = 7.7 Hz, 2H), 7.38 (m, 8H), 7.21 (d, J = 8.2 Hz, 2H), 6.85 (d, J = 8.2 Hz, 2H), 6.77 (s, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.7, 151.9, 144.3, 140.2, 133.1, 130.1, 128.9, 128.6, 128.0, 127.4, 125.9, 125.4, 123.0, 114.0, 104.7, 55.3. HRMS (ESI) calcd. for $C_{22}H_{19}N_2O$ $[M + H]^+$ 327.1492, found 327.1492.

*5-(4-Fluorophenyl)-1,3-diphenyl-1H-pyrazole (**3u**).* Yield: 20.5 mg, 65%. Yellow solid, m.p. 144-146 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (d, J = 7.5 Hz, 2H), 7.43 (t, J = 7.4 Hz, 2H), 7.38-7.30 (m, 6H), 7.24 (t, J = 6.3 Hz, 2H), 7.01 (t, J = 8.2 Hz, 2H), 6.79 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.7 (d, J = 248.8 Hz), 152.0, 143.4, 140.0, 133.0, 130.6 (d, J = 8.2 Hz), 129.0, 128.7, 128.1, 127.6, 126.8 (d, J = 3.4 Hz), 125.8, 125.3, 115.6 (d, J = 21.7 Hz), 105.2. HRMS (ESI) calcd. for $C_{21}H_{16}FN_2$ $[M + H]^+$ 315.1292, found 315.1292.

*5-(4-Chlorophenyl)-1,3-diphenyl-1H-pyrazole (**3v**).* Yield: 26.8 mg, 81%. White solid, m.p. 103-105 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (d, J = 7.7 Hz, 2H), 7.44 (t, J = 7.3 Hz, 2H), 7.41-7.28 (m, 8H), 7.21 (d, J = 8.0 Hz, 2H), 6.82 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 143.2, 139.9, 134.4, 132.9, 130.0, 129.08, 129.05, 128.8, 128.7, 128.1, 127.7, 125.9, 125.4, 105.3. HRMS (ESI) calcd. for $C_{21}H_{16}ClN_2$ $[M + H]^+$ 331.0997, found 331.0997.

*5-(4-Bromophenyl)-1,3-diphenyl-1H-pyrazole (**3w**).* Yield: 27.7 mg, 74%. Yellow solid, m.p. 129-131 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 (d, J = 7.6 Hz, 2H), 7.40 (m, 10H), 7.15 (d, J = 7.9 Hz, 2H), 6.83 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 143.2, 139.9, 132.8, 131.8, 130.2, 129.5, 129.1, 128.7, 128.1, 127.7, 125.9, 125.4, 122.6, 105.3. HRMS (ESI) calcd. for $C_{21}H_{16}BrN_2$ $[M + H]^+$ 375.0491, found 375.0492.

*1,3-Diphenyl-5-(4-(trifluoromethyl)phenyl)-1H-pyrazole (**3x**).* Yield: 21.3 mg, 58%. White solid, m.p. 154-156 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 (d, J = 7.7 Hz, 2H), 7.59 (d, J = 8.0 Hz, 2H), 7.49-7.34 (m, 10H), 6.89 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 142.9, 139.7, 134.0, 132.7, 130.3 (q, J = 32.4 Hz), 129.2, 128.9, 128.7, 128.3, 127.9, 125.9, 125.5 (q, J = *19.0 Hz*), 125.4, 123.9 (q, J = 272.2 Hz), 105.8. HRMS (ESI) calcd. for $C_{22}H_{16}F_3N_2$ $[M + H]^+$ 365.1260, found 365.1259.

*5-(4-Nitrophenyl)-1,3-diphenyl-1H-pyrazole (**3y**).* Yield: 21.8 mg, 64%. White solid. m.p. 136-137 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.18 (d, J = 7.8 Hz, 2H), 7.92 (d, J = 7.6 Hz, 2H), 7.49-7.33 (m, 10H), 6.95 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.4, 147.3, 142.0, 139.6, 136.7, 132.5, 129.33, 129.27, 128.8, 128.4, 128.2, 125.8, 125.5, 123.8, 106.3. HRMS (ESI) calcd. for $C_{21}H_{16}N_3O_2$ $[M + H]^+$ 342.1237, found 342.1237.

*4-(1,3-Diphenyl-1H-pyrazol-5-yl)phenol (**3z**).* Yield: 15.5 mg, 50%. White solid. m.p. 221-223 ℃. ^{1}H NMR (400 MHz, Acetone-d_6) δ = 8.62 (s, 1H), 7.93 (d, J = 7.6 Hz, 2H), 7.43-7.27 (m, 8H), 7.13 (d, J = 7.4 Hz, 2H), 6.89 (s, 1H), 6.80 (d, J = 7.5 Hz, 2H). ^{13}C NMR (100 MHz, d_6-Acetone) δ = 157.7, 151.3, 144.6, 140.7, 133.6, 130.1, 128.8, 128.5, 127.7, 127.2, 125.5, 125.1, 121.9, 115.4, 104.4. HRMS (ESI) calcd. for $C_{21}H_{17}N_2O$ $[M + H]^+$ 313.1335, found 313.1335.

*5-(Naphthalen-2-yl)-1,3-diphenyl-1H-pyrazole (**3a'**).* Yield: 27.8 mg, 80%. White solid. m.p. 102-103 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 (d, J = 7.6 Hz, 2H), 7.88-7.74 (m, 4H), 7.54-7.41 (m, 6H), 7.34 (m, 5H), 6.95 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.1, 144.4, 140.2, 133.1, 133.0, 132.9, 129.0, 128.7, 128.2, 128.10, 128.06, 128.01, 127.98, 127.7, 127.5, 126.7, 126.6, 126.3, 125.9, 125.3, 105.6. HRMS (ESI) calcd. for $C_{25}H_{19}N_2$ $[M + H]^+$, 347.1543, found 347.1543.

*5-methyl-1,3-diphenyl-1H-pyrazole (**3b'**).* Yield: 16.8 mg, 72%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 – 7.84 (m, 2H), 7.57 - 7.46 (m, 4H), 7.40 (q, J = 7.6 Hz, 3H), 7.32 (t, J = 7.3 Hz, 1H), 6.54 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (100 MHz,

$CDCl_3$) δ = 151.7, 140.23, 140.18, 133.6, 129.2, 128.6, 127.8, 127.7, 125.9, 125.1, 104.5, 12.6. HRMS (ESI) calcd. for $C_{16}H_{15}N_2$ $[M + H]^+$, 235.1230, found 235.1233.

*1-Phenyl-2-(2,2,6,6-tetramethylpiperidin-1-yl)ethanone (**4a**).* Yield: 17.3 mg, 68%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.94 (d, J = 7.6 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 5.12 (s, 2H), 1.57 (dd, J = 19.5, 7.8 Hz, 1H), 1.52 – 1.44 (m, 4H), 1.37 – 1.30 (m, 1H), 1.19 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.8, 135.5, 133.2, 128.6, 128.0, 81.4, 60.2, 39.8, 32.8, 20.3, 17.1. HRMS (ESI) calcd. for $C_{17}H_{26}NO_2$ $[M + H]^+$ 276.1958, found 276.1957.

SUPPORTING INFORMATION

Copies of ^{1}H and ^{13}C NMR spectra for all products, the UV-vis absorption spectra of $Ir(ppy)_3$, **1a** and **2a** and steady state emission quenching spectra of excited $^*Ir(ppy)_3$ by **1a** or **2a**. This material is available free of charge via the internet at http://pubs.acs.org.

ACKNOWLEDGMENTS

We are grateful for financial support from the Ministry of Science and Technology of China (2013CB834804 and 2013CB834505), the National Natural Science Foundation of China (21390404, 91427303, and 21402217), Strategic Priority Research Program of the Chinese Academy of Science (XDB17030200), and the Chinese Academy of Sciences.

REFERENCES

[1] Prier, C. K.; Rankic, D. A.; MacMillan, D. W. *Chem. Rev.* **2013**, *113*, 5322.

[2] (a) Teplý, F. Collect. Czech. *Chem. Commun.* **2011**, *76*, 859. (b) Ischay, M. A.; Yoon, T. P. *Eur. J. Org. Chem.* **2012**, *77*, 3359. (c) Hari, D. P.; Konig, B. *Angew. Chem. Int. Ed.* **2013**, *52*, 4734. (d) Nicewicz, D. A.; Nguyen, T. M. *ACS Catal.* **2014**, *4*, 355. (e) Xie, J.; Jin, H.; Xu, P.; Zhu, C. *Tetrahedron Lett.* **2014**, *55*, 36. (f) Luca, O. R.; Gustafson, J. L.; Maddox, S. M.; Fenwick, A. Q.; Smith, D. C. *Org. Chem. Front.* **2015**, *2*, 823. (g) Pena-Lopez, M.; Rosas-Hernandez, A.; Beller, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 5006. (h) Tang, S.; Liu, K.; Liu, C.; Lei, A. W. *Chem. Soc. Rev.* **2015**, *44*, 1070. (i) Xuan, J.; Zhang, Z. G.; Xiao, W. J. *Angew. Chem. Int. Ed.* **2015**, *54*, 15632.

[3] (a) Shi, L.; Xia, W. *Chem. Soc. Rev.* **2012**, *41*, 7687. (b) Hu, J.; Wang, J.; Nguyen, T. H.; Zheng, N. *Beilstein J. Org. Chem.* **2013**, *9*, 1977. (c) Xuan, J.; Lu, L.Q.; Chen, J. R.; Xiao, W. J. *Eur. J. Org. Chem.* **2013**, *78*, 6755. (d) Yoon, T. P. *ACS Catal.* **2013**, *3*, 895. (e) Jahn, E.; Jahn, U. *Angew. Chem. Int. Ed.* **2014**, *53*, 13326.

[4] (a) Xu P.; Wang G. Q.; Zhu Y. C.; Li W. P.; Cheng Y. X.; Li S. H.; Zhu C. J. *Angew. Chem. Int. Ed.* **2016**, *55*, 2939. (b) Xie J.; Zhang T.; Chen F., N. Mehrkens; F. Rominger; M. Rudolph; Hashmi A. S. K. *Angew. Chem. Int. Ed.* **2016**, *55*, 1.

[5] (a) Sridhar, R.; Perumal, P. T.; Etti, S.; Shanmugam, G.; Ponnuswamy, M. N.; Prabavathy, V. R.; Mathivanan, N. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 6035. (b) Liu, J. J.; Sun, J.; Fang, Y. B.; Yang, Y. A.; Jiao, R. H.; Zhu, H. L. *Org. Biomol. Chem.* **2014**, *12*, 998. (c) Ouyang, G.; Cai, X. J.; Chen, Z.; Song, B. A.; Bhadury, P. S.; Yang, S.; Jin, L. H.; Xue, W.; Hu, D. Y.; Zeng, S. *J. Agric. Food Chem.* **2008**, *56*, 10160. (d) Abdel-Magid, A. F. *ACS Med. Chem. Lett.* **2014**, *5*, 730. (e) Chang, C. P.; Wu, C. H.; Song, J. S.; Chou, M. C.; Wong, Y. C.; Lin, Y.; Yeh, T. K.; Sadani, A. A.; Qu, M. H.; Chen, K. H.; Chen, P. H.; Kuo, P. C.; Tseng, C. T.; Chang, K. H.; Tseng, S. L.; Chao, Y. S.; Hung, M. S.; Shia, K. S. *J. Med. Chem.* **2013**, *56*, 9920. (f) Hwang, S. H.; Wagner, K. M.; Morisseau, C.; Liu, J. Y.; Dong, H.; Wecksler, A. T.; Hammock, B. D. *J. Med. Chem.* **2011**, *54*, 3037.

[6] Kumar, V.; Kaur, K.; Gupta, G. K.; Sharma, A. K. *Eur. J. Med. Chem.* **2013**, *69*, 735.

[7] (a) Penning, T. D.; Talley, J. J.; Bertenshaw, S. R.; Carter, J. S.; Collins, P. W.; Docter, S.; Graneto, M. J.; Lee, L. F.; Malecha, J. W.; Miyashiro, J. M.; Rogers, R. S.;

Rogier, D. J.; Yu, S. S.; Anderson, G. D.; Burton, E. G.; Cogburn, J. N.; Gregory, S. A.; Koboldt, C. M.; Perkins, W. E.; Seibert, K.; Veenhuizen, A. W.; Zhang, Y. Y.; Isakson, P. C. *J. Med. Chem.* **1997**, *40*, 1347. (b) Habeeb, A. G; Praveen Rao, P. N.; Knaus, E. E. *J. Med. Chem.* **2001**, *44*, 3039. (c) Penning, T. D.; Kramer, S. W.; Lee, L. F.; Collins, P. W.; Koboldt, C. M.; Seibert, K.; Veenhuizen, A. W.; Zhang, Y. Y.; Isakson, P. C. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 2121.

[8] (a)Terrett, N. K.; Bell, A. S.; Brown, D.; Ellis, P. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1819. (b) Dale, D. J.; Dunn, P. J.; Golightly, C.; Hughes, M. L.; Levett, P. C.; Pearce, A. K.; Searle, P. M.; Ward, G.; Wood, A. S. *Org. Proc. Res. Dev.* **2000**, *4*, 17.

[9] (a) Ojwach, S. O.; Darkwa, *J. Inorg. Chim. Acta.* 2011, *363*, 1947. (b) Singer, R. A.; Caron, S.; McDermott, R. E.; Arpin, P.; Do, N. M. *Synthesis* **2003**, *25*, 1727. (c) Singer, R. A.; Dore, M.; Sieser, J. E.; Berliner, M. A. *Tetrahedron Lett.* **2006**, *47*, 3727. (d) Kowalczyk, R.; Skarzewski, J. *Tetrahedron* **2005**, *61*, 623.

[10] (a) Zolfigol, M.; Azarifar, D.; Maleki, B. *Tetrahedron Lett,* **2004**, *45*: 2181. (b) Chai, L.; Zhao, Y.; Sheng, Q.; Liu, Z. Q. *Tetrahedron Lett*, **2006**, *47*: 9283. (c) Su, G.; Wu, W. T.; Wang, J. T.; Wu, L. M. *Chin Chem Lett*, **2008**, *19*, 1013. (d) Nakamichi, N.; Kawashita, Y.; Hayashi, M. *Org. Lett.* **2002**, *4*, 3955. (e) Kawashita, Y.; Hayashi, M. *Molecules*, **2009**, *14*, 3073. (f) Ananthnag G. S,; Adhikari A.; Balakrishna M. S.; *Catal Commun*, **2014**, *43*, 240. (g) Ye, P.; Wang, D.-H.; Chen, B.; Meng, Q.-Y.; Tung, C.-H. Wu, L.-Z. *Sci. China Chem.* **2016**,*59*, 175.

[11] (a) L. Knorr, Ber. **1883**, 16, 2587. (b) Silva, V. L. M.; Silva, A. M. S.; Pinto D. C. G. A.; Cavaleiro, J. A. S.; Elguero, J. *Eur. J. Org. Chem.* **2004**, *117*, 4348. (c) Heller, S. T.; Natarajan, S. R. *Org. Lett.* **2006**, *8*, 2675. (d) Vickerstaffe, E.; Warrington, B. H.; Ladlow, M.; Ley, S. V. *J. Comb. Chem.* **2004**, *6*, 332. (e) Singh, S. K.; Reddy, M. S.; Shivaramakrishna, S.; Kavitha, D.; Vasudev, R.; Moses, B. J.; Sivalakshmidevi, A.; Rao, Y. *Tetrahedron Lett.* **2004**, *45*, 7679. (f) Polshettiwar, V.; Varma, R. S. *Tetrahedron* **2010**, *66*, 1091. (g) DeAngelis, A.; Wang, D. H.; Buchwald S. L. *Angew. Chem., Int. Ed.* **2013**, *52*, 1. (h) Wei, J. J.; Yu, H. F.; Yu, Z. K. *Tetrahedron Lett.* **2011**, *52*, 5884.

[12] (a) Zhang, T. H.; Bao, W. L. *J. Org. Chem.* **2013**, *78*, 1317. (b) Hu, J. T.; Chen, S.;

Sun, Y. H.; Yang, J.; Rao, Y. *Org. Lett.* **2012**, *14*, 5030. (c) Li, X. W.; He, L.; Chen, H. J.; Wu, W. Q.; Jiang, H. F. *J. Org. Chem.* **2013**, *78*, 3636. (d) Zhang, G. W.; Zhao, Y.; Ge, H. B. *Angew. Chem. Int. Ed.* **2013**, *52*, 2559. (e) Metin, Z.; Arif, K. *J. Org. Chem.* **2011**, *76*, 9379. (f) Liu, P.; Pan, Y. M.; Xu, Y. L.; Wang, H. S. *Org. Biomol. Chem.* **2012**, *10*, 4696. (g) Li, Z. L.; Liu, J. H.; Huang, Z. W.; Yang, Y.; Xia C. G.; Li, F. W. *ACS Catal.* **2013**, *3*, 839. (h) Pratibha, R.; Manhulika, S.; Jaya, S.; Jagdamba, S. *RSC Adv.* **2014**, *4*, 779.

[13] Johanna, S.; Burkhard, K.; *Green Chem.* **2016**, doi: 10.1039/C6GC01101B.

[14] Lei, T,; Liu, W. Q.; Li, J.; Huang, M.-Y.; Yang, B.; Meng, Q.-Y.; Chen, B.; Tung, C.-H.; Wu, L.-Z. *Org. Lett.* **2016**, *18*, 2479.