Received: 18 May 2018 | Revised: 5 July 2018 | Accepted: 9 July 2018

DOI: 10.1002/aoc.4532

FULL PAPER

WILEY Applied Organometallic Chemistry

$Cu_{1.5}PMo_{12}O_{40}$-catalyzed condensation cyclization for the synthesis of substituted pyrazoles

Guo-Ping Yang[1,3] | Xing He[1] | Bing Yu[2] | Chang-Wen Hu[1]

[1] Key Laboratory of Cluster Science of Ministry of Education, Beijing Key Laboratory of Photoelectronic/Electrophotonic, School of Chemistry and Chemical Engineering, Beijing Institute of Technology, Beijing 100081, P. R. China

[2] College of Chemistry and Molecular Engineering, Zhengzhou University, Zhengzhou 450001, Henan Province, P. R. China

[3] China Academy of Engineering Physics, P. R. China

Correspondence
Bing Yu, College of Chemistry and Molecular Engineering, Zhengzhou University, Zhengzhou 450001, Henan Province, P. R. China.
Email: bingyu@zzu.edu.cn

Chang-Wen Hu, Key Laboratory of Cluster Science of Ministry of Education, Beijing Key Laboratory of Photoelectronic/Electrophotonic, School of Chemistry and Chemical Engineering, Beijing Institute of Technology, Beijing 100081, P. R. China.
Email: cwhu@bit.edu.cn

Funding information
National Natural Science Foundation of China, Grant/Award Numbers: 21501010 and 21671019; 973 Program, Grant/Award Number: 2014CB932103; the 111 Project, Grant/Award Number: B07012

A convenient and direct approach has been developed for the preparation of pyrazole derivatives by the condensation cyclization of hydrazines/hydrazide and 1,3-diketones in the presence of $Cu_{1.5}PMo_{12}O_{40}$ (0.33 mol%) under mild conditions (r.t.-60 °C, 10–30 min). Notably, the reaction was found to be scalable as 99% yield was obtained when the reaction was performed at a 5-mmol scale. This solvent-free and halogen-free catalytic system represents an effective economic and environmentally friendly method for the construction of pyrazoles.

KEYWORDS
condensation reaction, copper, hydrazine, polyoxometalates, pyrazole

1 | INTRODUCTION

Nitrogen-containing heterocycles have attracted widespread attention in the field of synthetic organic chemistry due to their wide and diverse applications in pharmaceutical and agrochemical fields.[1] Particularly, the pyrazole ring is a prominent structure motif that was found as the core structure of numerous drugs,[2] such as Celecoxib, Deracoxib, Penthiopyrad, Lonazolac, Razaxaban, and Rimonabant, which are valuable biologically and pharmaceutically active organic molecules.

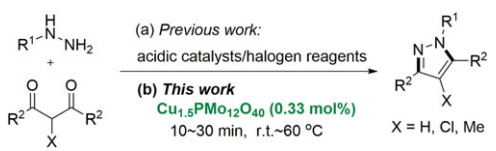
Due to the important of the pyrazoles, it is therefore not surprising that many synthetic methods have been developed for the construction of pyrazole scaffold.[3] For instance, the pyrazole ring can be synthesized via the reaction of hydrazines with unsaturated aldehydes/ketones,[4] or 1,3-dicarbonyl compounds,[5] 1,3-dipolar cycloaddition of diazo compounds with alkenes,[6]

alkynes,[7] or 1,3-dicarbonyl compounds,[8] oxidative coupling of enaminones and nitriles,[9] etc. Among these methods hitherto developed, the most generally useful one is based on the condensation-cyclization reaction of hydrazines and 1,3-dicarbonyl compounds. For example, in 2004, the Wang's group[5] reported the sulfuric acid catalyzed condensation cyclization between hydrazines and 1,3-diketones, affording pyrazole derivatives. Moreover, various protocols employed microwave,[10] or acidic catalysts,e.g., Sc $(OTf)_3$,[11] polystyrene supported sulfonic acid,[12] layered zirconium sulfophenyl phosphonate catalysis,[13] were reported to be efficient for the preparation pyrazoles. Each of those reported procedures has its own merit, meanwhile, those methods suffer from various drawbacks such as harsh or sensitive reaction conditions, difficulties of catalyst preparation, long reaction time, inconvenient operation, etc. Therefore, there is a great need to develop a more convenient operation, much greener, and suitable for industrial production methods.

In the course of our continuing efforts in developing polyoxometalate-catalyzed reactions,[14] we herein report a practical, high efficiency, and environmentally benign protocol for pyrazoles synthesis by employing $Cu_{1.5}PMo_{12}O_{40}$ (0.33 mol%) as catalyst under mild conditions (Scheme 1).

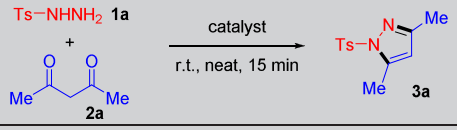
2 | RESULTS AND DISCUSSION

To optimize the reaction conditions, we studied the condensation of *p*-toluenesulfonyl hydrazide **1a** with acetylacetone **2a** using various catalysts. As shown in Table 1, the reaction without any catalyst led to the desired pyrazole **3a** in yield of 34% at room temperature for 15 min (entry 1). Then we attempted to use some Lewis acids, such as Zn $(OAc)_2$, $AlCl_3{\cdot}6H_2O$, $InCl_3$, and Cu $(OTf)_2$, and Bronsted acids, i.e. CH_3COOH and $H_3PMo_{12}O_4$ to catalyze the reaction under identical conditions. Accordingly, the desired product **3a** was obtained in yields of 66%, 72%, 75%, 84%, 56%, and 56% (entries 2–7). From these results, we can speculate that the catalytic activity of copper-based catalyst is probably better than others. Subsequently, a series of copper salts like $CuSO_4{\cdot}5H_2O$, Cu $(NO_3)_2{\cdot}3H_2O$, $CuCl_2{\cdot}2H_2O$, CuBr·DMS, Cu $(acac)_2$, Cu $(OAc)_2{\cdot}2H_2O$ were surveyed as catalyst for the model reaction. All those copper salts showed good activities (65–90% yields, entries 8–13). Among these, Cu $(NO_3)_2{\cdot}3H_2O$ was the most promising and delivered the desired product **3a** in 90% yield, indicating that the counter anion of copper catalyst has a profound impact on the activity (entry 9). However, from an industrial point of view, scalability and catalyst selectivity are significantly important factors; therefore, a more active catalyst is still required.



SCHEME 1 Condensation-cyclization reaction of hydrazines and 1,3-dicarbonyl compounds

TABLE 1 Optimization of the reaction conditions[a]



Entry	Catalyst	Catalyst loading (mol%)	Yield[b] [%]
1	-	-	34
2	Zn $(OAc)_2$	3	66
3	$AlCl_3{\cdot}6H_2O$	3	72
4	$InCl_3$	3	75
5	Cu $(OTf)_2$	3	84
6	CH_3COOH	3	56
7	$H_3PMo_{12}O_{40}$	1	56
8	$CuSO_4{\cdot}5H_2O$	3	88
9	Cu $(NO_3)_2{\cdot}3H_2O$	3	90
10	$CuCl_2{\cdot}2H_2O$	3	88
11	CuBr·DMS	3	83
12	Cu $(acac)_2$	3	75
13	Cu $(OAc)_2{\cdot}2H_2O$	3	65
14	$Cu_{1.5}PMo_{12}O_{40}$	2	>99
15	$Cu_{1.5}PMo_{12}O_{40}$	0.33	>99
16[c]	$Cu_{1.5}PMo_{12}O_{40}$	0.33	>99

[a]Reaction conditions: hydrazide **1a** (1 mmol), 1,3-diketone **2a** (1 mmol), catalyst, solvent-free, r.t., 15 min. Ts = *p*-toluenesulfonyl; DMS = dimethyl sulphide.

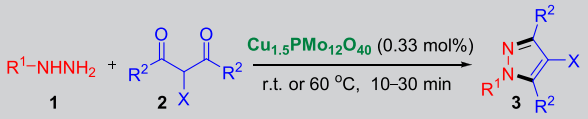
[b]The yields were determined by GC with biphenyl as the internal standard.

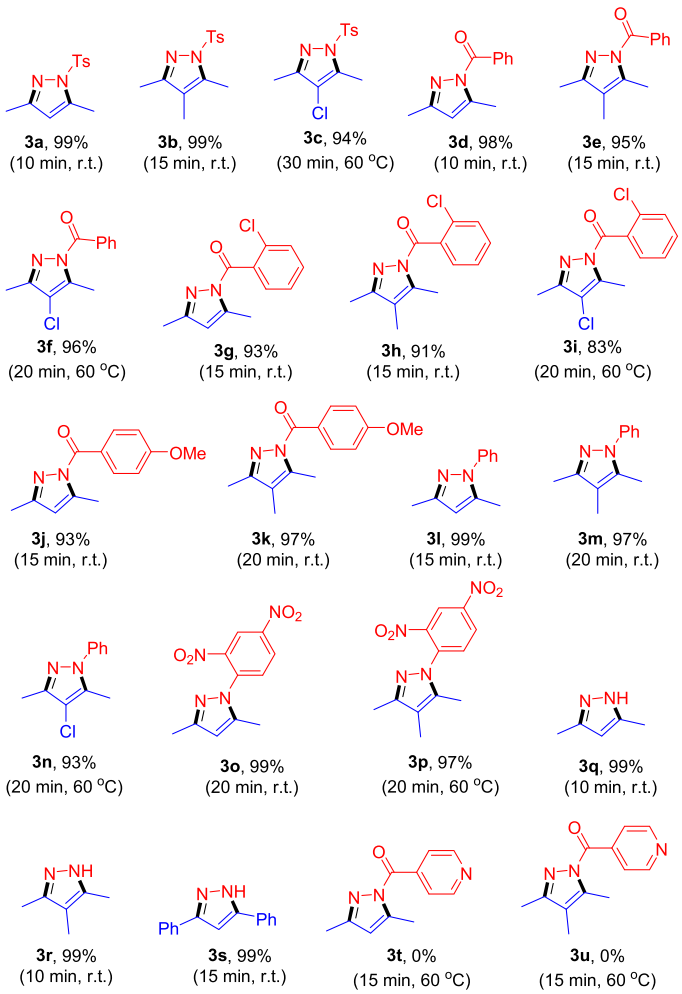
[c]The time is 10 min.

It is known that $[PMo_{12}O_{40}]^{3-}$ is an excellent soft base anion, which might enhance the catalytic activity of copper ion.[15] Then the polyacid salt $Cu_{1.5}PMo_{12}O_{40}$ was synthesized as a catalyst for the condensation reaction of **1a** and **2a**.[16] To our delight, the condensation reaction provided the product **3a** in almost quantitative yield catalyzed by 2 mol% of $Cu_{1.5}PMo_{12}O_{40}$ (entry 14). To evaluate the catalyst efficiency, the catalyst loadings and reaction time were further decreased (entries 15 and 16). Finally, the target pyrazole product **3a** could be obtained in excellent yield by using 0.33 mol% of $Cu_{1.5}PMo_{12}O_{40}$ as catalyst at room temperature for 10 min (entry 16).

With these optimized conditions in hand, we next focused our attention on substrate scope to determine

TABLE 2 Substrate scope of the condensation reaction[a]

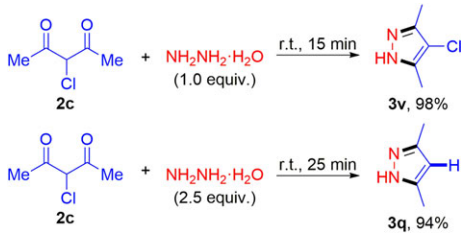




[a]Reaction conditions: hydrazine (1 mmol), 1,3-diketone (1 mmol), $Cu_{1.5}PMo_{12}O_{40}$ (0.33 mol%), solvent-free. Isolated yields were given.

the generality of this procedure. As summarized in Table 2, a variety of pyrazole derivatives were constructed by the condensation of hydrazines and 1,3-diketones. The products **3a** and **3b**, from $TsNHNH_2$ and acetylacetones, were obtained in almost quantitative yields at room temperature for 10 min and 15 min, respectively. As for the electron withdrawing group containing substrate,e.g., 3-chloro-2,4-pentanedione, longer reaction time (30 min) and elevated temperature (60 °C) were necessary to achieve an excellent yield of **3c**. The reaction of electron-rich or electron-poor benzohydrazides showed high reactivity to afford the corresponding pyrazoles **3d**-**k** in good to excellent yields (83–98%). However, it is obvious that the substrates with electron-withdrawing substituents displayed lower reactivities. Therefore, 60 °C was generally required. Moreover, the aromatic hydrazine derivatives, such as phenylhydrazine and (2,4-dinitrophenyl) hydrazine, were also worked well in this protocol, providing the corresponding product **3 l**-**p** in excellent yields. The simple hydrazine hydrate showed good reactivity for the construction of pyrazole **3q**-**s**. Unfortunately, the heterocyclic hydrazine was not suitable for this procedure even at 60 °C (**3 t** and **3u**), probably due to the coordination effect of heteroatom and copper, which may poison the catalyst. Unfortunately, the unsymmetrical 1,3-dicarbonyl compound ethyl 3-oxo-3-phenylpropanoate did not show any reactivity with **1a** in the presence of $Cu_{1.5}PMo_{12}O_{40}$ at r.t. or 60 °C for 30 min.

Interestingly, the reaction of hydrazine hydrate and 3-chloro-2,4-pentanedione (**2c**) delivered different products by using different equivalents of hydrazine hydrate under room temperature. As shown in Scheme 2, the

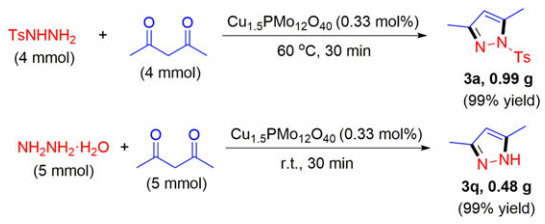


SCHEME 2 Reaction of 3-chloro-2,4-pentanedione and hydrazine hydrate

condensation product **3v** was obtained in 98% yield when the 1.0 equivalent of hydrazine hydrate was applied; while the excess amount of hydrazine hydrate (2.5 equiv.) was employed, the condensation-dehalogenation product **3q** was observed in 94% yield. We surmised that the condensation was fast and efficient to form **3v**, then the excess amount of hydrazine hydrate could act as a base for the dehalogenation of **3v** providing **3q** as product.

Notably, this procedure is scalable and practical. Almost quantitative yields were obtained when the reaction was conducted on gram scale under room temperature by the catalysis of $Cu_{1.5}PMo_{12}O_{40}$ (0.33 mol%) albeit with higher temperature or longer reaction time (Scheme 3).

To gain further insights into this transformation, the blank experiment of (2,4-dinitrophenyl) hydrazine **1f** and 3-methylpentane-2,4-dione **2b** was conducted with $Cu_{1.5}PMo_{12}O_{40}$ catalyst at room temperature. The condensation product **3p'** was detected by GC–MS as major product, while **3p** was the minor product (see the Supporting Information). Compared with the $Cu_{1.5}PMo_{12}O_{40}$-catalyzed reaction at 60 °C, it was clear that the pyrazole was constructed via a step wised condensation-cyclization reaction, and the catalyst played an important role in the cyclization of **3p'** to form the pyrazole **3p** (Scheme 4).



SCHEME 3 Gram scale reactions

3 | CONCLUSIONS

In conclusion, we have presented an efficient protocol for the condensation reaction of hydrazines/hydrazide and 1,3-diketones to synthesize pyrazoles employing $Cu_{1.5}PMo_{12}O_{40}$ as a halogen-free catalyst under mild conditions. Various pyrazoles were constructed in excellent yields. Furthermore, the reaction was proved to be scalable at a gram scale with excellent yields. The reaction proceeded with low catalyst loadings and short reaction times, which represents an economic and environmentally friendly method.

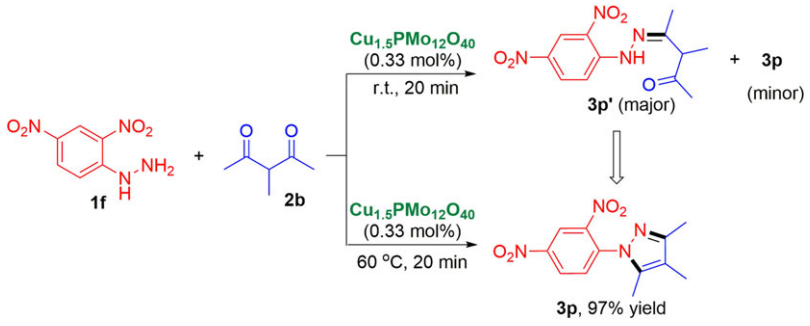
4 | EXPERIMENTAL SECTION

4.1 | Preparation of the catalyst[16]

The aqueous solution of $H_3PMo_{12}O_{40}$ was neutralized by adding a required amount of Ba $(OH)_2{\cdot}8H_2O$ (1.5 equiv.), and then the required amount of $CuSO_4{\cdot}5H_2O$ (1.5 equiv.) was added. After eliminating the formed $BaSO_4$ precipitate by filtration, the aqueous $Cu_{1.5}PMo_{12}O_{40}$ solution was obtained. After bubbling nitrogen to the resulting solution, water was evaporated under reduced pressure. The obtained compound was dried under vacuum at 60 °C overnight, and then characterized by FT-IR and ESI-MS (see the Supporting Information).

4.2 | Typical procedure of the $Cu_{1.5}PMo_{12}O_{40}$ catalyzed condensation reaction

To an 8-mL reaction vial, *p*-toluenesulfonyl hydrazide (1 mmol), acetylacetone (1 mmol), $Cu_{1.5}PMo_{12}O_{40}$ (0.33 mol%) were added. Then the reaction was carried out in screw cap vials with a Teflon seal at r.t. for the desired time. After reaction, the mixture was purified by



SCHEME 4 Control experiments

column chromatography (petroleum ether/EtOAc) to afford the desired products.

4.3 | Characterization Data of the Product

4.3.1 | 3,5-dimethyl-1-tosyl-1*H*-pyrazole (3a)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.82 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 5.89 (s, 1H), 2.49 (s, 3H), 2.40 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 153.40, 145.18, 144.08, 135.37, 129.90, 127.55, 110.77, 21.65, 13.83, 13.10; EI-MS: *m/z* (%) =186.2 (100), 250.1 (1) [M^+].

4.3.2 | 3,4,5-trimethyl-1-tosyl-1*H*-pyrazole (3b)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.80 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 2.39 (s, 6H), 2.14 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 153.69, 144.86, 139.60, 135.62, 129.82, 127.50, 117.20, 21.65, 12.44, 11.33, 8.02; EI-MS: *m/z* (%) = 200.2 (100), 264.1 (10) [M^+].

4.3.3 | 4-chloro-3,5-dimethyl-1-tosyl-1*H*-pyrazole (3c)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.83 (d, J = 7.6 Hz, 2H), 7.20 (d, J = 7.6 Hz, 2H), 2.49 (s, 3H), 2.42 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 150.91, 145.70, 139.31, 134.76, 130.09, 127.79, 113.78, 21.72, 11.92, 11.26; EI-MS: *m/z* (%) = 91.2 (100), 284.1 (11) [M^+].

4.3.4 | (3,5-dimethyl-1*H*-pyrazol-1-yl)(phenyl) methanone (3d)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.99 (d, J = 8 Hz, 2H), 7.56 (t, J = 8 Hz, 1H), 7.46 (t, J = 8 Hz, 2H), 6.06 (s, 1H), 2.64 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 168.45, 152.16, 145.11, 133.36, 132.45, 131.38, 127.87, 111.11, 14.36, 13.90; EI-MS: *m/z* (%) =105.2 (100), 200.1 (39) [M^+].

4.3.5 | phenyl(3,4,5-trimethyl-1*H*-pyrazol-1-yl) methanone (3e)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.96 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.2 Hz, 2H), 2.56 (s, 3H), 2.20 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 168.36, 152.49, 140.45, 133.71, 132.19, 131.26, 127.80, 117.48, 12.55, 12.39, 7.72; EI-MS: *m/z* (%) =105.2 (100), 214.2 (35) [M^+].

4.3.6 | (4-chloro-3,5-dimethyl-1*H*-pyrazol-1-yl)(phenyl)methan-one (3f)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.95 (d, J = 8 Hz, 2H), 7.58 (t, J = 8 Hz, 1H), 7.46 (t, J = 8 Hz, 2H), 2.64 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 167.90, 149.57, 140.35, 132.74, 132.50, 131.38, 127.96, 114.86, 12.35, 11.81; EI-MS: *m/z* (%) =105.2 (100), 234.1 (24) [M^+].

4.3.7 | (2-chlorophenyl)(3,5-dimethyl-1*H*-pyrazol-1-yl) methanone (3 g)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.33–7.79 (m, 4H), 6.05 (s, 1H), 2.66 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 167.43, 153.23, 144.49, 135.12, 131.70, 131.21, 129.71, 129.36, 126.35, 111.78, 14.25, 13.94; EI-MS: *m/z* (%) =199.2 (100), 234.1 (0) [M^+].

4.3.8 | (2-chlorophenyl)(3,4,5-trimethyl-1*H*-pyrazol-1-yl)methan-one (3 h)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31–7.46 (m, 4H), 2.59 (s, 3H), 2.11 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 167.25, 153.68, 139.76, 135.52, 131.56, 130.99, 129.63, 129.25, 126.33, 118.30, 12.47, 7.70; EI-MS: *m/z* (%) = 213.2.2 (100), 248.1 (1) [M^+].

4.3.9 | (4-chloro-3,5-dimethyl-1*H*-pyrazol-1-yl)(2-chlorophenyl)-methanone (3i)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34–7.46 (m, 4H), 2.67 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 167.01, 150.66, 134.28, 131.82, 131.50, 129.75, 129.44, 126.41, 115.52, 12.24, 11.85; EI-MS: *m/z* (%) = 139.1 (100), 268.1 (1) [M^+].

4.3.10 | (3,5-dimethyl-1*H*-pyrazol-1-yl)(4-methoxyphenyl)methan-one (3j)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.05 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 6.04 (s, 1H), 3.86 (s, 3H), 2.61 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 167.54, 163.20, 151.67, 144.99, 134.00, 125.35, 113.28, 110.73, 55.47, 14.27, 13.88; EI-MS: *m/z* (%) =135.2 (100), 230.2 (29) [M^+].

4.3.11 | (4-methoxyphenyl)(3,4,5-trimethyl-1*H*-pyrazol-1-yl)meth-anone (3 k)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.02 (d, J = 8.0 Hz, 2H), 6.94 (d, J = 7.6 Hz, 2H), 3.87 (s, 3H), 2.53 (s, 3H), 2.21 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 167.51, 163.01, 151.97, 140.42, 133.85, 125.70, 117.08, 113.22, 55.45, 12.48, 12.37, 7.74; EI-MS: m/z (%) =135.2 (100), 244.2 (33) [M^+].

4.3.12 | 3,5-dimethyl-1-phenyl-1*H*-pyrazole (3 l)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.33–7.43 (m, 5H), 5.99 (s, 1H), 2.30 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 148.95, 139.96, 139.35, 128.97, 127.21, 124.75, 106.90, 13.52, 12.38; EI-MS: m/z (%) = 172.2 (100) [M^+].

4.3.13 | 3,4,5-trimethyl-1-phenyl-1*H*-pyrazole (3 m)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.29–7.42 (m, 5H), 2.25 (s, 3H), 2.21 (s, 3H) 1.98 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 148.08, 140.16, 136.07, 128.97, 126.97, 124.68, 113.25, 11.89, 10.97, 8.21; EI-MS: m/z (%) = 186.2 (100) [M^+].

4.3.14 | 4-chloro-3,5-dimethyl-1-phenyl-1*H*-pyrazole (3n)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.35–7.48 (m, 5H), 2.30 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 146.06, 139.79, 135.70, 129.18, 127.72, 124.56, 109.83, 11.42, 10.84; EI-MS: m/z (%) = 206.1 (100) [M^+].

4.3.15 | 1-(2,4-dinitrophenyl)-3,5-dimethyl-1*H*-pyrazole (3o)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.80 (s, 1H), 8.53 (d, J = 8.8 Hz, 1H), 7.70 (d, J = 8.8 Hz, 1H), 6.10 (s, 1H), 2.26 (d, J = 6 Hz, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 152.39, 146.24, 145.67, 140.88, 137.97, 129.35, 127.31, 121.02, 108.91, 13.50, 11.63; EI-MS: m/z (%) = 262.1 (100) [M^+].

4.3.16 | 1-(2,4-dinitrophenyl)-3,4,5-trimethyl-1*H*-pyrazole (3p)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.77 (s, 1H), 8.50 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 8.8 Hz, 1H), 2.19 (s, 6H), 1.99 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 152.01, 145.73, 145.29, 138.21, 137.04, 128.87, 127.24, 121.06, 115.86, 11.99, 10.40, 8.22; EI-MS: m/z (%) = 276.1 (100) [M^+].

4.3.17 | 3,5-dimethyl-1*H*-pyrazole (3q)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.88 (s, 1H), 5.82 (s, 1H), 2.27 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 144.46, 104.14, 12.23; EI-MS: m/z (%) = 96.1 (100) [M^+].

4.3.18 | 3,4,5-trimethyl-1*H*-pyrazole(3r)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.56 (s, 1H), 2.18 (s, 6H), 1.90 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 142.10, 110.59, 103.91, 10.79, 7.54; EI-MS: m/z (%) = 109.1 (100), 110.1 (83) [M^+].

4.3.19 | 3,5-diphenyl-1*H*-pyrazole (3 s)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 11.01 (s, 1H), 7.33–7.75 (m, 10H), 6.85 (d, J = 0.8 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 170.18, 147.71, 130.27, 127.85, 127.22, 124.58, 99.07, 59.40, 20.04, 13.17; EI-MS: m/z (%) =220.2 (100) [M^+].

4.3.20 | 4-chloro-3, 5-dimethyl-1*H*-pyrazole (3v)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.54 (s, 1H), 2.25 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 141.01, 107.89, 10.38; EI-MS: m/z (%) =130.1 (100) [M^+].

ACKNOWLEDGMENTS

We thank the Natural Science Foundation of China (21501010, 21671019), 973 Program (2014CB932103) and the 111 Project (B07012) for financial support.

ORCID

Bing Yu http://orcid.org/0000-0002-2423-1212

REFERENCES

[1] a) E. Marcantoni, M. Petrini, *Adv. Synth. Catal.* **2016**, *358*, 3657; b) S. Chiba, *Tetrahedron Lett.* **2016**, *57*, 3678; c) M. Gao, B. Xu, *Chem. Rec.* **2016**, *16*, 1701. d) X. X. Guo, D. W. Gu, Z. X. Wu, W. B. Zhang, *Chem. Rev.* **2015**, *115*, 1622; e) B. Zhang, A. Studer, *Chem. Soc. Rev.* **2015**, *44*, 3505; f) J. Cornil, L. Gonnard, C. Bensoussan, A. Serra-Muns, C. Gnamm, C. Commandeur, M. Commandeur, S. Reymond, A. Guérinot, J. Cossy, *Acc. Chem. Res.* **2015**, *48*, 761; g) B. Yu, L.-N. He, *ChemSusChem* **2015**, *8*, 52. (h) C.-V. T. Vo, J. W. Bode, *J. Org. Chem.* **2014**, *79*, 2809.

[2] a) Z. Xu, C. Gao, Q.-C. Ren, X.-F. Song, L.-S. Feng, Z.-S. Lv, *Eur. J. Med. Chem.* **2017**, *139*, 429; b) A. Ansari, A. Ali, M. Asif, Shamsuzzaman, *New J. Chem.* **2017**, *41*, 16.

[3] a) L. Wang, X. Yu, X. Feng, M. Bao, *J. Org. Chem.* **2013**, *78*, 1693; b) J. Zhang, Y. Shao, H. Wang, Q. Luo, J. Chen, D. Xu, X. Wan, *Org. Lett.* **2014**, *16*, 3312; c) X. Yu, N. Huang, X. Feng, Y. Yamamoto, M. Bao, *Synthesis* **2014**, *46*, 2422.

[4] a) H.-L. Liu, H.-F. Jiang, M. Zhang, W.-J. Yao, Q.-H. Zhu, Z. Tang, *Tetrahedron Lett.* **2008**, *49*, 3805; b) D. B. Grotjahn, S. Van, D. Combs, D. A. Lev, C. Schneider, M. Rideout, C. Meyer, G. Hernandez, L. Mejorado, *J. Org. Chem.* **2002**, *67*, 9200; c) M. C. Bagley, M. C. Lubinu, C. Mason, *Synlett* **2007**, *2007*, 0704; d) D. Sar, R. Bag, A. Yashmeen, S. S. Bag, T. Punniyamurthy, *Org. Lett.* **2015**, *17*, 5308.

[5] Z.-X. Wang, H.-L. Qin, *Green Chem.* **2004**, *6*, 90.

[6] X. Deng, N. S. Mani, *J. Org. Chem.* **2008**, *73*, 2412.

[7] Y. Hari, S. Tsuchida, R. Sone, T. Aoyama, *Synthesis* **2007**, *2007*, 3371.

[8] B. S. Gerstenberger, M. R. Rauckhorst, J. T. Starr, *Org. Lett.* **2009**, *11*, 2097.

[9] J. J. Neumann, M. Suri, F. Glorius, *Angew. Chem. Int. Ed.* **2010**, *49*, 7790.

[10] B. R. Vaddula, R. S. Varma, J. Leazer, *Tetrahedron Lett.* **2013**, *54*, 1538.

[11] W. Xiong, J.-X. Chen, M.-C. Liu, J.-C. Ding, H.-Y. Wu, W.-K. Su, *J. Braz. Chem. Soc.* **2009**, *20*, 367.

[12] V. Polshettiwar, R. S. Varma, *Tetrahedron Lett.* **2008**, *49*, 397.

[13] M. Curini, O. Rosati, V. Campagna, F. Montanari, G. Cravotto, M. Boccalini, *Synlett* **2005**, *2005*, 2927.

[14] a) X. Feng, T. Yang, X. He, B. Yu, C.-W. Hu, *Appl. Organomet. Chem.* **2018**, *32*, e4314; b) G.-P. Yang, N. Zhang, N.-N. Ma, B. Yu, C.-W. Hu, *Adv. Synth. Catal.* **2017**, *359*, 926.

[15] a) Y. Izumi, K. Matsuo, K. Urabe, *J. Mol. Catal.* **1983**, *18*, 299; b) D. E. Katsoulis, *Chem. Rev.* **1998**, *98*, 359; c) S.-S. Wang, G.-Y. Yang, *Chem. Rev.* **2015**, *115*, 4893; d) M. Egi, M. Umemura, T. Kawai, S. Akai, *Angew. Chem. Int. Ed.* **2011**, *50*, 12197; e) M.-Y. Wang, Q.-W. Song, R. Ma, J.-N. Xie, L.-N. He, *Green Chem.* **2016**, *18*, 282.

[16] A. Aouissi, D. Al-Dhayan, Z. A. Al-Othman, A. Lokbaichi, *Asian J. Chem.* **2012**, *24*, 3899.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Yang G-P, He X, Yu B, Hu C-W. $Cu_{1.5}PMo_{12}O_{40}$-catalyzed condensation cyclization for the synthesis of substituted pyrazoles. *Appl Organometal Chem*. 2018;e4532. https://doi.org/10.1002/aoc.4532