JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Metal-Free Iodine-Catalyzed Synthesis of Fully Substituted Pyrazoles and Its Sulphenylation

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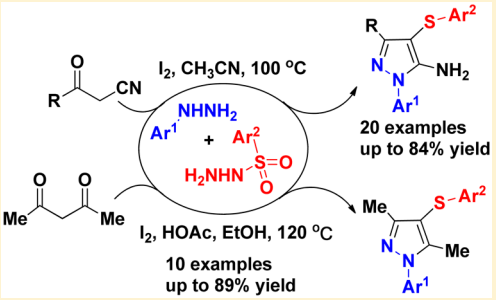
Supporting Information

ABSTRACT: A direct and metal-free access toward fully substituted pyrazoles and its sulphenylation has been established through an iodine-mediated three-component [3 + 2] annulation of β-ketonitrile (or pentane-2,4-dione), arylhydrazines, and aryl sulfonyl hydrazides. The reaction allows the formation of one C−S and two C−N bonds by the multiple bond cleavage including sulfur−oxygen, sulfur−nitrogen, and carbon−oxygen bonds. The method features low-cost and readily accessible substrates, bond-forming efficiency, and broad substrate scopes as well as simple one-pot operation, which makes this strategy highly attractive.

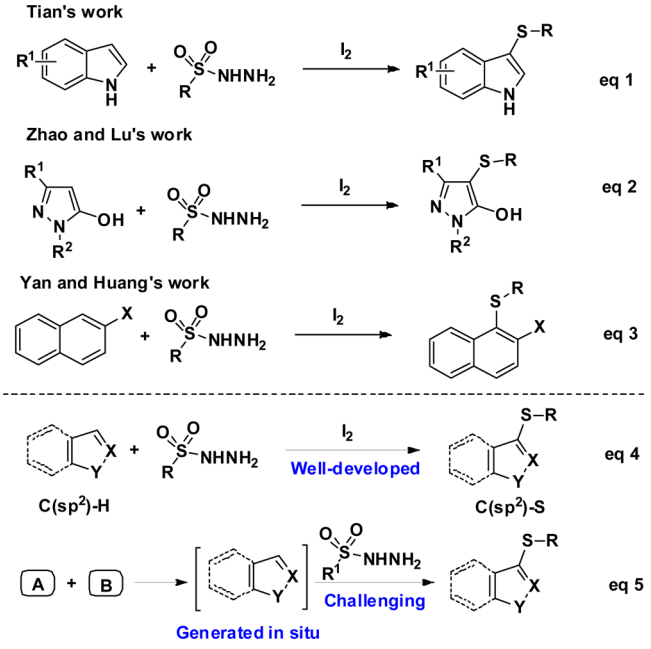


INTRODUCTION

Sulfur-containing compounds have extensive applications in the fields of organic synthesis, pharmaceutical industry, and agrochemicals as well as materials science.[1] Organosulfur compounds widely exist in drugs and natural products.[2] Substantial efforts have been devoted to powerful and reliable access to new C−S bond-forming reactions, which made it more powerful and applicable.[3] Basically, the transition-metal-catalyzed variants have taken a pivotal position, and a variety of transition-metal species including Pd,[4] Cu,[5] and Fe[6] have been utilized in C−S bond formation. However, these methods encounter limitations with respect to the use of expensive or toxic metal salts and foul-smelling and volatile sulfur sources such as thiols,[7] disulfides,[8] TIPS-SH,[9] and thiolates.[10] To address these issues, the investigation of other alternative sulfur sources like thiourea,[11] potassium ethyl xanthogenate,[12] thiocyanate,[13] and metal sulfides[14] has been conducted, but most of these approaches suffer from many drawbacks such as a narrow substrate scope and harsh reaction conditions. Hence, the exploration of new, green, and practical methods, especially metal-free pathways, to access C−S bond formation using stable and environmentally friendly reagents is still highly desired but full of challenge.

Sulphonyl hydrazides have emerged as ideal sulphenylation agents for the synthesis of sulfur-containing compounds[15] due to their stable nature, easy availability, high reactivity, and eco-friendly conversions (byproducts are only water and N_2). Very recently, Tian and co-workers pioneered the I_2-catalyzed sulphenylation reaction of sulphonyl hydrazides and indoles affording indole thioethers (Scheme 1, eq 1).[16] Subsequently, Zhao, Lu, and co-workers reported I_2-catalyzed sulphenylation of pyrazolones[17] and benzo[*b*]furans[18] using sulphonyl hydrazides as a sulphenylation agent (Scheme 1, eq 2). The

Scheme 1. Profiling Applications of Sulphenylation



sulphenylation of naphthols and naphthylamines was developed by Yan and Huang (Scheme 1, eq 3).[19] Generally, these reactions can be summarized into the direct sulphenylation of the electron-rich aryl or heterocyclic rings (Scheme 1, eq 4). However, in sharp contrast, an efficient three-component

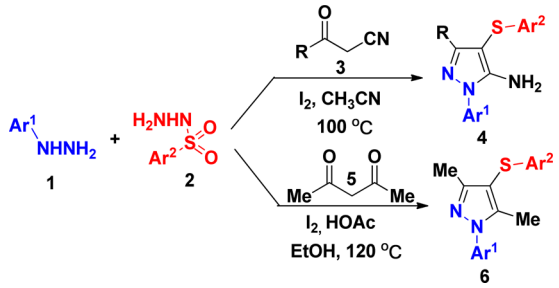
Received: June 7, 2015
Published: July 16, 2015

DOI: 10.1021/acs.joc.5b01280
J. Org. Chem. 2015, 80, 8217−8224

reaction allowing direct formation of heterocycles and its sulphenylation in particular has met with little success (Scheme 1, eq 5) but represents a highly desirable methodology considering its bond-forming efficiency, functional group tolerance, and high levels of selectivity.

Pyrazoles constitute a privileged scaffold present in a wide variety of synthetic and natural products of medicinal interest.[20] Molecules possessing this valuable motif have been reported to exert a wide range of biological activities, such as antibacterial,[21] antiviral,[22] anticancer,[23] antidiabetic,[24] antiobesity,[25] anti-inflammatory,[26] but efficient methods to access densely functionalized forms of this scaffold, especially its sulphenylation, are scarce.[17] Considering the valuable potential of pyrazoles and the continuation of our project on multicomponent reactions,[27] we decided to evaluate the feasibility of the synthesis of pyrazoles and its sulphenylation by using readily available β-ketonitrile, arylhydrazines, and sulphonyl hydrazides, based on the factors that the annulation of β-ketonitrile and arylhydrazines could generate in situ electron-rich pyrazole-5-amines,[28] followed by a I_2-catalyzed sulphenylation with sulphonyl hydrazides, thereby transforming them into fully substituted pyrazoles. Herein, we present the realization of this concept, which was achieved by controlling different reactivity of two hydrazines in a one-pot manner (Scheme 2). Using pentane-2,4-dione **5** as replacement for β-

Scheme 2. I_2-Catalyzed Synthesis of Fully Substituted Pyrazoles

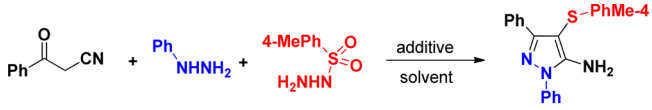


ketonitrile **3**, this I_2-catalyzed reaction process involved [3 + 2] cyclization/sulphenylation sequence, enabling a direct strategy for the assemble of new fully substituted pyrazoles **6** with moderate to good yields utilizing two C–N bonds and one C–S bond formation (Scheme 2).

RESULTS AND DISCUSSION

Initially, we investigated the reaction of 3-oxo-3-phenylpropanenitrile (**1a**) with phenylhydrazine (**2a**) and 4-methylbenzenesulfonohydrazide (**3a**) under various conditions. As depicted in Table 1, treatment of **1a** with **2a** and **3a** in the presence of 20 mol % of I_2 in CH_3CN at 100 °C afforded the expected product **4a** in 51% yield. Raising the loading of iodine delivered the higher yield of **4a** (entry 1 vs entries 2–3), and the use of 50 mol % of I_2 resulted in the best result. With the further increase of the loading of iodine to 1.0 equiv, the yield of **4a** did not improve (entry 4). Afterward, the subsequent evaluation of different solvents was conducted in the presence of I_2 (compare entries 5–7). The use of tetrahydrofuran generated the product **4a** with a slightly lower yield (entry 5). The identical reaction performed in 1,2-dichloroethane (DCE) lowered the yield to 59% (entry 6). A much lower yield was isolated by the use of EtOH as a solvent (entry 7). An inferior

Table 1. Optimization of Reaction Conditions for Forming Product 4a[a]



1a 2a 3a 4a

entry	cat. (mol %)	t (°C)	solvent	yield (%)[b]
1	I_2 (20)	100	CH_3CN	51
2	I_2 (30)	100	CH_3CN	61
3	I_2 (50)	100	CH_3CN	74
4	I_2 (100)	100	CH_3CN	74
5	I_2 (50)	100	THF	67
6	I_2 (50)	100	DCE	59
7	I_2 (50)	100	EtOH	40
8	I_2 (50)	80	CH_3CN	25
9	I_2 (50)	120	CH_3CN	72

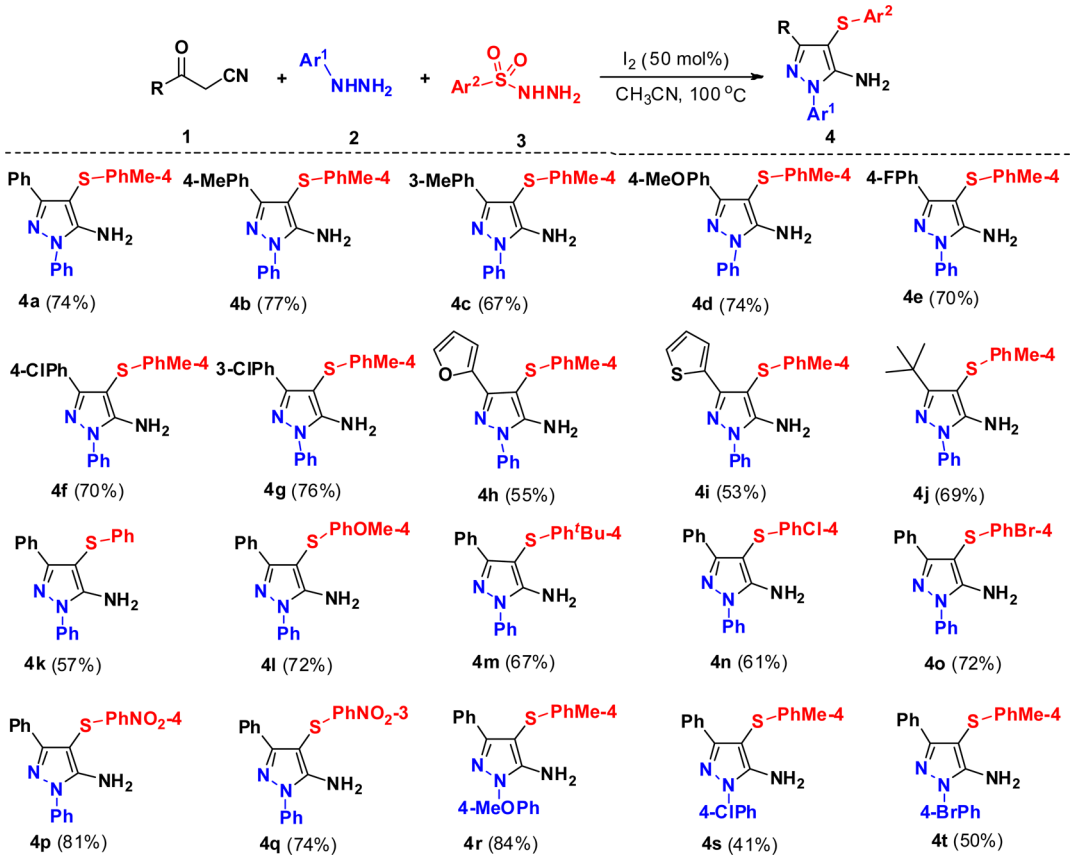
[a]Reaction conditions: All reactions were performed with **1a** (1.0 mmol), **2a** (1.5 mmol), **3a** (1.5 mmol), catalyst, and solvent (2.5 mL) in the sealed reaction tube under air conditions. [b]Isolated yield is based on **1a**.

outcome was observed when the reaction promoted by 50 mol % of I_2 was carried out at lower reaction temperature (entry 8). Elevating the temperature to 120 °C did not show improvement and even gave rise to a diminished chemical yield (entry 9). These experimental facts indicated that the reaction temperature seemed to exert a significant influence on the reactivity.

With the established optimal conditions, the scope of this three-component sulphenylation reaction was examined by conducting a variety of β-ketonitriles **1** to react with various simple aryl hydrazines **2** and sulphonyl hydrazides **3** (Scheme 3). First, the influence of substituents in the phenyl ring of β-ketonitriles **1** was investigated, which found that the sulphenylation reaction tolerated a broad spectrum of substituted β-ketonitriles bearing both electron-donating and electron-withdrawing groups under the optimized conditions. The variant of substituents that resided at different positions on the phenyl ring, such as Me, MeO, F, and Cl, was compatible. Additionally, a significant drop in the yields was observed for substrates possessing heteroaryl moiety such as furan and thiophene rings, as has been demonstrated with substrates (**1h** and **1i**), giving their expected products **4h** and **4i** in 55% and 53% yields, respectively. Notably, pivaloyl acetonitrile (**1j**) was well-suited for this present transformation, successfully converting into the corresponding sulphenylated product **4j** in a 69% yields. After the successful utilization of various β-ketonitriles, we next extended our investigation to the electronic nature of substituents on both aryl sulphonyl hydrazide (Ar^2) and aryl hydrazine (Ar^1) moieties. As per our expectation, arylsulfonyl hydrazides bearing electron-donating, electron-neutral, and electron-withdrawing groups showed high reactivity and gave high yields (Scheme 3, **4k–4o**). Even for challenging cases in which a strong electron-withdrawing effect exists on the *para* or *meta* position on the aromatic ring (**3g** and **3h**), good yields of 81% and 74% were obtained. Unfortunately, benzyl sulfonylhydrazide did not work in the reaction. Similarly, a variety of aryl hydrazine **2** with different functional groups like methoxy, chloro, and bromo can enable the reaction to occur smoothly, resulting in moderate to good yields (41%–84%) of the products **4r–4t**. The structures of the resultant products **4**

DOI: 10.1021/acs.joc.5b01280
J. Org. Chem. 2015, 80, 8217–8224

Scheme 3. Three-Component Synthesis of 4-Arylthiopyrazol-5-amines[a,b]



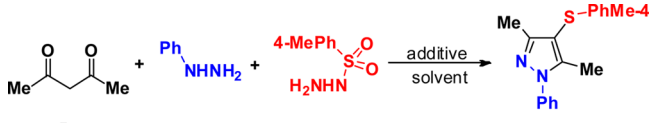
[a]Reaction conditions: All reactions were performed with **1** (1.0 mmol), **2** (1.5 mmol), **3** (1.5 mmol), I_2 (0.5 mmol), and CH_3CN (2.5 mL) in the sealed reaction tube at 100 °C under air conditions for 5 h. [b]Isolated yield is based on **1**.

have been confirmed by NMR and HR-MS spectral analysis. In addition, one of them (**4a**) has been unambiguously determined by X-ray diffractional analysis. In general, these sulphenylation-based three-component reactions provide new examples for forming richly decorated pyrazoles, which are ubiquitous structural cores in substantial bioactive compounds.

After our success with functional pyrazoles **4**, we attempted to further examine the reaction scope using pentane-2,4-dione **5** to replace *β*-ketonitrile **3**. The one-pot reaction of **2a** with **3a** and **5** was conducted under the conditions described above. The expected 3,5-dimethylpyrazole **6a** was obtained but with a dramatically deteriorated yield (41%) (Table 2, entry 1). Increasing the loading of iodine to 1.0 equiv failed to improve the yield of **6a** (entry 2). Next, we adjusted solvents for the optimized conditions. THF and DCE were then tried, and DCE gave the desired product **6a** in 50% yield (entry 4). Exchanging EtOH for DCE delivered a slightly higher yield (54% yield, entry 5). After careful optimizations, it is found that the use of 0.5 equiv of HOAc as an additive in EtOH at 120 °C was the most suitable condition for the current three-component reaction, providing product **6a** in the best yield of 70% (entry 6).

After the feasible reaction conditions have been validated, we set out to investigate its scope by reacting aryl hydrazines **2** with arylsulfonyl hydrazides **3** and pentane-2,4-dione **5** (Scheme 4). The presence of various substituents, including methyl, methoxyl, chloro, and bromo groups, on the hydrazinyl-attached aryl ring (Ar^1) all worked well, giving access to a series of new fully substituted pyrazoles **6b**–**6e** with

Table 2. Optimization of Reaction Conditions for Forming Product 6a[a]



entry	cat. (mol %)	*t* (°C)	solvent	yield[b] (%)
1	I_2 (50)	120	CH_3CN	41
2	I_2 (100)	120	CH_3CN	40
3	I_2 (50)	120	THF	20
4	I_2 (50)	120	DCE	50
5	I_2 (50)	120	EtOH	54
6	I_2 (50)	120	EtOH	70[c]

[a]Reaction conditions: All reactions were performed with **5** (1.0 mmol), **2a** (1.5 mmol), **3a** (1.5 mmol), catalyst, and solvent (2.5 mL) in the sealed reaction tube under air conditions for 5 h. [b]Isolated yield is based on **5**. [c]HOAc (0.5 mmol) as an additive.

47%–89% chemical yields. It is found in Scheme 4 that the electronic nature of aryl hydrazines imposed an evident impact on the reaction efficiency because aryl hydrazines substituted with electron-donating groups delivered higher yields than those substituted with electron-neutral or -withdrawing groups (**6b**, **6c** vs **6a**, **6d** and **6e**). Alternatively, arylsulfonyl hydrazides **3** carrying either electronically neutral, rich, or poor groups could be successfully engaged in the three-component [3 + 2] annulation, resulting in acceptable yields of the products **6f**–**6j**

DOI: 10.1021/acs.joc.5b01280
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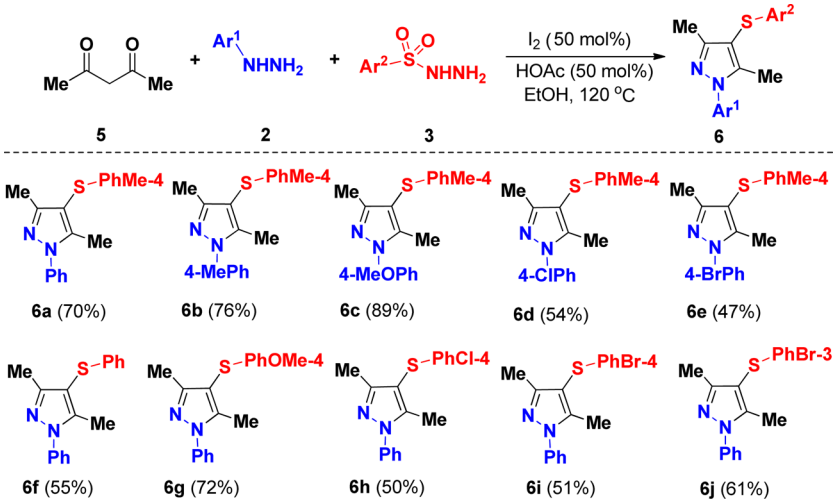
Scheme 4. Three-Component Synthesis of 3,5-Dimethyl-4-arylthiopyrazoles[a,b]

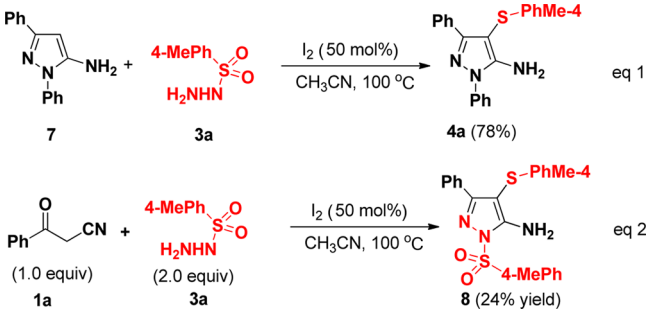


[a]Reaction conditions: All reactions were performed with **5** (1.0 mmol), **2** (1.5 mmol), **3** (1.5 mmol), I_2 (0.5 mmol), HOAc (0.5 mmol), and EtOH (2.5 mL) in the sealed reaction tube at 120 °C under air conditions for 5 h. [b]Isolated yield is based on **5**.

(up to 72%). Notably, halogen-containing arylsulfonyl hydrazides could be utilized and well-tolerated under the optimal conditions, providing the expected products in good yields, which offer possible potential for further functionalizations by cross-coupling reactions.

In order to gain reasonable insight into the reaction mechanism, 1,3-diphenyl-1H-pyrazol-5-amine **7** was treated with **3a** under the standard conditions, generating the corresponding 1,3-diphenyl-4-(*p*-tolylthio)-1H-pyrazol-5-amine **4a** in a 78% chemical yield (Scheme 5, eq 1). This

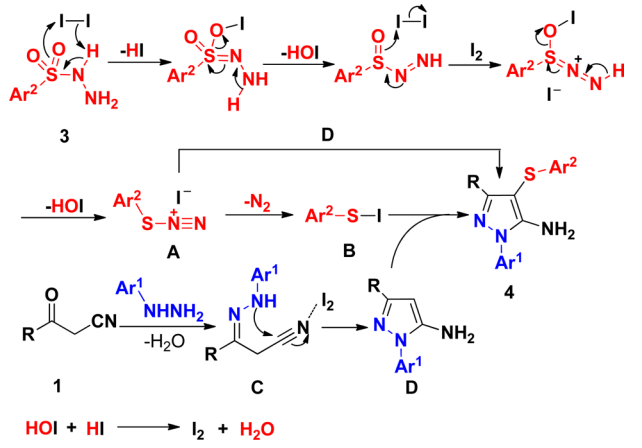
Scheme 5. Some Control Experiments



observation proves that [3 + 2] annulation for the formation of pyrazol-5-amines occurred prior to sulphenylation step. Treatment of 1 equiv of 3-oxo-3-phenylpropanenitrile (**1a**) with 2 equiv of 4-methylbenzenesulfonohydrazide (**3a**) gave the expected pyrazol-5-amines **8** but with a much lower yield (24%), which indicates that the pyrazole ring linked with a strong electron-withdrawing group is unfavorable for electrophilic substitution (Scheme 5, eq 2).

On the basis of previous reports[16−19] and from the observation of the experimental results, a mechanism analogous to the one recently proposed[18] was envisaged for this reaction (Scheme 6). Aryl sulphonyl hydrazides **3** mediated by molecular iodine continuously release HI and HOI, giving rise to the thiodiazonium **A** which eliminated one molecule of nitrogen to access intermediate **B**. Then, intermediate **A** or **B** undergoes a Friedel−Crafts-type reaction with electron-rich

Scheme 6. Proposed Mechanism for Forming Products 4



pyrazol-5-amines **D**, generated in situ from I_2-catalyzed [3 + 2] annulation of *β*-ketonitrile with aryl hydrazines, to yield final sulphenylated pyrazol-5-amines **4**. In these steps, the reaction between the released HI and HOI regenerate iodine to continue the catalytic cycle.

In conclusion, we have established a new I_2-catalyzed three-component [3 + 2] annulation for the selective formation of fully substituted pyrazoles through in situ-generated C(sp^2)-H sulphenylation. The reaction simultaneously installs one C−S and two C−N bonds through the multiple bond cleavage including sulfur−oxygen, sulfur−nitrogen, and carbon−oxygen bonds, showing that the synthetic strategy could facilitate us to access richly decorated pyrazoles with a wide diversity in substituents. The mild reaction conditions, flexible modification of pyrrole skeleton, and reliable scalability as well as broad substrate scopes make this three-component annulation strategy highly viable for future applications.

EXPERIMENTAL SECTION

General Information. All one-pot reactions were carried out in a 25 mL Schlenk tube equipped with a magnetic stir bar under air. Arylsulfonyl hydrazides **3** were prepared according to the known literatures.[29] All other reagents were obtained from commercial

DOI: 10.1021/acs.joc.5b01280
J. Org. Chem. 2015, 80, 8217−8224

sources and used as received, if not stated otherwise. All melting points are uncorrected. The NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on a 400 MHz instrument with TMS as internal standard. Chemical shifts (δ) were reported in ppm with respect to TMS. Data are represented as follows: chemical shift, mutiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant (J, Hz) and integration. HRMS analyses were carried out using a TOF-MS instrument with an ESI source. X-ray crystallographic analysis was performed with a SMART CCD and a P4 diffractometer.

Example for the synthesis of ***4a****.* 3-Oxo-3-phenylpropanenitrile (**1a**, 1.0 mmol, 145 mg), phenylhydrazine (**2a**, 1.5 mmol, 108 mg), and 4-methylbenzenesulfonohydrazide (**3a**, 1.5 mmol, 186 mg) were introduced in a sealed 10 mL reaction tube, I_2 (0.5 mmol, 127 mg) and CH_3CN (2.5 mL) were then successively added, and the mixture stirred at 100 °C for 5 h. After completion of the reaction (monitored by TLC), the reaction mixture was down to room temperature. Then, organic solvent was concentrated by a rotary evaporator, and the residue was purified by column chromatography (eluents, petroleum ether/ethyl acetate 15:1) to afford the pure product **4a**.

*1,3-Diphenyl-4-(p-tolylthio)-1H-pyrazol-5-amine (****4a****).* Yellow solid, 264 mg, 74% yield; mp 123−124 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.87 (d, J = 6.8 Hz, 2H), 7.72 (d, J = 8.2 Hz, 2H), 7.58−7.54 (m, 2H), 7.43−7.32 (m, 4H), 7.10 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 5.77 (s, 2H,), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.3, 151.8, 139.3, 135.5, 134.8, 133.3, 130.2, 129.8, 128.7, 128.6, 127.5, 127.4, 125.5, 123.7, 84.9, 20.9; IR (KBr, ν, cm^{-1}) 3412, 3307, 3067, 2920, 1637, 1616, 1596, 1453, 691; HRMS (ESI-TOF): m/z calcd for $C_{22}H_{18}N_3S$ [M − H]$^-$, 356.1216; found, 356.1194.

*1-Phenyl-3-(p-tolyl)-4-(p-tolylthio)-1H-pyrazol-5-amine (****4b****).* Yellow solid, 286 mg, 77% yield; mp 158−159 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.77 (d, J = 8.0 Hz, 2H), 7.71 (d, J = 7.6 Hz, 2H), 7.57−7.53 (m, 2H), 7.42−7.38 (m, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 7.00 (d, J = 8.4 Hz, 2H), 5.79 (s, 2H), 2.28 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.3, 151.7, 139.4, 137.9, 135.5, 134.7, 130.5, 130.2, 129.8, 129.2, 127.4, 127.3, 125.5, 123.6, 84.9, 21.3, 20.9; IR (KBr, ν, cm^{-1}) 3409, 3304, 3016, 2917, 2851, 1637, 1617, 1595, 1434, 703; HRMS (ESI-TOF): m/z calcd for $C_{23}H_{20}N_3S$ [M − H]$^-$, 370.1371; found, 370.1368.

*1-Phenyl-3-(m-tolyl)-4-(p-tolylthio)-1H-pyrazol-5-amine (****4c****).* Yellow solid, 248 mg, 67% yield; mp 132−133 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.73−7.66 (m, 4H), 7.58−7.54 (m, 2H), 7.43−7.39 (m, 1H), 7.25−7.22 (m, 1H), 7.14−7.10 (m, 3H), 7.02 (d, J = 8.0 Hz, 2H), 5.76 (s, 2H), 2.28 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.3, 151.8, 139.3, 137.6, 135.6, 134.8, 133.2, 130.2, 129.8, 129.2, 128.5, 128.1, 127.2, 125.7, 124.6, 123.7, 85.2, 21.6, 20.9; IR (KBr, ν, cm^{-1}) 3407, 3297, 2924, 2853, 1637, 1617, 1595, 1491, 703; HRMS (ESI-TOF): m/z calcd for $C_{23}H_{20}N_3S$ [M − H]$^-$, 370.1371; found, 370.1365.

*3-(4-Methoxyphenyl)-1-phenyl-4-(p-tolylthio)-1H-pyrazol-5-amine (****4d****).* Yellow solid, 286 mg, 74% yield; mp 139−140 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.81 (d, J = 8.8 Hz, 2H), 7.71 (d, J = 8.0 Hz, 2H), 7.56−7.52 (m, 2H), 7.41−7.37 (m, 1H), 7.10 (d, J = 8.0 Hz, 2H), 7.00 (d, J = 8.0 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 5.77 (s, 2H), 3.74 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 159.6, 152.1, 151.7, 139.4, 135.6, 134.7, 130.2, 129.8, 128.7, 127.3, 125.8, 125.4, 123.6, 114.1, 84.6, 55.5, 20.9; IR (KBr, ν, cm^{-1}) 3411, 3301, 1637, 1614, 1595, 1432, 1252, 703; HRMS (ESI-TOF): m/z calcd for $C_{23}H_{20}N_3OS$ [M − H]$^-$, 386.1326; found, 386.1348.

*3-(4-Fluorophenyl)-1-phenyl-4-(p-tolylthio)-1H-pyrazol-5-amine (****4e****).* Yellow solid, 263 mg, 70% yield; mp 130−131 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.93−7.90 (m, 2H), 7.73−7.71 (m, 2H), 7.58−7.54 (m, 2H), 7.43−7.39 (m, 1H), 7.23−7.19 (m, 2H), 7.11 (d, J = 8.0 Hz, 2H), 7.03−7.01 (m, 2H), 5.80 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 163.7, 162.5 ($^1J_{CF}$ = 243.6), 151.9, 151.4, 139.2, 135.3, 134.8, 130.3, 129.8, 129.4 ($^3J_{CF}$ = 8.2), 127.5, 125.4, 123.7, 115.6 ($^2J_{CF}$ = 21.2), 84.7, 20.9; IR (KBr, ν, cm^{-1}) 3412, 3234, 3070, 2922, 1637, 1615, 1525, 1436, 1370, 691; HRMS (ESI-TOF): m/z calcd for $C_{22}H_{17}FN_3S$ [M − H]$^-$, 374.1126; found, 374.1152.

*3-(4-Chlorophenyl)-1-phenyl-4-(p-tolylthio)-1H-pyrazol-5-amine (****4f****).* Yellow solid, 274 mg, 70% yield; mp 141−142 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.91 (d, J = 8.0 Hz, 2H), 7.71−7.43 (m, 7H), 7.09−7.00 (m, 4H), 5.84 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.0, 151.0, 139.2, 135.2, 134.9, 133.2, 132.1, 130.3, 129.8, 129.0, 128.8, 127.6, 125.5, 123.8, 84.9, 20.9; IR (KBr, ν, cm^{-1}) 3412, 3235, 3069, 2918, 1637, 1615, 1532, 1434, 1369, 691; HRMS (ESI-TOF): m/z calcd for $C_{22}H_{17}ClN_3S$ [M − H]$^-$, 390.0837; found, 390.0857.

*3-(3-Chlorophenyl)-1-phenyl-4-(p-tolylthio)-1H-pyrazol-5-amine (****4g****).* Yellow solid, 297 mg, 76% yield; mp 119−120 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.93 (d, J = 1.6 Hz, 1H), 7.89−7.87 (m, 1H), 7.74−7.72 (m, 2H), 7.58−7.55 (m, 2H), 7.44−7.39 (m, 3H), 7.11 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.0 Hz, 2H), 5.87 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.1, 150.6, 139.1, 135.3, 135.1, 135.0, 133.4, 130.7, 130.3, 129.8, 128.4, 127.7, 126.9, 125.8, 125.6, 123.8, 85.1, 20.9; IR (KBr, ν, cm^{-1}) 3406, 3295, 3069, 2921, 2853, 1637, 1617, 1596, 1491, 703, 731; HRMS (ESI-TOF): m/z calcd for $C_{22}H_{17}ClN_3S$ [M − H]$^-$, 390.0837; found, 390.0830.

*3-(Furan-2-yl)-1-phenyl-4-(p-tolylthio)-1H-pyrazol-5-amine (****4h****).* Brown solid, 191 mg, 55% yield; mp 154−155 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm)7.70−7.68 (m, 2H), 7.57−7.53 (m, 2H), 7.43−7.39 (m, 1H), 7.11−7.03 (m, 4H), 6.86 (d, J = 3.3 Hz, 1H), 6.52−6.51 (m, 1H), 5.88 (s, 2H), 2.23 (s, 3H,); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 151.5, 147.3, 145.1, 143.0, 139.2, 134.9, 134.9, 130.2, 129.8, 127.6, 125.8, 123.7, 111.8, 109.3, 84.4, 20.9; IR (KBr, ν, cm^{-1}) 3399, 3322, 3053, 2917, 1636, 1595, 1427, 1226, 698; HRMS (ESI-TOF): m/z calcd for $C_{20}H_{16}N_3OS$ [M − H]$^-$, 346.1008; found, 346.0984.

*1-Phenyl-3-(thiophen-2-yl)-4-(p-tolylthio)-1H-pyrazol-5-amine (****4i****).* Brown solid, 192 mg, 53% yield; mp 161−162 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.69−7.53 (m, 5H), 7.48 (d, J = 4.0 Hz, 1H), 7.43−7.40 (m, 1H), 7.11−7.03 (m, 5H), 5.89 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 151.9, 148.0, 139.0, 135.3, 135.0, 134.9, 130.2, 129.8, 127.8, 127.6, 126.4, 125.7, 125.6, 123.8, 84.6, 20.9; IR (KBr, ν, cm^{-1}) 3397, 3320, 2923, 1593, 1462, 1228, 698; HRMS (ESI-TOF): m/z calcd for $C_{20}H_{16}N_3S_2$ [M − H]$^-$, 362.0785; found, 362.0784.

*3-tert-Butyl-1-phenyl-4-(p-tolylthio)-1H-pyrazol-5-amine (****4j****).* White solid, 233 mg, 69% yield; mp 154−155 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.64 (d, J = 8.0 Hz, 2H), 7.53−7.49 (m, 2H), 7.37−7.33 (m, 1H), 7.10−7.08 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.0 Hz, 2H), 5.50 (s, 2H), 2.23 (s, 3H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 161.4, 151.7, 139.6, 135.8, 134.2, 130.0, 129.7, 126.9, 125.0, 123.2, 83.9, 33.6, 29.6, 20.9; IR (KBr, ν, cm^{-1}) 3400, 3304, 3068, 2930, 2867, 1616, 1449, 1594, 701; HRMS (ESI-TOF): m/z calcd for $C_{20}H_{22}N_3S$ [M − H]$^-$, 336.1534; found, 336.1549.

*1,3-Diphenyl-4-(phenylthio)-1H-pyrazol-5-amine (****4k****).* Yellow solid, 196 mg, 57% yield; mp 126−127 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.88−7.86 (m, 2H), 7.74−7.72 (m, 2H), 7.59−7.55 (m, 2H), 7.44−7.28 (m, 6H), 7.14−7.12 (m, 3H), 5.82 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.4, 151.9, 139.3, 139.1, 133.3, 129.8, 129.6, 128.7, 128.6, 127.5, 127.4, 125.4, 125.2, 123.7, 84.3; IR (KBr, ν, cm^{-1}) 3451, 3350, 3057, 1607, 1533, 1438, 687; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{16}N_3S$ [M − H]$^-$, 342.1064; found, 342.1066.

*4-(4-Methoxyphenylthio)-1,3-diphenyl-1H-pyrazol-5-amine (****4l****).* Yellow solid, 269 mg, 72% yield; mp 111−112 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.93 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H), 7.58−7.54 (m, 2H), 7.43−7.33 (m, 4H), 7.11−7.09 (m, 2H), 6.90−6.88 (m, 2H), 5.83 (s, 2H), 3.69 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 158.0, 152.1, 151.8, 139.4, 133.4, 129.8, 129.4, 128.7, 128.5, 127.5, 127.5, 123.7, 115.4, 86.2, 55.6; IR (KBr, ν, cm^{-1}) 3454, 3353, 3058, 2941, 2840, 1606, 1532, 1436, 1243, 690; HRMS (ESI-TOF): m/z calcd for $C_{22}H_{18}N_3OS$ [M − H]$^-$, 372.1170; found, 372.1170.

*4-(4-tert-Butylphenylthio)-1,3-diphenyl-1H-pyrazol-5-amine (****4m****).* Brown solid, 267 mg, 67% yield; mp 131−132 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.94−7.92 (m, 2H), 7.74−7.72 (m,

DOI: 10.1021/acs.joc.5b01280
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2H), 7.58−7.54 (m, 2H), 7.43−7.30 (m, 6H), 7.06−7.04 (m, 2H), 5.81 (s, 2H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.3, 151.8, 148.0, 139.3, 135.5, 133.4, 129.8, 128.7, 128.6, 127.5, 127.5, 126.5, 125.1, 123.7, 84.8, 34.5, 31.5; IR (KBr, ν, cm^{-1}) 3446, 3354, 3058, 2955, 2865, 1601, 1530, 1428, 694; HRMS (ESI-TOF): m/z calcd for $C_{25}H_{24}N_3S$ [M − H]$^-$, 398.1690; found, 398.1694.

4-(4-Chlorophenylthio)-1,3-diphenyl-1H-pyrazol-5-amine (**4n**). Yellow solid, 230 mg, 61% yield; mp 113−114 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.85−7.83 (m, 2H), 7.73−7.70 (m, 2H), 7.58−7.54 (m, 2H), 7.44−7.33 (m, 6H), 7.14−7.11 (m, 2H), 5.89 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.3, 152.0, 139.2, 138.4, 133.1, 130.0, 129.8, 129.5, 128.7, 128.7, 127.6, 127.4, 126.9, 123.8, 83.7; IR (KBr, ν, cm^{-1}) 3447, 3343, 3055, 2921, 2848, 1608, 1533, 1437, 739, 691; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{15}ClN_3S$ [M − H]$^-$, 376.0674; found, 376.0661.

4-(4-Bromophenylthio)-1,3-diphenyl-1H-pyrazol-5-amine (**4o**). Yellow solid, 303 mg, 72% yield; mp 127−128 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.85−7.72 (m, 4H), 7.58−7.37 (m, 8H), 7.08 (d, J = 8.0 Hz, 2H), 5.93 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.3, 152.0, 139.2, 138.9, 133.1, 132.3, 129.8, 128.7, 128.7, 127.6, 127.4, 127.2, 123.8, 118.1, 83.5; IR (KBr, ν, cm^{-1}) 3446, 3340, 3053, 1608, 1534, 1436, 691, 557; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{15}BrN_3S$ [M − H]$^-$, 420.0164; found, 420.0145.

4-(4-Nitrophenylthio)-1,3-diphenyl-1H-pyrazol-5-amine (**4p**). Brown solid, 314 mg, 81% yield; mp 128−129 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 8.16 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.60−7.56 (m, 2H), 7.45−7.42 (m, 1H), 7.39−7.33 (m, 5H), 6.08 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.4, 152.1, 149.7, 145.2, 139.1, 132.9, 129.8, 128.8, 127.7, 127.4, 125.4, 124.7, 124.0, 81.8; IR (KBr, ν, cm^{-1}) 3412, 3331, 3061, 1620, 1595, 1496, 1442, 700; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{15}N_4O_2S$ [M − H]$^-$, 387.0915; found, 387.0916.

4-(3-Nitrophenylthio)-1,3-diphenyl-1H-pyrazol-5-amine (**4q**). Brown solid, 287 mg, 74% yield; mp 145−146 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.99−7.96 (m, 1H), 7.88−7.87 (m, 1H), 7.84−7.82 (m, 2H), 7.73−7.71 (m, 2H), 7.60−7.56 (m, 4H), 7.45−7.34 (m, 4H), 6.06 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.4, 152.1, 148.9, 142.4, 139.1, 133.0, 131.5, 131.0, 129.9, 128.8, 128.8, 127.7, 127.4, 123.9, 120.3, 119.3, 82.4; IR (KBr, ν, cm^{-1}) 3425, 3343, 3056, 1613, 1595, 1498, 1436, 700; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{15}N_4O_2S$ [M − H]$^-$, 387.0915; found, 387.0921.

1-(4-Methoxyphenyl)-3-phenyl-4-(p-tolylthio)-1H-pyrazol-5-amine (**4r**). Yellow solid, 324 mg, 84% yield; mp 122−123 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.87−7.85 (m, 2H), 7.60−7.58 (m, 2H), 7.37−7.31 (m, 3H), 7.10 (d, J = 8.8 Hz, 4H), 7.02 (d, J = 8.0 Hz, 2H), 5.64 (s, 2H$_2$), 3.83 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 158.7, 151.8, 151.8, 135.6, 134.7, 133.4, 132.2, 130.2, 128.6, 128.4, 127.4, 125.7, 125.4, 114.9, 84.2, 55.9, 20.9; IR (KBr, ν, cm^{-1}) 3444, 3347, 3012, 2925, 1610, 1509, 1457, 1255, 700; HRMS (ESI-TOF): m/z calcd for $C_{23}H_{20}N_3OS$ [M − H]$^-$, 386.1326; found, 386.1335.

1-(4-Chlorophenyl)-3-phenyl-4-(p-tolylthio)-1H-pyrazol-5-amine (**4s**). Brown solid, 160 mg, 41% yield; mp 123−124 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.89−7.86 (m, 2H), 7.77−7.74 (m, 2H), 7.63−7.60 (m, 2H), 7.39−7.32 (m, 3H), 7.10 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.4 Hz, 2H), 5.91 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.6, 152.1, 138.2, 135.4, 134.8, 133.1, 131.7, 130.2, 129.7, 128.7, 127.5, 125.5, 125.4, 85.3, 20.9; IR (KBr, ν, cm^{-1}) 3413, 3353, 3015, 2920, 1613, 1532, 1446, 736, 692; HRMS (ESI-TOF): m/z calcd for $C_{22}H_{17}ClN_3S$ [M − H]$^-$, 390.0831; found, 390.0824.

1-(4-Bromophenyl)-3-phenyl-4-(p-tolylthio)-1H-pyrazol-5-amine (**4t**). Yellow solid, 218 mg, 50% yield; mp 105−106 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.88−7.86 (m, 2H), 7.75−7.68 (m, 4H), 7.39−7.32 (m, 3H), 7.10 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 5.91 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.6, 152.1, 138.6, 135.4, 134.8, 133.1, 132.6, 130.2, 128.7, 127.5, 125.6, 125.5, 120.0, 85.3, 20.9; IR (KBr, ν, cm^{-1}) 3448, 3351, 3051, 2920, 1605, 1531, 1446, 692, 573; HRMS (ESI-TOF): m/z calcd for $C_{22}H_{17}BrN_3S$ [M − H]$^-$, 434.0326; found, 434.0332.

Example for the Synthesis of **6**. Pentane-2,4-dione (**5**, 1.0 mmol, 100 mg), phenylhydrazine (**2a**, 1.5 mmol, 108 mg), and 4-methylbenzenesulfonohydrazide (**3a**, 1.5 mmol, 186 mg) were introduced in a sealed 10 mL reaction tube, I_2 (0.5 mmol, 127 mg), and HOAc (0.5 mmol) as well as EtOH (2.5 mL) were then successively added, and the mixture stirred at 120 °C for 5 h. After completion of the reaction (monitored by TLC), the reaction mixture was down to room temperature. Then, organic solvent was concentrated by a rotary evaporator, and the residue was purified by column chromatography (eluents, petroleum ether/ethyl acetate 15:1) to afford the pure product **6a**.

3,5-Dimethyl-1-phenyl-4-(p-tolylthio)-1H-pyrazole (**6a**). White solid, 206 mg, 70% yield; mp 102−103 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.60−7.52 (m, 4H), 7.46−7.42 (m, 1H), 7.10 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 2.33 (s, 3H), 2.24 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.2, 144.3, 139.9, 135.1, 134.3, 130.3, 129.7, 128.2, 126.2, 124.8, 106.2, 20.9, 12.3, 11.8; IR (KBr, ν, cm^{-1}) 3008, 2918, 1637, 1616, 1594, 1447, 696; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{19}N_2S$ [M + H]$^+$, 295.1270; found, 295.1272.

3,5-Dimethyl-1-(p-tolyl)-4-(p-tolylthio)-1H-pyrazole (**6b**). Yellow solid, 234 mg, 76% yield; mp 72−74 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.33 (d, J = 8.4 Hz, 2H), 7.24 (s, 1H), 7.04−6.95 (m, 5H), 2.39 (s, 3H), 2.32−2.26 (m, 9H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 153.1, 144.2, 139.7, 137.0, 130.8, 129.2, 129.0, 128.0, 126.7, 124.7, 105.7, 12.1, 11.6; IR (KBr, ν, cm^{-1}) 2921, 1637, 1614, 1593, 1412, 712; HRMS (ESI-TOF): m/z calcd for $C_{19}H_{21}N_2S$ [M + H]$^+$, 309.1426; found, 309.1430.

1-(4-Methoxyphenyl)-3,5-dimethyl-4-(p-tolylthio)-1H-pyrazole (**6c**). White solid, 288 mg, 89% yield; mp 98−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) δ 7.40 (d, J = 8.8 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 7.02−6.99 (m, 4H), 3.87 (s, 3H), 2.31 (d, J = 3.2 Hz, 9H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 158.2, 151.9, 143.2, 133.9, 133.8, 132.0, 128.8, 125.4, 124.8, 113.4, 105.1, 54.7, 20.0, 11.2, 10.5; IR (KBr, ν, cm^{-1}) 2922, 1637, 1616, 1587, 1496, 1270, 703; HRMS (ESI-TOF): m/z calcd for $C_{19}H_{21}N_2OS$ [M + H]$^+$, 325.1375; found, 325.1369.

1-(4-Chlorophenyl)-3,5-dimethyl-4-(p-tolylthio)-1H-pyrazole (**6d**). Yellow solid, 177 mg, 54% yield; mp 106−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) δ 7.33 (d, J = 1.2 Hz, 4H), 6.94 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 2.24 (s, 3H), 2.18 (d, J = 3.2 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 153.5, 144.0, 138.4, 135.0, 134.4, 133.4, 129.7, 129.3, 125.9, 125.7, 107.4, 20.9, 12.2, 11.7; IR (KBr, ν, cm^{-1}) 2922, 1637, 1616, 1594, 1490, 800, 703; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{18}ClN_2S$ [M + H]$^+$, 329.0880; found, 329.0881.

1-(4-Bromophenyl)-3,5-dimethyl-4-(p-tolylthio)-1H-pyrazole (**6e**). Pale yellow solid, 175 mg, 47% yield; mp 84−85 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.52 (d, J = 8.8 Hz, 2H), 7.29 (d, J = 8.8 Hz, 2H), 6.96 (d, J = 8.0 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 2.27 (s, 3H), 2.20 (d, J = 2.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 159.9, 147.5, 144.2, 134.1, 132.7, 128.3, 127.0, 125.5, 120.4, 114.9, 114.2, 113.0, 96.1, 87.8, 75.4, 55.4, 27.9; IR (KBr, ν, cm^{-1}) 3060, 2923, 1615, 1594, 1470, 697, 578; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{18}BrN_2S$ [M + H]$^+$, 373.0375; found, 373.0386.

3,5-Dimethyl-1-phenyl-4-phenylthio-1H-pyrazole (**6f**). White solid, 154 mg, 55% yield; mp 71−72 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.40 (d, J = 4.4 Hz, 4H), 7.33−7.29 (m, 1H), 7.17−7.13 (m, 2H), 7.03−6.97 (m, 3H), 2.26 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 152.3, 143.3, 138.8, 137.3, 128.3, 128.0, 127.0, 124.5, 124.1, 123.8, 105.2, 11.2, 10.7; IR (KBr, ν, cm^{-1}) 3001, 2926, 1637, 1616, 1595, 1461, 698; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{17}N_2S$ [M + H]$^+$, 281.1113; found, 281.1112.

4-(4-Methoxyphenylthio)-3,5-dimethyl-1-phenyl-1H-pyrazole (**6g**). Yellow solid, 223 mg, 72% yield; mp 84−85 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.50−7.49 (m, 4H), 7.42−7.40 (m, 1H), 7.11−7.08 (m, 2H), 6.84−6.82 (m, 2H), 3.78 (s, 3H), 2.39 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 156.9, 151.9, 142.7, 138.8, 128.2, 127.8, 127.2, 126.8, 123.7, 113.7, 106.8, 54.4, 11.2, 10.7; IR (KBr, ν, cm^{-1}) 3001, 2926, 1637, 1616, 1596, 1461, 698; HRMS (ESI-

DOI: 10.1021/acs.joc.5b01280
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TOF): m/z calcd for $C_{18}H_{19}N_2OS$ $[M + H]^+$, 311.1219; found, 311.1223.

4-(4-Chlorophenylthio)-3,5-dimethyl-1-phenyl-1H-pyrazole (**6h**). Pale brown solid, 157 mg, 50% yield; mp 128−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.41−7.40 (m, 4H), 7.33−7.30 (m, 1H), 7.12 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 2.26 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 153.1, 144.2, 139.7, 136.9, 130.8, 129.2, 129.0, 128.0, 126.7, 124.7, 105.7, 12.1, 11.6; IR (KBr, ν, cm^{-1}) 3001, 2926, 1637, 1616, 1596, 1461, 769, 698; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{16}ClN_2S$ $[M + H]^+$, 315.0723; found, 315.0729.

4-(4-Bromophenylthio)-3,5-dimethyl-1-phenyl-1H-pyrazole (**6i**). White solid, 183 mg, 51% yield; mp 130−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.60−7.53 (m, 4H), 7.49−7.46 (m, 3H), 7.02−7.00 (m, 2H), 2.32 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.2, 144.7, 139.8, 137.7, 132.4, 129.7, 128.3, 127.7, 124.8, 118.5, 105.0, 12.2, 11.7; IR (KBr, ν, cm^{-1}) 3051, 2929, 1637, 1616, 1596, 1461, 703, 578; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{16}BrN_2S$ $[M + H]^+$, 359.0218; found, 359.0227.

4-(3-Bromophenylthio)-3,5-dimethyl-1-phenyl-1H-pyrazole (**6j**). White solid, 218 mg, 61% yield; mp 72−73 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.62−7.53 (m, 4H), 7.48−7.44 (m, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.27−7.22 (m, 2H), 7.05−7.02 (m, 1H), 2.33 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 152.2, 144.8, 140.9, 139.8, 131.7, 129.7, 128.6, 128.3, 127.5, 124.9, 124.5, 122.9, 104.5, 12.2, 11.7; IR (KBr, ν, cm^{-1}) 1637, 1616, 1593, 1455, 699, 578; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{16}BrN_2S$ $[M + H]^+$, 359.0218; found, 359.0220.

Example for the Synthesis of **8**. 3-Oxo-3-phenylpropanenitrile (**1a**, 1.0 mmol, 145 mg) and 4-methylbenzenesulfonohydrazide (**3a**, 3.0 mmol, 372 mg) were introduced in a sealed 10 mL reaction tube. I_2 (0.5 mmol, 127 mg) and CH_3CN (2.5 mL) were then successively added, and the mixture stirred at 120 °C for 5 h. After completion of the reaction (monitored by TLC), the reaction mixture was down to room temperature. Then, organic solvent was concentrated by a rotary evaporator, and the residue was purified by column chromatography (eluents, petroleum ether/ethyl acetate 15:1) to afford the pure product **8**.

3-Phenyl-4-(p-tolylthio)-1-tosyl-1H-pyrazol-5-amine (**8**). Yellow solid; 105 mg, 24% yield; mp 66−67 °C; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.92 (d, J = 8.4 Hz, 1H), 7.71−7.69 (m, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.37−7.35 (m, 3H), 7.01 (d, J = 8.0 Hz, 2H), 6.75−6.71 (m, 4H), 2.42 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 157.5, 155.4, 146.6, 135.1, 134.0, 133.8, 131.5, 130.8, 130.2, 129.8, 128.8, 127.9, 127.9, 125.2, 84.9, 21.7, 20.8; IR (KBr, ν, cm^{-1}) 3412, 3307, 3067, 1630, 1611, 1598, 1450; HRMS (ESI-TOF): m/z calcd for $C_{23}H_{20}N_3O_2S_2$ $[M - H]^-$, 434.0997; found, 434.0992.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for all pure products and X-ray crystal data (CIF) for **4a**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01280.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for financial support from the NSFC (nos. 21232004, 21272095, and 21472071), PAPD of Jiangsu Higher Education Institutions, the Qing Lan Project (12QLG006), the Outstanding Youth Fund of Jiangsu Normal University (YQ2015003), and Natural Science Foundation of Jiangsu Normal University (14XLR005). We thank Prof. Changsheng Yao from Jiangsu Normal University for his generous help.

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DOI: 10.1021/acs.joc.5b01280
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