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Transition Metal-Free De Novo Synthesis of Sulfonated Pyrazoles from Sulfonyl Hydrazides, 1,3-Diketones, and Sodium Sulfinates at Room Temperature

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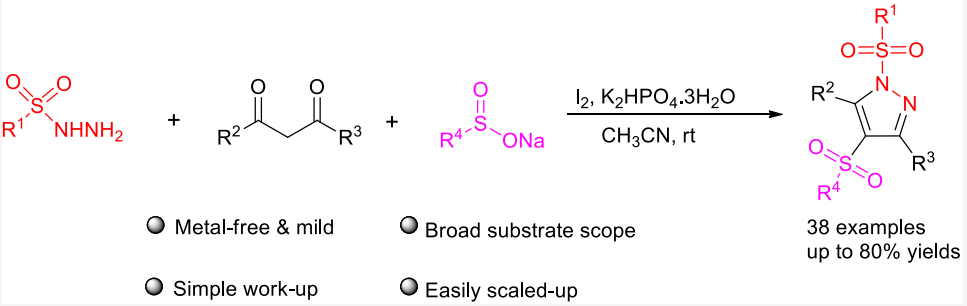

ABSTRACT: A transition metal-free method for de novo construction of diverse sulfonated pyrazoles from readily available sulfonyl hydrazides, 1,3-diketones, and sodium sulfinates was established under mild conditions. Pyrazoles bearing two different sulfonyl groups were obtained in one step. The method features a diversity of substituents of the pyrazole products and a remarkably simple work-up.

INTRODUCTION

Pyrazole skeletons have gained considerable attention due to their wide existence in pharmaceuticals and biologically active compounds,[1] which shows a variety of bioactivities, e.g. antimicrobial,[2] anticancer,[3] antiinflammatory,[4] antiproliferation,[5] agricultural insecticide,[6] and antioxidation activity.[7] Besides, pyrazoles also play important roles in coordinating chemistry, organometallic chemistry, and latent fingermarks analysis.[8] In addition, substituents on the pyrazole skeleton might also play important roles in the activities. At this point, it is meaningful to develop efficient methods for constructing pyrazoles bearing diverse functional groups.[9] Sulfone groups, often uncovered in biologically active molecules, agrochemicals, and materials, constitute one of the most valuable sorts of organic functional groups.[10] Incorporation of sulfone group into particular skeletons is a frequently used strategy to gain better activities during the drug design.[11] Given these viewpoints, the synthesis of sulfonated pyrazoles has evoked lots of interest from synthetic chemists.[12−15]

Conventional approaches targeting this consist of cycloaddition of reagents in which sulfone groups were pre-installed and remained untouched during the reaction and oxidation of pyrazoles with thioether groups.[12,13] In 2014, Wan et al. reported the pioneering synthesis of sulfonated pyrazoles from sulfonyl hydrazides and 1,3-diketones, in which sulfonyl hydrazides function as both the ring component and sulfonyl precursor (eq 1).[14a] Recently, this dual-role-sulfonyl-hydrazide

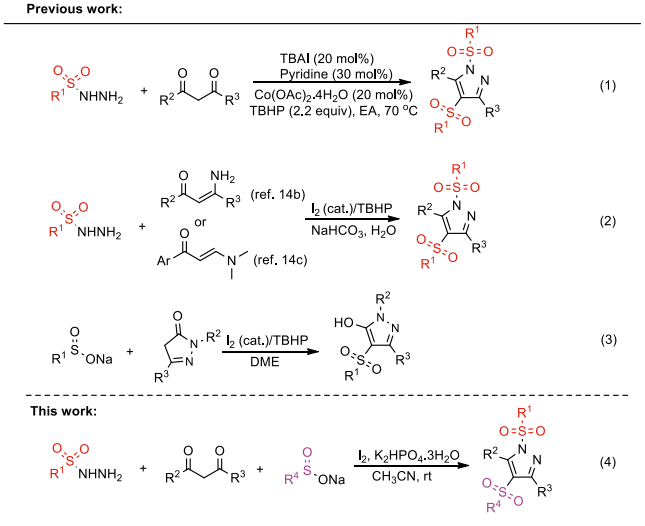

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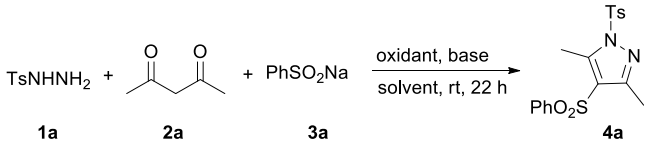
Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a 4a

entry	oxidant (equiv)	solvent	base (equiv)	isolated yield (%)
1	I_2 (2.0)	CH_3CN	$K_2HPO_4{\cdot}3H_2O$ (1.5)	58
2	I_2 (2.0)	EA	$K_2HPO_4{\cdot}3H_2O$ (1.5)	40
3	I_2 (2.0)	THF	$K_2HPO_4{\cdot}3H_2O$ (1.5)	36
4	I_2 (2.0)	DMSO	$K_2HPO_4{\cdot}3H_2O$ (1.5)	33
5	I_2 (2.0)	1,4-dioxane	$K_2HPO_4{\cdot}3H_2O$ (1.5)	41
6	I_2 (2.0)	DMA	$K_2HPO_4{\cdot}3H_2O$ (1.5)	37
7	I_2 (2.0)	NMP	$K_2HPO_4{\cdot}3H_2O$ (1.5)	35
8	I_2 (1.5)	CH_3CN	$K_2HPO_4{\cdot}3H_2O$ (1.5)	57
9	I_2 (1.1)	CH_3CN	$K_2HPO_4{\cdot}3H_2O$ (1.5)	50
10	I_2 (1.5)	CH_3CN	$NaHCO_3$ (1.5)	32
11	I_2 (1.5)	CH_3CN	NaOAc (1.5)	35
12	I_2 (1.5)	CH_3CN	K_2CO_3 (1.5)	11
13	I_2 (1.5)	CH_3CN	KOH (1.5)	32
14	I_2 (1.5)	CH_3CN	^{t}BuOK (1.5)	29
15	I_2 (1.5)	CH_3CN	$K_2HPO_4{\cdot}3H_2O$ (0.8)	58
16	I_2 (1.5)	CH_3CN	$K_2HPO_4{\cdot}3H_2O$ (0.6)	51
17	I_2 (1.5)	CH_3CN	K_2HPO_4 (0.8)	46
18[b]	I_2 (1.5)	CH_3CN		42
19		CH_3CN	K_2HPO_4 (0.8)	n.d.[c]
20	I_2 (0.2) + TBHP (3)	CH_3CN	$K_2HPO_4{\cdot}3H_2O$ (0.8)	11
21	I_2 (0.2) + DTBP (3)	CH_3CN	$K_2HPO_4{\cdot}3H_2O$ (0.8)	16

[a]Reaction conditions: 4-methylbenzenesulfonohydrazide (**1a**) (0.5 mmol), pentane-2,4-dione (**2a**) (0.6 mol), sodium 4-methylbenzenesulfinate (**3a**) (1.0 mol), oxidant, base, solvent (4.5 mL), air, and rt. [b]The reaction was carried out at 35 °C. [c]n.d. = not detected.

strategy was applied to the reactions of sulfonyl hydrazides with enaminones, affording sulfonated pyrazoles under mild conditions (eq 2).[14b,c] This strategy makes full use of the sulfonyl hydrazides involved in the reaction; however, it could only introduce two identical sulfonyl groups to the pyrazole skeleton. Compared to sulfonyl hydrazides, sodium sulfinates are more environmentally benign sulfone sources. In 2017, Wang et al. reported a molecular iodine-catalyzed direct sulfonation of preformed pyrazolones with sodium sulfinates (eq 3).[15] Although these methods are inspiring, more general and efficient protocols are still much in demand to get over the existing limitations such as extra steps to prepare active precursors, applying excess amounts of organometallic reagents, harsh reaction conditions, tedious work-up procedures, and limited substrate scope or low yields. Aiming at developing a green, practical, and efficient method for constructing diverse sulfonated pyrazoles, we speculated that the target compounds might be produced from readily available 1,3-dielectrophiles, sulfonyl hydrazides, and sodium sulfinates, in which the latter two reagents might serve as the sulfonyl precursors at the same time in the reaction, giving rise to pyrazoles with more tunable structures. As a verification, we herein reported a novel strategy for the synthesis of diverse sulfonated pyrazoles through a molecular iodine-promoted multicomponent reaction of sulfonyl hydrazides, 1,3-diketones, and sodium sulfinates (eq 4).

RESULTS AND DISCUSSION

Initial reactivity assays were conducted with 4-methylbenzenesulfonohydrazide **1a**, pentane-2,4-dione **2a**, and sodium benzenesulfinate **3a** as model substrates. To our delight, in the presence of I_2 (2.0 equiv) and $K_2HPO_4{\cdot}3H_2O$ (1.5 equiv) in CH_3CN at room temperature, the desired pyrazole **4a** was obtained in 58% isolated yield (Table 1, entry 1). Other solvents such as ethyl acetate, tetrahydrofuran (THF), dimethyl sulfoxide (DMSO), 1,4-dioxane, dimethylacetamide (DMA), and *N*-methyl-2-pyrrolidone (NMP) also work in the reaction, albeit providing pyrazole **4a** in inferior yields (Table 1, entries 2−7). A comparable yield of pyrazole **4a** was obtained when decreasing the loading of iodine to 1.5 equiv, while further decreasing to 1.1 equiv gave only 50% yield (Table 1, entries 8 and 9). Further investigation of other bases revealed that $K_2HPO_4{\cdot}3H_2O$ was the best choice (Table 1, entries 10−14). The optimal amount of $K_2HPO_4{\cdot}3H_2O$ was found to be 0.8 equiv, although a 42% isolated yield of **4a** was produced at 35 °C even without $K_2HPO_4{\cdot}3H_2O$ (Table 1, entries 15, 16, and 18). These results indicate that the base $K_2HPO_4{\cdot}3H_2O$ plays a promotive part in the transformation, but not an indispensable one. Iodine is essential in this transformation as the desired product **4a** was not observed in the absence of iodine (Table 1, entry 19). Applying a catalytic amount of iodine (20 mol %) and 3 equiv of additional oxidant (TBHP or DTBP) did not yield pyrazole **4a** in a satisfactory yield; only 11 and 16% yields were obtained, respectively (Table 1, entries 20 and 21).

With the optimal conditions in hand, we then examined the generality of the method by applying various sulfonyl hydrazides, 1,3-diketones, and sodium sulfinates. The scope of sulfonyl hydrazides was first investigated. As exhibited in Table 2, various aryl sulfonyl hydrazides bearing electron-donating or -withdrawing substituents were compatible in this reaction, affording pyrazoles **4a**−**4q** in yields of 47−67% under

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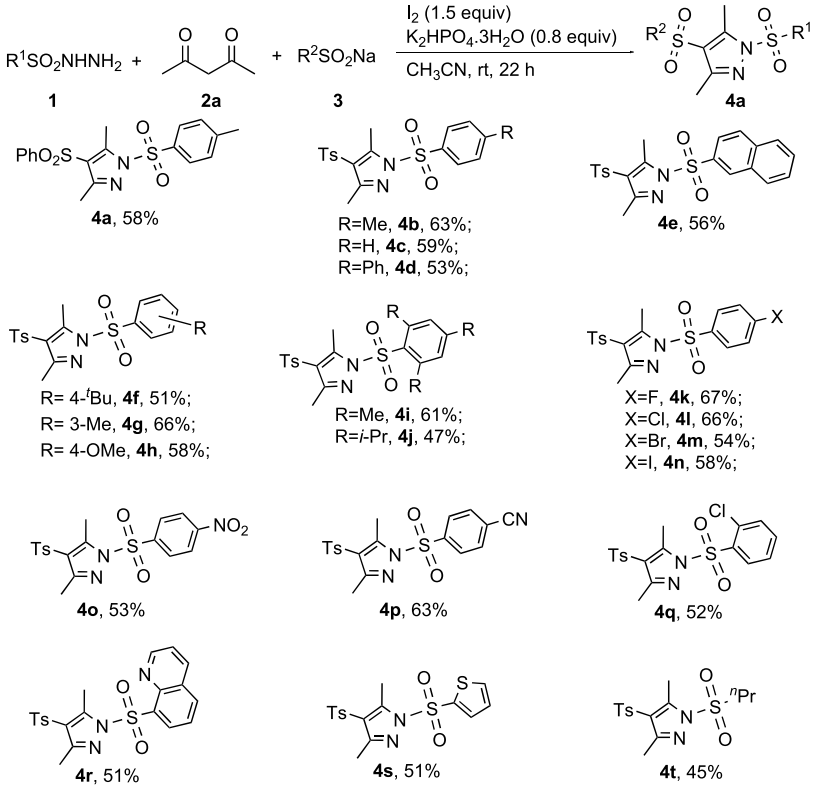
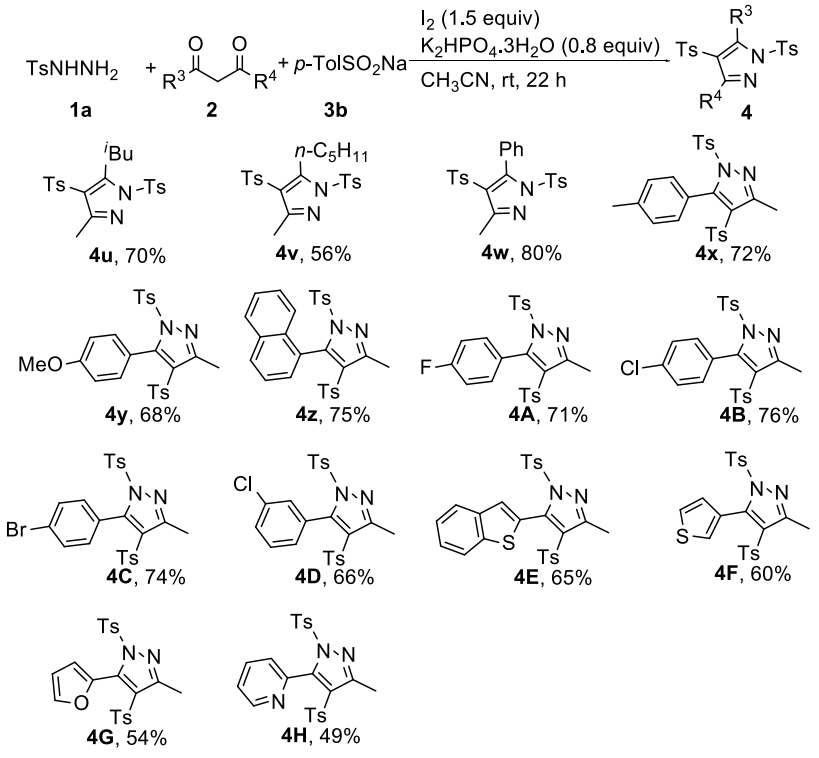
Table 2. Substrate Scope of Sulfonyl Hydrazides[a]



[a]Reaction conditions: **1** (0.5 mmol), **2a** (0.6 mmol), **3** (1.0 mmol), I_2 (0.75 mmol), K_2HPO_4 $3H_2O$ (0.4 mmol), CH_3CN (4.5 mL), air, rt, and 22 h.

Table 3. Substrate Scope of 1,3-Diketones[a]



[a]Reaction conditions: **1a** (0.5 mmol), **2** (0.6 mmol), **3b** (1.0 mmol), I_2 (0.75 mmol), $K_2HPO_4 \cdot 3H_2O$ (0.4 mmol), CH_3CN (4.5 mL), air, rt, and 22 h.

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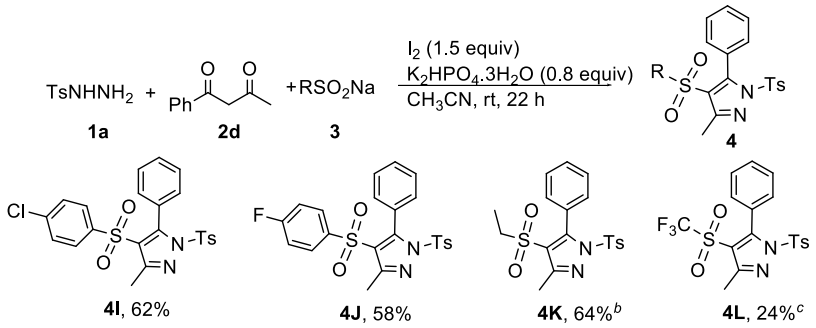
Table 4. Substrate Scope of Sodium Sulfinates[a]



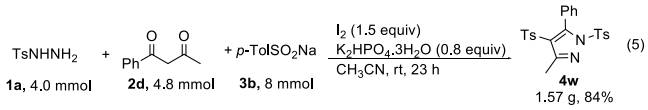
[a]Reaction conditions: **1a** (0.5 mmol), **2d** (0.6 mmol), **3** (1.0 mmol), I_2 (0.75 mmol), $K_2HPO_4{\cdot}3H_2O$ (0.4 mmol), CH_3CN (4.5 mL), air, rt, and 22 h. [b]Sodium ethanesulfinate (2.0 mmol) was used. [c]Sodium trifluoromethanesulfinate (2.0 mmol) was used.

mild reaction conditions. The electronic properties of the substituents on the aromatic ring of aryl sulfonyl hydrazides did not show much influence on yields. It is notable that the functional groups such as fluoro, chloro, bromo, iodo, nitro, and cyano were well tolerated in this transformation, allowing the further elaboration of the corresponding products. Heteroaryl sulfonyl hydrazides such as quinoline-8-sulfonohydrazide and thiophene-2-sulfonohydrazide were also suitable substrates in the reaction, producing the corresponding pyrazoles **4r** and **4s** in 51% yields. Remarkably, the aliphatic sulfonyl hydrazide, which was ineffective in the previous report,[14] was an adaptable substrate as well in this protocol, affording pyrazole **4t** in a 45% isolated yield.

Next, the reactivity of nonsymmetrical 1,3-diketones in this reaction was surveyed with 4-methylbenzenesulfonohydrazide (**1a**) and sodium *p*-toluenesulfinate (**3b**) under the standard conditions. As shown in Table 3, a variety of nonsymmetrical 1,3-diketones were suitable substrates in this method. When 6-methylheptane-2,4-dione was applied in the protocol, the corresponding pyrazole **4u** was produced in 70% yield and excellent regioselectivity.[16] Nonane-2,4-dione, which contains a longer carbon chain, was also smoothly converted into the desired product **4v** in 56% yield under the optimal conditions. The investigation was then directed to 1,3-diketones with an aryl group. 1-Phenylbutane-1,3-dione proved to be quite active under the standard conditions, furnishing **4w** in 80% yield. In addition, 1-arylbutane-1,3-diones bearing methoxy, fluoro, chloro, and bromo substituents on the aryl ring were all compatible in the reaction, yielding the corresponding functionalized pyrazole products in 68−76% yields (Table 3, **4y** and **4A**-**4D**). 1,3-Diketones with a heteroaryl group such as benzo[*b*]thiophen-2-yl, 3-thiophenyl, 2-furanyl, and 2-pyridinyl suited the standard conditions as well, constructing pyrazoles **4E**−**4H** with two heteroaryl rings in 49−65% yields.

The generality of sodium sulfinates was examined by the reaction with 4-methylbenzenesulfonohydrazide (**1a**) and 1-phenylbutane-1,3-dione (**2d**) (Table 4). Sodium 4-chlorobenzene sulfinate (**3c**) and sodium 4-fluorobenzene sulfinate (**3d**) were less effective than sodium *p*-toluenesulfinate (**3b**) in this method, generating the corresponding products **4I** and **4J** in 62 and 58% yield (*vs* **4w**, 80%), respectively. Encouragingly, aliphatic sodium sulfinate, e.g., sodium ethanesulfinate, was fit with the protocol as well, furnishing pyrazole **4K** in 64% yield under slightly modified conditions. The Langlois reagent (CF_3SO_2Na) also survived in the reaction; however, only 24% yield of product **4L** was obtained.

To test the practicality of the method for the synthesis of fully substituted pyrazoles, a gram-scale reaction was carried out. Under the standard conditions, the reaction of 4-methylbenzenesulfonohydrazide (**1a**, 4.0 mmol), 1-phenylbutane-1,3-dione (**2d**, 4.8 mmol), and sodium *p*-toluenesulfinate (**3b**, 8.0 mmol) proceeded smoothly, providing 1.57 g of pyrazole **4w** in 84% yield (eq 5). It is remarkable that the pure product was obtained through a simple filtration, thus dramatically reducing the time and solvents consumed during the conventional work-up.



To gain more insight into the mechanism of the reaction, some control experiments were carried out. Under the standard conditions, the desired product **4a** was not detected when pyrazole **5** was subjected to the reaction (Scheme 1a), indicating that the reaction would probably not proceed through a cyclization−sulfonylation process. When a radical scavenger 2,6-di-*tert*-butyl-4-methylphenol (BHT) or 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) was added to the reaction system, the desired product **4a** was provided in 49 and 56% yield, respectively (Scheme 1b,c), showing little influence on the reaction effectivity. These results suggested that a radical process was not likely involved in this method.

Based on the results of control experiments, a plausible mechanism for the reaction is depicted in Scheme 2. Sulfonyl iodide **6** is easily generated from sodium sulfinate **3** and molecular iodine.[15,17] The condensation of sulfonyl hydrazide and 1,3-diketone afforded imine **7**, which then undergoes tautomerization to produce its enol form **8**. A following nucleophilic attack of the enol form **8** toward the in situ generated sulfonyl iodide **6** yields intermediate **9**, which finally produces the desired product **4** by an intramolecular condensation.

CONCLUSIONS

To conclude, a molecular iodine-promoted transition metal-free method for the synthesis of sulfonated pyrazoles from readily available sulfonyl hydrazides, 1,3-diketones, and sodium sulfinates has been established under mild conditions. Sulfonyl hydrazides and sodium sulfinates each offer a sulfonyl group in the reaction, improving the diversity of the desired products. The protocol features broad substrate scope and easy

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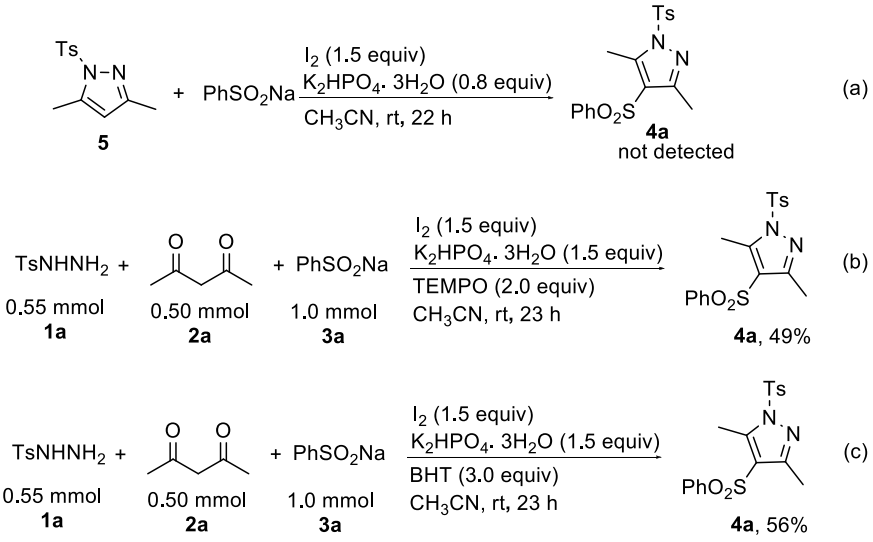
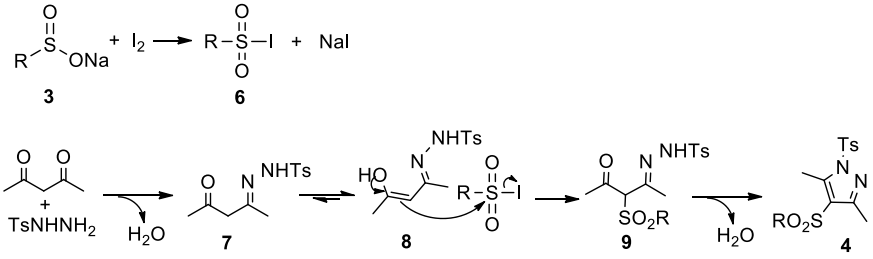
Scheme 1. Control Experiments



Scheme 2. Plausible Reaction Mechanism



manipulation. Considering its green conditions and simple operation, the protocol might be fairly appealing in synthetic chemistry. Further mechanistic study and elaboration of the methodology to construct other diversely substituted heterocyclic compounds is being pursued in our laboratory.

EXPERIMENTAL SECTION

General Methods. All commercially available reagents were used without further purification. Analytical TLC was performed on glass-backed plates precoated with silica gel, which were visualized by UV fluorescence (λ_{max} = 254 nm). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer (^{1}H: 400 MHz; ^{13}C: 100 MHz), using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. All ^{1}H NMR spectra are reported in parts per million (ppm) downfield of TMS and were measured relative to the signals at 0 ppm (TMS). All ^{13}C NMR spectra were reported in ppm relative to the residual $CHCl_3$ (77.0 ppm) and were obtained with ^{1}H-decoupling. Data for ^{1}H NMR are described as follows: chemical shift (δ in ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; sep, septet; m, multiplet; br, broad signal), coupling constant (Hz), integration. Data for ^{13}C NMR are described in terms of chemical shift (δ in ppm). High-resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometer. Melting points were measured on the X4 melting point apparatus and uncorrected.

Sulfonyl hydrazides[18] and 1,3-diketones[19] were prepared according to the reported procedures.

General Procedure for the Synthesis of Pyrazoles 4. To a Schlenk tube (10 mL) were added sulfonyl hydrazide (0.5 mmol), 1,3-diketone (0.6 mmol, 1.2 equiv), sodium sulfinate (1.0 mmol, 2.0 equiv), $K_2HPO_4{\cdot}3H_2O$ (0.4 mmol, 0.8 equiv), I_2 (0.75 mmol, 1.5 equiv), and 4.5 mL of CH_3CN sequentially under air. Then, the tube was sealed and the reaction mixture was stirred at room temperature for 22 h. It was then quenched (consumption of residual I_2) with saturated $Na_2S_2O_3$ solution, forming a white precipitate. Filtration of the suspension gave the crude product. The crude product was washed with water (15 mL) and petroleum ether (15 mL) sequentially to afford pure product **4**.

*3,5-Dimethyl-4-(phenylsulfonyl)-1-tosyl-1H-pyrazole (**4a**).* The title compound was obtained as a white solid (113.6 mg, 58%). Mp 120−122 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.83 (m, 4H), 7.61 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 2.86 (s, 3H), 2.45 (s, 3H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.1, 146.8, 146.5, 142.0, 133.7, 133.4, 130.2, 129.2, 128.1, 126.5, 121.3, 21.7, 21.6, 13.6, 11.6; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{18}H_{18}N_2O_4S_2Na$: 413.0606; found: 413.0610.

*3,5-Dimethyl-1,4-ditosyl-1H-pyrazole (**4b**).*[14a,b] The title compound was obtained as a white solid (127.3 mg, 63%). Mp 123−125 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 2.85 (s, 3H), 2.44 (s, 3H), 2.41 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.1, 146.6, 146.5, 144.5, 139.2, 133.9, 130.2, 129.9, 128.1, 126.6, 121.7, 21.7, 21.5, 13.6, 11.6.

*3,5-Dimethyl-1-(phenylsulfonyl)-4-tosyl-1H-pyrazole (**4c**).* The title compound was obtained as a white solid (116.2 mg, 59%). Mp 155−156 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.4 Hz, 2H), 7.77−7.66 (m, 3H), 7.58 (t, J = 7.4 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 2.86 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.3, 146.8, 144.5, 139.1, 136.9, 135.0, 129.9, 129.6, 128.0, 126.6, 121.9, 21.5, 13.6, 11.7; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{18}H_{18}N_2O_4S_2Na$: 413.0606; found: 413.0615.

*1-([1,1′-Biphenyl]-4-ylsulfonyl)-3,5-dimethyl-4-tosyl-1H-pyrazole (**4d**).* The title compound was obtained as a white solid (123.3 mg, 53%). Mp 162−164 °C.

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^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 2H), 7.79−7.72 (m, 4H), 7.59 (d, J = 8.0 Hz, 2H), 7.53−7.41 (m, 3H), 7.32 (d, J = 8.0 Hz, 2H), 2.89 (s, 3H), 2.42 (s, 3H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.4, 148.1, 146.8, 144.6, 139.2, 138.5, 135.2, 129.9, 129.1, 129.0, 128.7, 128.2, 127.4, 126.7, 121.9, 21.5, 13.7, 11.8; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{24}H_{22}N_2O_4S_2Na$: 489.0919; found: 489.0923.

*3,5-Dimethyl-1-(naphthalen-2-ylsulfonyl)-4-tosyl-1H-pyrazole (**4e**).* The title compound was obtained as a white solid (125.0 mg, 56%). Mp 148−150 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.00 (t, J = 9.0 Hz, 2H), 7.92 (d, J = 8.0 Hz, 2H), 7.83(dd, J = 8.6, 1.4 Hz, 2H), 7.76−7.62 (m, 4H), 7.30 (d, J = 8.0 Hz, 2H), 7.53−7.41 (m, 3H), 7.32 (d, J = 8.0 Hz, 2H), 2.91 (s, 3H), 2.40 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.3, 146.8, 144.5, 139.1, 135.7, 133.6, 131.8, 130.4, 130.1, 130.0, 129.9, 129.6, 128.1, 128.0, 126.6, 122.0, 121.9, 21.5, 13.6, 11.8; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{22}H_{20}N_2O_4S_2Na$: 463.0762; found: 463.0765.

*1-((4-(Tert-butyl)phenyl)sulfonyl)-3,5-dimethyl-4-tosyl-1H-pyrazole (**4f**).* The title compound was obtained as a white solid (114.3 mg, 51%). Mp 151−152 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.8 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 2.84 (s, 3H), 2.41 (s, 3H), 2.37 (s, 3H), 1.34 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.3, 151.2, 146.7, 144.5, 139.2, 133.8, 129.9, 128.0, 126.69, 126.66, 121.8, 35.4, 30.9, 21.5, 13.7, 11.7; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{22}H_{26}N_2O_4S_2Na$: 469.1232; found: 469.1232.

*3,5-Dimethyl-1-(m-tolylsulfonyl)-4-tosyl-1H-pyrazole (**4g**).* The title compound was obtained as a white solid (132.2 mg, 66%). Mp 130−131 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.76 (m, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.52−7.40 (m, 2H), 7.32 (d, J = 8.0 Hz, 2H), 2.85 (s, 3H), 2.44 (s, 3H), 2.42 (s, 3H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.2, 146.7, 144.5, 140.1, 139.2, 136.7, 135.9, 129.9, 129.4, 128.2, 126.6, 125.2, 121.8, 21.5, 21.2, 13.6, 11.7; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{19}H_{20}N_2O_4S_2Na$: 427.0762; found: 427.0767.

*1-((4-Methoxyphenyl)sulfonyl)-3,5-dimethyl-4-tosyl-1H-pyrazole (**4h**).* The title compound was obtained as a white solid (121.5 mg, 58%). Mp 132−135 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H), 2.84 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.8, 151.0, 146.4, 144.5, 139.3, 130.7, 129.9, 128.0, 126.7, 121.6, 114.8, 55.8, 21.5, 13.7, 11.7; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{19}H_{20}N_2O_5S_2Na$: 443.0711; found: 443.0720.

*1-(Mesitylsulfonyl)-3,5-dimethyl-4-tosyl-1H-pyrazole (**4i**).* The title compound was obtained as a white solid (132.3 mg, 61%). Mp 181−182 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 6.99 (s, 2H), 2.82 (s, 3H), 2.53 (s, 6H), 2.42 (s, 3H), 2.31 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.0, 146.3, 145.2, 144.4, 141.1, 139.4, 132.2, 131.3, 129.9, 126.7, 120.9, 22.5, 21.5, 21.1, 13.6, 11.5; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{21}H_{24}N_2O_4S_2Na$: 455.1075; found: 455.1084.

*3,5-Dimethyl-4-tosyl-1-((2,4,6-triisopropylphenyl)sulfonyl)-1H-pyrazole (**4j**).* The title compound was obtained as a white solid (120.8 mg, 47%). Mp 145−147 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.19 (s, 2H), 4.01 (sep, J = 6.7 Hz, 2H), 2.92 (sep, J = 6.9 Hz, 1H), 2.73 (s, 3H), 2.42 (s, 3H), 2.34 (s, 3H), 1.26 (d, J = 6.8 Hz, 6H), 1.13 (d, J = 6.8 Hz, 12H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.5, 152.1, 149.5, 145.5, 144.3, 139.5, 130.2, 129.8, 126.6, 124.2, 121.0, 34.2, 29.6, 24.2, 23.3, 21.5, 13.4, 13.1; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{27}H_{36}N_2O_4S_2Na$: 539.2014; found: 539.2015.

*1-((4-Fluorophenyl)sulfonyl)-3,5-dimethyl-4-tosyl-1H-pyrazole (**4k**).* The title compound was obtained as a white solid (135.5 mg, 67%). Mp 182−184 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06−8.00 (m, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.29−7.22 (m, 2H), 2.86 (s, 3H), 2.43 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.4 (d, J = 257.8 Hz), 151.5, 146.8, 144.6, 139.1, 132.9 (d, J = 3.9 Hz), 131.3 (d, J = 9.3 Hz), 129.9, 126.7, 122.0, 117.0 (d, J = 22.8 Hz), 21.5, 13.6, 11.7; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{18}H_{17}FN_2O_4S_2Na$: 431.0511; found: 431.0517.

*1-((4-Chlorophenyl)sulfonyl)-3,5-dimethyl-4-tosyl-1H-pyrazole (**4l**).* The title compound was obtained as a white solid (140.6 mg, 66%). Mp 159−160 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.55 (d, J = 8.8 Hz, 2H), 7.32 (t, J = 8.0 Hz, 2H), 2.86 (s, 3H), 2.43 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.7, 146.9, 144.6, 142.0, 139.1, 135.3, 130.0, 129.6, 126.7, 122.1, 21.5, 13.7, 11.7; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{18}H_{17}ClN_2O_4S_2Na$: 447.0216; found: 447.0225.

*1-((4-Bromophenyl)sulfonyl)-3,5-dimethyl-4-tosyl-1H-pyrazole (**4m**).* The title compound was obtained as a white solid (126.7 mg, 54%). Mp 198−199 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.4 Hz, 2H), 7.77−7.68 (m, 4H), 7.32 (d, J = 8.0 Hz, 2H), 2.85 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.7, 146.9, 144.6, 139.1, 135.8, 133.0, 130.7, 130.0, 129.6, 126.7, 122.1, 21.5, 13.7, 11.7; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{18}H_{17}BrN_2O_4S_2Na$: 490.9711; found: 490.9715.

*1-((4-Iodophenyl)sulfonyl)-3,5-dimethyl-4-tosyl-1H-pyrazole (**4n**).* The title compound was obtained as a white solid (149.2 mg, 58%). Mp 184−186 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.8 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 2.85 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.6, 146.9, 144.6, 139.1, 138.9, 136.4, 129.9, 129.2, 126.7, 122.1, 103.5, 21.5, 13.7, 11.7; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{18}H_{17}IN_2O_4S_2Na$: 538.9572; found: 538.9573.

*3,5-Dimethyl-1-((4-nitrophenyl)sulfonyl)-4-tosyl-1H-pyrazole (**4o**).* The title compound was obtained as a white solid (115.2 mg, 53%). Mp 228−230 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 9.2 Hz, 2H), 8.21 (d, J = 8.8 Hz, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H), 2.89 (s, 3H), 2.43 (s, 3H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.5, 151.3, 147.5, 144.9, 142.3, 139.0, 130.1, 129.8, 126.8, 124.8, 122.8, 21.6, 13.7, 11.8; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{18}H_{17}N_3O_6S_2Na$: 458.0456; found: 458.0459.

*1-((4-Cyanophenyl)sulfonyl)-3,5-dimethyl-4-tosyl-1H-pyrazole (**4p**).* The title compound was obtained as a white solid (130.7 mg, 63%). Mp 210−211 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 2.88 (s, 3H), 2.43 (s, 3H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.3, 147.4, 144.8, 140.8, 138.9, 133.3, 130.0, 128.9, 126.8, 122.6, 118.7, 116.6, 55.8, 21.6, 13.7, 11.8; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{19}H_{17}N_3O_4S_2Na$: 438.0560; found: 438.0558.

*1-((2-Chlorophenyl)sulfonyl)-3,5-dimethyl-4-tosyl-1H-pyrazole (**4q**).* The title compound was obtained as a white solid (110.4 mg, 52%). Mp 139−141 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.62 (td, J = 7.8, 1.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 2.95 (s, 3H), 2.43 (s, 3H), 2.30 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.5, 148.9, 144.5, 139.3, 135.9, 134.8, 132.9, 132.4, 132.2, 129.9, 127.6, 126.6, 121.2, 21.5, 13.6, 12.1; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{18}H_{17}ClN_2O_4S_2Na$: 447.0216; found: 447.0219.

*8-((3,5-Dimethyl-4-tosyl-1H-pyrazol-1-yl)sulfonyl)quinoline (**4r**).* The title compound was obtained as a white solid (112.7 mg, 51%). Mp 204−206 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (dd, J = 8.4, 1.6 Hz, 1H), 8.68 (dd, J = 7.2, 1.2 Hz, 1H), 8.22 (dd, J = 8.4, 1.6 Hz, 1H), 8.15 (dd, J = 8.4, 1.2 Hz, 1H), 7.78−7.68 (m, 3H), 7.48 (dd, J = 8.4, 4.4 Hz, 1H), 7.31 (d, J = 8.4 Hz, 2H), 3.24 (s, 3H), 2.44 (s, 3H), 2.22 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.3, 151.2, 151.0, 144.2,

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143.4, 139.8, 136.6, 135.7, 134.0, 133.4, 129.8, 128.7, 126.6, 125.5, 122.5, 120.5, 21.5, 13.7, 12.6; HRMS (TOFMS) m/z $[M + Na]^+$ calcd for $C_{21}H_{19}N_3O_4S_2Na$: 464.0715; found: 464.0717.

*3,5-Dimethyl-1-(thiophen-2-ylsulfonyl)-4-tosyl-1H-pyrazole (**4s**).* The title compound was obtained as a white solid (101.3 mg, 51%). Mp 146−147 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, J = 3.6, 1.2 Hz, 1H), 7.79 (dd, J = 4.8, 1.2 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.16 (t, J = 4.6 Hz, 1H), 2.88 (s, 3H), 2.43 (s, 3H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.5, 146.8, 144.6, 139.1, 136.4, 136.2, 135.8, 129.9, 128.1, 126.7, 122.1, 21.5, 13.7, 11.8; HRMS (TOFMS) m/z $[M + Na]^+$ calcd for $C_{16}H_{16}N_2O_4S_3Na$: 419.0170; found: 419.0175.

*3,5-Dimethyl-1-(propylsulfonyl)-4-tosyl-1H-pyrazole (**4t**).* The title compound was obtained as a white solid (80.9 mg, 45%). Mp 97−98 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 3.51−3.42 (m, 2H), 2.83 (s, 3H), 2.43 (s, 6H), 1.83−1.71 (m, 2H), 1.04 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.4, 147.6, 144.6, 139.2, 130.0, 126.6, 121.6, 56.2, 21.5, 16.5, 13.6, 12.4, 11.5; HRMS (TOFMS) m/z $[M + Na]^+$ calcd for $C_{15}H_{20}N_2O_4S_2Na$: 379.0762; found: 379.0762.

*5-Isobutyl-3-methyl-1,4-ditosyl-1H-pyrazole (**4u**).*[14a] The title compound was obtained as a white solid (155.8 mg, 70%). Mp 166−167 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 3.29 (d, J = 7.6 Hz, 2H), 2.44 (s, 3H), 2.42 (s, 3H), 2.29−2.17 (m, 4H), 0.98 (s, 3H), 0.97 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.4, 151.3, 146.3, 144.3, 139.3, 134.2, 129.9, 129.7, 128.4, 126.8, 121.4, 32.8, 30.1, 22.1, 21.7, 21.5, 13.7.

*3-Methyl-5-pentyl-1,4-ditosyl-1H-pyrazole (**4v**).* The title compound was obtained as a white solid (128.8 mg, 56%). Mp 111−113 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 3.30−3.22 (m, 2H), 2.45 (s, 3H), 2.42 (s, 3H), 2.33 (s, 3H), 1.63−1.49 (m, 2H), 1.47−1.28 (m, 4H), 0.91 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.8, 151.3, 146.4, 144.4, 139.3, 134.1, 130.0, 129.8, 128.3, 126.8, 120.8, 31.9, 30.2, 25.4, 22.1, 21.7, 21.5, 13.9, 13.7; HRMS (TOFMS) m/z $[M + Na]^+$ calcd for $C_{23}H_{28}N_2O_4S_2Na$: 483.1388; found: 483.1388.

*3-Methyl-5-phenyl-1,4-ditosyl-1H-pyrazole (**4w**).*[14a,b] The title compound was obtained as a white solid (187.8 mg, 80%). Mp 184−186 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.56−7.48 (m, 3H), 7.37 (t, J = 7.8 Hz, 2H), 7.30−7.22 (m, 4H), 7.13−7.03 (m, 4H), 2.57 (s, 3H), 2.42 (s, 3H), 2.35 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.0, 147.8, 146.4, 144.2, 138.5, 133.8, 130.6, 130.1, 129.9, 129.3, 128.3, 127.3, 127.1, 126.2, 124.1, 21.7, 21.5, 14.0.

*3-Methyl-5-(p-tolyl)-1,4-ditosyl-1H-pyrazole (**4x**).* The title compound was obtained as a white solid (173.7 mg, 72%). Mp 186−187 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.0 Hz, 2H), 7.34−7.23 (m, 4H), 7.19 (d, J = 7.6 Hz, 2H), 7.12 (d, J = 7.6 Hz, 2H), 6.98 (d, J = 7.6 Hz, 2H), 2.54 (s, 3H), 2.47 (s, 3H), 2.43 (s, 3H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.0, 148.2, 146.3, 144.2, 140.3, 138.6, 133.9, 130.5, 129.8, 129.3, 128.3, 128.1, 127.1, 124.0, 123.1, 21.6, 21.5, 21.4, 14.0; HRMS (TOFMS) m/z $[M + Na]^+$ calcd for $C_{25}H_{24}N_2O_4S_2Na$: 503.1075; found: 503.1083.

*5-(4-Methoxyphenyl)-3-methyl-1,4-ditosyl-1H-pyrazole (**4y**).*[14b] The title compound was obtained as a white solid (169.7 mg, 68%). Mp 211−213 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.6 Hz, 2H), 7.32−7.21 (m, 4H), 7.12 (d, J = 7.2 Hz, 2H), 7.01 (d, J = 7.6 Hz, 2H), 6.89 (d, J = 7.6 Hz, 2H), 3.90 (s, 3H), 2.55 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.0, 151.0, 148.2, 146.3, 144.2, 138.7, 134.0, 132.2, 129.9, 129.3, 128.3, 127.1, 124.1, 117.9, 112.8, 55.3, 21.7, 21.5, 14.1.

*3-Methyl-5-(naphthalen-1-yl)-1,4-ditosyl-1H-pyrazole (**4z**).* The title compound was obtained as a white solid (193.4 mg, 75%). Mp 200−203 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.45−7.35 (m, 3H), 7.29−7.21 (m, 1H), 7.11 (d, J = 7.6 Hz, 2H), 7.08−6.99 (m, 3H), 6.76 (d, J = 8.0 Hz, 2H), 6.67 (d, J = 8.8 Hz, 1H), 2.68 (s, 3H), 2.36 (s, 3H), 2.12 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.0, 146.3, 145.8, 143.9, 137.5, 133.3, 132.6, 132.0, 130.7, 129.7, 129.5, 128.9, 128.5, 128.0, 127.1, 126.3, 125.7, 125.1, 124.9, 124.3, 123.8, 21.6, 21.2, 14.2; HRMS (TOFMS) m/z $[M + Na]^+$ calcd for $C_{28}H_{24}N_2O_4S_2Na$: 539.1075; found: 539.1082.

*5-(4-Fluorophenyl)-3-methyl-1,4-ditosyl-1H-pyrazole (**4A**).* The title compound was obtained as a white solid (172.4 mg, 71%). Mp 177−180 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.0 Hz, 2H), 7.33−7.23 (m, 4H), 7.14 (d, J = 7.6 Hz, 2H), 7.11−7.03 (m, 4H), 7.15 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 2.55 (s, 3H), 2.44 (s, 3H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.8 (d, J = 250.3 Hz), 151.0, 146.7 (d, J = 23.6 Hz), 144.4, 138.5, 133.8, 132.8 (d, J = 8.6 Hz), 130.0, 129.4, 128.3, 127.0, 124.3, 122.1 (d, J = 3.3 Hz), 114.8, 114.6, 21.7, 21.4, 14.0; HRMS (TOFMS) m/z $[M + Na]^+$ calcd for $C_{24}H_{21}N_2O_4S_2FNa$: 507.0824; found: 507.0836.

*5-(4-Chlorophenyl)-3-methyl-1,4-ditosyl-1H-pyrazole (**4B**).*[14b] The title compound was obtained as a white solid (190.8 mg, 76%). Mp 189−191 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.34−7.24 (m, 4H), 7.15 (d, J = 7.6 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 2.55 (s, 3H), 2.44 (s, 3H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.2, 146.7, 146.6, 144.6, 138.5, 136.7, 133.8, 132.0, 130.0, 129.5, 128.4, 127.8, 127.1, 124.7, 124.1, 21.7, 21.5, 14.0.

*5-(4-Bromophenyl)-3-methyl-1,4-ditosyl-1H-pyrazole (**4C**).* The title compound was obtained as a white solid (203.3 mg, 74%). Mp 185−187 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 2.55 (s, 3H), 2.44 (s, 3H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.1, 146.6, 146.5, 144.5, 138.4, 133.7, 132.2, 130.7, 130.0, 129.5, 128.3, 127.1, 125.2, 124.9, 124.4, 21.7, 21.5, 13.9; HRMS (TOFMS) m/z $[M+H]^+$ calcd for $C_{24}H_{22}N_2O_4S_2Br$: 545.0204; found: 545.0204.

*5-(3-Chlorophenyl)-3-methyl-1,4-ditosyl-1H-pyrazole (**4D**).* The title compound was obtained as a white solid (166.5 mg, 66%). Mp 162−164 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 7.2 Hz, 2H), 7.48 (d, J = 8.0 Hz, 1H), 7.39−7.27 (m, 5H), 7.15 (d, J = 7.2 Hz, 2H), 7.05 (d, J = 7.2 Hz, 1H), 6.78 (s, 1H), 2.58 (s, 3H), 2.45 (s, 3H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.0, 146.7, 145.7, 144.6, 138.3, 133.7, 133.5, 130.3, 130.2, 130.1, 129.5, 128.9, 128.8, 128.4, 128.0, 127.2, 124.5, 21.7, 21.5, 14.0; HRMS (TOFMS) m/z $[M + Na]^+$ calcd for $C_{24}H_{21}N_2O_4S_2ClNa$: 523.0529; found: 523.0540.

*5-(Benzo[b]thiophen-2-yl)-3-methyl-1,4-ditosyl-1H-pyrazole (**4E**).* The title compound was obtained as a white solid (168.4 mg, 65%). Mp 199−201 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.87−7.78 (m, 2H), 7.69 (d, J = 7.6 Hz, 2H), 7.49−7.36 (m, 4H), 7.27 (d, J = 7.2 Hz, 2H), 7.14 (s, 1H), 7.03 (d, J = 7.6 Hz, 2H), 2.57 (s, 3H), 2.43 (s, 3H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.2, 146.7, 144.5, 141.7, 140.4, 138.2, 137.9, 133.6, 130.0, 129.8, 129.4, 128.6, 127.4, 126.0, 125.6, 124.75, 124.72, 124.5, 122.0, 21.7, 21.5, 14.1; HRMS (TOFMS) m/z $[M + Na]^+$ calcd for $C_{26}H_{22}N_2O_4S_3Na$: 545.0639; found: 545.0650.

*3-Methyl-5-(thiophen-3-yl)-1,4-ditosyl-1H-pyrazole (**4F**).* The title compound was obtained as a white solid (141.1 mg, 60%). Mp 206−208 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.0 Hz, 2H), 7.35−7.22 (m, 6H), 7.12 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 4.4 Hz, 1H), 2.57 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.1, 146.5, 144.3, 143.3, 138.5, 133.8, 129.9, 129.7, 129.4,

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128.3, 127.04, 124.8, 124.6, 124.4, 21.7, 21.5, 14.1; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{22}H_{20}N_2O_4S_3Na$: 495.0483; found: 495.0490.

*5-(Furan-2-yl)-3-methyl-1,4-ditosyl-1H-pyrazole (**4G**).* The title compound was obtained as a white solid (124.5 mg, 54%). Mp 194−196 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 2H), 7.64−7.59 (m, 1H), 7.51 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 6.72 (d, J = 3.6 Hz, 1H), 6.63−6.58 (m, 1H), 2.50 (s, 3H), 2.44 (s, 3H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.2, 146.6, 144.62, 144.56, 138.5, 137.5, 136.8, 133.7, 130.0, 129.6, 128.6, 127.2, 125.7, 116.3, 111.3, 21.7, 21.5, 13.9; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{22}H_{20}N_2O_5S_2Na$: 479.0711; found: 479.0717.

*2-(3-Methyl-1,4-ditosyl-1H-pyrazol-5-yl)pyridine (**4H**).* The title compound was obtained as a white solid (114.5 mg, 49%). Mp 196−198 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75−8.70 (m, 1H), 7.88−7.80 (m, 3H), 7.57 (d, J = 8.4 Hz, 2H), 7.50−7.43 (m, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 2.43 (s, 6H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.1, 148.8, 146.9, 146.43, 146.39, 144.4, 138.6, 135.6, 133.7, 130.0, 129.6, 128.8, 127.3, 126.6, 124.5, 123.7, 21.8, 21.5, 13.5; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{23}H_{21}N_3O_4S_2Na$: 490.0871; found: 490.0877.

*4-((4-Chlorophenyl)sulfonyl)-3-methyl-5-phenyl-1-tosyl-1H-pyrazole (**4I**).* The title compound was obtained as a white solid (152.1 mg, 62%). Mp 191−194 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58−7.49 (m, 3H), 7.38 (t, J = 7.8 Hz, 2H), 7.32−7.23 (m, 6H), 7.04 (d, J = 7.2 Hz, 2H), 2.58 (s, 3H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.8, 147.9, 146.5, 139.8, 139.7, 133.6, 130.5, 130.2, 129.9, 128.9, 128.5, 128.3, 127.4, 125.9, 123.4, 21.6, 14.0; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{23}H_{19}N_2O_4S_2ClNa$: 509.0372; found: 509.0376.

*4-((4-Fluorophenyl)sulfonyl)-3-methyl-5-phenyl-1-tosyl-1H-pyrazole (**4J**).* The title compound was obtained as a white solid (136.8 mg, 58%). Mp 181−183 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57−7.48 (m, 3H), 7.42−7.32 (m, 4H), 7.30−7.23 (m, 2H), 7.04 (d, J = 7.6 Hz, 2H), 6.96 (t, J = 8.4 Hz, 2H), 2.58 (s, 3H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.3 (d, J = 254.5 Hz), 150.9, 147.8, 146.5, 137.4 (d, J = 3.4 Hz), 133.7, 130.6, 130.3, 129.94 (d, J = 9.8 Hz), 129.93, 128.3, 127.5, 126.0, 123.6, 115.9 (d, J = 22.1 Hz), 21.7, 14.1; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{23}H_{19}N_2O_4S_2FNa$: 493.0668; found: 493.0674.

*4-(Ethylsulfonyl)-3-methyl-5-phenyl-1-tosyl-1H-pyrazole (**4K**).* The title compound was obtained as a white solid (128.7 mg, 64%). Mp 154−156 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60−7.51 (m, 3H), 7.49−7.41 (m, 2H), 7.31−7.22 (m, 4H), 2.72 (q, J = 7.2 Hz, 2H), 2.53 (s, 3H), 2.44 (s, 3H), 1.14 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.8, 148.4, 146.6, 133.9, 130.60, 130.55, 130.0, 128.4, 127.7, 126.0, 120.8, 50.7, 21.6, 13.9, 6.9; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{19}H_{20}N_2O_4S_2Na$: 427.0762; found: 427.0769.

*3-Methyl-5-phenyl-1-tosyl-4-((trifluoromethyl)sulfonyl)-1H-pyrazole (**4L**).* The title compound was obtained as a white solid (53.3 mg, 24%). Mp 139−142 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.4 Hz, 2H), 7.57 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 7.6 Hz, 2H), 2.53 (s, 3H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.0, 152.7, 147.2, 133.2, 130.8, 130.22, 130.18, 128.8, 127.5, 124.8, 119.6 (q, J = 322.7 Hz), 113.1, 21.8, 13.5; HRMS (TOFMS) m/z [M + Na]$^+$ calcd for $C_{18}H_{15}N_2O_4S_2F_3Na$: 467.0323; found: 467.0330.

Gram-Scale Reaction. To a 25 mL Schlenk tube were added 4-methylbenzenesulfonohydrazide (**1a**) (745 mg, 4.0 mmol), 1-phenylbutane-1,3-dione (**2d**) (779 mg, 4.8 mmol), sodium 4-methylbenzenesulfinate (**3b**) (1.43 g, 8.0 mmol), $K_2HPO_4{\cdot}3H_2O$ (730.6 mg, 3.2 mmol), I_2 (1.53 g, 6.0 mmol), and 12 mL of CH_3CN sequentially under air. Then, the tube was sealed and the reaction mixture was stirred at room temperature for 23 h. It was then quenched (consumption of residual I_2) with saturated $Na_2S_2O_3$ solution, forming a white precipitate. Filtration of the suspension gave the crude product. Washing the crude product with water (100 mL) and petroleum ether (100 mL) sequentially afforded the pure product **4w** as a white solid (1.57 g, 84%).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00171.

^{1}H NMR and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

Dedicated to the cherished memory of Dr. Negish.

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