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Note

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Substituent-Oriented Synthesis of Substituted Pyrazoles/ Chromeno[3,2-*c*]Pyrazoles *via* Sequential Reactions of Chromones/3-chlorochromones and Tosylhydrazones

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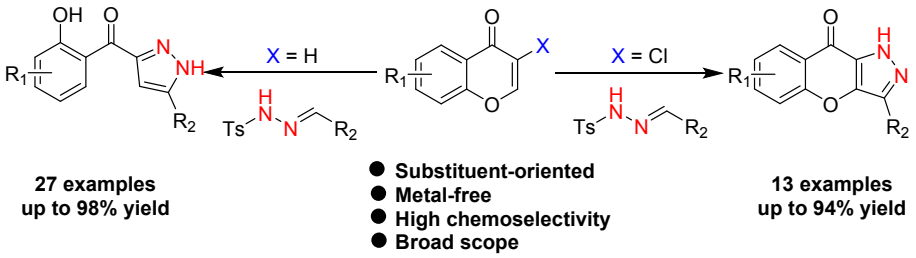


ABSTRACT: A facile and efficient synthetic strategy for chemoselective synthesis of monocyclic/tricyclic-fused pyrazoles was developed and it was oriented by different 3-position substituents (H or Cl) on the chromones. The reaction proceeded in a one-pot sequential way with a broad substrate scope and moderate to excellent yields.

Chromone and its derivatives, which are found in a wide variety of synthetic and natural products exhibiting important biological activities, are greatly useful building blocks for synthesis of various heterocycles due to their three strong electrophilic centres that could react with numerous nucleophilic reagents, especially as an excellent Michael reaction acceptor accompanied by ring-opening process.[1] Accordingly, simple, effective diversity-oriented synthesis based on chromones to construct bioactive heterocyclic scaffolds has piqued enough interest of synthetic chemists.

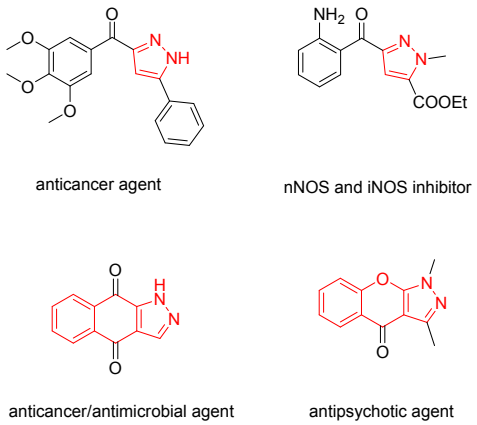
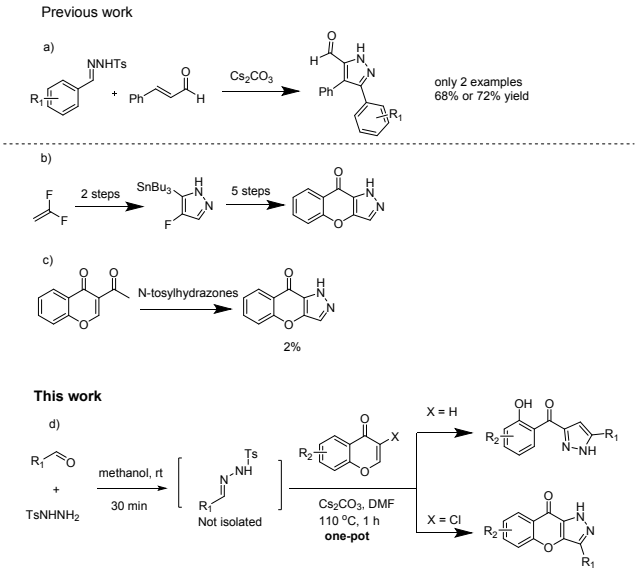


Figure 1. Representative examples of bioactive monocyclic/tricyclic-fused pyrazole derivatives.

Among those bioactive heterocyclic scaffolds, pyrazoles are fascinating and versatile examples of five-membered heterocycles with broad pharmaceutical and agrochemical activities including antitumor[2], antimicrobial[3], anti-hypercholesterolemia[4], anti-inflammatory[5], and inhibitory activity towards nNOS/iNOS[6] (Figure 1). Additionally, as an important subset of fused compounds, tricyclic-fused pyrazoles have also shown excellent properties such as lower toxicity and higher activity due to the introduction of other heterocycles,[7] which enables themselves to become promising structural cores of various pharmacologically active substances (Figure 1).[8] Besides the classic numerous accesses to monocyclic pyrazoles (condensation reaction and 1, 3-dipolar cycloaddition reaction using alkynes or alkenes with appropriate leaving groups)[9], this scaffold also had been synthesized *via* the reaction of cinnamaldehyde and tosylhydrazone recently, only two examples being given with lower regioselectivity and moderate yields (Scheme 1a).[10] However, the synthesis of tricyclic chromeno[3,2-*c*]pyrazoles is extremely limited. The reported procedure involved a side reaction of 3-acetylchromone with diazomethane[11] (Scheme 1c) or a multistep synthesis starting from 1, 1-difluoroethylene[12] (Scheme 1b), which have been known to suffer from obvious drawbacks. Recently, an attempt using *N*-tosylhydrazones and chromone-3-carboxaldehyde had been made to synthesize this kind of compounds, but xanthones instead of chromeno[3,2-*c*]pyrazoles were obtained.[13] Owing to all mentioned above, it is still challenging and highly desirable to design a practical and straightforward synthetic method for constructing monocyclic/tricyclic-fused pyrazoles simultaneously, especially by substituent-oriented synthesis strategy with a tunable atom (H or Cl) from easily obtained starting materials.

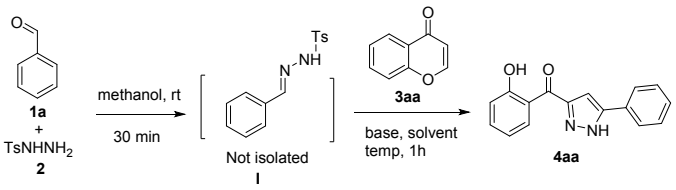
Scheme 1. Strategies for Synthesis of Monocyclic Pyrazoles/ Chromeno[3,2-*c*]Pyrazoles



Inspired by our previous studies on constructing bioactive heterocyclic scaffolds based on chromones[14], we envisioned that a one-pot reaction of tosylhydrazones and chromones/3-halogenated chromones in the presence of a base could be achieved to prepare ring-opening and ring-closing products under the same reaction conditions (Scheme 1d). As we expected, monocyclic/tricyclic-fused pyrazoles were chemoselectively obtained respectively, which was controlled by using different substituents on 3-position of chromones (H or Cl). The structures of two products **4ao**[15] and **5a**[16] were unambiguously confirmed by X-ray crystallographic analysis (shown in Supporting Information).

At the outset of our study, we treated chromone (**3aa**) with benzaldehyde (**1a**) and tosylhydrazide (**2**) as the model substrates in a one-pot, two-step sequential version to optimize the reaction conditions (Table 1). To our delight, NaOH as the base and DMF as the solvent at 110 °C for 1 h led to a 72% yield (Table 1, entry 1). Motivated by this result, a range of bases were tested, suggesting that the bases of this reaction had a significant effect on the isolated yields of the product (Table 1, entries 1-6). Among them Cs_2CO_3 was found to be the optimal base with an excellent yield of 98% (Table 1, entry 2), while no desired product was detected as for Na_3PO_4, Na_2CO_3, and Et_3N (Table 1, entries 3, 5, and 6). Subsequently, screening of solvents indicated that polar solvents were favorite in the reactions and DMF was the best choice as well as DMSO (Table 1, entries 7-11 *vs* 2). Besides, further studies showed that increasing the amount of **1a** and **2** had no obvious effect on the yield (Table 1, entry 12), whereas a decrease for **1a** and **2** led to incomplete full conversion of the starting material (Table 1, entry 13). Taking temperature into consideration, we found lower the temperature to 80 °C could decrease the yield obviously (Table 1, entry 14). Actually, we have also investigated the one-pot, one-step way and one-pot, two-step way without the concentration process of tosylhydrazone intermediate respectively, however, the yield of pyrazole **4aa** was not satisfactory (Table 1, entries 15 and 16). Therefore, the optimal reaction conditions were found to include benzaldehyde (1.2 equiv.), tosylhydrazide (1.4 equiv.) and Cs_2CO_3 (3.0 equiv.) in DMF (2.0 mL) at 110 °C for 1 h.

Table 1. Optimization of Reaction Conditions[a]



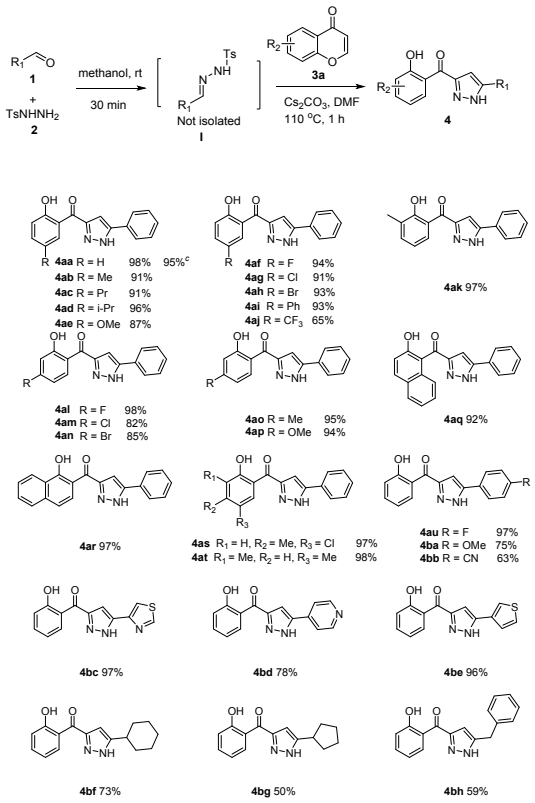
entry	base	solvent	temp (°C)	yield[b] (%)
1	NaOH	DMF	110	72
2	**Cs_2CO_3**	**DMF**	**110**	**98**
3	Na_3PO_4	DMF	110	n.d.
4[c]	t-BuONa	DMF	110	78
5	Na_2CO_3	DMF	110	n.d.
6	Et_3N	DMF	110	n.d.
7	Cs_2CO_3	EtOH	110	10
8	Cs_2CO_3	toluene	110	n.d.
9	Cs_2CO_3	dioxane	110	52
10	Cs_2CO_3	DMSO	110	95
11	Cs_2CO_3	MeCN	110	33
12[c]	Cs_2CO_3	DMF	110	97
13[d]	Cs_2CO_3	DMF	110	90
14	Cs_2CO_3	DMF	80	58
15[e]	Cs_2CO_3	DMF	110	48
16[f]	Cs_2CO_3	methanol /DMF	110	82

[a] Reaction conditions: **1a** (0.36 mmol, 1.2 equiv.) and **2** (0.42 mmol, 1.4 equiv.) in methanol (2.0 mL) were stirred for 30 min at rt and evaporated to dryness; then compound **3aa** (0.3 mmol, 1.0 equiv.), base (0.9 mmol, 3.0 equiv.) and solvent (2.0 mL) were added, heated for another 1 h. [b] Isolated yields. [c] 1.5 equiv. of **1a** and 1.8 equiv. of **2** were used. [d] 1.0 equiv. of **1a** and 1.2 equiv. of **2** were used. [e] A one-pot, one-step method was used. [f] A one-pot, two-step method without concentration was used.

With the optimal conditions identified, we embarked on exploring the scope of this method with a variety of substrates. The results for 29 successful examples are summarized in Scheme 2. Pleasingly, various substituted chromones with electron-donating groups or electron-withdrawing groups were broadly tolerated, furnishing pyrazoles **4aa–4bh** in good to excellent yields regardless of steric hindrances and substitution positions on the aromatic ring. Moreover, multi-substituted chromones including fused-chromones such as naphthalene derivatives also delivered the corresponding products in excellent yields (Scheme 2, **4aq-4at**,). To further explore the one-pot, two-step sequential synthesis of pyrazoles, the scope of aldehydes was then surveyed (Scheme 2, **4au-4bh**). As illustrated in Scheme 2, the aromatic aldehydes bearing electron-withdrawing group afforded better yield of the corresponding product than that with electron-donating group (Scheme 2, **4au** *vs* **4ba**), whereas strong electron-withdrawing groups such as cyano group gave a relatively lower yield (Scheme 2, 4**bb**). Heteroaromatics were also compatible with the reaction (Scheme 2. **4bc-4be**). Gratifyingly, aliphatic aldehydes were found to be suitable

substrates as well under the standard conditions leading to the desired products in acceptable yields (Scheme 2, **4bf-4bh**), which provided a novel strategy for introduction of various aliphatic chains or alicyclic rings to pyrazole skeleton.

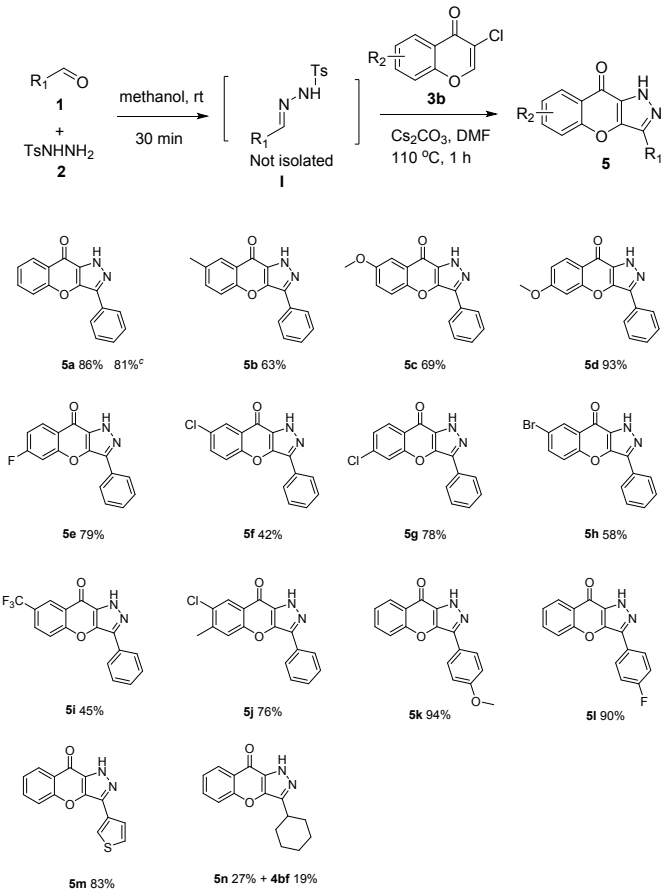
Scheme 2. Synthesis of Monocyclic Pyrazoles *via* One-Pot, Two-Step Reaction of Aldehydes, Tosylhydrazide, and Chromones[a, b]



[a] Reaction conditions: **1** (0.36 mmol, 1.2 equiv.) and **2** (0.42 mmol, 1.4 equiv.) in methanol (2.0 mL) were stirred for 30 min at rt and evaporated to dryness; then compound **3a** (0.3 mmol, 1.0 equiv.), base (0.9 mmol, 3.0 equiv.) and solvent (2.0 mL) were added, heated for another 1 h. [b] Isolated yields. [c] The procedure was scaled up to a gram scale.

After successfully synthesizing monocyclic pyrazoles from 3-unsubstituted-chromones, we turned our attention to 3-chlorochromones (Scheme 3). As expected, the reaction underwent further cyclization to form the tricyclic system, and the yield of the product **5a** was 86% under previous optimized conditions (Scheme 3, **5a**). Notably, the efficiency of this transformation was significantly influenced by the electronic properties of the substituents on the chromone ring, on which with electron-donating groups showing more favorable reactivity than those electron-withdrawing groups in terms of isolated yields (Scheme 3, **5b**, **5c** *vs* **5f**, **5h**, **5i**; **5d** *vs* **5e**, **5g**). In addition, both substrates of aromatic aldehydes with electron-donating groups and electron-withdrawing substituents performed well to give similar results (Scheme 3, **5k**, **5l**), while no desired product was obtained for 4-nitrobenzaldehyde. This may be caused by the unstability of 4-nitrobenzaldehyde in the presence of base and nucleophile. The reaction of heteroaromatic aldehyde also proceeded smoothly and provided very good yield (Scheme 3, **5m**). However, a relatively lower yield was obtained when aliphatic aldehyde such as cyclohexanaldehyde was used, and quite a few ring-opening byproducts were produced simultaneously (Scheme 3, **5n**).

Scheme 3. Synthesis of Tricyclic Chromeno[3,2-*c*]Pyrazoles [a, b]

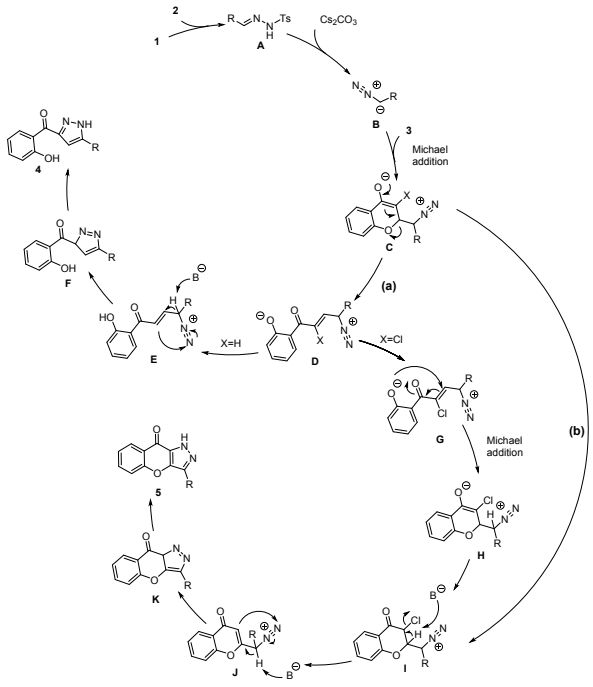


[a] Reaction conditions: **1** (0.36 mmol, 1.2 equiv.) and **2** (0.42 mmol, 1.4 equiv.) in methanol (2.0 mL) were stirred for 30 min at rt and evaporated to dryness; then compound **3b** (0.3 mmol, 1.0 equiv.), base (0.9 mmol, 3.0 equiv.) and solvent (2.0 mL) were added, heated for another 1 h. [b] Isolated yields. [c] The procedure was scaled up to a gram scale.

To demonstrate the synthetic utility of our protocol, we scaled up the reaction to a gram scale, whereby the monocyclic and tricyclic-fused pyrazole **4aa** and **5a** were furnished with yields of 95% and 81%, respectively (Scheme 2, Scheme 3).

Differential formation of monocyclic or tricyclic-fused pyrazoles could be explained by plausible mechanisms as depicted in Scheme 4. The common steps involve the formation of hydrazone intermediate **A** generated from condensation of aldehyde **1** and tosylhydrazine **2**, which subsequently transforms into intermediate **B** in the presence of Cs_2CO_3. Then an intermolecular Michael addition between **3** and **B** affords intermediate **C** which undergoes ring opening to give intermediate **D** based on the literature precedents (path a)[14a,c,d]. However, different pathways appear when chromones with different atoms/groups on position 3 are introduced. 3-Unsubstituted undergo an intramolecular cyclization reaction under alkaline conditions followed by a 1, 3-hydrogen shift to yield the monocyclic pyrazole products **4**, while 3-chlorochromones experience more complicated procedures, including an intramolecular Michael addition and keto-enol tautomerism to produce intermediate **I**. Afterwards, Cl^- would be eliminated from **I** to provide intermediate **J**. Finally, **J** could be converted to the tricyclic pyrazole products **5** *via* an intramolecular cyclization and a 1, 5-hydrogen shift similar to monocyclic products **4**. Moreover, intermediate **I** might be obtained from intermediate **C** directly without the ring-opening/ring-closing process to furnish the tricyclic-fused pyrazoles as well (path b). Besides, the possibility of a [3 + 2]-cycloaddition mechanism for synthesis of the two skeletons could not be excluded.

Scheme 4. Proposed Mechanism



In conclusion, we have demonstrated a one-pot sequential reaction for chemoselective synthesis of monocyclic pyrazoles and tricyclic-fused pyrazoles, which was oriented by different substituents on position 3 of chromones. This practical and easily handled protocol, with good substrate availability and great regioselectivity, could occur under a broad substrate scope in short reaction time without any extra additive metal. Moreover, the reactions could be carried out in moderate to excellent yields and scaled-up easily. Further studies on the application of these products are under investigation in our laboratory.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all solvents and other reagents are commercially available and used without further purification. All reagents were weighed and handled in air at room temperature. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 300-400 mesh silica gel in petroleum ether. NMR spectra were recorded on Brucker AVANCE 300 NMR spectrometer or Brucker AVANCE III 400 NMR spectrometer or Brucker AVANCE III 500 NMR spectrometeror or Brucker AVANCE III 600 NMR spectrometer. Chemical shifts were reported in parts per million (ppm, δ). Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), heptet (hept), multipet (m) and broad (br). Low and high-resolution mass spectra (LRMS and HRMS) were recorded on a Finnigan/MAT-95 (EI), Finnigan LCQ/DECA and Micromass Ultra Q-TOF (ESI) spectrometer. Melting points were measured by Büchi 510 melting point apparatus.

General procedure for the synthesis of chromones. All synthesized starting chromenones **3aa-3at** were known compounds. However, only a CAS Registry Number existed for **3aj** by SciFinder searching. The chromones were prepared by the addition of the corresponding substituted *o*-hydroxyacetophenone (2 mmol) with *N*, *N*-dimethylformamide dimethyl acetal (DMF-DMA), followed by cyclization by

hydrogen chloride according to a reported protocol except compound **3aq** and **3ar**.[14c,17] The cyclization process of **3aq** and **3ar** was completed without anything[18] or by T3P®[19], respectively.

6-(trifluoromethyl)-4*H*-chromen-4-one (3aj): As a light yellow solid (317 mg, 74%), m. p. 50-53 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (s, 1H), 7.93 – 7.87 (m, 2H), 7.59 (d, *J* = 8.8 Hz, 1H), 6.41 (d, *J* = 6.1 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 176.4, 158.0, 155.6, 130.2 (d, *J* = 3.2 Hz), 127.8 (q, *J* = 33.7 Hz), 124.7, 124.0 (q, *J* = 4.0 Hz), 123.4 (d, *J* = 272.4 Hz), 119.4, 113.5. HRMS (EI-DFS) m/z: [M]$^+$ calcd for $C_{10}H_5F_3O_2$, 214.0236; found 214.0238.

General procedure for the synthesis of 3-chlorochromones. All synthesized starting 3-chlorochromenones **3ba-3bh** were known compounds except compound **3bi**, and **3bj** also only had a CAS Registry Number. 3-Chlorochromones were prepared by the addition of the corresponding substituted *o*-hydroxyacetophenone (2 mmol) with *N*, *N*-dimethylformamide dimethyl acetal (DMF-DMA), followed by cyclization and an chlorination process by iodine monochloride (**3ba-3bc, 3be-3bh**)[14a,20] or *N*-Chlorosuccinimide (NCS) (**3bd, 3bi, 3bj**)[1b,21] according to a reported protocol.

3-chloro-6-(trifluoromethyl)-4*H*-chromen-4-one (3bi): As a white solid (278 mg, 56%), m. p. 121-123 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.60 – 8.57 (m, 1H), 8.21 (s, 1H), 7.94 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 171.4, 157.4, 152.4, 130.6 (d, *J* = 3.1 Hz), 128.4 (q, *J* = 33.9 Hz), 124.5 (q, *J* = 4.1 Hz), 123.3, 123.2 (q, *J* = 272.5 Hz), 121.7, 119.5. HRMS (EI-DFS) m/z: [M]$^+$ calcd for $C_{10}H_4ClF_3O_2$, 247.9846; found 247.9845.

3,6-dichloro-7-methyl-4*H*-chromen-4-one (3bj): As a white solid (420 mg, 92%), m. p. 148-150 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.19 (s, 1H), 8.12 (s, 1H), 7.37 (s, 1H), 2.51 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 154.2, 151.9, 143.6, 132.5, 125.6, 122.3, 120.6, 119.8, 20.8. HRMS (EI-DFS) m/z: [M]$^+$ calcd for $C_{10}H_6Cl_2O_2$, 227.9739; found 227.9732.

General procedure for the synthesis of monocyclic substituted-pyrazoles(4aa–4bh). A 5 mL reaction tube equipped with a magnetic stirrer was charged with aldehyde (0.36 mmol), tosylhydrazide (78 mg, 0.42 mmol), methanol (2 mL). The mixture was stirred at room temperature for 30 min. After removing the solvent in vacuo, chromones (0.3 mmol), Cs_2CO_3 (293 mg, 0.9 mmol), and DMF (2 mL) were added, and the reaction mixture was heated at 110 °C under open atmosphere until pyrazole formation was complete. Then the mixture was extracted with EtOAc (10 mL × 3), and washed with brine (10 mL), dried over anhydrous Na_2SO_4 and evaporated to dryness to yield a crude reaction product, which was purified by silica gel chromatography eluted with PE: EtOAc = 5:1 to give the product as yellow solid.

Gram-scale preparation of 4aa. A 100 mL reaction tube equipped with a magnetic stirrer was charged with benzaldehyde (836 μL, 8.22 mmol), tosylhydrazide (1786 mg, 9.59 mmol), methanol (40 mL). The mixture was stirred at room temperature for 30 min. After removing the solvent in vacuo, chromones (1000 mg, 6.85 mmol), Cs_2CO_3 (6696 mg, 20.55 mmol), and DMF (40 mL) were added, and the reaction mixture was heated at 110 °C under open atmosphere until pyrazole formation was complete. Then the mixture was extracted with EtOAc (40 mL × 3), and washed with brine (40 mL), dried over anhydrous Na_2SO_4 and evaporated to dryness to yield a crude reaction product, which was purified by silica gel chromatography eluted with PE: EtOAc = 5:1 to give the product as yellow solid (1719 mg, 95%).

(2-hydroxyphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4aa): As a light yellow solid (78 mg, 98%), m. p. 155-157 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 12.02 (s, 1H), 8.46 (d, *J* = 8.0 Hz, 1H), 7.78 – 7.71 (m, 2H), 7.54 (ddd, *J* = 8.7, 7.2, 1.7 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.43 – 7.38 (m, 1H), 7.21 (s, 1H), 7.07 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.01 – 6.95 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ

189.4, 163.4, 136.7, 132.4, 130.1, 129.1, 129.0, 125.7, 119.2, 119.1, 118.5, 106.7. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{14}N_2O_2$, 265.0972; found 265.0965.

(2-hydroxy-5-methylphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ab): As a light yellow solid (76 mg, 91%), m. p. 171-173 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.24 – 8.15 (m, 1H), 7.93 – 7.85 (m, 2H), 7.50 (t, J = 7.7 Hz, 2H), 7.45 – 7.33 (m, 3H), 6.94 (d, J = 8.3 Hz, 1H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 189.8, 158.7, 145.9, 136.4, 132.4, 130.0, 129.5, 129.0, 128.0, 125.9, 121.5, 117.7, 106.3, 20.5. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{16}N_2O_2$, 279.1128; found 279.1121.

(2-hydroxy-5-propylphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ac): As a light yellow solid (83 mg, 91%), m. p. 109-110 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.42 – 8.16 (m, 1H), 7.90 (d, J = 7.7 Hz, 2H), 7.50 (t, J = 7.6 Hz, 2H), 7.46 – 7.33 (m, 3H), 6.96 (d, J = 8.4 Hz, 1H), 2.59 – 2.51 (m, 2H), 1.60 (h, J = 7.4 Hz, 2H), 0.92 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 190.0, 159.2, 135.9, 132.8, 132.1, 129.5, 129.0, 125.9, 121.3, 117.7, 106.4, 36.8, 24.7, 14.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{20}N_2O_2$, 307.1441; found 307.1449.

(2-hydroxy-5-isopropylphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ad): As a light yellow solid (87 mg, 96%), m. p. 144-146 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 (s, 1H), 7.92 – 7.86 (m, 2H), 7.54 – 7.47 (m, 2H), 7.47 – 7.38 (m, 2H), 7.35 (s, 1H), 6.97 (d, J = 8.5 Hz, 1H), 2.97 – 2.84 (m, 1H), 1.23 (d, J = 6.9 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 189.9, 159.01, 145.6, 139.0, 133.9, 130.0, 129.5, 129.0, 125.9, 121.4, 117.8, 106.3, 33.0, 24.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{20}N_2O_2$, 307.1441; found 307.1445.

(2-hydroxy-5-methoxyphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ae): As a light yellow solid (77 mg, 87%), m. p. 136-139 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 – 7.74 (m, 3H), 7.50 (t, J = 7.6 Hz, 2H), 7.44 – 7.37 (m, 1H), 7.36 (s, 1H), 7.19 (dd, J = 9.0, 3.2 Hz, 1H), 6.97 (d, J = 9.0 Hz, 1H), 3.77 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 189.4, 154.8, 151.9, 129.5, 129.0, 125.9, 122.8, 121.8, 118.8, 115.6, 106.4, 56.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{16}N_2O_3$, 295.1077; found 295.1081.

(5-fluoro-2-hydroxyphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4af): As a light yellow solid (79 mg, 94%), m. p. 183-185 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.72 – 8.34 (m, 1H), 7.94 – 7.85 (m, 2H), 7.56 – 7.47 (m, 2H), 7.46 – 7.35 (m, 2H), 6.93 – 6.84 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 188.9, 166.4 (d, J = 252.7 Hz), 163.4, 135.6, 129.5, 129.1, 126.0, 118.8, 107.2 (d, J = 22.2 Hz), 106.4, 104.5 (d, J = 23.9 Hz). HRMS (EI-DFS) m/z: $[M]^+$calcd for $C_{16}H_{11}FN_2O_2$, 282.0799; found 282.0797.

(5-chloro-2-hydroxyphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ag): As a light yellow solid (82 mg, 91%), m. p. 191-193 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.60 – 8.04 (m, 1H), 7.88 (d, J = 7.6 Hz, 2H), 7.58 – 7.47 (m, 3H), 7.42 (t, J = 7.4 Hz, 1H), 7.34 (s, 1H), 7.05 (d, J = 8.8 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 188.9, 158.5, 134.2, 131.2, 129.6, 129.2, 125.9, 124.3, 122.8, 119.5, 106.1. HRMS (EI-DFS) m/z: $[M]^+$ calcd for $C_{16}H_{11}ClN_2O_2$, 298.0504; found 298.0509.

(5-bromo-2-hydroxyphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ah): As a light yellow solid (96 mg, 93%), m. p. 202-205 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.69 – 8.15 (m, 1H), 7.91 – 7.80 (m, 2H), 7.63 (dd, J = 8.8, 2.5 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.40 (t, J = 7.3 Hz, 1H), 7.32 (s, 1H), 6.98 (d, J = 8.8 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 189.4, 158.8, 137.0, 134.1, 129.6, 129.2, 125.9, 124.6, 120.0, 110.2, 106.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{13}BrN_2O_2$, 343.0077; found 343.0079.

(4-hydroxy-[1, 1'-biphenyl]-3-yl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ai): As a light yellow solid (96 mg, 93%), m. p. 156-158 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.72 (s, 1H), 7.94 – 7.88 (m, 2H), 7.85 (dd, J = 8.6, 2.4 Hz, 1H), 7.70 – 7.63 (m, 2H), 7.54 – 7.44 (m, 4H), 7.44 – 7.31 (m, 3H), 7.14 (d, J = 8.5 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 189.4, 159.6, 139.3, 133.0, 130.9, 130.2, 129.0, 128.9, 128.6, 127.0, 126.1, 125.4, 122.0, 117.9, 105.9. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{22}H_{18}N_2O_2$, 341.1285; found 341.1293.

(2-hydroxy-5-(trifluoromethyl)phenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone(4aj): As a light yellow solid (44 mg, 65%), m. p. 151-154 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.40 (s, 1H), 7.88 (d, J = 7.4 Hz, 2H), 7.66 (d, J = 7.7 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.36 (t, J = 7.3 Hz, 1H), 7.30 (s, 1H), 7.03 (d, J = 8.5 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 185.8, 165.6, 148.8, 131.2, 130.5, 129.8, 129.4, 128.6, 125.8, 125.3 (d, J = 270.5 Hz), 124.0, 121.3, 116.9, 105.5. HRMS (EI-DFS) m/z: [M]$^+$ calcd for $C_{17}H_{11}F_3N_2O_2$, 332.0767; found 332.0763.

(2-hydroxy-3-methylphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ak): As a light yellow solid (81 mg, 97%), m. p. 143-145 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.66 – 8.52 (m, 1H), 7.95 – 7.86 (m, 2H), 7.60 – 7.46 (m, 3H), 7.46 – 7.36 (m, 2H), 6.94 (t, J = 7.7 Hz, 1H), 2.25 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 190.9, 160.9, 145.3, 137.4, 131.3, 129.5, 129.1, 126.6, 126.0, 119.2, 118.9, 106.6, 15.9. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{17}H_{16}N_2O_2$, 279.1128; found 279.1120.

(4-fluoro-2-hydroxyphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4al): As a light yellow solid (82 mg, 98%), m. p. 167-170 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.83 – 8.30 (m, 1H), 7.93 – 7.83 (m, 2H), 7.50 (dd, J = 8.3, 6.8 Hz, 2H), 7.45 – 7.39 (m, 1H), 7.36 (s, 1H), 6.94 – 6.84 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 189.3, 166.4 (d, J = 252.4 Hz), 163.3, 135.6, 129.5, 129.1, 126.0, 118.8, 107.2 (d, J = 22.0 Hz), 106.3, 104.5 (d, J = 23.8 Hz). HRMS (EI-DFS) m/z: [M]$^+$ calcd for $C_{16}H_{11}FN_2O_2$, 282.0799; found 282.0798.

(4-chloro-2-hydroxyphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4am): As a light yellow solid (74 mg, 82%), m. p. 190-192 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.47 – 8.21 (m, 1H), 7.96 (dd, J = 7.3, 1.7 Hz, 2H), 7.58 (dd, J = 8.3, 6.8 Hz, 2H), 7.54 – 7.46 (m, 1H), 7.42 (s, 1H), 7.22 – 7.10 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 188.8, 160.7, 139.0, 133.8, 129.5, 129.1, 125.9, 121.8, 119.6, 117.4, 106.2. HRMS (EI-DFS) m/z: [M]$^+$ calcd for $C_{16}H_{11}ClN_2O_2$, 298.0504; found 298.0509.

(4-bromo-2-hydroxyphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4an): As a light yellow solid (88 mg, 85%), m. p. 200-202 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 – 8.00 (m, 1H), 7.94 – 7.85 (m, 2H), 7.51 (t, J = 7.6 Hz, 2H), 7.42 (t, J = 7.4 Hz, 1H), 7.34 (s, 1H), 17.25 (d, J = 1.8 Hz, 1H), 7.21 (dd, J = 8.4, 1.9 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 189.5, 160.3, 133.7, 129.5, 129.1, 127.8, 125.9, 122.4, 120.3, 106.2. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{16}H_{13}BrN_2O_2$, 343.0077; found 343.0085.

(2-hydroxy-4-methylphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ao):As a light yellow solid (80 mg, 95%), m. p. 155-158 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 12.10 (s, 1H), 8.30 (d, J = 8.2 Hz, 1H), 7.74 (d, J = 7.4 Hz, 2H), 7.49 – 7.41 (m, 2H), 7.41 – 7.35 (m, 1H), 7.18 (s, 1H), 6.87 (s, 1H), 6.77 (dd, J = 8.3, 1.6 Hz, 1H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 188.8, 163.6, 148.5, 132.2, 130.3, 129.1, 128.9, 125.8, 120.6, 118.5, 116.8, 106.6, 22.1. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{17}H_{16}N_2O_2$, 279.1128; found 279.1133.

(2-hydroxy-4-methoxyphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ap): As a light yellow solid (83 mg, 94%), m. p. 139-141 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 12.71 (s, 1H), 11.64 (s, 1H), 8.51 – 8.17 (m, 1H), 7.73 (d, J = 7.8 Hz, 2H), 7.48 – 7.32 (m, 3H), 7.19

– 7.09 (m, 1H), 6.55 – 6.42 (m, 2H), 3.85 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, Chloroform-*d*) δ 166.7, 166.6, 134.1, 129.0, 128.8, 125.7, 113.0, 108.1, 106.2, 101.1, 55.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{16}N_2O_3$, 295.1077; found 295.1086.

(2-hydroxynaphthalen-1-yl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4aq): As a light yellow solid (87 mg, 92%), m. p. 124-127 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 7.94 – 7.85 (m, 2H), 7.85 – 7.77 (m, 2H), 7.48 – 7.28 (m, 6H), 7.25 (d, *J* = 8.9 Hz, 1H), 7.13 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, DMSO-d_6) δ 153.1, 131.8, 131.0, 129.0, 128.4, 128.3, 127.6, 127.1, 125.5, 123.2, 123.0, 120.0, 118.7, 105.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{16}N_2O_2$, 315.1128; found 315.1133.

(1-hydroxynaphthalen-2-yl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4ar): As a yellow solid (92 mg, 97%), m. p. 185-188 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.89 – 8.67 (m, 1H), 8.38 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.94 – 7.84 (m, 3H), 7.71 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H), 7.59 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.49 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.45 – 7.36 (m, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, DMSO-d_6) δ 190.8, 163.0, 152.0, 143.9, 137.2, 130.9, 129.6, 129.2, 128.0, 127.7, 126.6, 126.0, 124.8, 124.2, 118.6, 113.2, 106.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{16}N_2O_2$, 315.1128; found 315.1127.

(5-chloro-2-hydroxy-3-methylphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4as): As a light yellow solid (90 mg, 97%), m. p. 194-196 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.87 – 8.30 (m, 1H), 7.89 – 7.80 (m, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.34 (s, 1H), 7.01 (s, 1H), 2.34 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, DMSO-d_6) δ 188.6, 159.8, 143.9, 132.4, 129.6, 129.2, 125.9, 123.5, 120.2, 106.1, 20.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{15}ClN_2O_2$, 313.0738; found 313.0743.

(2-hydroxy-3,5-dimethylphenyl)(5-phenyl-1*H*-pyrazol-3-yl)methanone (4at): As a yellow solid (86 mg, 98%), m. p. 135-137 °C. ^1H NMR (400 MHz, Chloroform-*d*) δ 12.08 (s, 1H), 8.01 – 7.90 (m, 1H), 7.73 (d, *J* = 7.4 Hz, 2H), 7.46 – 7.34 (m, 3H), 7.23 – 7.19 (m, 1H), 7.16 (s, 1H), 2.27 (s, 3H), 2.26 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 159.8, 138.9, 129.4, 129.0, 128.8, 127.6, 127.2, 125.8, 118.1, 106.8, 20.6, 15.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{18}N_2O_2$, 293.1285; found 293.1293.

(5-(4-fluorophenyl)-1*H*-pyrazol-3-yl)(2-hydroxyphenyl)methanone (4au): As a light yellow solid (82 mg, 97%), m. p. 155-158 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.31 – 8.16 (m, 1H), 7.90 (dd, *J* = 8.5, 5.4 Hz, 2H), 7.51 (ddd, *J* = 9.1, 7.3, 1.7 Hz, 1H), 7.36 – 7.24 (m, 3H), 7.06 – 6.92 (m, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, DMSO-d_6) δ 188.96, 162.07 (d, *J* = 245.6 Hz), 159.92, 134.96, 131.97, 127.59 (d, *J* = 8.4 Hz), 126.41, 121.64, 118.89, 117.36 (d, *J* = 4.2 Hz), 115.86 (d, *J* = 21.7 Hz), 105.97. HRMS (EI-DFS) m/z: $[M]^+$ calcd for $C_{16}H_{11}FN_2O_2$, 282.0799; found 282.0798.

(2-hydroxyphenyl)(5-(4-methoxyphenyl)-1*H*-pyrazol-3-yl)methanone (4ba): As a light yellow solid (65 mg, 75%), m. p. 155-157 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.57 – 8.28 (m, 1H), 7.84 – 7.75 (m, 2H), 7.53 (ddd, *J* = 8.7, 7.3, 1.7 Hz, 1H), 7.23 (s, 1H), 7.11 – 6.94 (m, 4H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, DMSO-d_6) δ 190.4, 160.8, 160.0, 135.6, 132.8, 127.4, 121.7, 119.4, 117.8, 114.9, 105.4, 55.7. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{16}N_2O_3$, 295.1077; found 295.1081.

4-(3-(2-hydroxybenzoyl)-1*H*-pyrazol-5-yl)benzonitrile (4bb): As a light yellow solid (55 mg, 63%), m. p. 170-172 °C. ^1H NMR (600 MHz, DMSO-d_6) δ 8.14 – 8.04 (m, 3H), 7.90 (d, *J* = 7.9 Hz, 2H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.44 (s, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.92 (t, *J* = 7.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, DMSO-d_6) δ 187.2, 160.2, 148.2, 146.8, 136.5, 134.9, 133.2, 132.0, 126.2, 123.2, 119.3, 118.7, 118.6, 110.2, 107.5. HRMS (EI-DFS) m/z: $[M]^+$ calcd for $C_{17}H_{15}N_2O_3$, 295.1077; found 295.1081.

(2-hydroxyphenyl)(5-(thiazol-4-yl)-1*H*-pyrazol-3-yl)methanone (4bc): As a light yellow solid (80 mg, 97%), m. p. 222-225 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.26 (d, J = 1.9 Hz, 1H), 8.51 – 8.24 (m, 1H), 8.22 (d, J = 2.0 Hz, 1H), 7.54 (ddd, J = 8.6, 7.2, 1.7 Hz, 1H), 7.30 (s, 1H), 7.08 – 6.95 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 189.8, 160.4, 155.8, 146.1, 135.5, 132.6, 122.1, 119.4, 117.8, 116.5, 106.9. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{13}H_{11}N_3O_2S$, 272.0488; found 272.0496.

(2-hydroxyphenyl)(5-(pyridin-4-yl)-1*H*-pyrazol-3-yl)methanone (4bd): As a light yellow solid (62 mg, 78%), m. p. 231-233 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.66 (d, J = 5.3 Hz, 2H), 8.07 (s, 1H), 7.93 – 7.84 (m, 2H), 7.59 – 7.48 (m, 2H), 7.08 – 6.96 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 188.2, 159.6, 150.8, 135.3, 131.9, 122.7, 120.1, 119.6, 117.7, 108.4. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{15}H_{13}N_3O_2$, 266.0924; found 266.0928.

(2-hydroxyphenyl)(5-(thiophen-3-yl)-1*H*-pyrazol-3-yl)methanone (4be): As a light yellow solid (78 mg, 96%), m. p. 170-172 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.44 – 8.23 (m, 1H), 8.00 (d, J = 3.2 Hz, 1H), 7.69 (dd, J = 5.0, 2.9 Hz, 1H), 7.62 (dd, J = 5.0, 1.3 Hz, 1H), 7.53 (ddd, J = 8.7, 7.2, 1.8 Hz, 1H), 7.24 (s, 1H), 7.07 – 6.95 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 189.7, 160.3, 135.2, 132.4, 131.0, 127.7, 126.0, 122.2, 121.7, 119.1, 117.5, 106.0. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{14}H_{12}N_2O_2S$, 271.0536; found 271.0538.

(5-cyclohexyl-1*H*-pyrazol-3-yl)(2-hydroxyphenyl)methanone (4bf): As a light yellow solid (59 mg, 73%), m. p. 107-109 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.53 – 8.43 (m, 1H), 7.57 – 7.51 (m, 1H), 7.04 – 6.94 (m, 2H), 6.70 (s, 1H), 2.76 (tt, J = 11.3, 3.7 Hz, 1H), 2.05 – 1.99 (m, 2H), 1.82 (dq, J = 10.9, 3.6 Hz, 2H), 1.74 (dd, J = 12.4, 4.0 Hz, 1H), 1.58 – 1.23 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 189.9, 161.3, 151.1, 149.2, 135.1, 132.7, 121.4, 118.4, 118.0, 104.7, 34.8, 32.4, 25.7, 25.6. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{16}H_{20}N_2O_2$, 271.1441; found 271.1443.

(5-cyclopentyl-1*H*-pyrazol-3-yl)(2-hydroxyphenyl)methanone (4bg): As a light yellow solid (43 mg, 56%), m. p. 113-115 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (d, J = 7.8 Hz, 1H), 7.55 – 7.45 (m, 1H), 7.01 – 6.89 (m, 2H), 6.66 (s, 1H), 3.10 (p, J = 8.1 Hz, 1H), 2.11 – 1.97 (m, 2H), 1.78 – 1.66 (m, 2H), 1.67 – 1.51 (m, 4H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 190.8, 161.3, 150.0, 135.6, 133.2, 121.4, 119.2, 117.8, 105.5, 36.5, 33.1, 25.1. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{15}H_{16}N_2O_2$, 257.1285; found 257.1285.

(5-benzyl-1*H*-pyrazol-3-yl)(2-hydroxyphenyl)methanone (4bh): As a light yellow solid (50 mg, 59%), m. p. 116-117 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.50 (s, 1H), 7.56 (ddd, J = 8.6, 7.2, 1.7 Hz, 1H), 7.42 – 7.27 (m, 5H), 7.07 – 6.97 (m, 2H), 6.72 (s, 1H), 4.11 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 190.6, 160.7, 138.8, 135.2, 132.6, 128.7, 128.6, 126.6, 121.2, 119.0, 117.5, 107.5, 31.3. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{17}H_{16}N_2O_2$, 279.1128; found 279.1133.

General procedure for the synthesis of chromeno[3,2-*c*]pyrazoles (5a-5n). A 5 mL reaction tube equipped with a magnetic stirrer was charged with aldehyde (0.36 mmol), tosylhydrazide (78 mg, 0.42 mmol), methanol (2 mL). The mixture was stirred at room temperature for 30 min. After removing the solvent in vacuo, 3-chlorochromone (0.3 mmol), Cs_2CO_3 (293 mg, 0.9 mmol),and DMF (2 mL) were added, and the reaction mixture was heated at 70 °C under open atmosphere until chromeno[3,2-*c*]pyrazoles formation was complete. Then the mixture was extracted with EtOAc (10 mL × 3), and washed with brine (10 mL), dried over anhydrous Na_2SO_4 and evaporated to dryness to yield a crude product, which was purified by silica gel chromatography eluted with PE: EtOAc = 2:1 to give the product as a yellow solid.

Gram-scale preparation of 5a. A 100 mL reaction tube equipped with a magnetic stirrer was charged with benzaldehyde (676 μL, 6.65

mmol), tosylhydrazide (1444 mg, 7.76 mmol), methanol (40 mL). The mixture was stirred at room temperature for 30 min. After removing the solvent in vacuo, 3-chlorochromone (1000 mg, 5.54 mmol), Cs_2CO_3 (5412 mg, 16.61 mmol), and DMF (40 mL) were added, and the reaction mixture was heated at 110 °C under open atmosphere until pyrazole formation was complete. Then the mixture was extracted with EtOAc (40 mL × 3), and washed with brine (40 mL), dried over anhydrous Na_2SO_4 and evaporated to dryness to yield a crude reaction product, which was purified by silica gel chromatography eluted with PE: EtOAc = 2:1 to give the product as yellow solid (1180 mg, 81%).

3-phenylchromeno[3,2-*c*]pyrazol-9(1*H*)-one (5a): As a light yellow solid (67 mg, 86%), m. p. 270-272 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 14.47 (s, 1H), 8.34 – 8.26 (m, 1H), 8.14 (d, J = 7.6 Hz, 2H), 7.95 – 7.85 (m, 2H), 7.62 – 7.52 (m, 3H), 7.45 (t, J = 7.4 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 168.3, 156.6, 143.5, 136.6, 135.3, 131.2, 129.5, 128.8, 127.9, 126.4, 126.1, 125.0, 122.6, 119.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{12}N_2O_2$, 263.0815; found 263.0818.

7-methyl-3-phenylchromeno[3,2-*c*]pyrazol-9(1*H*)-one (5b): As a light yellow solid (52 mg, 63%), m. p. >300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 14.44 (s, 1H), 8.17 – 8.09 (m, 2H), 8.07 – 8.03 (m, 1H), 7.77 (d, J = 8.6 Hz, 1H), 7.70 (dd, J = 8.7, 2.2 Hz, 1H), 7.56 (t, J = 7.7 Hz, 2H), 7.48 – 7.41 (m, 1H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 168.2, 154.9, 143.5, 136.5, 136.3, 134.4, 131.2, 129.5, 128.7, 127.9, 126.0, 125.6, 122.3, 119.1, 20.8. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{14}N_2O_2$, 277.0972; found 277.0972.

7-methoxy-3-phenylchromeno[3,2-*c*]pyrazol-9(1*H*)-one (5c): As a light yellow solid (60 mg, 69%), m. p. 265-268 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 14.45 (s, 1H), 8.13 (d, J = 7.7 Hz, 2H), 7.85 (d, J = 9.2 Hz, 1H), 7.64 (d, J = 3.1 Hz, 1H), 7.57 (t, J = 7.6 Hz, 2H), 7.50 (dd, J = 9.2, 3.2 Hz, 1H), 7.44 (t, J = 7.4 Hz, 1H), 3.90 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 168.0, 156.3, 151.3, 143.6, 136.4, 131.2, 129.5, 128.7, 127.6, 126.1, 124.3, 123.2, 120.9, 106.2, 56.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{14}N_2O_3$, 293.0921; found 293.0926.

6-methoxy-3-phenylchromeno[3,2-*c*]pyrazol-9(1*H*)-one (5d): As a light yellow solid (81 mg, 93%), m. p. 276-278 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.19 – 8.09 (m, 3H), 7.56 (t, J = 7.7 Hz, 2H), 7.49 – 7.40 (m, 1H), 7.29 (d, J = 2.4 Hz, 1H), 7.04 (dd, J = 8.9, 2.4 Hz, 1H), 3.94 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 167.7, 164.5, 158.3, 142.9, 135.2, 130.6, 129.1, 128.3, 127.3, 125.6, 116.0, 113.9, 101.2, 56.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{14}N_2O_3$, 293.0921; found 293.0927.

6-fluoro-3-phenylchromeno[3,2-*c*]pyrazol-9(1*H*)-one (5e): As a light yellow solid (67 mg, 79%), m. p. 237-240 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.31 (dd, J = 8.9, 6.5 Hz, 1H), 8.13 – 8.07 (m, 2H), 7.78 (dd, J = 9.9, 2.4 Hz, 1H), 7.55 (t, J = 7.7 Hz, 2H), 7.46 – 7.41 (m, 1H), 7.39 (td, J = 8.5, 2.5 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 167.9, 165.8 (d, J = 252.5 Hz), 157.8 (d, J = 14.0 Hz), 143.5, 130.6, 129.4, 129.1 (d, J = 11.1 Hz), 128.8, 126.0, 119.9, 113.5 (d, J = 22.9 Hz), 106.1 (d, J = 26.2 Hz). HRMS (EI-DFS) m/z: $[M]^+$ calcd for $C_{16}H_9FN_2O_2$, 280.0643; found 280.0640.

7-chloro-3-phenylchromeno[3,2-*c*]pyrazol-9(1*H*)-one (5f): As a light yellow solid (37 mg, 42%), m. p. 250-253 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.13 (d, J = 1.5 Hz, 1H), 8.11 – 8.05 (m, 2H), 7.91 – 7.86 (m, 2H), 7.54 (t, J = 7.6 Hz, 2H), 7.46 – 7.40 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 167.5, 155.1, 143.4, 134.9, 130.5, 129.4, 129.2, 128.8, 126.0, 125.2, 123.9, 121.7, 110.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{10}ClN_2O_2$, 296.0347; found 296.0343.

6-chloro-3-phenylchromeno[3,2-*c*]pyrazol-9(1*H*)-one (5g): As a light yellow solid (69 mg, 78%), m. p. 252-255 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.20 (d, J = 8.5 Hz, 1H), 8.07 (d, J = 7.7 Hz, 2H), 7.96 (d, J = 2.1 Hz, 1H), 7.55 – 7.48 (m, 3H), 7.41 (dd, J = 8.2, 6.4 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 1687.0, 156.7, 143.2, 139.4, 135.4, 130.6, 129.4, 128.9, 128.7, 128.1, 126.0, 125.3, 121.6, 119.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{11}ClN_2O_2$, 297.0425; found 297.0427.

7-bromo-3-phenylchromeno[3,2-*c*]pyrazol-9(1*H*)-one (5h): As a light yellow solid (60 mg, 58%), m. p. 278-280 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 (d, J = 2.6 Hz, 1H), 8.12 – 8.06 (m, 2H), 8.01 (dd, J = 9.0, 2.6 Hz, 1H), 7.83 (d, J = 9.0 Hz, 1H), 7.56 (t, J = 7.7 Hz, 2H), 7.44 (t, J = 7.4 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 167.4, 155.5, 143.3, 137.6, 135.5, 130.0, 129.5, 128.8, 128.3, 126.0, 124.3, 121.9, 117.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{10}BrN_2O_2$, 339.9842; found 339.9822.

3-phenyl-7-(trifluoromethyl)chromeno[3,2-c]pyrazol-9(1*H*)-one (5i): As a light yellow solid (45 mg, 45%), m. p. 155-157 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ14.63 (s, 1H), 8.54 – 8.46 (m, 1H), 8.22 (d, J = 7.3 Hz, 1H), 8.18 – 8.07 (m, 3H), 7.57 (d, J = 6.5 Hz, 2H), 7.45 (d, J = 6.3 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 167.2, 158.2, 143.5, 136.6, 131.2, 130.8, 130.0, 129.4, 128.8, 127.8, 126.0, 124.1 (q, J = 272.2, 271.6 Hz), 123.8, 122.7, 121.2. HRMS (EI-DFS) m/z: $[M]^+$ calcd for $C_{17}H_9F_3N_2O_2$, 330.0609; found 330.0611.

7-chloro-5-methyl-3-phenylchromeno[3,2-*c*]pyrazol-9(1*H*)-one (5j): As a light yellow solid (71 mg, 76%), m. p. 286-287 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.03 – 7.99 (m, 2H), 7.95 (s, 1H), 7.67 (s, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.40 (t, J = 7.4 Hz, 1H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 166.8, 154.3, 143.1, 142.8, 135.0, 130.3, 129.7, 129.0, 128.4, 125.6, 125.0, 121.4, 120.9, 20.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{13}ClN_2O_2$, 311.0582; found 311.0579.

3-(4-methoxyphenyl)chromeno[3,2-*c*]pyrazol-9(1*H*)-one (5k): As a light yellow solid (82 mg, 94%), m. p. 250-253 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.28 (dd, J = 7.9, 1.7 Hz, 1H), 8.08 – 8.01 (m, 2H), 7.89 (ddd, J = 8.6, 6.8, 1.8 Hz, 1H), 7.83 (dd, J = 8.5, 1.1 Hz, 1H), 7.52 (ddd, J = 8.1, 6.8, 1.2 Hz, 1H), 7.16 – 7.09 (m, 2H), 3.84 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 168.7, 159.7, 156.6, 142.8, 135.2, 127.4, 126.4, 124.8, 123.3, 122.7, 119.3, 114.9, 55.7. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{13}N_2O_3$, 292.0842; found 292.0842.

3-(4-fluorophenyl)chromeno[3,2-*c*]pyrazol-9(1*H*)-one (5l): As a light yellow solid (75 mg, 90%), m. p. >300 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.27 (dd, J = 8.0, 1.6 Hz, 1H), 8.17 – 8.10 (m, 2H), 7.88 (ddd, J = 8.7, 6.9, 1.7 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 8.8 Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 168.2, 162.0 (d, J = 245.5 Hz), 156.2, 142.7, 134.9, 134.6, 128.1, 127.7 (d, J = 8.2 Hz), 127.1, 126.0, 124.6, 122.3, 118.9, 116.1 (d, J = 21.7 Hz). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{10}FN_2O_2$, 280.0643; found 280.0647.

3-(thiophen-3-yl)chromeno[3,2-*c*]pyrazol-9(1*H*)-one (5m): As a yellow solid (66 mg, 83%), m. p. 250-252 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.26 (dd, J = 8.0, 1.8 Hz, 1H), 8.16 – 8.10 (m, 1H), 7.89 – 7.81 (m, 2H), 7.77 – 7.72 (m, 2H), 7.49 (ddd, J = 8.0, 6.6, 1.6 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ 168.3, 156.2, 142.3, 134.8, 131.1, 127.4, 126.1, 125.4, 124.5, 122.5, 122.4, 119.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_{10}N_2O_2S$, 269.0379; found 269.0377.

3-cyclohexylchromeno[3,2-*c*]pyrazol-9(1*H*)-one (5n): As a light yellow solid (22 mg, 27%), m. p. 180-181 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.29 (dd, J = 8.0, 1.8 Hz, 1H), 7.89 (ddd, J = 8.7, 7.0, 1.8 Hz, 1H), 7.78 (d, J = 8.3 Hz, 1H), 7.56 – 7.50 (m, 1H), 3.01 (tt, J =

11.7, 3.6 Hz, 1H), 2.12 – 2.04 (m, 2H), 1.86 (dq, J = 10.7, 3.5 Hz, 2H), 1.80 – 1.65 (m, 3H), 1.53 – 1.42 (m, 2H), 1.40 – 1.31 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, DMSO-d_6) δ 168.8, 156.4, 143.2, 135.0, 126.4, 124.6, 122.7, 119.1, 35.4, 31.8 26.2, 26.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{18}N_2O_2$, 269.1285; found 269.1280.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Crystallographic data and characterization of new compounds (^1H and ^{13}C NMR spectra).

X-ray data for compound **4ao.**

X-ray data for compound **5a.**

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Notes

The authors declare no competing financial interest.

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