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One-pot synthesis of 2*H*-phenanthro[9,10-*c*]pyrazoles from isoflavones by two dehydration processes†

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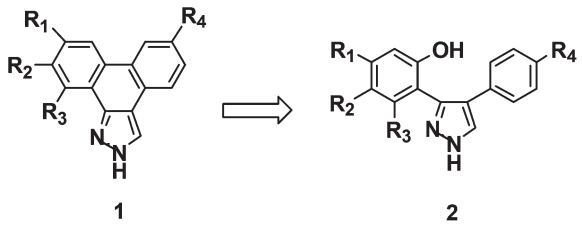
An environmentally friendly and efficient method was developed for one-pot synthesis of a series of 2*H*-phenanthro[9,10-*c*]pyrazoles in EtOH by two dehydration processes. Firstly, 3,4-diaryl-1*H*-pyrazoles were synthesized by the cyclocondensation of isoflavones and hydrazine hydrate in refluxing EtOH. Secondly, the final target products 2*H*-phenanthro[9,10-*c*]pyrazoles were given by photocyclization and dehydration of 3,4-diaryl-1*H*-pyrazoles in 1 : 1 (v/v) EtOH–H_2O. The advantages of this method are catalyst-free, short synthetic routes, mild reaction conditions and easy work-up. In addition, the fluorescence properties of 2*H*-phenanthro[9,10-*c*]pyrazoles were determined.

Introduction

Pyrazole and its derivatives, although scarcely found in nature, constitute an interesting family of heterocycles due to their wide applications. For instance, they are shown to possess important biological and pharmaceutical activities[1] such as anti-inflammatory,[2] antipyretic,[3] antitumor,[4] gastric secretion stimulatory,[5] anti-depressant,[6] antibacterial,[7] antifilarial agents,[8] anti-obesity,[9] estrogen receptor agonist,[10] HIV-1 reverse transcriptase inhibitors[11] and anti-hyperglycemic activities.[12] They are also useful intermediates for industrial products.[13] In addition, pyrazole derivatives are also used as insecticides, herbicides and fungicides.[14] Due to promising pharmacological and agrochemical applications, 3,4-diarylpyrazoles are being used as inhibitors of heat-shock protein 90 (HSP90) and as therapeutics of cancer.[15] Syntheses of 3,4-diarylpyrazoles have been reported over the past decades.[16] Isoflavone, as one kind of nature product, shows remarkable biological anticancer and cardiovascular protection, *etc*.[17] We have synthesized 3,4-diaryl-1*H*-pyrazoles by a one-pot procedure based on the reaction of natural isoflavones with hydrazine hydrate.[18]

Following our investigations on the development of new methodologies for the access to novel polyheterocyclic derivatives, we planned the synthesis of 2*H*-phenanthro[9,10-*c*]-pyrazoles **1** by cyclization of the corresponding 3,4-diaryl-1*H*-pyrazoles **2** (Scheme 1). Although many syntheses of pyrazoles and derivatives have been developed,[19] the syntheses of phenanthropyrazole compounds have been rarely reported. Reimlinger[20] synthesized 2*H*-phenanthro[9,10-*c*]pyrazole by the reaction of diazofluorene with acetylene in an autoclave. Alberti[21] reported that diazotization of 4-(*o*-aminophenyl)-5-phenylpyrazoles and treatment of the diazonium salt with H_3PO_2 have given 2*H*-phenanthro[9,10-*d*]pyrazoles. 1-Phenyl-1*H*-phenanthro[9,10-*c*]pyrazole has been synthesized by irradiation of 1,4,5-triphenylpyrazole in the presence of iodine.[22] These synthetic processes are usually complicated, time-consuming and carried out in the hazardous organic solvents or under harsh conditions, even accompanied with harmful by-products.



Scheme 1 The retrosynthetic analysis of 2*H*-phenanthro[9,10-*c*]pyrazoles.

Encouraged by the fact that Nayak and Wan[23] obtained photocyclization product triphenylene during the photolysis of 2″-hydroxy[1,1′; 2′,1″]terphenyl in 1 : 2 (v/v) H_2O–CH_3CN. We attempted to synthesize 2*H*-phenanthro[9,10-*c*]pyrazoles **1** by the photocyclization and dehydration of 3,4-diaryl-1*H*-pyrazoles **2**. Herein, an environmentally friendly and efficient procedure for one-pot synthesis of 2*H*-phenanthro[9,10-*c*]pyrazoles

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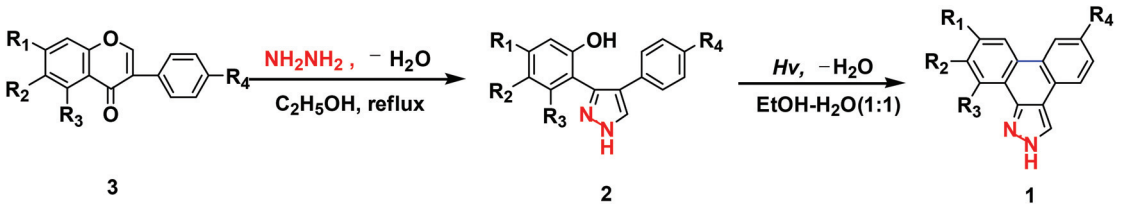


Scheme 2 One-pot synthesis of 2*H*-phenanthro[9,10-*c*]pyrazoles.

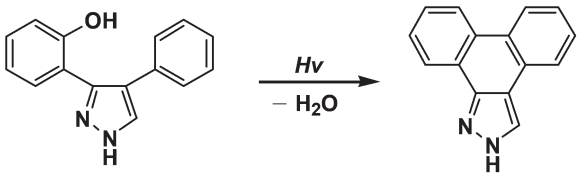
1 from isoflavones **3** in EtOH was developed by two dehydration processes (Scheme 2).

Results and discussion

Optimization of the solvents in photocyclization reaction

According to the literature method,[18] we synthesized the intermediate **2a**. The photocyclization reaction of **2a** in different solvents was investigated. It was found that only a trace of the target product **1a** was obtained when **2a** was irradiated at $\lambda \geq 300$ nm with a medium-pressure mercury lamp (500 W) at about 20 °C in Me_2CO or CH_2Cl_2 for 12 h (trace, Table 1, entries 1–2). And in EtOH, MeOH or MeCN, the photocyclization reaction was slow and the yield of product **1a** was lower after irradiating **2a** for 6 h (32%–36%; Table 1, entries 3–5), while the addition of same volume of water to them could efficiently accelerate the reaction and increase its yield (74%–82%, Table 1, entries 6–8), the reason is that the addition of water is favorable to excited state intramolecular proton transfer (ESIPT).[23] From the economical and environmental point of view, EtOH–H_2O (1 : 1) was finally chosen as the reaction medium for all further reactions.

Table 1 Photocyclization of **2a** in different solvents[a]



Entry	Solvent	Time (h)	Yield **1**[b] (%)
1	CH_2Cl_2	12 h	Trace
2	Me_2CO	12 h	Trace
3	EtOH	6 h	36%
4	MeOH	6 h	32%
5	MeCN	6 h	35%
6	EtOH–H_2O (1 : 1)	4 h	82%
7	MeOH–H_2O (1 : 1)	4 h	74%
8	MeCN–H_2O (1 : 1)	4 h	80%

[a] The intermediate **2a** (0.236 g, 1 mmol) was dissolved in different solvents (100 mL). The solution was irradiated at $\lambda \geq 300$ nm with a medium-pressure mercury lamp (500 W) under an argon atmosphere at about 20 °C until **2a–u** was consumed completely as indicated by thin-layer chromatography (TLC). [b] Yield of isolated product after column chromatography based on **2a**.

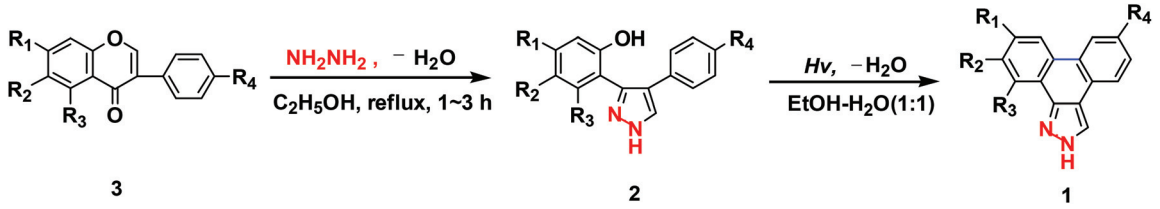
One-pot synthesis of 2*H*-phenanthro[9,10-*c*]pyrazoles

During the cyclocondensation of isoflavone **3** with hydrazine hydrate, EtOH was the best solvent according to literature.[18] EtOH–H_2O (1 : 1) was chosen as reaction medium for photocyclization reactions. Hence, 2*H*-phenanthro[9,10-*c*]pyrazoles **1** were synthesized by one-pot procedure from isoflavone **3**. First, the intermediates 3,4-diaryl-1*H*-pyrazoles **2** were synthesized by the cyclocondensation of isoflavones and 80% hydrazine hydrate in refluxing EtOH. Three representative compounds **2a**, **2b** and **2t** were synthesized in excellent yields (**2a**: 96%; **2b**: 98%; **2t**: 93%) according to literature methods.[18] That is to say, the electronic effect from the substrate had no significant impact on the overall yields of **2**. Then, the mixture was directly adjusted to pH = 6–7 with a solution of 3 M HCl, and diluted with 40 mL EtOH and 50 mL redistilled water. The solution was irradiated with a medium-pressure mercury lamp (500 W) under an argon atmosphere at about 20 °C. Finally, 2*H*-phenanthro[9,10-*c*]pyrazoles **1** were successfully obtained by one-pot synthetic route (Scheme 2). The advantage of one-pot synthesis mainly lies in its short routine, operational simplicity and good yields.

Impact of different isoflavones on the yields of photocyclization products

During the photocyclization of the intermediate **2**, the electronic effect from the isoflavones **3** had a significant impact on the yields of the product **1**. The isoflavone skeletons carrying electron-donating substituents including –Me, –OMe, –i-OPr or –OH can react efficiently to give the corresponding products in good yield (77–89%, Table 2, entries 2–15), while when they carried the electron-withdrawing substituents such as –F, or $-CF_3$, the corresponding product is only obtained in lower yields (32–68%, Table 2, entries 16–21). In addition, the position of the substituents in the isoflavones also has an effect on the yields of product **1**. For an instance, in **3k** and **3l**, where the electron-donating substituent –OMe was located on ring A and ring B of the isoflavones, the yield of the corresponding product **1k** (84%, Table 2, entry 11) is higher than that of **1l** (76%, Table 2, entry 12). For another, **3p** and **3r** carried the electron-withdrawing substituents –F: when –F was on ring A of the isoflavone, the yield of **1p** (38%, Table 2, entry 16) is lower than **1r**, in which –F was on ring B of the isoflavone (64%, Table 2, entry 18). A conclusion can be drawn that the impact of the substituents on ring B is less than that on ring A in substrates.

Table 2 One-pot synthesis of 2*H*-phenanthro[9,10-*c*]pyrazole compounds (**1a–u**) from isoflavones (**3a–u**) by two different dehydration process[a]

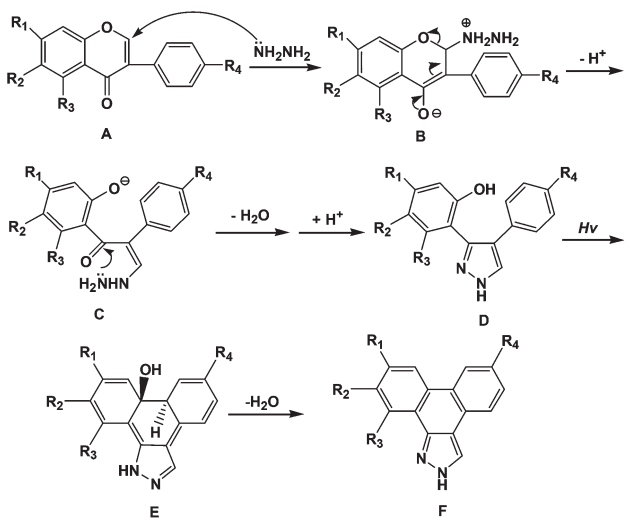


Entry	Substrate	R_1	R_2	R_3	R_4	Product	Time[b]	Yield[c] (%)
1	**3a**	H	H	H	H	**1a**	6 h	75%
2	**3b**	i-OPr	H	H	H	**1b**	3 h	86%
3	**3c**	i-OPr	H	H	Me	**1c**	3 h	89%
4	**3d**	i-OPr	H	H	OMe	**1d**	3 h	85%
5	**3e**	OH	H	H	H	**1e**	4 h	83%
6	**3f**	OH	H	H	OH	**1f**	4 h	84%
7	**3g**	OMe	H	H	OH	**1g**	6 h	79%
8	**3h**	OH	H	H	OMe	**1h**	4 h	81%
9	**3i**	OMe	H	H	OMe	**1i**	6 h	78%
10	**3j**	OBz	H	H	OMe	**1j**	6 h	77%
11	**3k**	OMe	H	H	H	**1k**	4 h	84%
12	**3l**	H	H	H	OMe	**1l**	5 h	76%
13	**3m**	H	H	H	Me	**1m**	4 h	82%
14	**3n**	OMe	H	H	Me	**1n**	4 h	83%
15	**3o**	OMe	H	Me	H	**1o**	4 h	86%
16	**3p**	H	F	H	H	**1p**	12 h	38%
17	**3q**	H	F	H	Me	**1q**	10 h	46%
18	**3r**	H	H	H	F	**1r**	8 h	64%
19	**3s**	OMe	H	H	F	**1s**	8 h	68%
20	**3t**	OMe	H	H	CF_3	**1t**	12 h	32%
21	**3u**	i-OPr	H	H	CF_3	**1u**	12 h	33%

[a] All reactions were carried out on the scale of 1 mmol **3a–u** and 2 mmol 80% hydrazine hydrate in refluxing 10 mL EtOH until the complete disappearance of **3a–u** (1–3 h). The mixture was adjusted to pH = 6–7 with a solution of 3 M HCl, and diluted with 40 mL EtOH and 50 mL redistilled water. The diluted solution was irradiated at $\lambda \geq 300$ nm with a medium-pressure mercury lamp (500 W) under an argon atmosphere at about 20 °C until **2a–u** was consumed completely as indicated by TLC. [b] The photocyclization reaction time of **2a–u**. [c] Yield of isolated product after column chromatography based on **3a–u**.

Mechanism for two dehydration processes

A plausible mechanism for the formation of 2*H*-phenanthro-[9,10-*c*]pyrazoles is depicted in Scheme 3. The Michael-addition mechanism can be proposed for the cyclocondensation between isoflavones and hydrazine hydrate.[24] First, one nitrogen atom of hydrazine, as a nucleophile, attacks the C(2) position of isoflavone **A** to produce the intermediate **B**, which opens the benzopyranone ring to generate **C**. Another nitrogen atom of hydrazine attacks the –C═O group, which, upon loss of H_2O and protonation, leads to condensation product **D**. Then, under the radiation of UV light, the phenolic hydroxyl group of **D** attacks the *ortho*-position of the other benzene ring to give the addition products **E**; the intermediate **E** is unstable, and loses H_2O to obtain the final target products **F**.



Scheme 3 Proposed mechanism for two dehydration processes.

Tautomeric forms of 2*H*-phenanthro[9,10-*c*]pyrazoles

Being similar to pyrazoles,[25] 2*H*-phenanthro[9,10-*c*]pyrazoles also exist in tautomeric forms (Scheme 4). For ^{1}H NMR of **1b**,

Scheme 4 Alternative tautomeric forms of 2*H*-phenanthro[9,10-*c*]pyrazoles.

with DMSO-d_6 as solvent, a major proton peak at 13.9 ppm accompanied by a minor peak at 13.6 ppm, and some small peaks also appeared in the aromatic region; in DMSO-d_6 with added D_2O as solvent, the deuterium (^{2}H)-exchange experiments simplified the spectra, and the peak at 13.9 ppm and 13.6 ppm disappeared. The results of deuterium (^{2}H)-exchange of **1b** indicated that 2*H*-phenanthro[9,10-*c*]pyrazoles has two tautomeric forms. In addition, the ^{1}H NMR results of 2*H*-phenanthro[9,10-*c*]pyrazoles showed that the type and position of the substituents in the 2*H*-phenanthro[9,10-*c*]pyrazoles affected the ratios of tautomers. For examples, from the integral areas of two proton peaks (13–14 ppm) at N atom, we can find the ratio of tautomers is 3 : 2 in **1o**, 4.56 : 1 in **1b** and 4 : 1 in **1s**.

Fluorescence properties of 2*H*-phenanthro[9,10-*c*]pyrazoles

2*H*-Phenanthro[9,10-*c*]pyrazoles have blue-purple fluorescence. For **1**, **1i**, **1a** and **1p** were chosen to determine the fluorescence properties. As is illustrated in Fig. 1, the maximum excitations of **1i**, **1a** and **1p** appear at 257, 255 and 253 nm, respectively, which have a slight blue shift with the change of substituents in 2*H*-phenanthro[9,10-*c*]pyrazoles. The photo-luminescence spectra of **1a** have a sharp emission peak at 361 nm accompanied by two shoulders around 345 nm and 375 nm. For **1p**, it has the similar emission bands, which has an emission maxima of 358 nm with a slight blue shift compared with its analogue **1a**. While **1i** has a red shift relative to analogue **1a** with the sharp emission peak of 375 nm and a shoulder of 373 nm. When there are electron-donating substituents on the 2*H*-phenanthro[9,10-*c*]pyrazole, its fluorescence intensity increases obviously and the peak is red-shifted. When carrying electron-with drawing substituents on the 2*H*-phenanthro-[9,10-*c*]pyrazole, its fluorescence emission peak decreases significantly in intensity and is blue-shifted in position.

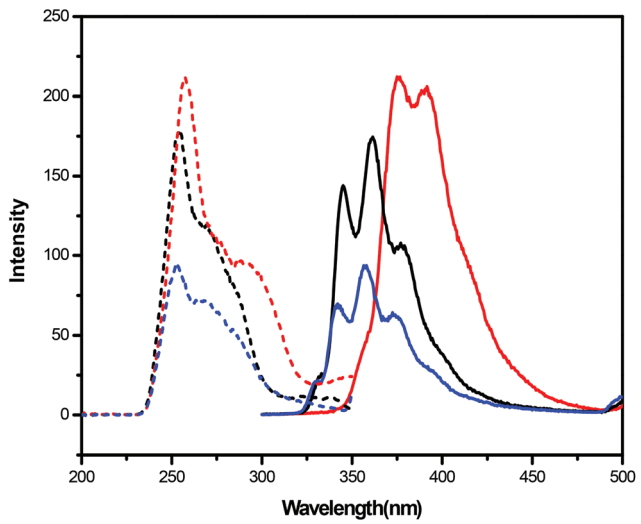


Fig. 1 Excitation spectra (EX, dash lines) and emission spectra (EM, solid lines) of compounds **1i** (red), **1a** (black) and **1p** (blue) in chloroform (1×10^{-6} mol L^{-1}).

Conclusions

In summary, a novel protocol for one-pot syntheses of 2*H*-phenanthro[9,10-*c*]pyrazoles from isoflavones by two dehydration processes in EtOH was developed. First, 3,4-diaryl-1*H*-pyrazoles were synthesized by the cyclocondensation of isoflavone and hydrazine hydrate in refluxing EtOH, which was followed by a photocyclization process in 1 : 1 EtOH–H_2O to give the final target products 2*H*-phenanthro[9,10-*c*]pyrazoles. This procedure offers several notable advantages including operational simplicity, mild reaction conditions, excellent yields and being friendly to environment. It is an efficient method for one-pot synthesis of the nitrogen-containing fused heterocycle compounds. The fluorescence properties studies showed that 2*H*-phenanthro[9,10-*c*]pyrazoles had strong blue-purple fluorescence.

Experimental section

Melting points were measured by a X-5 micromelting point apparatus and are uncorrected. NMR spectra were recorded on a Bruker AM 300 instrument or Bruker AM 400 instrument using DMSO-d_6 solvent peaks. High resolution mass spectra (HRMS) was recorded using electron-spray ionization (ESI) technique and IR spectra were recorded on a Nicollet 170SX FT-IR spectrophotometer with KBr pellets. All the irradiation experiments were performed in a BL-GHX-V photochemical reactor equipped with a 500 W medium-pressure mercury lamp. The fluorescent spectra were recorded on a Perkin Elmer LS55 luminescence spectrometer. TLC was performed on silica gel 60 GF254 plates. The silica gel (size 200–300 mesh) used for the column chromatography was purchased from Qingdao Haiyang Chemistry Plant (China).

General procedure for the synthesis of 2*H*-phenanthro[9,10-*c*]-pyrazoles (1)

3,4-Diaryl-1*H*-pyrazoles were synthesized according to the literature method.[18] Hydrazine hydrate (80%, 5 mmol) and isoflavone **3** (1 mmol) were added to an EtOH solution (10 mL) and the mixture was refluxed at 80 °C until **3a–u** was consumed completely indicative by TLC (1–3 h). The mixture was adjusted to pH = 6–7 with a solution of 3 M HCl, and diluted with 40 mL EtOH and 50 mL redistilled water. The solution was contained in 100 mL quartz tubes, deaerated by bubbling Ar for 30 min and irradiated at $\lambda \geq 300$ nm with a medium-pressure mercury lamp (500 W), which were cooled to about 20 °C with tap water by means of an internal cold finger. The progress of reaction was monitored by TLC at regular intervals until the intermediate **2a–u** had disappeared completely. Then, the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel using petroleum ether–ethyl acetate or chloroform–methanol to give the corresponding product (**1a–u**), and characterized by ^{1}H NMR, ^{13}C NMR, IR and HRMS.

2*H*-Phenanthro[9,10-*c*]pyrazole (1a). Isolated as a yellow powder; m.p. 242.3–244.9 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 7.55 (s, 1H), 7.64–7.68 (m, 3H), 8.32 (s, 1H), 8.49 (s, 1H), 8.62–8.78 (m, 3H), 14.07 (br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 116.2, 122.4, 123.8, 123.9, 124.1, 125.1, 126.9, 127.1, 127.2, 127.4, 127.6, 129.5; IR (KBr), ν (cm^{-1}) 3403, 3098, 2922, 1611, 1544, 1455, 1197, 1075, 950, 862, 756. HRMS (*m*/*z*): calc. for $C_{15}H_{10}N_2$ $[M + H]^+$ 219.0922, found 219.0910.

9-Isopropoxy-2*H*-phenanthro[9,10-*c*]pyrazole (1b). Isolated as a yellow powder; m.p. 212.0–213.2 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 1.37 (d, 6H, J = 5.7 Hz), 4.98 (m, 1H), 7.38 (d, 1H, J = 7.5 Hz), 7.56 (m, 1H), 7.62 (m, 1H), 8.23 (s, 1H), 8.30 (d, 1H, J = 7.5 Hz), 8.38 (d, 1H, J = 8.1 Hz), 8.55 (s, 1H), 8.76 (d, 1H J = 8.1 Hz), 13.89 (br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 21.9, 69.5, 108.9, 115.0, 115.2, 117.4, 123.6, 124.0, 124.2, 124.7, 126.7, 127.2, 127.6, 131.3, 133.8, 136.0, 156.7; IR (KBr), ν (cm^{-1}) 3689, 3155, 2928, 2358, 1714, 1475, 1202, 1061, 955, 758; HRMS (*m*/*z*): calc. for $C_{18}H_{16}N_2O$ $[M + H]^+$ 277.1341, found 277.1334.

9-Isopropoxy-6-methyl-2*H*-phenanthro[9,10-*c*]pyrazole (1c). Isolated as an orange powder; m.p. 263.1–264.2 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 1.36 (d, 6H, J = 6.0 Hz), 2.54 (s, 3H), 4.95 (m, 1H), 7.34 (d, 1H, J = 7.5 Hz), 7.45 (d, 1H, J = 7.8 Hz), 8.16 (d, 1H, J = 7.5 Hz), 8.20 (s, 1H), 8.35 (d, 1H, J = 7.8 Hz), 8.48 (s, 1H), 8.55 (s, 1H), 13.81 (br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 21.6, 69.5, 109.1, 115.1, 115.2, 117.2, 123.5, 123.9, 124.0, 124.7, 126.7, 129.0, 131.1, 133.6, 133.9, 135.7, 156.6; IR (KBr), ν (cm^{-1}) 3703, 3148, 3017, 2924, 1719, 1584, 1461, 1258, 1177, 1122, 951, 856, 812, 759; HRMS (*m*/*z*): calc. for $C_{19}H_{18}N_2O$ $[M + H]^+$ 291.1497, found 291.1480.

9-Isopropoxy-6-methoxy-2*H*-phenanthro[9,10-*c*]pyrazole(1d). Isolated as a pink powder; m.p. 248.1–249.0 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 1.36 (d, 6H, J = 6.0 Hz), 3.94 (s, 3H), 4.96 (m, 1H), 7.27 (d, 1H, J = 7.2 Hz), 7.37 (d, 1H, J = 7.2 Hz), 8.10–8.18 (m, 3H), 8.36 (d, 1H, J = 8.1 Hz), 8.45 (s, 1H), 13.77 (br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 21.9, 55.5, 69.5, 106.8, 109.7, 115.2, 115.3, 116.6, 117.1, 121.0, 123.9, 124.9, 128.0, 130.9, 133.2, 135.1, 156.5, 156.9; IR (KBr), ν (cm^{-1}) 3702, 3094, 2980, 2916, 1720, 1582, 1460, 1277, 1185, 1122, 957, 861, 817; HRMS (*m*/*z*): calc. for $C_{19}H_{18}N_2O_2$ $[M + H]^+$ 307.1447, found 307.1430.

2*H*-Phenanthro[9,10-*c*]pyrazol-9-ol (1e). Isolated as a pink powder; m.p. 279.2–280.1 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 7.22 (m, 1H), 7.51–7.61 (m, 2H), 8.05 (s, 1H), 8.26–8.31 (m, 3H), 8.51 (s, 1H), 10.00 (s, 1H), 13.79 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 108.4, 114.7, 116.9, 123.7, 123.9, 124.8, 127.5, 131.4, 133.7, 133.8, 133.9, 156.8; IR (KBr), ν (cm^{-1}) 3159, 2923, 1706, 1623, 1458, 1321, 1195, 1085, 947, 847, 754; HRMS (*m*/*z*): calc. for $C_{15}H_{10}N_2O$ $[M + H]^+$ 235.0871, found 235.0858.

2*H*-Phenanthro[9,10-*c*]pyrazole-6,9-diol (1f). Isolated as a grey powder; m.p. 324.6–325.2 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 7.18–7.22 (m, 2H), 7.85 (d, 2H, J = 8.4 Hz), 8.11 (d, 1H, J = 7.5 Hz), 8.28 (d, 1H, J = 8.4 Hz), 8.40 (s, 1H), 9.62 (s, 1H), 9.92 (s, 1H), 13.62 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 108.1, 108.2, 114.9, 116.8, 117.1, 117.2, 119.9, 123.9, 125.0, 125.1, 128.6, 130.9, 131.5, 154.8, 156.5; IR (KBr), ν (cm^{-1}) 3262, 2922, 1628, 1587, 1462, 1230, 1084, 952, 758. HRMS (*m*/*z*): calc. for $C_{15}H_{10}N_2O_2$ $[M + H]^+$ 251.0821, found 251.0816.

9-Methoxy-2*H*-phenanthro[9,10-*c*]pyrazol-6-ol (1g). Isolated as a pink powder; m.p. 241.6–243.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm) 3.99 (s, 3H), 7.16 (d, 1H, J = 8.4 Hz), 7.34 (d, 1H, J = 8.4 Hz), 7.99 (s, 2H), 8.11 (d, 1H, J = 8.4 Hz), 8.35 (d, 1H, J = 8.4 Hz), 8.43 (s, 1H), 9.65 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm) 55.3, 106.3, 108.6, 115.4, 116.2, 117.3, 119.9, 123.9, 125.0, 128.3, 130.7, 154.9, 158.2. IR (KBr), ν (cm^{-1}) 3574, 3226, 2927, 2560, 1626, 1586, 1468, 1238, 1187, 1052, 950, 817; HRMS (*m*/*z*): calc. for $C_{16}H_{12}N_2O_2$ $[M + H]^+$ 265.0977, found 265.0974.

6-Methoxy-2*H*-phenanthro[9,10-*c*]pyrazol-9-ol (1h). Isolated as a brown powder; m.p. 268.8–270.0 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 3.96 (s, 3H), 7.23–7.27 (m, 2H), 7.96 (1s, 1H), 8.06 (1s, 1H), 8.18 (d, 1H, J = 8.4 Hz), 8.30 (d, 1H, J = 8.4 Hz), 8.47 (s, 1H), 9.97 (s 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 55.8, 106.7, 109.2, 115.2, 116.9, 117.5, 121.6, 124.4, 125.6, 128.5, 131.5, 157.1, 157.3; IR (KBr), ν (cm^{-1}) 3630, 3435, 3207, 2599, 1627, 1465, 1236, 1056, 950, 811; HRMS (*m*/*z*): calc. for $C_{16}H_{12}N_2O_2$ $[M + H]^+$ 265.0977, found 265.0974.

6,9-Dimethoxy-2*H*-phenanthro[9,10-*c*]pyrazole (1i). Isolated as a pink powder; m.p. 261.2–261.6 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 4.00 (s, 6H), 7.32 (br, 1H), 7.40 (br, 1H), 8.15–8.20 (m, 3H), 8.38 (d, 1H, J = 8.4 Hz), 8.48 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 55.5, 107.1, 107.2, 115.1, 116.1, 116.3, 121.2, 123.9, 125.0, 128.1, 130.8, 156.9, 158.4; IR (KBr), ν (cm^{-1}) 3688, 3142, 2906, 2358, 1732, 1627, 1469, 1285, 1239, 1189, 1032, 949, 861, 809; HRMS (*m*/*z*): calc. for $C_{17}H_{14}N_2O_2$ $[M + H]^+$ 279.1134, found 279.1131.

9-Benzyloxy-6-methoxy-2*H*-phenanthro[9,10-*c*]pyrazole (1j). Isolated as a pink powder; m.p. 277.8–279.9 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm) 3.98 (s, 3H), 5.38 (s, 2H), 7.27–7.45 (m, 5H), 7.58 (m, 2H), 8.10 (s, 1H), 8.19 (d, 1H, J = 8.0 Hz), 8.28 (s, 1H), 8.39 (d, 1H, J = 8.0 Hz), 8.49 (s, 1H), 13.77 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm) 55.5, 69.7, 106.9, 108.4, 115.2, 116.5, 116.6, 116.7, 121.2, 123.9, 125.0, 127.9, 128.4, 130.8, 137.1, 156.9, 157.5; IR (KBr), ν (cm^{-1}) 3685, 3134, 2926, 2358, 1624, 1586, 1467, 1237, 1188, 1064, 1033, 951, 824, 736. HRMS (*m*/*z*): calc. for $C_{22}H_{18}N_2O_2$ $[M + H]^+$ 355.1447, found 355.1445.

9-Methoxy-2*H*-phenanthro[9,10-*c*]pyrazole (1k). Isolated as an orange powder; m.p. 254.1–255.7 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 4.00 (s, 3H), 7.37 (s, 1H), 7.54 (s, 1H), 7.63 (s, 1H), 8.21 (s, 1H), 8.29 (s, 1H), 8.40 (s, 1H), 8.58 (br, 1H), 8.75 (s, 1H), 13.88 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 55.5, 106.6, 115.1, 116.3, 123.7, 123.9, 124.2, 124.8, 127.6, 131.2, 133.8, 133.9, 158.6; IR (KBr), ν (cm^{-1}) 3699, 3100, 2925, 1728, 1621, 1584, 1474, 1225, 1031, 950, 857, 756; HRMS (*m*/*z*): calc. for $C_{16}H_{12}N_2O$ $[M + H]^+$ 249.1028, found 249.1014.

6-Methoxy-2*H*-phenanthro[9,10-*c*]pyrazole (1l). Isolated as a pink powder; m.p. 245.4–246.7 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 3.97 (s, 3H), 7.30 (br, 1H), 7.69–7.73 (m, 2H), 8.19–8.24 (m, 2H), 8.44–8.84 (m, 3H), 13.95 (br, 1H); ^{13}C NMR

(75 MHz, DMSO-d_6), δ (ppm) 55.4, 106.5, 116.4, 116.6, 120.7, 121.3, 122.3, 124.5, 125.0, 126.8, 127.4, 128.3, 129.0, 133.3, 134.9, 157.1; IR (KBr), ν (cm^{-1}) 3138, 3006, 2946, 1714, 1622, 1581, 1458, 1243, 1207, 1071, 1032, 952, 865, 825, 767; HRMS (*m*/*z*): calc. for $C_{16}H_{12}N_2O$ $[M + H]^+$ 249.1028, found 249.1006.

6-Methyl-2*H*-phenanthro[9,10-*c*]pyrazole (1m). Isolated as an orange powder; m.p. 256.2–257.5 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm) 2.55 (s, 3H), 7.46 (d, 1H, J = 8.0 Hz), 7.65–7.72 (m, 2H), 8.20 (d, 1H, J = 8.0 Hz), 8.46 (d, 1H, J = 8.0 Hz), 8.54 (s, 1H), 8.59 (s, 1H), 8.78 (d, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm) 21.4, 116.4, 121.1, 122.3, 123.6, 123.7, 123.9, 124.1, 124.4, 127.0, 127.2, 128.9, 129.3, 133.7, 134.2, 135.5; IR (KBr), ν (cm^{-1}) 3700, 3096, 2910, 1582, 1455, 1194, 1074, 951, 820, 764; HRMS (*m*/*z*): calc. for $C_{16}H_{12}N_2$ $[M + H]^+$ 233.1079, found 233.1072.

9-Methoxy-6-methyl-2*H*-phenanthro[9,10-*c*]pyrazole (1n). Isolated as an orange powder; m.p. 238.2–238.8 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 2.55 (s, 3H), 4.00 (s, 3H), 7.34 (s, 1H), 7.43 (s, 1H), 8.16 (br, 2H), 8.36 (1s, 1H), 8.53 (br, 2H), 13.81 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 21.3, 55.5, 106.5, 115.2, 116.2, 123.5, 123.9, 124.0, 124.8, 126.7, 127.2, 127.2, 128.9, 131.1, 133.5, 133.6, 133.9, 158.5; IR (KBr), ν (cm^{-1}) 3387, 3097, 2922, 1633, 1584, 1465, 1281, 1229, 1070, 951, 861, 816; HRMS (*m*/*z*): calc. for $C_{17}H_{14}N_2O$ $[M + H]^+$ 263.1184, found 263.1182.

9-Methoxy-11-methyl-2*H*-phenanthro[9,10-*c*]pyrazole (1o). Isolated as a white powder; m.p. 240.2–241.1 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 3.01 (s, 3H), 3.98 (s, 3H), 7.17 (s, 1H), 7.54 (br, 2H), 8.05 (br, 1H), 8.26 (br, 1H), 8.68–8.81 (m, 2H), 13.68 (br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 24.3, 55.2, 104.6, 115.9, 117.7, 122.4, 125.1, 127.4, 127.6, 132.4, 132.5, 135.5, 137.2, 157.5; IR (KBr), ν (cm^{-1}) 3251, 2954, 1613, 1462, 1204, 1074, 941, 840, 743; HRMS (*m*/*z*): calc. for $C_{17}H_{14}N_2O$ $[M + H]^+$ 263.1184, found 263.1179.

10-Fluoro-2*H*-phenanthro[9,10-*c*]pyrazole (1p). Isolated as a yellow powder; m.p. 229.6–230.9 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 7.56–7.65 (m, 3H), 8.24–8.33 (m, 2H), 8.63–8.70 (m, 2H), 8.86 (s, 1H), 14.05 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 107.4, 107.6, 115.1, 115.3, 117.0., 123.7, 123.8 125.3, 126.2, 127.4, 131.4, 134.0, 134.1, 135.3, 159.9; IR (KBr), ν (cm^{-1}) 3698, 3107, 2920, 1720, 1622, 1584, 1459, 1175, 1075, 951, 870, 763; HRMS (*m*/*z*): calc. for $C_{15}H_9N_2F$ $[M + H]^+$ 237.0828, found 237.0811.

10-Fluoro-6-methyl-2*H*-phenanthro[9,10-*c*]pyrazole (1q). Isolated as an orange powder; m.p. 292.3–293.4 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 2.54 (s, 3H), 7.48–7.52 (m, 2H), 8.19 (br, 2H), 8.50–8.57 (m, 2H), 8.84 (br, 1H), 13.97 (br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 21.4, 107.4, 107.5, 115.0, 115.1, 117.0, 123.7, 123.8, 123.9, 126.0, 126.7, 127.1, 128.8, 133.8, 134.5, 160.2; IR (KBr), ν (cm^{-1}) 3686, 3146, 2923, 1714, 1627, 1550, 1464, 1378, 1178, 1083, 950, 865, 819, 773; HRMS (*m*/*z*): calc. for $C_{17}H_{11}FN_2$ $[M + H]^+$ 251.0985, found 251.0968.

6-Fluoro-2*H*-phenanthro[9,10-*c*]pyrazole (1r). Isolated as an orange powder; m.p. 232.1–234.4 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 7.52 (s, 1H), 7.69–7.75 (m, 2H), 8.36 (s, 1H), 8.46–8.59 (m, 3H), 8.78 (s, 1H), 14.08 (br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 109.4, 109.6, 115.7, 115.9, 121.3, 122.4, 123.5, 124.7, 125.8, 127.2, 128.0, 128.8, 133.8, 135.5, 160.9; IR (KBr), ν (cm^{-1}) 3705, 3097, 2920, 1716, 1625, 1462, 1378, 1277, 1231, 1188, 1127, 1064, 952, 855, 824; HRMS (*m*/*z*): calc. for $C_{15}H_9FN_2$ $[M + H]^+$ 237.0828, found 237.0812.

6-Fluoro-9-methoxy-2*H*-phenanthro[9,10-*c*]pyrazole (1s). Isolated as a yellow powder; m.p. 310.8–311.6 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm) 4.00 (s, 3H), 7.39 (d, 1H, J = 8.0 Hz), 7.50 (m, 1H), 8.18 (s, 1H), 8.31–8.39 (m, 2H), 8.53 (s, 1H), 8.60 (d, 1H, J = 8.0 Hz), 13.89 (br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 55.6, 106.9, 109.8, 110.0, 114.8, 115.4, 115.8, 117.2, 123.9, 125.7, 128.4, 130.6, 133.7, 135.6, 158.6, 159.1; IR (KBr), ν (cm^{-1}) 3684, 3097, 2924, 1716, 1626, 1469, 1377, 1274, 1228, 1179, 1067, 1033, 954, 862, 815. HRMS (*m*/*z*): calc. for $C_{16}H_{12}FN_2O$ $[M + H]^+$ 267.0934, found 267.0913.

9-Methoxy-6-trifluoromethyl-2*H*-phenanthro[9,10-*c*]pyrazole (1t). Isolated as a yellow powder; m.p. 232.1–233.7 °C. ^{1}H NMR (300 MHz, DMSO-d_6), δ (ppm) 4.03 (s, 3H), 7.43 (br, 1H), 7.91 (d, 1H, J = 8.1 Hz), 8.28–8.54 (m, 3H), 8.66 (s, 1H), 9.05 (br, 1H), 14.03 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 55.7, 106.9, 114.4, 117.4, 121.6, 123.4, 124.1, 124.7, 125.7, 127.4, 127.5, 128.6, 130.6, 134.5, 136.9, 158.9; IR (KBr), ν (cm^{-1}) 3684, 3145, 2933, 1715, 1625, 1588, 1476, 1326, 1280, 1121, 1031, 949, 829, 775; HRMS (*m*/*z*): calc. for $C_{17}H_{11}F_3N_2O$ $[M + H]^+$ 317.0902, found 317.0876.

9-Isopropoxy-6-trifluoromethyl-2*H*-phenanthro[9,10-*c*]pyrazole (1u). Isolated as a yellow powder; m.p. 263.7–265.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm) 1.36 (d, 6H, J = 6.0 Hz), 5.03 (m, 1H), 7.41 (s, 1H), 7.89 (d, 1H, J = 7.2 Hz), 8.10–8.46 (m, 3H), 8.62 (s, 1H), 9.03 (br, 1H), 14.02 (br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6), δ (ppm) 21.8, 69.7, 109.6, 114.4, 118.2, 121.5, 121.6, 123.4, 124.1, 124.7, 125.3, 126.1, 127.4, 130.7, 134.4, 134.5, 157.1; IR (KBr), ν (cm^{-1}) 3686, 3146, 2981, 2932, 1714, 1625, 1586, 1471, 1378, 1324, 1180, 1120, 952, 829, 774; HRMS (*m*/*z*): calc. for $C_{19}H_{15}F_3N_2O$ $[M + H]^+$ 345.1215, found 345.1196.

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