

Synthesis of styryl pyrazolones and evaluation of their potential antioxidant activities

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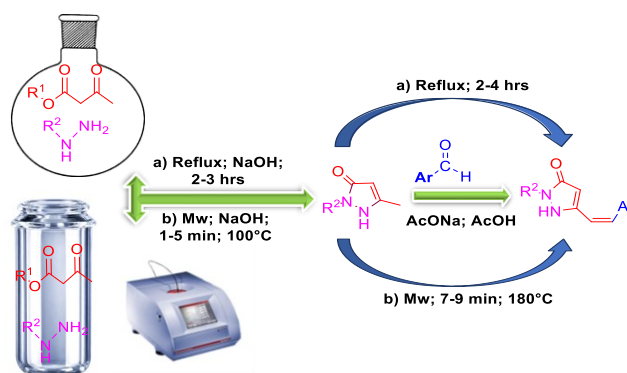
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Abstract

A library of 5-(styryl)-1,2-dihydro-3H-pyrazol-3-ones is reported via an efficient, environmentally friendly, one-pot stepwise procedure. The target compounds were obtained in excellent yields and exhibited high purity without requiring extensive purification. The synthesized styryl pyrazolones were further assessed for their *in vitro* antioxidant activity. Several compounds demonstrated significant free radical scavenging activity, with some outperforming the standard antioxidant Trolox, thereby indicating their potential as promising candidates for further pharmacological development.



Keywords: Microwave-assisted, green synthesis, one-pot stepwise, styryl pyrazolone, antioxidant activity

Introduction

Research into heterocyclic compounds has flourished over the years, primarily due to their diverse applications in medicinal and synthetic chemistry. Nitrogen-containing heterocycles represent an important class of compounds that serve as key structural frameworks in many physiologically active molecules and functional materials.^{1,2} Pyrazole and pyrazolone derivatives, in particular, have attracted a lot of interest due to its pharmacological properties such as anticancer, anti-inflammatory, antimicrobial, anti-AIDS, antitumor, anti-hyperglycemic, anti-insecticidal, anti-pyretic, antianxiolytic, and anticonvulsant activities.^{3,4} Furthermore, pyrazolone has demonstrated tremendous promise in pharmaceutical research, particularly in the development of therapeutic agents for Cerebral Ischaemia and Cardiovascular diseases.⁵ In addition, styryl-containing compounds have received considerable interest owing to their structural diversity and significant biological activities.⁶ Their conjugated systems also impart favorable physicochemical characteristics, such as enhanced stability and electron delocalization, which contribute to their biological activity and synthetic versatility.⁷ The incorporation of a styryl moiety into pyrazolone may therefore lead to compounds with improved biological potential.

In recent years, one-pot synthesis (OPS) has emerged as an efficient strategy in organic synthesis due to its advantages, such as low cost, high mass efficiency, ease of use, and reduced waste disposal. Among the major OPS strategies, cascade reactions, multicomponent reactions (MCRs), and one-pot stepwise synthesis (OPSS); the one-pot stepwise approach is regarded as particularly versatile and practical. This is due to its broader flexibility in optimizing reaction parameters, enabling efficient substrate scope exploration, scalability, and compatibility with diverse reaction types. Furthermore, OPSS offers the advantages of solvent exchange and controlled stepwise temperature regulation, thereby overcoming challenges associated with the solubility and reactivity of intermediates.⁸ Thus, for this reason, we use OPSS for the synthesis of styryl pyrazolones.

Addressing the dual challenges of sustainable chemical synthesis and the discovery of effective antioxidant agents, this study outlines the development and biological evaluation of a novel series of styryl pyrazolone derivatives. We report an eco-friendly, microwave-assisted one-pot protocol that successfully eliminates the need for toxic solvents and catalysts. To translate this synthetic achievement into potential therapeutic value, we further explore their *in vitro* antioxidant properties through DPPH and FRAP assays. Ultimately, this work seeks to highlight how targeted structural modifications can yield potent, environmentally friendly candidates for combating oxidative stress.

Results and Discussion

Optimization of the compound 5a. A systematic optimization of reaction conditions was undertaken to establish an efficient protocol for the synthesis of styryl pyrazolones. In the initial step, equimolar quantities of ethyl acetoacetate **1** (2 mmol) and hydrazine hydrate **2** (2 mmol) were subjected to conventional heating. No product formation was observed at ambient temperature in the absence of a solvent under stirring conditions, even upon prolonged reaction times. However, the introduction of a basic inorganic catalyst NaOH (2 mmol) facilitated the formation of the desired pyrazolone intermediate **3**. The reaction required 3 hrs and afforded yields of 75 %. In contrast, microwave irradiation (MWI) at 100 °C significantly reduced the reaction time to 4 min, and enhanced the yield to 80 % [Table 1]. The compound **3a** was identified by their respective Mass, NMR and IR spectra ^{9,10} In the second step, pyrazolone **3** was reacted with 4-Hydroxybenzaldehyde **4** in an acidic medium affording **5-(4-Hydroxystyryl)-1,2-dihydro-3H-pyrazol-3-one (5a)** as a result of the activation of the methyl group via the Knoevenagel reaction.⁹ The influence of different techniques and solvents on reaction efficiency was then systematically evaluated.

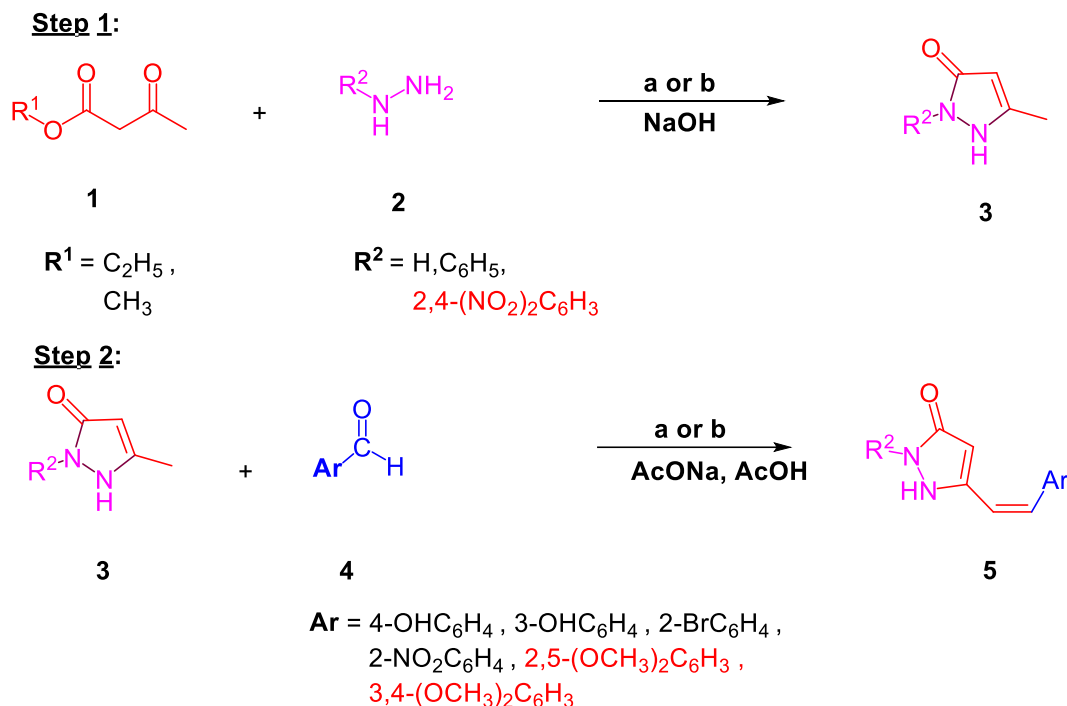
Synthesis of 5-(styryl)-1,2-dihydro-3H-pyrazol-3-one (5a-h) under microwave-assisted one-pot stepwise synthesis. In the initial step, equimolar quantities of 1,3-dicarbonyl compound **1** (2 mmol) and hydrazine derivative **2** (2 mmol) and a basic inorganic catalyst NaOH (2 mmol) were subjected to both conventional heating and microwave irradiation (MWI) facilitating the formation of the desired pyrazolone intermediate **3**. Under conventional heating, the reaction required 2-3 hrs and afforded yields of 53-75 %. In contrast, microwave irradiation (MWI) at 100 °C significantly reduced the reaction time to 1-5 min, and enhanced the yields to 78-95 % [Table 1]. In the subsequent step, the reaction of pyrazolone **3** with different benzaldehyde derivatives (**4**) in an acidic medium afforded the target styryl pyrazolones **5a-h**. Under conventional heating, condensation of the intermediate **3** with **4** required 2–4 hrs to complete the reaction, affording lower yields of styryl pyrazolones **5**. In contrast, solvent-free microwave-assisted conditions enabled rapid transformation, delivering significantly higher yields within 7-9 min [Scheme 1 (b)]. Accordingly, the overall reaction time taken for the two-step synthesis of **5a-h** under conventional heating was 6-9 hours, whereas MWI considerably shortened the reaction time to 8-14 minutes [Scheme 1, Table 2].

Collectively, these findings demonstrate that microwave irradiation is a superior strategy for the synthesis of styryl pyrazolones **5**, offering enhanced efficiency, reduced reaction time, and broader applicability compared to conventional methods. The method employed for the synthesized compounds does not involve the usage of any toxic organic solvents, and therefore, this procedure is classified as an eco-friendly pathway and follows green principles of chemistry.

The infrared spectrum analysis of compound **5a** displayed prominent absorption bands at 3271 cm⁻¹, assignable to the O–H stretching vibration; at 3199 and 3110 cm⁻¹ corresponding to N-H Stretch; at 1722 cm⁻¹ corresponding to the characteristic carbonyl (C=O) stretching; and at 1603 cm⁻¹, indicative of C=C stretching vibrations associated with the styryl framework. These diagnostic peaks are consistent with the expected functional groups of the synthesized scaffold. Furthermore, compounds **5b-h** exhibited comparable absorption features, thereby substantiating the successful incorporation of the styryl moiety and confirming the structural integrity of the entire series. Out of all the synthesized compounds, the product **5g** gives the best result with the yield percentage of 92%; this is due to the presence of the two methoxy groups at position 2 and 5.¹¹ In this work, a comparative study has been done between conventional heating and MWI and we have developed a novel compound of 5-(styryl)-1,2-dihydro-3H-pyrazol-3-one (**5a-h**) through catalyst-free, one-pot stepwise synthesis proceeding in excellent yields. All the products were characterized by using a variety of spectroscopic methods, such as nuclear magnetic resonance ¹H NMR and ¹³C NMR, mass spectrometry and infrared (IR) spectroscopy. Each product showed distinctive spectral characteristics that were in line with its structure.

Table 1 | List of synthesized pyrazolone **3**

Products	R ¹	R ²	Reflux ^a		Microwave Irradiation ^b	
			Time (hrs)	Yield (%)	Time (min)	Yield (%)
3a	C ₂ H ₅	H	3	75	4	80
3b	CH ₃	C ₆ H ₅	2	60	3	81
3c	C ₂ H ₅	2,4-(NO ₂) ₂ C ₆ H ₃	3	52	5	69
3d	C ₂ H ₅	H	2	59	3	86
3e	C ₂ H ₅	H	3	58	4	78
3f	CH ₃	H	2	55	2	81
3g	CH ₃	H	2	65	2	95
3h	C ₂ H ₅	H	3	53	1	86



Reaction Conditions: **a)** Conventional heating, ethanol 10 ml, **b)** Microwave, 100°C

Scheme 1 | Synthesis of 5-(styryl)-1,2-dihydro-3H-pyrazol-3-one (**5a-h**)

Table 2 | List of synthesized compounds

Products	R ¹	R ²	Ar	Reflux ^a		Microwave Irradiation ^b	
				Time (hrs)	Yield (%)	Time (min)	Yield (%)
5a	C ₂ H ₅	H	4-OHC ₆ H ₄	9	52	12	78
5b	CH ₃	C ₆ H ₅	4-OHC ₆ H ₄	8	56	13	79
5c	C ₂ H ₅	2,4-(NO ₂) ₂ C ₆ H ₃	4-OHC ₆ H ₄	9	45	14	69
5d	C ₂ H ₅	H	3-OHC ₆ H ₄	7	52	11	84
5e	C ₂ H ₅	H	2-BrC ₆ H ₄	6	43	12	76
5f	CH ₃	H	2-NO ₂ C ₆ H ₄	7	42	12	79
5g	CH ₃	H	2,5-(OCH ₃) ₂ C ₆ H ₃	6	55	8	92
5h	C ₂ H ₅	H	3,4-(OCH ₃) ₂ C ₆ H ₃	7	41	10	87

Reaction Conditions: **a)** Conventional heating, ethanol 10 ml, **b)** Microwave, 100 °C

In vitro studies of antioxidant activity. The antioxidant activities of the synthesized derivatives of styryl pyrazolone were evaluated in a series of in vitro tests by examining their radical scavenging ability and reducing potential using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay and the Ferric Reducing Antioxidant Power (FRAP) assay. Both the DPPH and FRAP methods are widely used to measure antioxidant capacity due to their rapid assessment process, ease of standardization, and notable absorbance at a wavelength of 517 nm and 700 nm.¹² Here, DPPH is based on the reduction of the stable violet colored

2,2-diphenyl-1-picrylhydrazyl radical by an antioxidant into colorless or pale yellow 2,2-diphenyl-1-picrylhydrazine, whereas, FRAP assay measures the antioxidant capacity by monitoring the reduction of the colorless $\text{Fe}^{3+}(\text{K}_3\text{Fe}(\text{CN})_6)$ complex to the intensely blue colored ferrous ion $\text{Fe}^{2+}(\text{K}_3\text{Fe}(\text{CN})_6)$ complex.²

2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay. Trolox was used as the positive control for the investigation to assess the ability of the synthesized 5-(styryl)-1,2-dihydro-3H-pyrazol-3-one to scavenge radicals. The pyrazolones were tested at different doses (20, 40, 60, 80, and 100 $\mu\text{g}/\text{mL}$) using DPPH. **Table 3** and **Figure 1** (see Supplementary Information) illustrate the results. We determined and identified the concentration of each chemical needed to scavenge 50% of the DPPH radical in the test medium. IC_{50} denotes the amount of antioxidants necessary to diminish the DPPH concentration in the test solution by fifty percent. The DPPH radical scavenging action is better when the IC_{50} value is lower. Antioxidant reduction capacity was assessed by determining the decline in DPPH radical absorbance at 517 nm. The IC_{50} values of the compounds **5g**, **5h**, and **5d** were the lowest, indicating that they exhibited superior antioxidant activity to Trolox, with an IC_{50} value of 47.06 $\mu\text{g}/\text{mL}$.

Table 3 | IC_{50} values and standard deviations of the samples and standard Trolox.

Compound	IC_{50} value ($\mu\text{g}/\text{mL}$)	Standard Deviation \pm ($\mu\text{g}/\text{mL}$)
5a	76.51	76.51 \pm 5.55
5b	55.65	55.65 \pm 7.38
5c	103.34	103.34 \pm 6.25
5d	45.54	45.54 \pm 5.72
5e	96.36	96.36 \pm 5.62
5f	91.00	91.00 \pm 5.74
5g	18.66	18.66 \pm 2.89
5h	35.67	35.67 \pm 4.86
Trolox	47.06	47.06 \pm 4.83

Ferric reducing antioxidant power (FRAP) assay. The FRAP test relies on the conversion of ferric ion (Fe^{3+}) to ferrous ion (Fe^{2+}). This test primarily assesses an antioxidant's capacity to degrade $\text{Fe}^{3+}(\text{K}_3\text{Fe}(\text{CN})_6)$ to generate a colored $\text{Fe}^{2+}(\text{K}_3\text{Fe}(\text{CN})_6)$ complex. The antioxidant's reducing ability is confirmed via a spectrophotometric analysis of a blue ferrous complex created by employing potassium ferricyanide as a reagent to interact with ferric ions. An increase in absorbance at 700 nm signifies antioxidant activity. The reducing power of any substance is defined by its ability to give an electron or a hydrogen atom to a metal atom.^{2,13} **Figure 2** (see Supplementary Information) illustrates the absorbance measurements of the synthesized compounds across various dilutions (20, 40, 60, 80, and 100 $\mu\text{g}/\text{mL}$).

Structure activity relationship (SAR) Studies. The spatial arrangement of substituents, particularly their stereochemistry, is crucial for biological activity, especially when specialized receptor interactions are necessary. This factor has demonstrated particular significance in the design of enzyme inhibitors, where exact spatial configurations dictate binding affinity and selectivity. Substitutions on the aromatic ring substantially influence the antioxidant activity of compounds (**5a–5h**). The antioxidant potency of the compounds was enhanced by the introduction of electron-donating and electron-withdrawing groups at the aromatic rings. All the compounds that exhibit the highest inhibitions contain methoxy and hydroxy substituents.¹⁴

The maximum effect against standard Trolox of IC_{50} of 47.06 $\mu\text{g/mL}$ was exhibited by compound **5g**, which contained a methoxy group, with an IC_{50} value of 18.66 $\mu\text{g/mL}$. The antioxidant activity was significantly enhanced by the introduction of a methoxy group. However, the bromo and nitro groups of compounds **5e**, **5c**, and **5f**, which have an electron-withdrawing group, exhibited lessened antioxidant activity. The synthesized compounds exhibited significant antioxidant activity in both DPPH and FRAP assays. In DPPH assay, high radical scavenging activity was observed by compound **5g**, **5h**, **5d** indicating effective hydrogen donating ability. Similarly, the FRAP assay showed strong reducing power, suggesting the presence of potent electron donating antioxidants.

Conclusions

In conclusion, we report the synthesis of a new series of styryl pyrazolone derivatives through a streamlined multicomponent reaction involving various 1,3-dicarbonyl compounds, hydrazine and substituted benzaldehydes using sodium hydroxide, sodium acetate and acetic acid. The novelty of this work lies in the diversity of both the starting materials and the synthesized products, allowing for structural variation and potential tuning of physicochemical and biological properties. To the best of our knowledge, this investigation is the first systematic synthesis of derivatives of styryl pyrazolones, which offers a simple, efficient, and versatile method for generating novel heterocyclic scaffolds with potential pharmaceutical relevance. This study demonstrates a solventless synthesis approach to a styryl pyrazolone derivative, 5-(Styryl)-1,2-dihydro-3H-Pyrazol-3-one, offering an environmentally friendly and efficient method. Synthesized styryl pyrazolone derivatives displayed potent antioxidant activity, with some surpassing Trolox, underscoring their promise as potential pharmacological leads. The synthesis of styryl pyrazolone compounds continues to hold significant value due to their diverse applications across pharmaceuticals, agriculture, and materials science. These results complement the growing body of work in sustainable organic synthesis and open avenues for further exploration of biologically active heterocycles.

Experimental section

General. All reagents were sourced from Merck, Avarice, Actylis, and Finsolv and were used without purification. The reactions were carried out using an Anton Paar Monowave 400 microwave digester. Melting points were determined using an Ikon melting point apparatus in open capillary tubes. IR spectra were obtained using a Perkin-Elmer 1725X FTIR spectrometer. Mass spectra were obtained using an Advion Express Mass Spectrophotometer. The NMR spectra were recorded using the Bruker spectrometer at 400 MHz for ^1H NMR and 101 MHz for ^{13}C NMR, with CDCl_3 and DMSO as solvents and tetramethylsilane (TMS) as the internal standard. The chemical shifts were denoted as δ (ppm). Elemental (CHN) analysis was conducted using a Eurovector elemental analyser (Elemental analyser EA3100). The *in vitro* antioxidant activity was measured using the Microplate Spectrophotometer (Thermo Scientific Multiskan SkyHigh version 2.0.35).

General procedure for the synthesis of pyrazolones (3a-h) under the conventional method: Pyrazolones **3** was synthesized using starting materials 1,3-dicarbonyl compound **1** (2 mmol), hydrazine **2** (2 mmol), and sodium hydroxide (2 mmol) with ethanol as a solvent in a round-bottom flask and refluxed for 2 to 3 hrs. The

reaction completion was monitored by thin-layer chromatography (TLC) and the crude reaction mixture was extracted with ethyl acetate. The crude product was further purified by column chromatography, eluting with an ethyl acetate/hexane mixture (20:80). The isolated product was then thoroughly dried under high vacuum to strip away any remaining solvent prior to characterization.

General procedure for the synthesis of styryl pyrazolones (5a-h) under the conventional method: Pyrazolone **3**, aldehyde derivatives **4** (2 mmol), sodium acetate (2 mmol), and acetic acid (2 mmol) were added, and the reaction mixture was refluxed for 2–4 hrs to synthesize styryl pyrazolones **5**. Completion of the reaction was monitored by thin-layer chromatography (TLC) using silica gel-coated aluminum plates with 20:80 ethyl acetate and hexane, after which the crude was extracted with ethyl acetate and further purified by column chromatography.

General procedure for synthesis of pyrazolones (3a-h) and styryl pyrazolones (5a-h) under microwave-assisted conditions: 1,3-dicarbonyl compound **1** (2 mmol), hydrazine **2** (2 mmol), and sodium hydroxide (2 mmol) were mixed thoroughly in a Pyrex test tube (glass vial G30 mL) and exposed to microwave irradiation for 1-5 min at 100°C, giving pyrazolone **3**. The reaction progress was monitored by thin-layer chromatography (TLC) on silica gel-coated aluminum plates using an ethyl acetate/hexane (20:80) solvent system. After completion was confirmed by TLC, the reaction mixture was extracted with ethyl acetate. The crude product was then purified by recrystallization from hot ethanol. In the second step, pyrazolone **3** is reacted with aldehyde **4** (2 mmol), sodium acetate (2 mmol), and acetic acid (2 mmol) to form styryl pyrazolones (**5a-h**) under microwave irradiation at 180°C for 7-9 min at the interval of 1 min (**Table 2**). The progress of the reaction was monitored by thin-layer chromatography (TLC) using silica gel-coated aluminum plates, with an ethyl acetate/hexane (20:80) solvent as the mobile phase. After confirming completion of the reaction by TLC, the reaction mixture was extracted with ethyl acetate, and the solvent was subsequently removed under reduced pressure using a rotary evaporator. The resulting crude product was purified by recrystallization from hot ethanol. Accordingly, the overall reaction time taken for the two-step synthesis of **5a-h** under conventional heating was 6-9 hrs, whereas MWI considerably shortened the reaction time to 8-14 min [**Scheme 1, Table 2**]. The structures of the synthesized compounds were established using various spectroscopic methods, including infrared (IR) spectroscopy, mass spectrometry, and nuclear magnetic resonance (¹H NMR and ¹³C NMR), each exhibiting characteristic signals consistent with the proposed structures.

The structures of all synthesized compounds were confirmed using spectral analysis (IR, ¹H NMR, ¹³C NMR, and mass spectrometry) along with CHN elemental analysis. All compounds displayed the expected characteristic signals consistent with their proposed structures. The corresponding data are presented below.

Spectral Analytical Data

5-(4-Hydroxystyryl)-1,2-dihydro-3H-pyrazol-3-one (5a). Yield 78%, Light Orange Solid, mp.-195-197 °C (Recrystallized from hot ethanol); IR (KBr) Cm^{-1} : 3271 (O-H), 3199 (N-H), 3110 (N-H), 1722 (C=O), 1603 (C=C), 1293 (C-N), 1121 (C-N), 731 (C-H); ¹H NMR (400 MHz, DMSO) δ 7.74 – 7.72 (s, 1H, O-H), 7.68 (s, 1H, N-H), 6.96 (d, $J = 8.2$ Hz, 2H, CH=CH), 6.59 – 6.50 (m, 4H, Ar-H), 5.20 (s, 1H, N-H), 4.60 (s, 1H, C-H); ¹³C NMR (101 MHz, DMSO) δ 167.40, 161.06, 135.59, 131.97, 129.12, 128.75, 114.79, 104.17, 89.14; MS: m/z 200.7 (M)⁺. Calcd for C₁₁H₁₀N₂O₂: C, 65.34; H, 4.98; N, 13.85% Anal. Found: C, 65.09; H, 4.64; N, 13.54%.

5-(4-Hydroxystyryl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (5b). Yield 79%, Brick red Solid, mp.-160-162 °C (Recrystallized from hot ethanol), IR (KBr) Cm^{-1} : 3403 (O-H), 3202 (N-H), 1710 (C=O), 1616 (C=C), 1341 (C-N), 1197 (C-O), 760 (C-H); $^1\text{H NMR}$ (400 MHz, DMSO) δ 10.84 (s, 1H, O-H), 8.64 (d, $J = 8.8$ Hz, 2H, Ar-H), 7.94 (d, $J = 8.6$ Hz, 2H, CH=CH), 7.72 (d, $J = 10.3, 7.3$ Hz, 2H, Ar-H), 7.46 – 7.43 (m, 3H, Ar-H), 6.95 (d, $J = 8.7$ Hz, 2H, Ar-H), 4.85 (s, 1H, N-H), 4.29 (s, 1H, C-H); $^{13}\text{C NMR}$ (101 MHz, DMSO) δ 163.79, 152.52, 139.20, 138.13, 132.21, 129.64, 129.50, 125.63, 125.06, 119.00, 118.58, 116.57, 62.04; MS: m/z 279.1 (M)⁺. Calcd for $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_2$: C, 73.37; H, 5.07; N, 10.07% Anal. Found: C, 72.99; H, 5.15; N, 9.98%.

2-(2,4-Dinitrophenyl)-5-(4-hydroxystyryl)-1,2-dihydro-3H-pyrazol-3-one (5c). Yield 69%, Yellow crystal, mp.-60-62 °C (Recrystallized from hot ethanol), IR (KBr) Cm^{-1} : 3424 (O-H), 3312 (N-H), 1730 (C=O), 1622 (C=C), 1517 (N-O), 1337 (N-O), 1208 (C-N), 1027(C-O), 743 (C-H); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.09 (s, 1H, O-H), 9.13 (s, 1H, Ar-H), 8.28 – 7.98 (m, 4H, Ar-H), 7.97-7.94 (d, $J = 7.8$ Hz, 2H, CH=CH), 7.27 (d, $J = 6.9, 1.3$ Hz, 2H, Ar-H), 4.24 (s, 1H, N-H), 3.49 (s, 1H, C-H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.25, 150.80, 145.00, 138.19, 130.03, 129.46, 129.39, 123.39, 116.57, 77.36, 77.04, 76.73, 61.44, 44.50, 16.20; MS: m/z 367.3 (M)⁺. Calcd for $\text{C}_{17}\text{H}_{12}\text{N}_4\text{O}_6$: C, 55.44; H, 3.28; N, 15.21% Anal. Found: C, 54.99; H, 3.25; N, 15.18%.

5-(3-Hydroxystyryl)-1,2-dihydro-3H-pyrazol-3-one (5d). Yield 84%, Orange crystal, mp.-120-122 °C (Recrystallized from hot ethanol), IR (KBr) Cm^{-1} : 3272 (O-H), 3110 (N-H), 3088 (N-H), 1726 (C=O), 1602 (C=C), 1289 (C-N), 1121 (C-N), 759 (C-H); $^1\text{H NMR}$ (400 MHz, DMSO) δ 7.67 (s, 1H, O-H), 6.98 (s, 1H, N-H) 6.96 (m, 1H, Ar-H), 6.60 (s, 1H, Ar-H), 6.56 (d, $J = 7.8$ Hz, 2H, CH=CH), 6.49 (d, $J = 5.8$ Hz, 2H, Ar-H), 5.20 (s, 1H, N-H), 4.67 (s, 1H, C-H); $^{13}\text{C NMR}$ (101 MHz, DMSO) δ 173.51, 161.25, 157.41, 146.12, 140.60, 128.86, 118.69, 115.09, 112.70, 104.19, 89.26; MS: m/z 202.9 (M)⁺. Calcd for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_2$: C, 65.34; H, 4.98; N, 13.85% Anal. Found: C, 64.94; H, 4.72; N, 13.66%.

5-(2-Bromostyryl)-1,2-dihydro-3H-pyrazol-3-one (5e). Yield 76%, Soft pink crystal, mp.-180-182 °C (Recrystallized from hot ethanol), IR (KBr) Cm^{-1} : 3336 (N-H), 3136 (N-H), 1714 (C=O), 1617 (C=C), 1252 (C-N), 753 (C-N), 690 (C-Br); $^1\text{H NMR}$ (400 MHz, DMSO) δ 7.76 (s, 1H, N-H), 7.74 (d, $J = 7.5$ Hz, 2H, CH=CH), 7.46-7.21 (d, $J = 7.9, 1.2$ Hz, 2H, Ar-H), 7.07 – 7.01 (m, 2H, Ar-H), 5.21 (s, 1H, N-H), 5.01 (s, 1H, C-H); $^{13}\text{C NMR}$ (101 MHz, DMSO) δ 161.41, 160.88, 144.11, 140.02, 132.59, 131.69, 127.87, 127.36, 123.37, 102.44, 89.21; MS: m/z 262.9 (M)⁺. Calcd for $\text{C}_{11}\text{H}_9\text{BrN}_2\text{O}$: C, 49.84; H, 3.42; N, 10.57% Anal. Found: C, 49.53; H, 3.71; N, 10.67%.

5-(2-Nitrostyryl)-1,2-dihydro-3H-pyrazol-3-one (5f). Yield 79%, yellowish crystal, mp.-160-162 °C (Recrystallized from hot ethanol), IR (KBr) Cm^{-1} : 3404 (N-H), 3223(N-H), 1729 (C=O), 1622 (C=C), 1516 (N-O), 1209 (C-N), 744 (C-H); $^1\text{H NMR}$ (400 MHz, DMSO) δ 7.72 (s, 1H, N-H), 7.61 (d, $J = 7.9, 1.3$ Hz, 2H, CH=CH), 7.51 (d, $J = 1.2$ Hz, 2H, Ar-H), 7.35 – 7.33 (m, 2H, Ar-H), 5.34 (s, 1H, N-H), 5.18 (s, 1H, C-H); $^{13}\text{C NMR}$ (125 MHz, DMSO) δ 168.02, 147.47, 135.53, 133.25, 130.45, 130.38, 129.34, 125.09, 124.93, 122.95, 82.37; MS: m/z 232.1 (M)⁺. Calcd for $\text{C}_{11}\text{H}_9\text{N}_3\text{O}_3$: C, 57.14; H, 3.92; N, 18.17% Anal. Found: C, 56.75; H, 3.64; N, 18.58%.

5-(2,5-Dimethoxystyryl)-1,2-dihydro-3H-pyrazol-3-one (5g). Yield 92%, Colorless crystal, mp.-180-182 °C (Recrystallized from hot ethanol), IR (KBr) Cm^{-1} : 3336 (N-H), 3101 (N-H), 2834 (OCH_3), 2751 (OCH_3), 1703 (C=O), 1610 (C=C), 1220 (C-O), 1046(C-O), 754 (C-H); $^1\text{H NMR}$ (400 MHz, DMSO) δ 8.91 (s, 1H, NH), 7.33 (d, $J = 3.1$ Hz, 1H, Ar-H), 7.09 (d, $J = 9.2$ Hz, 1H, Ar-H), 6.73 (s, 1H, Ar-H), 6.60 (d, $J = 3.1$ Hz, 2H, CH=CH), 3.68 (s, 1H, N-H), 3.62 (s, 1H, C-H), 2.08 (s, 3H, OCH_3), 2.04 (s, 3H, OCH_3); $^{13}\text{C NMR}$ (101 MHz, DMSO) δ 161.39, 153.19,

150.47, 139.98, 122.53, 119.96, 116.98, 111.45, 110.19, 103.45, 89.19, 56.34, 55.54; **MS: m/z** 246.2 (M)⁺. **Calcd for C₁₃H₁₄N₂O₃**: C, 63.40; H, 5.73; N, 11.38% **Anal. Found**: C, 63.33; H, 5.48; N, 11.12%.

5-(3,4-Dimethoxystyryl)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (5h). Yield 87%, light orange crystal, mp.-140 °C (Recrystallized from hot ethanol), **IR (KBr) Cm⁻¹**: 3195 (N-H), 2860 (OCH₃), 2790 (OCH₃), 1728 (C=O), 1654 (C=C), 1292 (C-N), 1034 (C-O), 1022(C-O), 745 (C-H); **¹H NMR (400 MHz, DMSO) δ** 7.74 (d, *J* = 7.9 Hz, 2H, CH=CH), 7.58 (d, *J* = 1.3 Hz, 2H, Ar-H), 7.52 – 7.50 (m, 3H, Ar-H), 7.35 – 7.30 (m, 3H, Ar-H), 5.31 (s, 1H, N-H), 5.20 (s, 1H, C-H), 2.08 (s, 3H, OCH₃), 1.95 (s, 3H, OCH₃); **¹³C NMR (101 MHz, DMSO) δ** 173.32, 161.42, 160.93, 149.82, 140.23, 139.93, 138.42, 135.17, 133.26, 131.82, 131.29, 126.99, 123.76, 101.75, 89.24, 74.37, 68.21; **MS: m/z** 323.1(M)⁺. **Calcd for C₁₉H₁₈N₂O₃**: C, 70.79; H, 5.63; N, 8.69% **Anal. Found**: C, 70.58; H, 5.37; N, 8.72%.

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Supplementary Material

The authors confirm that all data supporting the findings of this study are available in the main article and the Supporting Information file.

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By checking the following box, the senior author acknowledges that they and the other authors have read, understood, and complied with the Instructions to Authors (ItA).