

An efficient synthesis of new pyrazolone-substituted C-acylimine derivatives by three-component reaction between arylglyoxal derivatives, arylamines and pyrazolone

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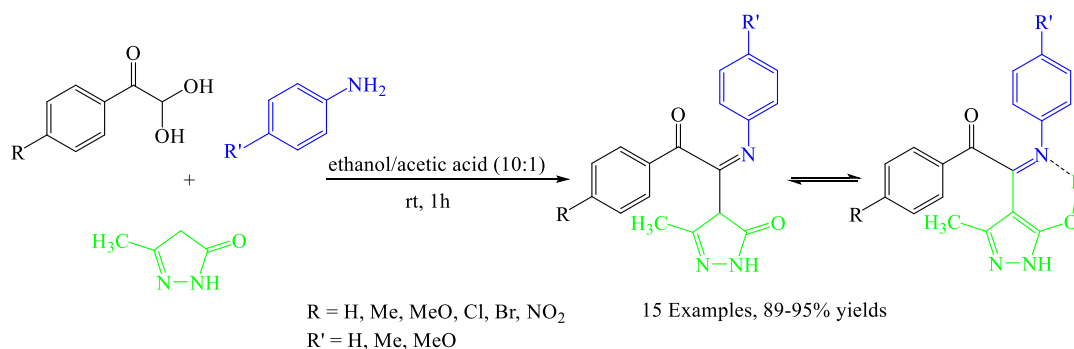
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Abstract

An effective protocol for synthesis of some new pyrazolone-substituted C-acylimine derivatives is reported through a one-pot three-component reaction between arylglyoxals, aniline derivatives and pyrazolone. All reactions were conducted in ethanol/acetic acid mixture as solvent and the stable products were obtained by simple filtering off the precipitated solids in high yields. The structures of all products were proved by ^1H and ^{13}C NMR and IR spectral and elemental analysis data.



Keywords: Arylglyoxals, C-acylimine, three-component reaction, pyrazolone, aniline,

Introduction

C-Acylimine is an important building block in organic chemistry in which the two heteroatoms oxygen and nitrogen are nucleophilic centers and the carbonyl and imine carbons show electrophilicity. These intermediates have found many applications for synthesis of a wide range of acyclic and cyclic nitrogen-containing organic compounds.¹⁻³ Reduction of these compounds or nucleophilic additions to their imine group have been widely used for synthesis of α -amino carbonyl compounds with important biological and pharmaceutical activities.⁴⁻⁸ C-Acylimines have been also reported as versatile intermediates for the synthesis of polyfunctionalized amino-compounds.^{9,10} C-Acylimines are generally prepared by condensation of glyoxal derivatives with amines.¹¹⁻¹⁷ A few other methods were also used for synthesis of C-acylimines such as NHC catalyzed arylation of aromatic aldehydes with imidoylchlorides,¹⁸ nitrosobenzene mediated C-C bond cleavage reaction with LHMDs¹⁷ and desulfonation of α -N-Boc sulfone ketone derivatives.²⁰ However, due to the importance of C-acylimines as key intermediates in organic chemistry, developing of new synthetic routes for their preparation is greatly desired.

Pyrazolone and its derivatives are a class of important aza-heterocyclic compounds with a variety of biological and farmaceutical activities and a variety of drug-like pyrazolone derivatives have been synthesized and investigated as candidates for medicinal features including antitumor, antimicrobial, anti-inflammatory activities, and so on.²¹

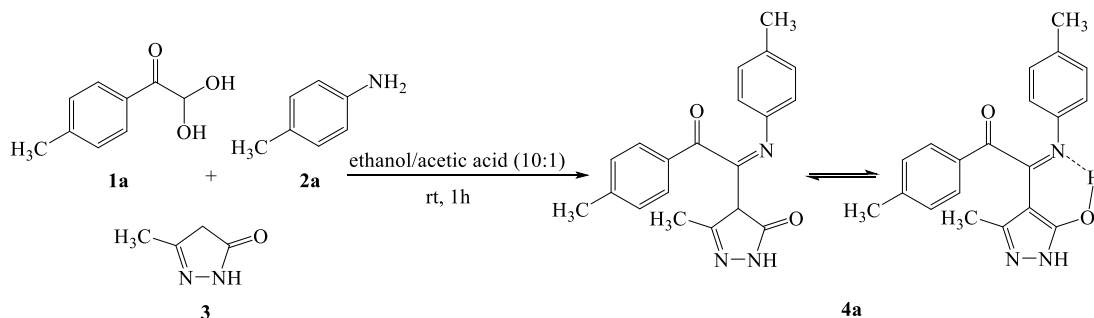
In continuation of our works on multicomponent reactions of arylglyoxals,²²⁻²⁴ we found that three-component reaction between arylglyoxal derivatives, arylamines and pyrazolone could be used as a simple and efficient method for synthesis of some new pyrazolone-substituted C-acylimine derivatives.

Results and Discussion

At first, three-component reaction between 4-methylphenylglyoxal monohydrate (**1a**), pyrazolone (**2**) and 4-methylaniline (**3a**) was studied (Scheme 1). A 1:1:1 molar ratio mixture of these compounds in 10:1 mixture of ethanol/acetic acid as solvent was stirred at room temperature. After 1 hour a solid product was precipitated which was filtered off and its structure was proved by elemental analysis and IR and NMR spectral data as C-acylimine **4a**. Compound **4a** may exist as two tautomers and the NMR spectra of this compound showed the presence of two tautomers in nearly 80:20 ratio. The ¹H NMR spectrum of **4a** showed three singlet signals at 1.98, 2.14 and 2.36 ppm for three methyl groups. The CH of pyrazolone moiety showed a single signal at 5.90 ppm. The aromatic protons were observed as doublet signals at 6.64 (6.52 for minor tautomer), 6.85, 7.32, and 8.00 (7.74 for minor tautomer) ppm. The NH and OH protons were observed as two D₂O-exchangable broad signals at 5.77 and 10.80 ppm, respectively. ¹H-decoupled ¹³C NMR spectrum of **4a** showed 16 distinct resonances in agreement with the suggested structure. Structure **4a** was also confirmed by the IR spectrum showing absorption bands at 3406, 3366 and 1679 cm⁻¹ for NH, OH and carbonyl groups, respectively.

Then the reaction conditions, including the solvent and temperature were optimized and the results are shown in Table 1.. When the reaction was carried out in solvents such as EtOH, H₂O, MeCN, and DMF at room temperature the product **4a** was obtained in 60, 30, 45 and 50% yields respectively (entries 4-7). When the reaction was carried out in refluxing ethanol/acetic acid mixture the yield was not improved and product **4a** was obtained in 95% yield after 4h (entry 2). Increasing the reaction time did not also improved the product

yield (entry 3). From these results ethanol/acetic acid mixture at room temperature was selected as the best reaction condition for synthesis of C-acylimine **4a**.



Scheme 1. Three-component reaction between 4-methylphenylglyoxal monohydrate, 4-methylaniline and pyrazolone for synthesis of C-acylimine **4a**

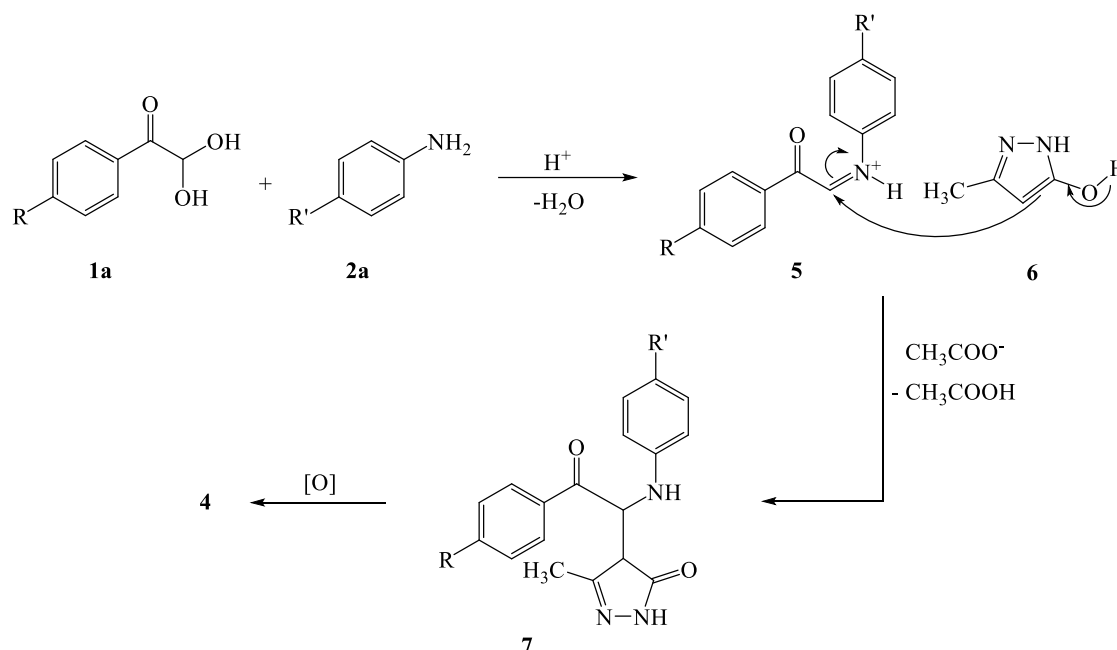
Table 1. Optimization of the reaction conditions for synthesis of compound **4a**^a

Entry	Solvent	Temperature (°C)	Time (minute)	Yield% ^a
1	EtOH/CH ₃ CO ₂ H (10:1)	25	60	95
2	EtOH/CH ₃ CO ₂ H (10:1)	78	240	95
3	EtOH/CH ₃ CO ₂ H (10:1)	25	120	95
4	EtOH	25	60	60
5	H ₂ O	25	120	30
6	CH ₃ CN	25	120	45
7	DMF	25	120	50

^aReaction conditions: 4-methylphenylglyoxal **1a** (1.0 mmol), 4-methylaniline **2a** (1.0 mmol), pyrazolone (1.0 mmol) and solvent (15 mL). ^bIsolated yield.

To explore the scope of this reaction, different arylglyoxals were reacted with aromatic amines and the results are shown in Table 2. The results showed that both the electron-poor and electron-rich arylglyoxals are compatible with the reaction and high yields of products were obtained. However, when an alkylglyoxal such as methylglyoxal was reacted with different aniline derivatives and pyrazolone under same reaction conditions no product could be isolated. It was also noted that when the arylglyoxals were reacted with electron-poor aniline derivatives such as chloroanilines or nitroanilines, related C-acylimines were not obtained.

The proposed mechanism for the formation of pyrazolone-substituted C-acylimine **4a** by the reaction between pyrazolone, arylglyoxal derivatives and aromatic amines is depicted in Scheme 2. The condensation of arylglyoxals with aniline derivatives promoted by acetic acid afforded the related iminium intermediate **5**. The iminium cation **5** was attacked by the enole of pyrazolone (**6**) to afford the aminoketone adduct **7** which was oxidized by air to afford C-acylimine **4**.

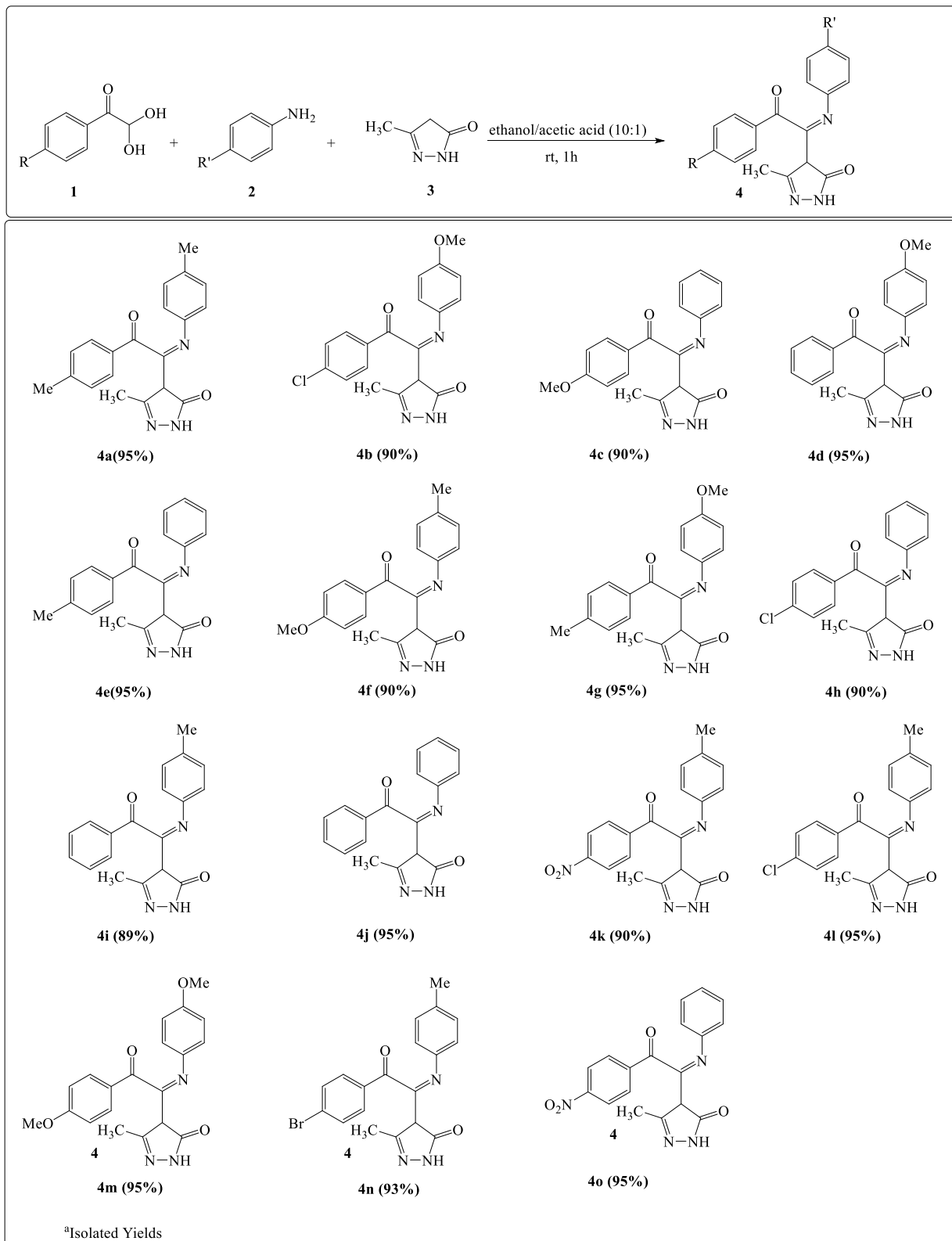


Scheme 2. Suggested mechanism for formation of C-acylimine **4** by three-component reaction between arylglyoxals, aniline derivatives and pyrazolone.

Conclusions

In conclusion we found that three-component reaction between arylglyoxals, aniline derivatives and pyrazolone in ethanol/acetic acid (10:1) mixture provides a facile one-pot method for synthesis of some new pyrazolone-substituted C-acylimine derivatives. It was found that different arylglyoxal derivatives with electron-withdrawing and electron-releasing groups are compatible with the reaction, but alkylglyoxals did not afford the desired products and only the starting materials were recovered. It was also found that electron-poor anilines and aliphatic amine didn't lead to any isolable product. The advantages of the method are readily available starting materials, simple and ambient reaction conditions, simple workup procedure and high yields of products.

Table 2. Synthesis of C-acylimine derivatives by three-component reaction between arylglyoxals, aniline derivatives and pyrazolone.^a



Experimental Section

General. All solvents and chemicals were purchased from commercial sources and used without further purification. The utilized arylglyoxals were prepared by the SeO₂-oxidation of the related aryl methylketones

on the basis of the reported procedure, and used as their monohydrates.²² Melting points were determined on a Melt-Tem II melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu IR-470 spectrometer. All of the NMR spectra were recorded on a Varian model UNITY Inova 500 MHz or Bruker DRX-300 Avance NMR spectrometer. Chemical shifts of ¹H and ¹³C are reported in parts per million (ppm) from tetramethylsilane (TMS) as an internal standard in DMSO as solvent.

General procedure. A mixture of aromatic amine derivative (1.0 mmol), arylglyoxal derivative (1.0 mmol) and 3-methyl-1*H*-pyrazol-4(5*H*)-one (1.0 mmol) was stirred at room temperature in ethanol/acetic acid (11mL, 10:1) for 1h. The precipitated solid was filtered off and washed with cold ethanol to afford the pure product.

(E)-3-methyl-4-(2-oxo-2-(*p*-tolyl)-1-(*p*-tolylimino)ethyl)-1*H*-pyrazol-5(4*H*)-one (4a). Yield: (95%); Yellow powder; mp 190-191 °C. IR (KBr) (ν_{max} , cm^{-1}): 1679 (C=O), 3366 (NH). ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 1.98, 2.14, 2.36 (9H, 3s, 3CH₃), 5.77 (1H, broad s, NH), 5.90 (1H, s, CH), 6.64 (6.52) (2H, d, *J* 8 Hz, Ar-H), 6.88 (6.84) (2H, d, *J* 8 Hz, Ar-H), 7.32 (2H, d, *J* 8 Hz, Ar-H), 8.00 (7.74) (2H, d, *J* 8 Hz, Ar-H), 10.77 (1H, broad s, OH) ppm. ¹³C-NMR (75 MHz, DMSO-*d*₆): δ = 10.78 (19.04), 20.55 (20.61), 21.60 (21.67) (3CH₃), 52.49 (56.52) (CH), 98.07, 113.50, 114.74, 124.99 (124.74), 128.73, 129.62, 129.70 (129.74), 132.89 (138.48), 144.19, 145.25 (146.13) (aromatic and C=N), 159.95 (C=O, amide), 195.50 (C=O, ketone) ppm. Anal Calcd for C₂₀H₁₉N₃O₂: C, 72.05; H, 5.74; N, 12.60%. Found: C, 71.93; H, 5.65; N, 12.77%.

(E)-4-(2-(4-chlorophenyl)-1-((4-methoxyphenyl)imino)-2-oxoethyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4b). Yield: (90%); Creamy powder; mp 159-160 °C. IR (KBr) (ν_{max} , cm^{-1}): 1679 (C=O), 3371 (NH). ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 1.98 (3H, s, CH₃), 3.63 (3H, s, OCH₃), 5.61 (1H, broad s, NH), 5.88 (1H, s, CH), 6.55-6.70 (4H, m, aromatic), 7.58 (2H, d, *J* 8 Hz, aromatic), 8.06 (2H, d, *J* 8 Hz, aromatic), 11.39 (1H, broad s, OH) ppm. ¹³C-NMR (75 MHz, DMSO-*d*₆): δ = 10.75 (CH₃), 53.19 (CH), 55.71 (55.74) (OCH₃), 97.63, 114.47, 114.84, 114.97, 115.93, 129.26, 130.47, 134.21, 138.59, 141.59 (Ar and C=N), 151.49 (C=O, amide), 195.15 (C=O, ketone) ppm. Anal Calcd for C₁₉H₁₆ClN₃O₃: C, 67.71; H, 4.36; N, 11.36%. Found: C, 67.80; H, 4.25; N, 11.43%.

(E)-4-(2-(4-methoxyphenyl)-2-oxo-1-(phenylimino)ethyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4c). Yield: (90%); Pink powder; mp 190 °C (decompose). IR (KBr) (ν_{max} , cm^{-1}): 1666 (C=O), 3375 (NH). ¹H-NMR (500 MHz, DMSO-*d*₆): δ = 1.95 (1.90) and 3.80 (3.79) (6H, 2s, 2 CH₃), 5.85 and 5.89 (2H, m, CH and NH), 6.67-7.00 (7H, m, aromatic), 7.77-8.05 (2H, m, aromatic), 10.86 (1H, broad s, OH) ppm. ¹³C-NMR (125 MHz, DMSO-*d*₆): δ = 10.76 (21.46) (CH₃), 52.11 (CH), 55.98 (OCH₃), 98.31, 113.31, 114.38, 114.58, 116.54 (116.41), 129.11 (129.23), 130.93, 138.55, 147.50 (148.62), 159.84 (aromatic and C=N), 163.65 (C=O, amide), 194.26 (C=O, ketone) ppm. Anal Calcd for C₁₉H₁₇N₃O₃: C, 68.05; H, 5.11; N, 12.53%. Found: C, 68.25; H, 5.15; N, 12.39%.

(E)-4-(1-((4-methoxyphenyl)imino)-2-oxo-2-phenylethyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4d). Yield: (95%); Grey powder; mp 168-169 °C. IR (KBr) (ν_{max} , cm^{-1}): 1680 (C=O), 3365 (NH). ¹H-NMR (500 MHz, DMSO-*d*₆): δ = 1.95 and 3.60 (3.61) (6H, 2s, 2CH₃), 5.56 (1H, broad s, NH), 5.87 (1H, s, CH), 6.52-6.69 (4H, m, aromatic), 7.44-7.58 (3H, m, aromatic), 8.04-8.05 (2H, m, aromatic), 11.06 (1H, broad s, OH) ppm. ¹³C-NMR (125 MHz, DMSO-*d*₆): δ = 10.73 (CH₃), 53.20 (CH), 55.76 (OCH₃), 97.98, 114.49, 114.90, 115.01, 115.74, 128.54, 129.06, 133.61, 135.53, 141.67, 151.53 (aromatic and C=N), 159.91 (C=O, amide), 196.09 (C=O, ketone) ppm. Anal Calcd for C₁₉H₁₇N₃O₃: C, 68.05; H, 5.11; N, 12.53%. C, 68.11; H, 5.10; N, 12.27%.

(E)-3-methyl-4-(2-oxo-1-(phenylimino)-2-(*p*-tolyl)ethyl)-1*H*-pyrazol-5(4*H*)-one (4e). Yield: (95%); Pink powder; mp 169 °C (decompose). IR (KBr) (ν_{max} , cm^{-1}): 1710 (C=O), 3385 (NH). ¹H-NMR (500 MHz, DMSO-*d*₆): δ = 1.90 (1.95) (CH₃), 5.88 (1H, s, CH), 5.92 (1H, broad s, NH), 6.47-6.68 (3H, m, aromatic), 6.97-7.03 (2H, m, aromatic), 7.27 (2H, m, aromatic), 7.75-7.95 (2H, m, aromatic), 11.03 (1H, broad s, OH) ppm. ¹³C-NMR (125 MHz, DMSO-*d*₆): δ = 10.73 (18.99) (CH₃), 21.47 (21.54) (CH₃), 56.49 (52.32), 98.029, 113.28, 114.39, 116.17 (116.56),

128.69 (129.11), 129.22 (129.65), 144.15 (138.56), 147.49 (148.90), 159.86 (aromatic), 172.39 (C=O amide), 195.35 (C=O ketone) ppm. Anal Calcd for C₁₉H₁₇N₃O₂: C, 71.46; H, 5.37; N, 13.16%.

(E)-4-(2-(4-methoxyphenyl)-2-oxo-1-(*p*-tolylimino)ethyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4f). Yield: (90%); Creamy powder; mp °C. IR (KBr) (ν_{max}, cm⁻¹): 1676(C=O), 3359 (NH). ¹H-NMR (500 MHz, DMSO-d₆): δ = 1.94, 2.11 (6H, 2s, 2CH₃), 3.80 (3H, s, OCH₃), 5.69 (1H, broad s, NH), 5.83 (1H, s, CH), 6.46 and 6.58 (6.80 and 6.83) (4H, 2d, *J* 8 Hz, aromatic), 6.9.2-7.01 (2H, m, aromatic), 8.04 (7.76) (2H, d, *J* 8 Hz, aromatic), 10.73 (1H, broad s, OH) ppm. ¹³C-NMR (125 MHz, DMSO-d₆): δ = 10.76, 20.49 (20.55) (2CH₃), 52.35 (CH), 55.97 (OCH₃), 98.38, 113.51, 114.35, 114.67, 124.97, 128.15, 129.56, 129.66, 130.91, 145.23 (146.23), (Ar and C=N), 163.62 (159.88) (C=O, amide), 194.42 (C=O, ketone) ppm. Anal Calcd for C₂₀H₁₉N₃O₃: C, 68.75; H, 5.48; N, 12.03%. Found: C, 68.80; H, 5.45; N, 12.22%.

(E)-4-(1-((4-methoxyphenyl)imino)-2-oxo-2-(*p*-tolyl)ethyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4g). Yield: (95%); Cedar green powder; mp 178-179 °C. IR (KBr) (ν_{max}, cm⁻¹): 1675 (C=O), 3371 (NH). ¹H-NMR (500 MHz, DMSO-d₆): δ = 1.93 and 2.33 (6H, 2s, 2CH₃), 3.59 (3.60) (3H, s, OCH₃), 6.52 (1H, broad s, NH), 6.53 (1H, s, CH), 6.54-6.68 (4H, m, aromatic), 7.23-7.28 (2H, m, aromatic), 7.68-7.98 (2H, m, aromatic), 11.15 (1H, broad s, OH). ¹³C-NMR (125 MHz, DMSO-d₆): δ = 10.73, 21.55 (2CH₃), 53.03 (CH), 55.76 (OCH₃), 89.61, 114.46, 114.90, 115.01, 115.71, 128.67, 129.61, 132.99, 141.70, 144.06, 151.49 (aromatic and C=N), 159.90 (C=O, amide), 195.66 (C=O, ketone) ppm. Anal Calcd for C₂₀H₁₉N₃O₃: C, 68.75; H, 5.48; N, 12.03%. Found: C, 68.67; H, 5.45; N, 12.11%.

(E)-4-(2-(4-chlorophenyl)-2-oxo-1-(phenylimino)ethyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4h). Yield: (90%); Creamy powder; mp 180-181 °C. IR (KBr) (ν_{max}, cm⁻¹): 1676 (C=O), 3378 (NH). ¹H-NMR (300 MHz, DMSO-d₆): δ = 2.00 (3H, s, CH₃), 5.95 (2H, m, CH and NH), 6.52-7.34 (3H, m, aromatic), 7.00-7.09 (2H, m, aromatic), 7.57(2H, d, *J* 9 Hz, aromatic), 8.08 (2H, d, *J* 9 Hz, aromatic), 10.74 (1H, broad s, OH) ppm. ¹³C-NMR (75 MHz, DMSO-d₆): δ = 10.77 (19.08), (CH₃), 52.54 (56.56) (CH), 97.51, 113.32, 114.53, 116.68 (116.37), 129.31 (129.20), 130.51, 134.10, 138.76 (138.68), 147.46, 148.75 (aromatic and C=N), 159.93 (C=O, amide), 194.85 (C=O, ketone) ppm. Anal Calcd for C₁₈H₁₄ClN₃O₂: C, 63.63; H, 4.15; N, 12.37%. Found: C, 63.59; H, 4.15; N, 12.35%.

(E)-3-methyl-4-(2-oxo-2-phenyl-1-(*p*-tolylimino)ethyl)-1*H*-pyrazol-5(4*H*)-one (4i). Yield: (89%); Yellow powder; mp 182-183 °C. IR (KBr) (ν_{max}, cm⁻¹): 1677 (C=O), 3376 (NH). ¹H-NMR (300 MHz, DMSO-d₆): δ = 2.02, 2.15 (6H, 2s, 2CH₃), 5.79 (1H, broad s, NH), 5.95 (1H, s, CH), 6.63 (6.52) (2H, d, *J* 9 Hz, aromatic), 6.86 (2H, m, aromatic), 7.49-7.64 (3H, m, aromatic), 8.08 (7.83) (2H, d *J* 8Hz, aromatic), 10.91 (1H, broad s, OH) ppm. ¹³C-NMR (75 MHz, DMSO-d₆): δ = 10.79, 20.56 (20.62) (2CH₃), 52.62 (56.53) (CH), 97.86, 113.51, 114.74, 125.04 (124.75), 128.62, 129.17, 129.75 (129.64), 133.75, 135.41 (138.59), 145.24 (146.13) (aromatic and C=N), 159.98 (C=O, amide), 195.91 (C=O, ketone) ppm. Anal Calcd for C₁₉H₁₇N₃O₂: C, 71.46; H, 5.37; N, 13.16%. Found: C, 71.39; H, 5.30; N, 13.22%.

(E)-3-methyl-4-(2-oxo-2-phenyl-1-(phenylimino)ethyl)-1*H*-pyrazol-5(4*H*)-one (4j). Yield: (95%); Pink powder; mp 188-189 °C. IR (KBr) (ν_{max}, cm⁻¹): 1679 (C=O), 3375 (NH). ¹H-NMR (300 MHz, DMSO-d₆): δ = 2.00 (3H, s, CH₃), 5.97 (2H, m, CH and NH), 6.51-6.73 (3H, m, aromatic), 7.00-7.09 (m, 2H, aromatic), 7.50-7.65 (3H, m, aromatic), 8.11 (7.85) (2H, d, *J* 9 Hz, aromatic), 10.87 (1H, broad s, OH) ppm. ¹³C-NMR (75 MHz, DMSO-d₆): δ = 10.78 (19.06) (CH₃), 52.39 (56.53) (CH), 97.77, 113.28, 114.45, 116.60 (116.25), 128.63, 129.18, 129.30, 133.79, 135.36 (138.63), 147.52 (148.89) (aromatic and C=N), 159.93 (C=O, amide), 195.75 (C=O, ketone) ppm. Anal Calcd for C₁₈H₁₅N₃O₂: C, 70.81; H, 4.95; N, 13.76%. Found: C, 70.80; H, 4.93; N, 13.68%.

(E)-3-methyl-4-(2-(4-nitrophenyl)-2-oxo-1-(*p*-tolylimino)ethyl)-1*H*-pyrazol-5(4*H*)-one (4k). Yield: (90%); Orange powder; mp 178-179 °C. IR (KBr) (ν_{max}, cm⁻¹): 1687 (C=O), 3386 (NH). ¹H-NMR (300 MHz, DMSO-d₆): δ = 2.00, 2.14 (6H, 2s, 2CH₃), 5.81 (1H, broad s, NH), 6.01 (1H, s, CH), 6.65 (6.54) (2H, d, *J* 9 Hz, aromatic), 6.86-6.89 (2H, m, aromatic), 8.24-8.33 (4H, m, aromatic), 10.76 (1H, broad s, OH) ppm. ¹³C-NMR (75 MHz, DMSO-

d6): δ = 10.72 (19.03), 20.55 (20.62) (2CH₃), 53.42 (56.52) (CH), 97.03, 113.58, 115.16, 124.18, 125.24, 129.63 (129.78), 129.89, 138.85, 140.61, 145.11, 150.28 (aromatic and C=N), 159.94 (C=O, amide), 195.23 (C=O, ketone) ppm. Anal Calcd for C₁₉H₁₆N₄O₄: C, 62.63; H, 4.43; N, 15.38%. Found: C, 62.70; H, 4.45; N, 15.27%.

(E)-4-(2-(4-chlorophenyl)-2-oxo-1-(p-tolylimino)ethyl)-3-methyl-1H-pyrazol-5(4H)-one (4l). Yield: (95%); Creamy powder; mp 179-180 °C. IR (KBr) (ν_{\max} , cm⁻¹): 1681 (C=O), 3368 (NH). ¹H-NMR (300 MHz, DMSO-d₆): δ = 1.98, 2.14 (6H, 2s, 2CH₃), 5.75 (1H, broad s, NH), 5.91 (1H, s, CH), 6.62 (6.52) (2H, 2d, *J* 9 Hz, aromatic), 6.84-6.88 (2H, 2H, 2d, *J* 9 Hz, aromatic), 7.58 (2H, d, *J* 9 Hz, aromatic), 8.06 (2H, d, *J* 9 Hz, aromatic) ppm. ¹³C-NMR (75 MHz, DMSO-d₆): δ = 10.75 (19.03), 20.54 (20.61) (2CH₃), 52.77 (56.52) (CH), 97.57, 113.52, 114.83, 125.11 (124.89), 129.27, 129.75 (129.62), 130.47, 134.17, 138.62, 145.17 (145.93) (aromatic and C=N), 159.92 (C=O, amide), 195.03 (C=O, ketone) ppm. Anal Calcd for C₁₉H₁₆ClN₃O₂: C, 64.50; H, 4.56; N, 11.88%. Found: C, 64.59; H, 4.55; N, 11.70%.

(E)-4-(2-(4-methoxyphenyl)-1-((4-methoxyphenyl)imino)-2-oxoethyl)-3-methyl-1H-pyrazol-5(4H)-one (4m). Yield: (95%); Grey powder; mp 173-174 °C. IR (KBr) (ν_{\max} , cm⁻¹): 1673 (C=O), 3367 (NH). ¹H-NMR (300 MHz, DMSO-d₆): δ = 1.97 (1.99), 3.63 (3.65), 3.85 (3.86) (9H, 3s, 3 CH₃), 5.58 (1H, broad s, NH), 5.84 (1H, s, CH), 6.57-7.06 (6H, m, aromatic), 7.81-8.10 (2H, m, aromatic), 10.89 (1H, broad s, OH) ppm. ¹³C-NMR (75 MHz, DMSO-d₆): δ = 10.80 (CH₃), 52.66 (CH), 55.73 and 56.01 (2OCH₃), 98.38, 114.40, 114.86 (114.97), 115.80, 128.14, 130.97, 138.43, 141.71 (142.05), 151.40, 159.96 (aromatic and C=N), 163.65 (C=O, amide), 194.53 (C=O, ketone) ppm. Anal Calcd for C₂₀H₁₉N₃O₄: C, 65.74; H, 5.24; N, 11.50%. Found: C, 65.69; H, 5.33; N, 11.41%.

(E)-4-(2-(4-bromophenyl)-2-oxo-1-(p-tolylimino)ethyl)-3-methyl-1H-pyrazol-5(4H)-one (4n). Yield: (93%); Yellow powder; mp 189-190 °C. IR (KBr) (ν_{\max} , cm⁻¹): 1680 (C=O), 3363 (NH). ¹H-NMR (300 MHz, DMSO-d₆): δ = 1.98, 2.14 (6H, 2s, 2CH₃), 5.75 (1H, broad s, NH), 5.91 (1H, s, CH), 6.62 (6.52) (2H, d, *J* 9 Hz, aromatic), 6.87 (2H, d, *J* 8 Hz, aromatic), 7.72 (2H, d, *J* 9 Hz, aromatic), 7.99 (2H, d, *J* 9 Hz, aromatic) 10.89 (broad s, OH) ppm. ¹³C-NMR (75 MHz, DMSO-d₆): δ = 10.76 (19.05), 20.55 (20.62) (2CH₃), 52.77 (56.52) (CH), 97.56, 113.53, 114.93, 125.11, 127.81, 129.62 (129.76), 130.58, 132.21, 134.52, 138.67, 145.17 (145.75) (aromatic and C=N), 159.92 (C=O, amide), 195.24 (C=O, ketone) ppm. Anal Calcd for C₁₉H₁₆BrN₃O₂: C, 57.30; H, 4.05; N, 10.55%. Found: C, 57.19; H, 4.11; N, 10.43%.

(E)-3-methyl-4-(2-(4-nitrophenyl)-2-oxo-1-(phenylimino)ethyl)-1H-pyrazol-5(4H)-one (4o). Yield: (95%); Orange powder; mp 161-162 °C. IR (KBr) (ν_{\max} , cm⁻¹): 1689 (C=O), 3374 (NH). ¹H-NMR (300 MHz, DMSO-d₆): δ = 2.01 (3H, s, CH₃), 6.03 (2H, s, CH and NH), 6.53-6.61 (1H, m, aromatic), 6.74 (2H, d, *J* 8 Hz, aromatic), 7.01-7.10 (2H, m, aromatic), 8.25 (2H, d, *J* 9 Hz, aromatic), 8.32 (2H, d, *J* 9 Hz, aromatic), 10.95 (1H, broad s, OH) ppm. ¹³C-NMR (75 MHz, DMSO-d₆): δ = 10.71 (19.04) (CH₃), 53.18 (56.51) (CH), 96.95, 113.36, 114.68, 116.78 (116.56), 124.19, 129.18 (129.31), 129.91, 140.57 (138.88), 147.41, 150.31 (aromatic and C=N), 159.89 (C=O, amide), 195.08 (C=O, ketone) ppm. Anal Calcd for C₁₈H₁₄N₄O₄: C, 61.71; H, 4.03; N, 15.99%. Found: C, 61.78; H, 4.12; N, 15.90%.

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