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# ONE-POT CHEMOSELECTIVE SYNTHESIS OF DIFFERENT PYRANO-PYRAZOLE DERIVATIVES

**Majid M. Heravi,* Mina Saeedi, Yahya S. Beheshtiha, and Hossein A. Oskooie**

Department of Chemistry, School of Sciences, Alzahra University, PO Box 1993891176, Vanak, Tehran, Iran
e-mail: mmh1331@yahoo.com

**Abstract** – One-pot chemoselective synthesis of different pyrano-pyrazole derivatives has been reported *via* two different conditions.

## INTRODUCTION

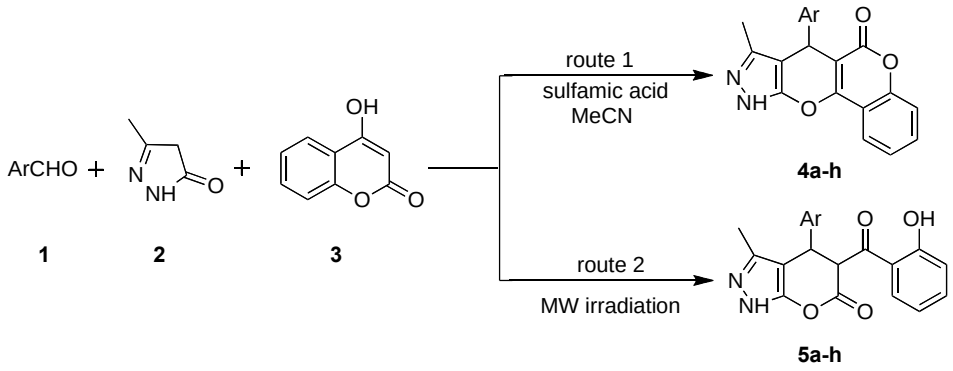
Chemoselective synthesis could be considered as a useful and practical tool for various applications in chemistry and biology. Consequently many reports have discussed chemoselectivity and practical choice of methods in synthetic organic chemistry.[1-4] Multicomponent reactions (MCRs) have drawn high efforts in recent years owing to exceptional synthetic efficiency, intrinsic atom economy, high selectivity and procedural simplicity.[5] These reactions constitute a valuable approach for creation of large libraries of structurally related, drug-like compounds, thereby enabling lead identification and lead optimization in drug discovery.[6] Chemoselective multicomponent reactions (MCRs) can be powerful tools in the drug discovery process for producing diverse arrays of compounds in one step and high yield.

Pyrano-pyrazole derivatives are known to possess a wide spectrum of important properties and great interest in them has been stimulated by some promising pharmacological applications. Besides, their utility in drug discovery has been extraordinary due to the remarkable therapeutic value of this class of heterocyclic compounds. They exhibit analgesic, anti-inflammatory activities and act as vasodilators, hypotensive and hypoglycemic agents.[7-9] Heterocyclic compounds containing pyrano-pyrazole derivatives have fungicidal properties as well.[10] Coumarine derivatives are widely distributed in nature and are reported to have biological activities such as anticoagulants, insecticidal, anthelminthincs, hypnotics, antifungal, phytoalexins and are known to be HIV protease inhibitors.[11]

The significance and importance of pyrano-pyrazole derivatives is the major driving force behind the scope of working on the synthesis of these heterocycles.

## RESULTS AND DISCUSSION

In the context of our interest in designing new ways for synthesis of heterocyclic compounds,[12-15] herein, we wish to report one-pot chemoselective synthesis of two different kinds of pyrano-pyrazole derivatives using aldehydes **1**, 3-methyl-1*H*-pyrazol-5(4*H*)-one **2** and 4-hydroxy-2*H*-chromen-2-one **3** according to the procedure outlined in the Scheme 1.




Scheme 1. One-pot chemoselective synthesis of different pyrano-pyrazole derivatives

This multicomponent reaction can attract the interest of the synthetic community because the formation of different condensation products can be expected depending on using microwave irradiation and heating under reflux condition.

At first, a one-pot three-component model reaction was conducted. A mixture of 4-nitrobenzaldehyde (1 mmol), 3-methyl-1*H*-pyrazol-5(4*H*)-one (1 mmol) and 4-hydroxy-2*H*-chromen-2-one (1 mmol) in acetonitrile (MeCN, 5 mL) was stirred. At room temperature and also under reflux condition neither **4a** nor **5a** obtained. When the model reaction was achieved in the presence of catalytic amount of sulfamic acid, **4a** was formed as the sole product in a good yield (85%) after the indicated time (Table 1).

Sulfamic acid ($NH_2SO_3H$, SA) is a dry, non-volatile, nonhygroscopic, odorless, white stable crystalline solid, commercially available and its efficiency in organic synthesis has been proved.[16] SA was found to work well with uniformly high chemoselectivity for cyclocondensation of 4-nitrobenzaldehyde with 3-methyl-1*H*-pyrazol-5(4*H*)-one and 4-hydroxy-2*H*-chromen-2-one. When different acidic and basic catalysts such as *p*-toluenesulfonic acid, HCl, $Et_3N$ and piperidine were examined, they were not effective and did not catalyze the model reaction efficiently. In addition, various conventional organic solvents (polar and non-polar) and $H_2O$ were investigated. As it can be seen in Table 2, the best results were

obtained by acetonitrile (Table 2). The starting materials did not fully react in ethanol, ethylene glycol and dichloromethane and no reaction happened in $H_2O$. The optimized reaction conditions showed that the use of 0.031 mol% of sulfamic acid was sufficient to get the maximum yield of product and higher amount of SA did not lead to significant improvement in yield of products.

Table 1. Synthesis of **4** via reaction of aromatic aldehydes, 3-methyl-1*H*-pyrazol-5(4*H*)-one and 4-hydroxy-2*H*-chromen-2-one in the presence of SA (3 mol%)

| Entry | Ar | Product | Time (h) | Yield (%)[a] |
|---|---|---|---|---|
| 1 | 4-$NO_2$-$C_6H_4$ | 4a | 4 h | 85 |
| 2 | 4-MeO-$C_6H_4$ | 4b | 5 h | 65 |
| 3 | 4-OH-$C_6H_4$ | 4c | 4.5 h | 80 |
| 4 | 1-naphthyl | 4d | 5 h | 80 |
| 5 | 2-furyl | 4e | 5.5 h | 75 |
| 6 | 3-$NO_2$-$C_6H_4$ | 4f | 4.5 | 80 |
| 7 | 4-F-$C_6H_4$ | 4g | 4 | 85 |
| 8 | $C_6H_5$ | 4h | 4.5 | 85 |

[a] Isolated yields.

Table 2. Effect of varying solvent on the yield of product **4a**

| Entry | Solvent | Yield (%)[a] |
|---|---|---|
| 1 | EtOH | 65 |
| 2 | MeCN | 85 |
| 3 | $CH_2Cl_2$ | 5 |
| 4 | ethylene glycol | 35 |
| 5 | $H_2O$ | - |

[a] Isolated yields.

In order to expand the scope of the present work, various aromatic aldehydes were examined and desired products were obtained. In all cases, aromatic aldehydes substituted with either electron-donating or electron-withdrawing groups underwent the reaction smoothly and gave the products in good yields. The results are summarized in Table 1.

In further study, the mentioned model reaction, mixture of 4-nitrobenzaldehyde (1 mmol), 3-methyl-1*H*-pyrazol-5(4*H*)-one (1 mmol) and 4-hydroxy-2*H*-chromen-2-one (1 mmol) was subjected to microwave irradiation. Interestingly, different product, pyrano[2,3-*c*]pyrazol-6-one derivative (**5a**) was obtained and thus the pronounced chemoselectivity was achieved under different conditions. To search for the optimal MW conditions and enhance the chemical yield, it seemed that choosing an appropriate solvent, power and temperature is of crucial importance. DMF resulted in higher yields than other solvents such as HOAc, DMF/HOAc, $H_2O$, ethylene glycol and EtOH. As it can be seen in Table 3, when the reaction was carried out in HOAc, ethylene glycol, EtOH and $H_2O$, the yield of the expected product is poor and a combination of starting materials and product was obtained. So DMF was chosen as the appropriate solvent. The model reaction was achieved at different power inputs as well. It was found that any products were not detected when the reaction was conducted at power input less than 450 W. In the case of higher power inputs any significant improvement in yield of corresponding products was not observed. The effect of temperature on the model reaction at power input 450 W in DMF was studied. The best results were obtained at 100 °C. Based on these optimized conditions, the process was then extended to other aromatic aldehydes and a series of compounds **5** were synthesized with this simple procedure. Their corresponding data are listed in Table 4.

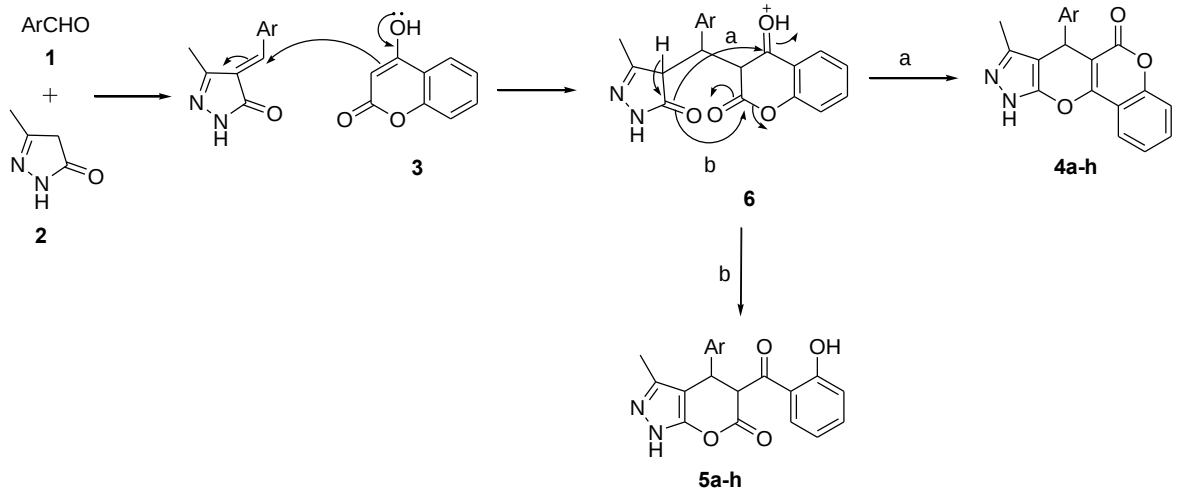
It should be noted that the model reaction was carried out in the presence of catalytic amount of SA (0.031 mol%) under MW conditions. The same result in terms of yield and reaction time were obtained and SA did not play any role in the reaction.

Table 3. Effect of varying solvent on the yield of product **5a**

| Entry | Solvent | Yield (%)[a] |
|---|---|---|
| 1 | - | - |
| 2 | EtOH | 45 |
| 3 | ethylene glycol | 55 |
| 4 | DMF | 80 |
| 5 | DMF-HOAc (5:1) | 45 |
| 6 | DMF-HOAc (5:2) | 40 |
| 7 | DMF-HOAc (1:1) | 50 |
| 8 | HOAc | 30 |
| 9 | $H_2O$ | - |

[a] Isolated yields.

Proposed mechanism for the synthesis of pyrano-pyrazole derivatives, **4** and **5**, is presented in Scheme 2.




Scheme 2. Proposed mechanism for the synthesis of **4** and **5**

Table 4. Synthesis of **5** via reaction of aromatic aldehydes, 3-methyl-1*H*-pyrazol-5(4*H*)-one and 4-hydroxy-2*H*-chromen-2-one under MW conditions

| Entry | Ar | Product | Time (min) | Yield (%)[a] |
|---|---|---|---|---|
| 1 | 4-$NO_2$-$C_6H_4$ | 5a | 4 min | 80 |
| 2 | 4-MeO-$C_6H_4$ | 5b | 6 min | 75 |
| 3 | 4-OH-$C_6H_4$ | 5c | 5 min | 75 |
| 4 | 1-naphthyl | 5d | 6 min | 85 |
| 5 | 2-furyl | 5e | 5 min | 80 |
| 6 | 3-$NO_2$-$C_6H_4$ | 5f | 5 min | 80 |
| 7 | 4-F-$C_6H_4$ | 5g | 4 min | 80 |
| 8 | $C_6H_5$ | 5h | 5 min | 85 |

[a] Isolated yields.

The first step may involve adduct formation by condensation of aromatic aldehyde **1** and 3-methyl-1*H*-pyrazol-5(4*H*)-one **2**, followed by attack of 4-hydroxy-2*H*-chromen-2-one **3** to give the intermediate **6**. In the presence of sulfamic acid under reflux conditions, ketone carbonyl is prone to be attacked by nucleophilic oxygen to form product **4**. Under microwave irradiation, the ester carbonyl is the reactive site in intermediate **6**. It seems that in this competitive reaction the related transition state is more polar and large microwave effect can be observed.[17] Consequently **5** is the desired product.

In conclusion, in this work we have demonstrated efficient and practical one-pot synthesis of

pyrano-pyrazole derivatives *via* reaction of 4-hydroxy-2*H*-chromen-2-one, 3-methyl-1*H*-pyrazol-5(4*H*)-one and aromatic aldehydes in two different conditions (microwave irradiation and heating under reflux condition). The one-pot combination not only preserves the synthesis of pyrano-pyrazoles in good yields but also consistently produces high chemoselectivity. The results indicated that aromatic aldehydes bearing either electron-withdrawing or electron-donating functional groups are proper for the both reactions.

## EXPERIMENTAL

Melting points were measured, using a capillary tube method with a Bamstead Electrothermal 9200 apparatus. $^{1}$H and $^{13}$C NMR spectra were recorded on a Bruker AQS-AVANCE spectrometer at 500 and 125 MHz, using TMS as an internal standard. FTIR spectra were recorded using, KBr disks on FT-IR Bruker Tensor 27 instrument. Mass spectra were documented on an Agilent Technology (HP) mass spectrometer operating at an ionization potential of 70 eV. The elemental analysis was performed with an Elemetar Analysensystem GmbH VarioEL CHNS mode.

### General procedure for the synthesis of compounds 4a-h

A mixture of 4-hydroxy-2*H*-chromen-2-one (1 mmol), 3-methyl-1*H*-pyrazol-5(4*H*)-one (1 mmol), an appropriate aldehyde (1 mmol), sulfamic acid (0.031 mol%) and acetonitrile (5 mL) was heated at reflux for indicated time as required to complete the reaction (Table 1). Upon completion of the reaction, monitored by TLC, the mixture was cooled to room temperature. The precipitated product was separated by filtration, washed with water and recrystallized using EtOH and $H_2O$.

### *13-Methyl-11-(4-nitrophenyl)-8,17-dioxa-14,15-diazatetracyclo[8.7.0$^{2,7}$.0$^{12,16}$]heptadeca-1(10),2(7),3,5,-12(16),13-hexaen-9-one (4a)*

Compound **4a** was obtained as yellow powder. Mp 209-211 °C. FTIR (KBr, cm$^{-1}$) $\nu_{max}$: 3223, 3069, 1704, 1611, 1555, 1517, 1417, 1347. $^{1}$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.37 (s, 3H, $CH_3$), 5.18 (s, 1H, CH), 7.33-8.23 (m, 8H, Ar), 12.99 (br, 1H, NH). $^{13}$C NMR (125 MHz DMSO-$d_6$) $\delta_C$: 10.9, 34.6, 104.7, 105.9, 116.7, 120.5, 124.1, 124.2, 125.0, 129.4, 132.5, 145.0, 146.7, 153.2, 161.2, 162.2, 165.4, 167.8. MS *m/z*: 43 (90), 195 (30), 239 (20), 376 (5) $[M + H]^+$. Anal. Calcd for $C_{20}H_{13}N_3O_5$: C, 64.00; H, 3.49; N, 11.20. Found: C, 64.14; H, 3.33; N, 11.31.

### *11-(4-Methoxyphenyl)-13-methyl-8,17-dioxa-14,15-diazatetracyclo[8.7.0$^{2,7}$.0$^{12,16}$]heptadeca-1(10),2(7),-3,5,12(16),13-hexaen-9-one (4b)*

Compound **4b** was obtained as yellow powder. Mp 188-189 °C. FTIR (KBr, cm$^{-1}$) $\nu_{max}$: 3426, 3080, 1669,

1608, 1563, 1458. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.36 (s, 3H, $CH_3$), 3.77 (s, 3H, -$OCH_3$), 6.32 (s, 1H, CH), 7.09-7.95 (m, 8H, Ar), 12.94 (br, 1H, NH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 10.9, 36.2, 55.7, 99.2, 104.6, 114.2, 115.3, 116.4, 123.8, 124.9, 128.5, 128.6, 131.8, 132.6, 134.5, 153.3, 157.7, 165.5, 168.1. MS *m/z*: 99 (90), 313 (30), 329 (30), 360 (10) $[M]^+$. Anal. Calcd for $C_{21}H_{16}N_2O_4$: C, 69.99; H, 4.48; N, 7.77. Found: C, 70.10; H, 4.51; N, 7.87.

***11-(4-Hydroxyphenyl)-13-methyl-8,17-dioxa-14,15-diazatetracyclo[8.7.0$^{2,7}$.0$^{12,16}$]heptadeca-1(10),2(7),-3,5,12(16),13-hexaen-9-one (4c)***

Compound **4c** was obtained as yellow powder. Mp 280-281 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3450, 3072, 1661, 1612, 1563, 1510. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.30 (s, 3H, $CH_3$), 5.71 (s, 1H, CH), 7.27-7.97 (m, 8H, Ar), 10.54 (br, 2H, NH, OH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 11.4, 35.9, 94.8, 108.0, 116.2, 117.0, 123.2, 124.6, 124.8, 131.5, 132.6, 143.5, 153.0, 158.6, 162.1, 163.3, 165.0, 166.0. MS *m/z*: 57 (100), 235 (35), 299 (40), 346 (10) $[M]^+$. Anal. Calcd for $C_{20}H_{14}N_2O_4$: C, 69.36; H, 4.07; N, 8.09. Found: C, 69.21; H, 4.26; N, 8.22.

***13-Methyl-11-(naphthalen-1-yl)-8,17-dioxa-14,15-diazatetracyclo[8.7.0$^{2,7}$.0$^{12,16}$]heptadeca-1(10),2(7),-3,5,12(16),13-hexaen-9-one (4d)***

Compound **4d** was obtained as yellow powder. Mp 201-202 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3374, 3051, 1660, 1610, 1565, 1434. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.33 (s, 3 H, $CH_3$), 6.20 (s, 1H, CH), 7.36-8.04 (m,11 H, Ar), 12.99 (br, 1H, NH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 11.0, 32.8, 105.7, 108.5, 116.4, 116.6, 124.0, 124.3, 124.7, 125.0, 125.8, 126.0, 126.3, 127.7, 129.6, 129.9, 131.9, 132.0, 134.5, 137.6, 144.3, 152.9, 153.1, 165.0. MS *m/z*: 235 (100), 299 (90), 380 (5) $[M]^+$. Anal. Calcd for $C_{24}H_{16}N_2O_3$: C, 75.78; H, 4.24; N, 7.36. Found: C, 75.86; H, 4.33; N, 7.30.

***11-(Furan-2-yl)-13-methyl-8,17-dioxa-14,15-diazatetracyclo[8.7.0$^{2,7}$.0$^{12,16}$]heptadeca-1(10),2(7),3,5,12-(16),13-hexaen-9-one (4e)***

Compound **4e** was obtained as brown powder. Mp 272-275 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3370, 3118, 1668, 1613, 1564, 1498. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.36 (s, 3H, $CH_3$), 5.69 (s, 1H, CH), 7.31-7.93 (m, 7H, Ar), 11.85 (br, 1H, NH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 11.9, 38.2, 92.8, 101.2, 108.1, 116.5, 121.2, 124.5, 124.8, 131.4, 136.2, 137.2, 141.1, 148.0, 158.1, 163.7, 165.1, 166.1. MS *m/z*: 41 (100), 105 (20), 178 (20), 320 (5) $[M]^+$. Anal. Calcd for $C_{18}H_{12}N_2O_4$: C, 67.50; H, 3.78; N, 8.75. Found: C, 67.39; H, 3.48; N, 8.40.

***13-Methyl-11-(3-nitrophenyl)-8,17-dioxa-14,15-diazatetracyclo[8.7.0$^{2,7}$.0$^{12,16}$]heptadeca-1(10),2(7),3,5,-***

***12(16),13-hexaen-9-one (4f)***

Compound **4f** was obtained as white powder. Mp 198-201 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3370, 3079, 1653, 1610, 1556, 1553. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.16 (s, 3H, $CH_3$), 5.67 (s, 1H, CH), 7.41-8.70 (m, 8H, Ar), 12.59 (br, 1H, NH). $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta_C$: 11.9, 39.1, 91.9, 103.4, 116.6, 117.2, 124.0, 124.5, 124.7, 128.2, 131.4, 133.3, 133.5, 136.2, 137.2, 148.7, 154.4, 162.7, 166.4, 166.5. MS *m/z*: 97 (100), 195 (30), 240 (40), 375 (5) $[M]^+$. Anal. Calcd for $C_{20}H_{13}N_3O_5$: C, 64.00; H, 3.49; N, 11.20. Found: C, 64.32; H, 3.71; N, 11.49.

***11-(4-Fluorophenyl)-13-methyl-8,17-dioxa-14,15-diazatetracyclo[8.7.0$^{2,7}$.0$^{12,16}$]heptadeca-1(10),2(7),3,-5,12(16),13-hexaen-9-one (4g)***

Compound **4g** was obtained as yellow powder. Mp 272-275 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3418, 1663, 1610, 1566. $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta_H$: 2.35 (s, 3H, $CH_3$), 5.66 (s, 1H, CH), 7.06-8.21 (m, 8H, Ar), 12.99 (br, 1H, NH). $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta_C$: 10.9, 36.4, 104.4, 115.6, 116.6, 120.5, 124.9, 125.0, 129.2, 131.9, 137.7, 145.0, 153.1, 153.3, 162.7, 165.4, 167.0, 168.2. MS *m/z*: 233 (100), 384 (5) $[M]^+$. Anal. Calcd for $C_{20}H_{13}FN_2O_3$: C, 68.96; H, 3.76; N, 8.04. Found: C, 69.05; H, 3.83; N, 8.14.

***13-Methyl-11-phenyl-8,17-dioxa-14,15-diazatetracyclo[8.7.0$^{2,7}$.0$^{12,16}$]heptadeca-1(10),2(7),3,5,12(16),-13-hexaen-9-one (4h)***

Compound **4h** was obtained as yellow powder. Mp 193-194 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3420, 3059, 1662, 1614, 1566. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.36 (s, 3H, $CH_3$), 5.68 (s, 1H, CH), 7.21-7.88 (m, 9H, Ar), 13.00 (br, 1H, NH). $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta_C$: 11.0, 36.9, 104.5, 105.5, 116.5, 116.6, 120.3, 124.3, 124.9, 125.9, 126.5, 129.4, 141.7, 144.5, 153.3, 162.7, 165.5, 166.9. MS *m/z*: 57 (100), 253 (80), 330 (10) $[M]^+$. Anal. Calcd for $C_{20}H_{14}N_2O_3$: C, 72.72; H, 4.27; N, 8.48. Found: C, 72.60; H, 4.56; N, 8.33.

**General procedure for the synthesis of compounds 5a-h**

A mixture of 4-hydroxy-2*H*-chromen-2-one (1 mmol), 3-methyl-1*H*-pyrazol-5(4*H*)-one (1 mmol), appropriate aldehyde (1 mmol) and DMF (4 mL) was irradiated in microwave oven at power input 450 W for specified time monitored by TLC, Table 4. After cooling, the reaction mixture was poured into ice water (10 mL). The precipitate was collected by filtration, washed with water and recrystallized using EtOH and $H_2O$.

***5-[(2-Hydroxyphenyl)carbonyl]-3-methyl-4-(4-nitrophenyl)-1H,4H,5H,6H-pyrno[2,3-c]pyrazol-6-one (5a)***

Compound **5a** was obtained as yellow powder. Mp 239-240 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3370, 3050, 1657, 1612, 1563, 1491, 1449, 1391. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$ : 2.15 (s, 3H, $CH_3$), 6.22 (s, 1H, CH), 6.42 (s, 1H, CH), 6.82-8.13 (m, 8H, Ar), 13.00 (br, 2H, NH, OH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 12.5, 38.9, 58.1, 105.1, 119.1, 119.4, 121.9, 128.8, 129.9, 130.5, 133.7, 139.5, 148.0, 148.1, 153.3, 165.0, 165.2, 195.0. MS *m/z*: 120 (100), 162 (60), 394 (5) $[M + H]^+$. Anal. Calcd for $C_{20}H_{15}N_3O_6$: C, 61.07; H, 3.84; N, 10.68. Found: C, 61.27; H, 3.92; N, 10.55.

***5-[(2-Hydroxyphenyl)carbonyl]-4-4(methoxyphenyl)-3-methyl-1H,4H,5H,6H-pyrno[2,3-c]pyrazol-6-one (5b)***

Compound **5b** was obtained as yellow powder. Mp 195-196 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3350, 3117, 1670, 1624, 1599, 1533.$^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.15 (s, 3H, $CH_3$), 3.70 (s, 3H, -$OCH_3$), 6.22 (s, 1H, CH), 6.38 (s, 1H, CH), 7.00-7.94 (m, 8 H, Ar), 13.00 (br, 2H, NH, OH). $^{13}$C NMR (125 MHz, DMSO-$d_6$): 11.9, 38.7, 53.9, 59.9, 105.3, 112.1, 118.1, 119.0, 128.4, 130.0, 133.8, 134.9, 139.4, 140.5, 155.5, 161.0, 165.0, 166.0, 195.0. MS *m/z*: 120 (100), 379 $[M + H]^+$. Anal. Calcd for $C_{21}H_{18}N_2O_5$: C, 66.66; H, 4.79; N. 7.40. Found: C, 66.44; H, 4.85; N, 7.51.

***4-(4-Hydroxyophenyl)-5-[(2-hydroxyphenyl)carbonyl]-3-methyl-1H,4H,5H,6H-pyrno[2,3-c]pyrazol-6-one (5c)***

Compound **5c** was obtained as yellow powder. Mp 230-232 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3185, 1675, 1611, 1566, 1510, 1440. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.15 (s, 3 H, $CH_3$), 6.22 (s, 1H, CH), 6.39 (s, 1H, CH), 7.11-8.10 (m, 8H, Ar), 13.00 (br, 3H, NH, OH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 12.3, 38.0, 59.8, 105.6, 115.0, 118.3, 119.1, 125.0, 128.1, 130.5, 132.0, 133.9, 139.0, 152.1, 158.9, 163.1, 164.1, 195.1. MS *m/z*: 202 (100), 265 (30), 364 (5) $[M]^+$. Anal. Calcd for $C_{20}H_{16}N_2O_5$: C, 65.93; H, 4.43; N, 7.69. Found: C, 65.83; H, 4.25; N, 7.38.

***5-[(2-Hydroxyphenyl)carbonyl]-3-methyl-4-(naphthalen-1-yl)-1H,4H,5H,6H-pyrno[2,3-c]pyrazol-6-one (5d)***

Compound **5d** was obtained as yellow powder. Mp 210-212 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3400, 3079, 1662. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.39 (s, 3H, $CH_3$), 6.20 (s, 1H, CH), 6.56 (s, 1H, CH), 7.26-8.25 (m, 11H, Ar), 13.00 (br, 2H, NH, OH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 11.3, 35.3, 60.8, 105.1, 108.6, 116.3, 120.6, 123.8, 124.2, 124.3, 124.9, 125.8, 126.8, 126.9, 127.7, 129.6, 132.1, 134.5, 137.7, 144.2, 152.9, 165.0, 165.1, 195.5. MS *m/z*: 120 (100), 258 (35), 398 (10) $[M]^+$. Anal. Calcd for $C_{24}H_{18}N_2O_4$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.66; H, 4.50; N, 7.31.

***4-(Furan-2-yl)-5-[(2-hydroxyphenyl)carbonyl]-3-methyl-1H,4H,5H,6H-pyrno[2,3-c]pyrazol-6-one (5e)***

Compound **5e** was obtained as light brown powder. Mp 213-215 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3401, 3146, 1666, 1613, 1563, 1502. $^1$H NMR (500 MHz,DMSO-$d_6$) $\delta_H$: 2.10 (s, 3H, $CH_3$), 6.20 (s, 1H, CH), 6.30 (s, 1H, CH), 7.00-7.58 (m, 7H, Ar), 13.00 (br, 2H, NH, OH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 11.2, 35.0, 57.0, 104.3, 117.9, 118.8, 119.1, 122.9, 125.9, 130.4, 134.5, 137.7, 139.0, 150.7, 158.1, 163.9, 168.1, 195.9. MS *m/z*: 120 (100), 176 (55), 162 (70), 337 (5) $[M-H]^+$. Anal. Calcd for $C_{18}H_{14}N_2O_5$: C, 63.90; H, 4.17; N, 8.28. Found: C, 64.00; H, 4.24; N, 8.35.

***5-[(2-Hydroxyphenyl)carbonyl]-3-methyl-4-(3-nitrophenyl)-1H,4H,5H,6H-pyrno[2,3-c]pyrazol-6-one (5f)***

Compound **5f** was obtained as white powder. Mp 230-231 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3450, 3058, 1659, 1613, 1565, 1493, 1448, 1390. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.15 (s, 3H, $CH_3$), 6.22 (s, 1H, CH), 6.42 (s, 1H, CH), 7.50-8.33 (m, 8H, Ar), 13.00 (br, 2H, NH, OH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 11.8, 39.2, 59.3, 105.3, 117.8, 119.0, 119.1, 122.0, 125.1, 125.3, 130.3, 131.1, 133.3, 138.4, 141.9, 145.7, 155.3, 165.0, 167.6, 195.9. MS *m/z*: 120 (100), 162 (60), 393 (5) $[M]^+$. Anal. Calcd for $C_{20}H_{15}N_3O_6$: C, 61.07; H, 3.48; N, 10.68. Found: C, 61.22; H, 3.33; N, 10.86.

***4-(4-Fluorophenyl)-5-[(2-hydroxyphenyl)carbonyl]-3-methyl-1H,4H,5H,6H-pyrno[2,3-c]pyrazol-6-one (5g)***

Compound **5g** was obtained as pale yellow powder. Mp 195-198 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3450, 3067, 1661, 1611, 1565, 1504. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.15 (s, 3H, $CH_3$), 6.22 (s, 1H, CH), 6.52 (s, 1H, CH), 7.00-7.83 (m, 8H, Ar), 13.00 (br, 2H, NH, OH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 11.9, 38.8, 59.8, 105.8, 113.3, 118.4, 119.1, 127.9, 128.1, 130.5, 134.0, 136.6, 138.9, 154.4, 159.7, 165.0, 166.7, 168.5, 196.0. MS *m/z*: 120 (100), 366 (10) $[M]^+$. Anal. Calcd for $C_{20}H_{15}FN_2O_4$: C, 65.57; H, 4.13; N, 7.65. Found: C, 35.44; H, 4.24; N, 7.34.

***5-[(2-Hydroxyphenyl)carbonyl]-3-methyl-4-phenyl-1H,4H,5H,6H-pyrno[2,3-c]pyrazol-6-one (5h)***

Compound **5h** was obtained as yellow powder. Mp 211-213 °C. FTIR (KBr, $cm^{-1}$) $\nu_{max}$: 3410, 3059, 1659, 1613, 1565, 1493. $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 2.15 (s, 3H, $CH_3$), 6.20 (s, 1H, CH), 6.35 (s, 1H, CH), 7.00-8.19 (m, 9H, Ar), 13.00 (br, 2H, NH, OH). $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta_C$: 12.1, 39.7, 60.1, 107.3, 118.1, 119.0, 119.1, 122.0, 125.0, 127.0, 131.5, 133.9, 140.0, 141.9, 153.5, 166.0, 167.1, 196.0. MS *m/z*: 120 (100), 271 (30), 348 (10) $[M]^+$. Anal. Calcd for $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04. Found: C, 68.75; H, 4.71; N, 7.95.

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