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# Synthesis of novel pyrazolic analogues of chalcones and their 3-aryl-4-(3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)-1-phenyl-1*H*-pyrazole derivatives as potential antitumor agents

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ABSTRACT

Novel (*E*)-1-aryl-3-(3-aryl-1-phenyl-1*H*-pyrazol-4-yl)prop-2-en-1-ones **5**/**6** (pyrazolic chalcones) were synthesized from a Claisen–Schmidt reaction of 3-aryl-1-phenylpyrazol-4-carboxaldehydes **4** with several acetophenone derivatives **1**. Subsequently, the microwave-assisted cyclocondensation reaction of chalcones **5**/**6** with hydrazine afforded the new racemic 3-aryl-4-(3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)-1-phenyl-1*H*-pyrazoles **7** or their *N*-acetyl derivatives **8** and **9** when reactions where carried out in DMF or acetic acid, respectively. Several of these compounds were screened by the US National Cancer Institute (NCI) for their ability to inhibit 60 different human tumor cell lines, where **5c** and **9g** showed remarkable activity mainly against leukemia (K-562 and SR), renal cancer (UO-31) and non-small cell lung cancer (HOP-92) cell lines, with the most important $GI_{50}$ values ranging from 0.04 to 11.4 μM, from the in vitro assays.



## 1. Introduction

The α,β-unsaturated ketones (chalcones) are considered to be precursors of flavonoids and isoflavonoids when found as naturally-occurring compounds, but it could be considered that their true importance is extended in two branches. The biological activity associated with them, including anti-inflammatory,[1–3] antimitotic,[4] anti-leishmanial,[5] anti-invasive,[6,7] anti-tuberculosis,[8] anti-fungal,[9] anti-malarial,[10,11] anti-tumor, and anti-oxidant properties;[12] as well as their recognized synthetic utility in the preparation of pharmacologically-interesting heterocyclic systems like pyrazolines, which have also been largely studied owing to their pharmacological activities, which includes anti-tumor,[13] anti-inflammatory,[14] anti-parasitary,[15] anti-depressive, anticonvulsant,[16] antimicrobial,[17] antinociceptives[18] and nitric oxide synthase inhibitors, associated with diseases such as Alzheimer, Huntington, and inflammatory arthritis.[19]

On the other hand, microwave radiation has gained the attention of chemists during the last decades due to its unique advantages, such as shorter reaction times, cleaner reaction products, higher yields and better selectivities, being a valuable alternative to accomplish more efficient syntheses of a variety of organic compounds with a considerable simplicity of operation and milder reaction conditions, when combined with the solvent-free approach, as it provides an opportunity to work with open vessels.[20–28]

In this way, targeting the preparation of the mentioned nitrogen containing heterocycles, we report herein the regioselective synthesis and citotoxic activities of (*E*)-1-aryl-3-(3-aryl-1-phenyl-1*H*-pyrazol-4-yl)prop-2-en-1-ones **5**/**6a–h** (pyrazolic chalcones) and 3-aryl-4-(3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)-1-phenyl-1*H*-pyrazoles **7a–h** and their *N*-acetyl derivatives **8**/**9a–h** by using microwave-assisted reaction conditions. Compounds **7a–h** and **8**/**9a–h** were obtained as racemic mixtures in all cases.

## 2. Results and discussion

### 2.1. Chemistry

In order to obtain the pyrazolic chalcones, the corresponding 4-formylpyrazolic precursors **4** were initially synthesized from the phenylhydrazones **3** (prepared by condensation of the respective acetophenones **1** and phenylhydrazine **2**); following a similar procedure described by Kira et al.[29] In this sense, the Vilsmeier–

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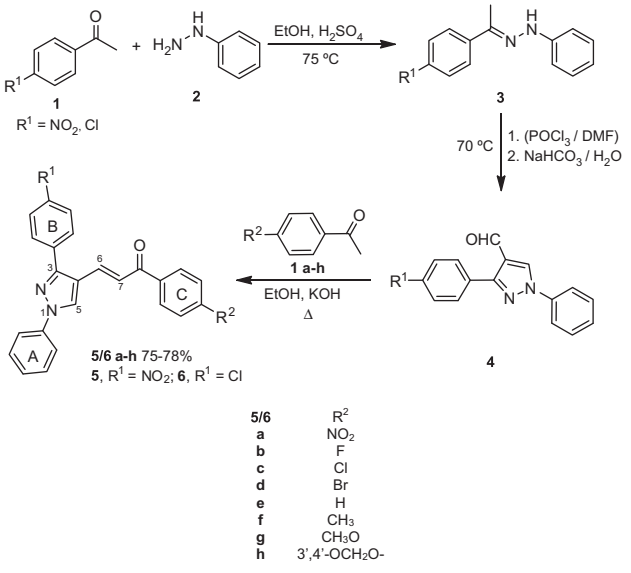
Haack reagent ($POCl_3$/DMF) was employed affording compounds **4** in 75–78% yield (Scheme 1). Compounds **4** were characterized by using IR, NMR, and MS techniques. Their analytical and spectroscopic data agreed with those reported in the literature[29] for the same compounds. Subsequently, the Claisen–Schmidt condensation of the obtained aldehydes **4** with the acetophenones **1a–h** afforded the corresponding pyrazolic chalcones **5**/**6a–h**, (Scheme 1).

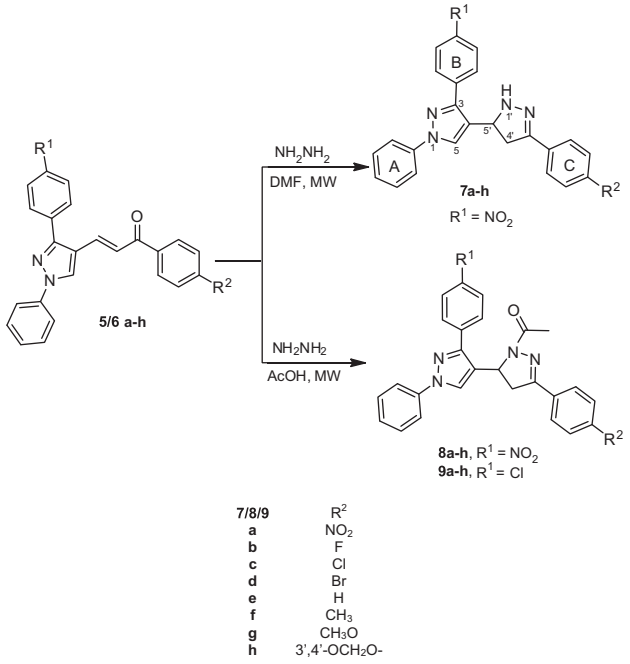
The structure elucidation of compounds **5**/**6a–h** was based on the spectral data (IR, $^1$H NMR, $^{13}$C NMR, and mass spectrometry). The IR spectra showed mainly absorption bands at 1662–1626 and 1521–1606 cm$^{-1}$ assigned to (C=O, C=N) and (C=C) functionalities, respectively. Particularly, the derivatives **5a–h** and **6a** showed typical absorption bands at 1337–1508 cm$^{-1}$ due to their $NO_2$ stretching vibrations. In the $^1$H NMR spectra of products **5**/**6** the H-6 and H-7 appears each one as a doublet at $\delta$ = 7.67–7.87 ppm and $\delta$ = 7.60–7.69 ppm, respectively, with coupling constant between them of $^3J$ = 13.0–15.9 Hz, which agrees with a *trans* configuration. Analysis of $^{13}$C, DEPT-135 and 2D-heteronuclear NMR spectra (HSQC and HMBC) provided the final structural elucidation of compounds **5** and **6**. Thus, the signal for C-6 is in the range of $\delta$ 118.6–123.5 ppm, the signal for C-7 appears at $\delta$ 132.1–134.8 ppm, while the C=O carbon atom appears at $\delta$ 186.8–189.0 ppm. Finally, the mass spectra of compounds **5**/**6** showed well-defined molecular ions with a characteristic fragmentation pattern involving the loss of the phenyl group in all cases.

Continuing with the synthetic approach, the microwave irradiation of a mixture of the chalcones **5a–h** (1.0 mmol) and hydrazine (1.3 mmol) in the presence of DMF as solvent (0.2 mL), afforded the desired products **7a–h** in good yields (Scheme 2). When the same reaction was carried out starting with chalcones **5**/**6a–h** in the presence of acetic acid (0.5 mL) instead of DMF, formation of different products was observed and identified as the corresponding *N*-acetyl derivatives **8**/**9a–h** (Scheme 2). This finding suggests that the acetic acid acted not only as solvent but also as acetylating agent.

Compounds **7–9** were obtained as racemic mixtures and were fully characterized by detailed (IR, NMR, and MS) measurements (Section 4). The IR spectra showed the expected absorption bands between 3289–3309 and 1600–1676 cm$^{-1}$ corresponding to the NH functionality for products **7** and to the C=O functionality for products **8**/**9**, respectively. In the $^1$H NMR spectra of compounds **7–9** the two methylenic 4′-H protons and the stereogenic 5′-H proton of the pyrazolinic moiety form an ABX spin system.




**Scheme 1.** Synthesis of the novel pyrazolic chalcones **5**/**6a–h**.




**Scheme 2.** Synthesis of the new pyrazoles **7a–h** and their *N*-acetyl derivatives **8**/**9a–h**.

Thus, the 4′-$H_A$ and 4′-$H_B$ appear each one as a double-doublet at $\delta$ = 2.94–3.28 ppm and $\delta$ = 3.44–3.95 ppm, respectively, with $^2J_{AB}$ = 16.1–18.0 Hz., while 5′-H appears as a double-doublet at $\delta$ = 5.08–5.82 ppm with $^3J_{AX}$ = 10.1–11.0 Hz for **7**, $^3J_{AX}$ = 5.4–5.6 Hz for **8**/**9** and $^3J_{BX}$ = 10.8–13.4 Hz for **7–9**. The NH protons of compounds **7** were not observed except for **7b** which appears as a singlet at $\delta$ = 7.19 ppm. The main signals in the $^{13}$C NMR for compounds **7–9** correspond to C-4′ at $\delta$ 39.5–42.2 ppm, C-5′ at $\delta$ 51.4–55.7 ppm and the quaternary C-3′ at $\delta$ 148.2–153.3 ppm. Finally, mass spectra of compounds **7–9** showed also well-defined molecular ions.

## 2.2. Anticancer activity

The two-stage screening process started with the evaluation of eight compounds (**5c**, **6b**, **6g**, **7b**, **7g**, **8c**, **9d**, and **9g**) selected by NCI, against the 60 cell lines at a single dose of 1.0 μM. The output from the single dose screen was reported as a mean graph available for analysis by the COMPARE program. The results of the primary assay showed that compounds **6b**, **6g**, **7b**, **7g**, **8c**, and **9d** were essentially inactive, while compounds **5c** and **9g** were declared active (Table 1).

Subsequently, a secondary screening process was performed, in order to determine the cytostatic activity of such compounds, against the 60 cell panel representing leukemia, melanoma and

**Table 1**
Results of primary anticancer assay for eight compounds selected by the NCI

| Compound | Activity[a] |
|---|---|
| **5c** | A |
| **6b** | NA |
| **6g** | NA |
| **7b** | NA |
| **7g** | NA |
| **8c** | NA |
| **9d** | NA |
| **9g** | A |

[a] Activity denoted as: A = active; NA = not active.

**Table 2**
In vitro testing expressed as growth inhibition of cancer cell lines for compounds **5c** and **9g**[a]

| Panel/cell line | Compounds | | | |
|---|---|---|---|---|
| | **5c** | | **9g** | |
| | $GI_{50}$[b] (μM) | $LC_{50}$[c] (μM) | $GI_{50}$[b] (μM) | $LC_{50}$[c] (μM) |
| *Leukemia* | | | | |
| RPMI-8226 | 1.86 | >100 | 1.73 | >100 |
| SR | 2.76 | >100 | 1.57 | 8.06 |
| CCRF-CEM | — | >100 | — | — |
| HL-60(TB) | >100 | >100 | — | — |
| K-562 | 0.09 | >100 | — | — |
| MOLT-4 | 0.87 | >100 | — | — |
| *Non-small cell lung cancer* | | | | |
| EKVX | 4.97 | >100 | — | >100 |
| HOP-62 | 26.0 | >100 | — | — |
| NCI-H226 | 3.77 | >100 | — | >100 |
| NCI-H23 | 4.99 | >100 | 1.77 | — |
| NCI-H460 | — | >100 | 1.98 | — |
| NCI-H522 | 6.41 | >100 | 2.20 | >100 |
| HOP-92 | — | >100 | 0.04 | — |
| NCI-H322M | — | >100 | — | >100 |
| A549/ATCC | — | >100 | — | >100 |
| *Colon* | | | | |
| COLO 205 | 2.09 | — | 2.16 | — |
| HCT-116 | 2.75 | >100 | 1.94 | — |
| HCT-15 | — | >100 | 3.09 | >100 |
| HT29 | — | >100 | — | >100 |
| KM12 | — | >100 | — | >100 |
| SW-620 | — | — | 3.48 | >100 |
| HCC-2998 | >100 | >100 | 2.21 | >100 |
| *CNS* | | | | |
| SF-295 | 2.32 | 74.1 | 2.48 | >100 |
| SF-539 | 3.95 | >100 | 1.87 | — |
| U251 | 2.09 | >100 | 1.71 | — |
| SF-268 | 3.12 | >100 | 4.55 | >100 |
| SNB-19 | 4.90 | >100 | — | >100 |
| SNB-75 | 1.55 | 24.0 | 2.76 | >100 |
| *Melanoma* | | | | |
| LOX IMVI | — | >100 | 1.66 | — |
| MALME-3M | 2.44 | >100 | — | >100 |
| MDA-MB-435 | — | >100 | — | >100 |
| SK-MEL-5 | >100 | >100 | 1.79 | — |
| UACC-257 | >100 | >100 | >100 | >100 |
| UACC-62 | 11.4 | >100 | 2.40 | >100 |
| SK-MEL-2 | 6.99 | 57.9 | — | >100 |
| M14 | — | >100 | — | >100 |
| SK-MEL-28 | — | >100 | — | >100 |
| *Ovarian* | | | | |
| IGROV1 | 3.54 | >100 | — | >100 |
| OVCAR-3 | 1.96 | >100 | — | — |
| OVCAR-4 | — | — | — | >100 |
| NCI/ADR-RES | 4.64 | >100 | 1.80 | — |
| OVCAR-8 | 6.32 | >100 | — | >100 |
| OVCAR-5 | >100 | >100 | 1.81 | >100 |
| SK-OV-3 | 12.5 | >100 | 2.14 | >100 |
| *Renal* | | | | |
| A498 | 3.14 | >100 | — | >100 |
| ACHN | 4.27 | >100 | 1.82 | — |
| CAKI-1 | 4.56 | >100 | 1.96 | — |
| RXF 393 | 2.08 | 9.87 | 1.82 | — |
| SN12C | — | >100 | — | >100 |
| TK-10 | 3.12 | >100 | — | >100 |
| UO-31 | 0.10 | >100 | — | >100 |
| 786-0 | 3.94 | >100 | — | — |
| *Prostate* | | | | |
| DU-145 | — | >100 | — | >100 |
| PC-3 | — | — | 2.35 | >100 |
| *Breast* | | | | |
| MCF7 | — | >100 | — | >100 |
| MDA-MB-231/ATCC | 2.45 | >100 | 1.88 | — |
| BT-549 | 2.25 | >100 | — | >100 |
| T-47D | 1.12 | >100 | 1.90 | — |
| MDA-MB-468 | 2.91 | >100 | — | >100 |
| HS 578T | 2.55 | >100 | — | >100 |

[a] Data obtained from NCI's in vitro disease-oriented human tumor cell lines screen.[31–33]

[b] $GI_{50}$ was the drug concentration resulting in a 50% reduction in the net protein increase (as measured by SRB staining) in control cells during the drug incubation. Determined at five concentration levels (100, 10, 1.0, 0.1, and 0.01 μM).

[c] $LC_{50}$ is a parameter of citotoxicity and reflects the molar concentration needed to kill 50% of the cells.

cancers of the lung, colon, brain, ovary, breast, prostate, and kidney; where the testing results were expressed according to the next three parameters: $GI_{50}$ which is the molar concentration of the compounds required to inhibit the growth of that cell line by 50% (relative to untreated cells). TGI as the molar concentration that causes total growth inhibition, and $LC_{50}$ which is a parameter of citotoxicity and reflects the molar concentration needed to kill 50% of the cells.[30] The compounds were evaluated at five concentration levels (100, 10, 1.0, 0.1, and 0.01 μM) and the test consisted of a 48 h continuous drug exposure protocol using sulforhodamide B (SRB) protein assay to estimate cell growth. Details of this evaluation method, and the complementary information related with the activity pattern over all cell lines, have been published.[31–33] As shown in Table 2, compound **5c** presented remarkable activity against 37 human tumor cell lines, being the most sensitive to growth inhibition K-562 of leukemia panel with $GI_{50}$ value of 0.09 μM and UO-31 of renal cancer panel displaying a $GI_{50}$ value of 0.10 μM (citotoxicity expressed as $LC_{50}$ with values >100 μM for both cell lines). Likewise, compound **9g** (active against 28 human tumor cell lines) was found especially effective against the cell line HOP-92 of non-small cell lung cancer panel exhibiting a remarkable $GI_{50}$ value of 0.04 μM ($LC_{50}$ >100 μM), as well as a $GI_{50}$ of 1.57 μM ($LC_{50}$ >100 μM) for cell line SR of leukemia panel. In summary, derivatives **5c** and **9g** showed significant activities with $GI_{50}$ ranges of 0.09–26.0 μM and 0.04–4.55 μM, respectively; where most of the $GI_{50}$ values of the screening process resulted in a sensitive range inferior of 20 μM denoting an outstanding activity in both cases. The values of citotoxicity associated with compounds **5c** and **9g** and measured as $LC_{50}$ are in most of the cell lines >100 μM (Table 2).

## 3. Conclusion

As a part of our current research work focused on the development of new bioactive heterocyclic compounds, the synthesis and anticancer screening of the novel pyrazolic chalcones **5**/**6a**–**h**, pyrazoles **7a**–**h** and their *N*-acetyl derivatives **8**/**9a**–**h** have been performed. The anticancer evaluation data revealed that among the eight compounds studied, derivatives **5c** and **9g** exhibited high activity patterns against different cancer cell lines with remarkable values in panels of non-small cell lung cancer, leukemia, and renal cancer. Owing to the significant results obtained, chemical studies are being conducted to improve the antitumor activity of such compounds, as well as other biological studies focused on antiviral and antifungal activity.

## 4. Experimental

Melting points were determined on a Buchi Melting Point Apparatus and are uncorrected. IR spectra were performed on a Shimadzu FTIR 8400 spectrometer in KBr disks. The $^{1}H$ and $^{13}C$

NMR spectra were run on a Bruker DPX 400 spectrometer operating at 400 MHz and 100 MHz, respectively, using DMSO-$d_6$ as solvent and TMS as internal standard. The mass spectra were obtained on a Hewlett Packard HP Engine-5989 spectrometer (equipped with a direct inlet probe) operating at 70 eV. The elemental analyses were carried out on a LECO CHNS-900 elemental analyzer. Reactions under microwave irradiation were performed using a CEM Discover™ monomode system with power/time control using a ramp of 100–300 W.

### 4.1. General procedure for the synthesis of the pyrazolic chalcones 5/6a–h

To a solution of 3-aryl-1-phenylpyrazol-4-carboxaldehyde **4** (1.0 mmol), acetophenone **1** (1.0 mmol) and ethanol (30.0 mL), a pellet of KOH was added. The reaction mixture was stirred at ambient temperature until formation of a precipitate. The solid obtained was isolated by filtration, washed and recrystalized from a (1:1) EtOH/DMF mixture.

#### 4.1.1. (*E*)-1-(4-Nitrophenyl)-3-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]prop-2-en-1-one (5a)

Green solid, 76% yield; mp: 244 °C. FTIR (KBr) $\nu$ ($cm^{-1}$): 1661 (C=O and C=N); 1517 and 1342 ($NO_2$); 1584 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.41 (t, 1H, $H_pA$, $J$ = 7.14 Hz), 7.56 (t, 2H, $H_mA$, $J$ = 8.20 Hz), 7.61 (d, 1H, H-7, 15.51 Hz), 7.68 (d, 1H, H-6, 15.30 Hz), 7.92 (d, 2H, $H_oA$, $J$ = 7.05 Hz), 7.97 (d, 2H, $H_oB$, $J$ = 8.89 Hz), 7.98 (d, 2H, $H_oC$, $J$ = 8.55 Hz), 8.25 (d, 2H, $H_mC$, $J$ = 8.60 Hz), 8.30 (d, 2H, $H_mB$, $J$ = 8.88 Hz), 9.19 (s, 1H, H-5) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 117.1 (C-4), 122.7 (C-6), 123.3 ($C_mB$), 126.3 ($C_pA$), 126.6 ($C_oA$), 128.3 ($C_mA$), 128.6 ($C_oB$), 128.7 ($C_oC$), 128.9 (C-5), 129.3 ($C_mC$), 134.8 (C-7), 136.3 ($C_iC$), 137.6 ($C_iA$), 138.4 ($C_iB$), 144.4 ($C_pC$), 147.2 ($C_pB$), 149.8 (C-3), 188.6 (C-8) ppm. MS (70 eV) $m/z$ (%): 440 (12, $M^+$), 279 (100), 77 (39). Anal. Calcd for $C_{24}H_{16}N_4O_5$: C, 65.45; H, 3.66; N, 12.77. Found: C, 65.54; H, 3.70; N, 12.69.

#### 4.1.2. (*E*)-1-(4-Fluorophenyl)-3-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]prop-2-en-1-one (5b)

Yellow solid, 76% yield; mp: 221 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1659 (C=O and C=N); 1602 (C=C); 1507 and 1343 ($NO_2$); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 6.61 (d, 2H, $H_oC$, $J$ = 8.89 Hz), 7.41 (t, 1H, $H_pA$, $J$ = 8.89 Hz), 7.59 (t, 2H, $H_mA$, $J$ = 7.86 Hz), 7.68 (d, 1H, H-7, $J$ = 15.51 Hz), 7.87 (d, 1H, H-6, $J$ = 15.30 Hz), 7.93 (d, 2H, $H_oA$, $J$ = 8.40 Hz), 7.95 (d, 2H, $H_oB$, $J$ = 8.88 Hz), 8.17 (d, 2H, $H_mC$, $J$ = 8.89 Hz), 8.37 (d, 2H, $H_mB$, $J$ = 8.89 Hz), 9.42 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 115.8 ($C_oC$), 118.7 (C-4), 122.0 (C-6), 124.0 ($C_mB$), 126.8 ($C_oA$), 127.5 ($C_pA$), 129.2 ($C_oB$), 129.3 (C-5), 129.7 ($C_mA$), 131.1 ($C_mC$), 133.3 (C-7), 138.3 ($C_iB$), 138.8 ($C_iA$), 147.2 ($C_pB$), 150.3 (C-3), 163.7 ($C_pC$), 166.2 ($C_iC$), 187.0 (C-8) ppm. MS (70 eV) $m/z$ (%): 413 (32, $M^+$), 244 (65), 123 (100), 77 (56). Anal. Calcd for $C_{24}H_{16}FN_3O_3$: C, 69.73; H, 3.90; N, 10.16. Found: C, 69.70; H, 3.95; N, 10.18.

#### 4.1.3. (*E*)-1-(4-Chlorophenyl)-3-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]prop-2-en-1-one (5c)

Yellow solid, 91% yield; mp: 224 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1660 (C=O and C=N); 1600 (C=C); 1507 and 1350 ($NO_2$); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.42 (t, 1H, $H_pA$, $J$ = 7.03 Hz), 7.55 (d, 2H, $H_mA$, $J$ = 7.03 Hz), 7.57 (d, 2H, $H_oA$, $J$ = 6.82 Hz), 7.60 (d, 1H, H-7, $J$ = 13.24 Hz), 7.67 (d, 1H, H-6, $J$ = 13.03 Hz), 7.93 (d, 2H, $H_oC$, $J$ = 7.63 Hz), 7.96 (d, 2H, $H_oB$, $J$ = 8.89 Hz), 8.01 (d, 2H, $H_mC$, $J$ = 8.01 Hz), 8.33 (t, 2H, $H_mB$, $J$ = 8.89 Hz), 9.17 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 117.8 (C-4), 118.6 (C-6), 122.4 ($C_oC$), 123.1 ($C_mB$), 126.7 ($C_pA$), 126.8 ($C_oA$), 128.6 ($C_oB$), 128.8 (C-5), 129.0 ($C_mA$), 129.3 ($C_mC$), 133.0 (C-7), 136.0 ($C_iC$), 137.3 ($C_pC$), 138.0 ($C_iB$), 138.5 ($C_iA$), 147.2 ($C_pB$), 149.7 (C-3), 187.5 (C-8) ppm. MS (70 eV) $m/z$ (%): 429 (13, $M^+$), 244 (61), 139 (100), 77 (90). Anal. Calcd for $C_{24}H_{16}ClN_3O_3$: C, 67.12; H, 3.79; N, 9.69. Found: C, 67.20; H, 3.85; N, 9.74.

#### 4.1.4. (*E*)-1-(4-Bromophenyl)-3-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]prop-2-en-1-one (5d)

Yellow solid, 95% yield; mp: 220 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1660 (C=O and C=N); 1599 (C=C); 1508 and 1352 ($NO_2$); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.41 (t, 1H, $H_pA$, $J$ = 7.65 Hz), 7.72 (d, 2H, $H_oC$, $J$ = 8.27 Hz), 7.56 (t, 2H, $H_mA$, $J$ = 7.24 Hz), 7.62 (d, 1H, H-7, $J$ = 15.50 Hz), 7.80 (d, 1H, H-6, $J$ = 15.7 Hz), 7.93 (d, 2H, $H_oA$, $J$ = 8.48 Hz), 7.95 (d, 2H, $H_mC$, $J$ = 8.30 Hz), 7.96 (d, 2H, $H_oB$, $J$ = 7.92 Hz), 8.33 (d, 2H, $H_mB$, $J$ = 7.96 Hz), 9.16 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 117.8 (C-4), 123.1 ($C_mB$), 122.4 (C-6), 126.2 ($C_pC$), 126.8 ($C_pA$), 128.6 ($C_oB$), 128.8 (C-5), 128.9 ($C_oA$), 129.4 ($C_mC$), 129.7 ($C_mA$), 131.0 ($C_oC$), 133.1 (C-7), 136.4 ($C_iC$), 138.0 ($C_iB$), 138.5 ($C_iA$), 147.2 ($C_pB$), 149.7 (C-3), 187.7 (C-8) ppm. MS (70 eV) $m/z$ (%): 473 (7, $M^+$), 183 (100), 244 (57), 77 (70). Anal. Calcd for $C_{24}H_{16}BrN_3O_3$: C, 60.77; H, 3.40; N, 8.86. Found: C, 60.80; H, 3.48; N, 8.79.

#### 4.1.5. (*E*)-3-[3-(4-Nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-1-phenyl-prop-2-en-1-one (5e)

Yellow solid, 92% yield; mp: 190 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1626 (C=O and C=N), 1595 (C=C), 1507 and 1339 ($NO_2$); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.42 (t, 1H, $H_pA$, $J$ = 7.00 Hz), 7.49 (d, 2H, $H_mC$, $J$ = 7.56 Hz), 7.55 (t, 2H, $H_mA$, $J$ = 7.15 Hz), 7.60 (t, 1H, $H_pC$, $J$ = 8.15 Hz), 7.62 (d, 1H, H-7, $J$ = 15.35 Hz), 7.67 (d, 1H, H-6, $J$ = 15.30 Hz), 7.91 (d, 2H, $H_oA$, $J$ = 7.40 Hz), 7.96 (d, 2H, $H_oB$, $J$ = 7.40 Hz), 7.98 (d, 2H, $H_oC$, $J$ = 8.15 Hz), 8.32 (d, 2H, $H_mB$, $J$ = 7.39 Hz), 9.15 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 118.0 (C-4), 123.0 (C-6), 124.1 ($C_mB$), 126.0 ($C_oC$), 126.3 ($C_pA$), 127.4 ($C_pC$), 127.8 (C-5), 128.0 ($C_oA$), 128.3 ($C_mA$), 128.7 ($C_oB$), 129.6 ($C_mC$), 133.1 (C-7), 135.0 ($C_iC$), 137.9 ($C_iB$), 139.0 ($C_iA$), 147.6 ($C_pB$), 149.7 (C-3), 189.0 (C-8) ppm. MS (70 eV) $m/z$ (%): 395 (36, $M^+$), 119 (100), 77 (78). Anal. Calcd for $C_{24}H_{17}N_3O_3$: C, 72.90; H, 4.33; N, 10.63. Found: C, 72.98; H, 4.33; N, 10.59.

#### 4.1.6. (*E*)-1-(4-Methylphenyl)-3-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]prop-2-en-1-one (5f)

Yellow solid, 89% yield; mp: 214 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1661 (C=O and C=N), 1596 (C=C), 1509 and 1350 ($NO_2$); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.40 (s, 3H, H–$CH_3$), 7.34 (d, 2H, $H_mC$, $J$ = 7.65 Hz), 7.40 (t, 1H, $H_pA$, $J$ = 7.45 Hz), 7.56 (t, 2H, $H_mA$, $J$ = 7.45 Hz), 7.64 (d, 1H, H-7, $J$ = 15.51 Hz), 7.69 (d, 1H, H-6, $J$ = 15.92 Hz), 7.91 (d, 2H, $H_oC$, $J$ = 7.60 Hz), 7.93 (d, 2H, $H_oA$, $J$ = 8.30 Hz), 7.96 (d, 2H, $H_oB$, $J$ = 7.31 Hz), 8.33 (d, 2H, $H_mB$, $J$ = 7.24 Hz), 9.15 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.3 (C–$CH_3$), 117.9 (C-4), 118.6 ($C_oC$), 122.9 (C-6), 123.1 ($C_mB$), 126.7 ($C_pA$), 127.6 ($C_oA$), 128.5 ($C_mC$), 128.6 ($C_oB$), 128.7 (C-5), 128.8 ($C_mA$), 132.1 (C-7), 134.9 ($C_pC$), 138.1 ($C_iB$), 138.5 ($C_iA$), 142.5 ($C_iC$), 147.1 ($C_pB$), 149.6 (C-3), 188.0 (C-8) ppm. MS (70 eV) $m/z$ (%): 409 (38, $M^+$), 244 (28), 119 (100), 77 (31). Anal. Calcd for $C_{25}H_{19}N_3O_3$: C, 73.34; H, 4.68; N, 10.26. Found: C, 73.44; H, 4.70; N, 10.16.

#### 4.1.7. (*E*)-1-(4-Methoxyphenyl)-3-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]prop-2-en-1-one (5g)

Yellow solid, 75% yield; mp: 205 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1657 (C=O and C=N), 1599 (C=C), 1507 and 1347 ($NO_2$), 1222 (O–$CH_3$); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 3.87 (s, 3H, H–$OCH_3$), 7.08 (d, 2H, $H_mC$, $J$ = 9.10 Hz), 7.41 (t, 1H, $H_pA$, $J$ = 7.44 Hz), 7.58 (t, 2H, $H_mA$, $J$ = 8.48 Hz), 7.67 (d, 1H, H-7, $J$ = 15.51 Hz), 7.87 (d, 1H, H-6, $J$ = 15.28 Hz), 7.94 (d, 2H, $H_oC$, $J$ = 9.12 Hz), 7.95 (d, 2H, $H_oA$, $J$ = 8.48 Hz), 8.08 (d, 2H, $H_oC$, $J$ = 9.10 Hz), 8.37 (d, 2H, $H_mB$, $J$ = 9.10 Hz), 9.17 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$)

$\delta$ 55.6 (C–$OCH_3$), 114.0 ($C_m$C), 117.8 (C-4), 122.3 ($C_m$B), 122.4 (C-6), 124.1 ($C_o$C), 127.0 ($C_o$A), 128.0 (C-5), 129.0 ($C_o$B), 129.5 ($C_m$A), 129.7 ($C_i$C), 132.2 ($C_p$A), 133.3 (C-7), 137.6 ($C_i$A), 138.2 ($C_i$B), 146.1 ($C_p$B), 149.7 (C-3), 163.8 ($C_p$C), 188.6 (C-8) ppm. MS (70 eV) *m*/*z* (%): 425 (9, $M^+$), 135 (100), 77 (45). Anal. Calcd for $C_{25}H_{19}N_3O_4$: C, 70.58; H, 4.50; N, 9.88. Found: C, 70.65; H, 4.48; N, 9.85.

#### 4.1.8. (*E*)-1-(3,4-Methylenedioxyphenyl)-3-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]prop-2-en-1-one (5h)

Green solid, 80% yield; mp: 169 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1657 (C=O and C=N), 1598 (C=C), 1507 and 1347 ($NO_2$), 1264 y 1102 (O–$CH_2$–O); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 6.07 (s, 2H, H–$CH_2$), 6.98 (d, 2H, $H_m$C, *J* = 8.03 Hz), 7.39 (t, 1H, $H_p$A, *J* = 7.53 Hz), 7.47 (s, 1H, $H_{o'}$C), 7.54 (t, 2H, $H_m$A, *J* = 7.53 Hz), 7.60 (d, 1H, H-7, *J* = 15.48), 7.63 (d, 1H, H-6, *J* = 15.57), 7.66 (d, 2H, $H_o$C, *J* = 8.03 Hz), 7.88 (d, 2H, $H_o$A, *J* = 7.78 Hz), 7.91 (d, 2H, $H_o$B, *J* = 8.78 Hz), 8.31 (d, 2H, $H_m$B, *J* = 8.79 Hz), 9.11 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 102.4 (C–$CH_2$), 108.5 ($C_m$C), 119.0 (C-4), 119.6 ($C_o$A), 123.5 (C-6), 124.3 ($C_m$B), 125.1 ($C_o$C), 127.9 ($C_p$A), 129.4 ($C_{o'}$C), 129.6 ($C_o$B), 129.7 (C-5), 130.0 ($C_m$A), 132.8 ($C_i$C), 132.9 (C-7), 138.2 ($C_p$C), 139.1 ($C_p$B), 139.4 ($C_i$A), 148.1 ($C_i$B), 148.5 (C-3), 150.7 ($C_{m'}$C), 187.7 (C-8) ppm. MS (70 eV) *m*/*z* (%): 439 (11, $M^+$), 279 (100), 149 (100), 77 (44). Anal. Calcd for $C_{25}H_{17}N_3O_5$: C, 68.33; H, 3.90; N, 9.56. Found: C, 68.28; H, 3.88; N, 9.58.

#### 4.1.9. (*E*)-3-[3-(4-Chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-1-(4-nitrophenyl)-prop-2-en-1-one (6a)

Green solid, 88% yield; mp: 234 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1662 (C=O and C=N), 1521 and 1348 ($NO_2$), 1521 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.39 (t, 1H, $H_p$A, *J* = 6.61 Hz), 7.55 (t, 2H, $H_m$A, *J* = 8.27 Hz), 7.57 (d, 2H, $H_o$B, *J* = 8.06 Hz), 7.60 (d, 1H, H-7, 15.50 Hz), 7.69 (d, 2H, $H_m$B, *J* = 8.48 Hz), 7.70 (d, 1H, H-6, 15.70 Hz), 7.91 (d, 2H, $H_o$A, *J* = 7.65 Hz), 8.17 (d, 2H, $H_o$C, *J* = 8.68 Hz), 8.32 (d, 2H, $H_m$C, *J* = 8.89 Hz), 9.15 (s, 1H, H-5) ppm. $^{13}$C NMR (DMSO-$d_6$) $\delta$ 117.13 (C-4), 118.5 ($C_o$A), 121.7 (C-6), 122.9 ($C_m$C), 126.6 ($C_p$A), 128.1 ($C_o$B), 128.7 ($C_o$C), 128.8 (C-5), 128.9 ($C_m$A), 129.3 ($C_m$B), 130.4 ($C_i$B), 133.15 ($C_p$B), 134.8 (C-7), 138.5 ($C_i$A), 142.4 ($C_i$C), 149.4 ($C_p$C), 151.1 (C-3), 187.8 (C-8) ppm. MS (70 eV) *m*/*z* (%): 429 (8, $M^+$), 279 (100), 77 (60). Anal. Calcd for $C_{24}H_{16}ClN_3O_3$: C, 67.06; H, 3.75; N, 9.78. Found: C, 67.19; H, 3.70; N, 9.77.

#### 4.1.10. (*E*)-3-[3-(4-Chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-1-(4-fluorophenyl)-prop-2-en-1-one (6b)

Yellow solid, 75% yield; mp: 166 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1660 (C=O and C=N), 1600 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.42 (t, 1H, $H_p$A, *J* = 8.69 Hz), 7.44 (d, 2H, $H_o$C, *J* = 8.89 Hz), 7.60 (t, 2H, $H_m$A, *J* = 8.48 Hz), 7.64 (d, 2H, $H_o$B, *J* = 7.44 Hz), 7.68 (d, 1H, H-7, *J* = 15.3 Hz), 7.70 (d, 2H, $H_o$A, *J* = 8.68 Hz), 7.87 (d, 1H, H-6, *J* = 15.5 Hz), 7.94 (d, 2H, $H_m$B, *J* = 7.45 Hz), 8.17 (d, 2H, $H_m$C, *J* = 8.89 Hz), 9.41 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 115.8 ($C_o$C), 117.8 (C-4), 118.7 ($C_m$B), 121.4 (C-6), 127.3 ($C_p$A), 128.7 ($C_o$B), 128.9 (C-5), 129.7 ($C_m$A), 130.0 ($C_o$A), 130.7 ($C_i$B), 131.1 ($C_m$C), 133.9 (C-7), 134.3 ($C_p$B), 138.8 ($C_i$A), 151.6 (C-3), 163.7 ($C_i$C), 166.2 ($C_p$C), 187.2 (C-8) ppm. MS (70 eV) *m*/*z* (%): 402 (9, $M^+$), 279 (100), 77 (49). Anal. Calcd for $C_{24}H_{16}ClFN_2O$: C, 71.55; H, 4.00; N, 6.95. Found: C, 71.50; H, 3.96; N, 6.99.

#### 4.1.11. (*E*)-1-(4-Chlorophenyl)-3-[3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]prop-2-en-1-one (6c)

Yellow solid, 90% yield; mp: 185 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1660 (C=O and C=N), 1598 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.42 (t, 1H, $H_p$A, *J* = 7.03 Hz), 7.58 (t, 2H, $H_m$A, *J* = 8.47 Hz), 7.62 (d, 2H, $H_o$B, *J* = 7.47 Hz), 7.65 (d, 2H, $H_o$C, *J* = 8.69 Hz), 7.68 (d, 1H, H-7, *J* = 15.50 Hz), 7.70 (d, 2H, $H_o$A, *J* = 7.86 Hz), 7.84 (d, 1H, H-6, *J* = 15.51 Hz), 7.94 (d, 2H, $H_m$B, *J* = 8.47 Hz), 8.10 (d, 2H, $H_m$C, *J* = 8.68 Hz), 9.41 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 117.8 (C-4), 118.7 (C-6), 121.2 ($C_m$B), 127.2 ($C_p$A), 128.7 ($C_o$C), 128.9 ($C_o$B), 129.0 (C-5), 129.7 ($C_m$A), 130.0 ($C_o$A), 130.3 ($C_m$C), 130.7 ($C_i$B), 133.6 ($C_i$A), 134.2 (C-7), 138.0 ($C_p$C), 138.8 ($C_p$B), 151.6 (C-3), 163.9 ($C_i$C), 187.4 (C-8) ppm. MS (70 eV) *m*/*z* (%): 418 (10, $M^+$), 279 (100), 77 (38). Anal. Calcd for $C_{24}H_{16}Cl_2N_2O$: C, 68.75; H, 3.85; N, 6.68. Found: C, 68.79; H, 3.80; N, 6.65.

#### 4.1.12. (*E*)-1-(4-Bromophenyl)-3-[3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]prop-2-en-1-one (6d)

Yellow solid, 96% yield; mp: 192 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1659 (C=O and C=N), 1597 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.42 (t, 1H, $H_p$A, *J* = 7.51 Hz), 7.59 (t, 2H, $H_m$A, *J* = 8.27 Hz), 7.62 (d, 2H, $H_o$C, *J* = 8.48 Hz), 7.68 (d, 1H, H-7, *J* = 15.52 Hz), 7.70 (d, 2H, $H_o$B, *J* = 8.69 Hz), 7.80 (d, 2H, $H_m$C, *J* = 8.48 Hz), 7.83 (d, 1H, H-6, *J* = 15.54 Hz), 7.94 (d, 2H, $H_o$A, *J* = 7.65 Hz), 8.02 (d, 2H, $H_m$B, *J* = 8.69 Hz), 9.41 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 117.8 (C-4), 118.7 ($C_o$A), 121.2 (C-6), 127.2 ($C_p$A), 127.3 ($C_i$B), 128.9 ($C_o$C), 129.0 (C-5), 129.7 ($C_m$A), 130.0 ($C_m$C), 130.2 ($C_m$B), 130.7 ($C_i$C), 131.8 ($C_o$B), 133.4 ($C_p$C), 134.3 (C-7), 136.5 ($C_p$B), 138.8 ($C_i$A), 151.6 (C-3), 187.6 (C-8) ppm. MS (70 eV) *m*/*z* (%): 462 (5, $M^+$), 464 (9), 279 (100), 77 (44). Anal. Calcd for $C_{24}H_{16}ClBrN_2O$: C, 62.16; H, 3.48; N, 6.04. Found: C, 62.10; H, 3.52; N, 6.14.

#### 4.1.13. (*E*)-3-[3-(4-Chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-1-phenyl-prop-2-en-1-one (6e)

Yellow solid, 78% yield; mp: 175 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1662 (C=O and C=N), 1606 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.42 (t, 1H, $H_p$A, *J* = 7.44 Hz), 7.58 (t, 2H, $H_m$A, *J* = 8.69 Hz), 7.60 (t, 1H, $H_p$C, *J* = 7.03 Hz), 7.61 (d, 2H, $H_m$B, *J* = 7.65 Hz), 7.61 (d, 2H, $H_m$C, *J* = 7.42 Hz), 7.63 (d, 2H, $H_o$B, *J* = 7.60 Hz), 7.69 (d, 1H, H-7, *J* = 15.71 Hz), 7.71 (d, 2H, $H_o$A, *J* = 8.48 Hz), 7.81 (d, 1H, H-6, *J* = 15.48 Hz), 8.10 (d, 2H, $H_o$C, *J* = 7.75 Hz), 9.43 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 117.8 (C-4), 118.7 (C-6), 121.7 ($C_m$B), 127.2 ($C_p$A), 127.3 ($C_i$B), 128.2 ($C_o$C), 128.7 ($C_m$C), 128.9 (C-5), 129.7 ($C_p$C), 129.8 ($C_m$A), 130.0 ($C_o$A), 130.8 ($C_o$B), 133.6 ($C_p$B), 133.8 (C-7), 137.6 ($C_i$C), 138.9 ($C_i$A), 151.6 (C-3), 188.7 (C-8) ppm. MS (70 eV) *m*/*z* (%): 384 (24, $M^+$), 279 (100), 77 (95). Anal. Calcd for $C_{24}H_{17}ClN_2O$: C, 74.90; H, 4.45; N, 7.28. Found: C, 74.94; H, 4.40; N, 7.32.

#### 4.1.14. (*E*)-3-[3-(4-Chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-1-(4-methylphenyl)-prop-2-en-1-one (6f)

Yellow solid, 76% yield; mp: 176 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1660 (C=O and C=N), 1595 (C=C); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.41 (s, 3H, H–$CH_3$), 7.39 (d, 2H, $H_m$C, *J* = 8.30 Hz), 7.42 (t, 1H, $H_p$A, *J* = 8.04 Hz), 7.60 (t, 2H, $H_m$A, *J* = 8.48 Hz), 7.63 (d, 2H, $H_o$B, *J* = 7.64 Hz), 7.66 (d, 1H, H-7, *J* = 15.93 Hz), 7.70 (d, 2H, $H_o$A, *J* = 8.68 Hz), 7.87 (d, 1H, H-6, *J* = 15.51 Hz), 7.85 (d, 2H, $H_m$B, *J* = 7.68 Hz), 8.01 (d, 2H, $H_o$C, *J* = 8.27 Hz), 9.42 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 21.1 (C–$CH_3$), 117.8 (C-4), 118.7 (C-6), 118.7 ($C_m$C), 121.7 ($C_m$B), 127.2 ($C_p$A), 128.9 ($C_o$B), 129.1 (C-5), 129.7 ($C_m$A), 130.0 ($C_o$A), 130.4 ($C_o$C), 130.8 ($C_i$B), 130.9 ($C_p$C), 133.3 (C-7), 133.5 ($C_p$B), 138.9 ($C_i$A), 143.5 ($C_i$C), 151.5 (C-3), 188.0 (C-8) ppm. MS (70 eV) *m*/*z* (%): 398 (4, $M^+$), 279 (100), 119 (40), 77 (39). Anal. Calcd for $C_{25}H_{19}ClN_2O$: C, 75.28; H, 4.80; N, 7.02. Found: C, 75.30; H, 4.84; N, 7.12.

#### 4.1.15. (*E*)-3-[3-(4-Chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-1-(4-methoxyphenyl)-prop-2-en-1-one (6g)

Yellow solid, 79% yield; mp: 167 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1659 (C=O and C=N), 1597 (C=C), 1219 (O–$CH_3$); $^1$H NMR (DMSO-$d_6$) $\delta$ 3.88 (s, 3H, H–$OCH_3$), 7.11 (d, 2H, $H_m$C, *J* = 8.89 Hz), 7.42 (t, 1H, $H_p$A,

$J$ = 7.45 Hz), 7.60 (t, 2H, $H_m$A, $J$ = 8.27 Hz), 7.62 (d, 2H, $H_o$B, $J$ = 7.76 Hz), 7.65 (d, 1H, H-7, $J$ = 15.51 Hz), 7.71 (d, 2H, $H_o$A, $J$ = 8.48 Hz), 7.87 (d, 1H, H-6, $J$ = 15.51 Hz), 7.95 (d, 2H, $H_m$B, $J$ = 8.47 Hz), 8.10 (d, 2H, $H_o$C, $J$ = 8.89 Hz), 9.40 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 55.5 (C–$OCH_3$), 114.0 ($C_m$C), 117.9 (C-4), 118.7 (C-6), 121.7 ($C_m$B), 127.2 ($C_p$A), 128.8 ($C_o$B), 128.9 (C-5), 129.6 ($C_m$A), 130.0 ($C_o$A), 130.4 ($C_i$C), 130.5 ($C_o$C), 130.8 ($C_i$B), 132.8 (C-7), 133.5 ($C_p$B), 138.9 ($C_i$A), 151.4 (C-3), 163.1 ($C_p$C), 186.8 (C-8) ppm. MS (70 eV) $m/z$ (%): 414 (20, $M^+$), 279 (100), 77 (49). Anal. Calcd for $C_{25}H_{19}ClN_2O_2$: C, 72.37; H, 4.62; N, 6.75. Found: C, 72.41; H, 4.68; N, 6.70.

#### 4.1.16. (*E*)-3-[3-(4-Chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-1-(3,4-methylenedioxyphenyl)-prop-2-en-1-one (6h)

Yellow solid, 82% yield; mp: 152 °C. FTIR (KBr), $\nu$ ($cm^{-1}$): 1657 (C=O and C=N), 1589 (C=C), 1258 and 1094 (O–$CH_2$–O); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 6.17 (s, 2H, H–$CH_2$), 7.11 (d, 2H, $H_m$C, $J$ = 8.27 Hz), 7.42 (t, 1H, $H_p$A, $J$ = 7.24 Hz), 7.59 (t, 2H, $H_m$A, $J$ = 7.65 Hz), 7.61 (s, 1H, $H_{o'}$C), 7.63 (d, 2H, $H_o$B, $J$ = 7.86 Hz), 7.64 (d, 1H, H-7, $J$ = 15.30 Hz), 7.70 (d, 2H, $H_o$A, $J$ = 8.68 Hz), 7.78 (d, 2H, $H_o$C, $J$ = 8.27 Hz), 7.84 (d, 1H, H-6, $J$ = 15.46 Hz), 7.94 (d, 2H, $H_m$B, $J$ = 7.86 Hz), 9.39 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 102.1 (C–$CH_2$), 108.1 ($C_m$C), 117.9 (C-4), 118.7 ($C_m$B), 121.6 (C-6), 124.6 ($C_o$C), 128.8 (C-5), 128.9 ($C_o$B), 129.2 ($C_p$A), 129.4 ($C_{o'}$C), 129.7 ($C_m$A), 130.0 ($C_o$A), 130.8 ($C_i$B), 132.3 ($C_p$B), 133.0 (C-7), 133.5 ($C_i$A), 138.9 ($C_{m'}$C), 138.9 ($C_p$C), 148.0 ($C_i$C), 151.5 (C-3), 186.4 (C-8) ppm. MS (70 eV) $m/z$ (%): 428 (11, $M^+$), 279 (39), 149 (100), 77 (41). Anal. Calcd for $C_{25}H_{17}ClN_2O_3$: C, 70.01; H, 4.00; N, 6.53. Found: C, 70.11; H, 3.96; N, 6.60.

### 4.2. General procedure for synthesis of pyrazoles 7a–h

A mixture of chalcone **5a–h** (1.0 mmol), hydrazine hydrate (1.3 mmol) and DMF (0.2 mL) was placed into an open Pyrex-glass vessel and subjected to microwave irradiation with magnetic stirring for 5 min and with a maximum power of 300 W. Reaction progress was monitored by TLC and the precipitate formed was filtered off and recrystallized from ethanol, affording compounds **7a–h**. The *N*-acetyl derivatives **8**/**9a–h** were obtained from chalcones **5**/**6a–h** following the same procedure and using AcOH instead of DMF.

#### 4.2.1. 3-(4-Nitrophenyl)-4-[3-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl]-1-phenyl-1*H*-pyrazole (7a)

Yellow solid, 94% yield; mp: 242 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 3300 (NH), 1675 (C=N), 1595 (C=C, Ar), 1506 and 1345 ($NO_2$). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 3.07 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 16.54 Hz, $J_{4a'-5'}$ = 10.54 Hz), 3.63 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 16.34 Hz, $J_{4b'-5'}$ = 11.37 Hz), 5.21 (t, 1H, H-5′, $J_{5'-4a'}$ = 10.96 Hz, $J_{5'-4b'}$ = 11.40 Hz), 7.45 (t, 1H, $H_p$-A, $J$ = 7.45 Hz), 7.51 (t, 2H, $H_m$-A, $J$ = 8.47 Hz), 7.84 (d, 2H, $H_o$-A, $J$ = 7.86 Hz), 7.93 (d, 2H, $H_o$-C, $J$ = 8.89 Hz), 8.07 (d, 2H, $H_o$-B, $J$ = 8.69 Hz), 8.24 (d, 2H, $H_m$-B, $J$ = 8.69 Hz), 8.33 (d, 2H, $H_m$-C, $J$ = 8.87 Hz), 8.68 (s, 1H, H-5). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 39.5 (C-4′), 55.6 (C-5′), 118.4 ($C_o$-A), 121.4 ($C_m$-C), 123.0 ($C_m$-B), 124.0 (C-4), 124.8 ($C_o$-B), 125.0 ($C_o$-C), 126.8 ($C_p$-A), 127.5 (C-5), 129.6 ($C_m$-A), 139.1 ($C_i$-A), 139.4 ($C_i$-B), 139.6 ($C_i$-C), 146.3 ($C_p$-B), 146.9 ($C_p$-C), 147.9 (C-3), 148.8 (C-3′). MS (70 eV) $m/z$ (%): 454 (100, $M^+$), 426 (13), 345 (10), 77 (21). Anal. Calcd for $C_{24}H_{18}N_6O_4$: C, 63.43; H, 3.99; N, 18.49. Found: C, 63.50; H, 3.93; N, 18.52.

#### 4.2.2. 4-[3-(4-Fluorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl]-3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazole (7b)

Yellow solid, 89% yield; mp: 217 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 3289 (NH), 1679 (C=N), 1590 (C=C, Ar), 1505 and 1346 ($NO_2$). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.99 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 16.29 Hz, $J_{4a'-5'}$ = 10.13 Hz), 3.49 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 16.36 Hz, $J_{4b'-5'}$ = 10.75 Hz), 5.13 (t, 1H, H-5′, $J_{5'-4a'}$ = 10.44 Hz, $J_{5'-4b'}$ = 11.00 Hz), 7.13 (m, 1H, $H_p$-C), 7.19 (s, 1H, NH), 7.33 (t, 2H, $H_p$-A, $J$ = 7.65 Hz), 7.50 (t, 2H, $H_m$-A, $J$ = 7.26 Hz), 7.65 (m, 2H, $H_m$-C,), 7.86 (d, 2H, $H_o$-A, $J$ = 7.65 Hz), 8.04 (d, 2H, $H_o$-B, $J$ = 8.89 Hz), 8.26 (d, 2H, $H_m$-B, $J$ = 8.69 Hz), 8.45 (s, 1H, H-5). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 39.7 (C-4′), 54.5 (C-5′), 114.5 ($C_o$-C), 118.2 ($C_o$-A), 122.8 ($C_m$-B), 123.7 (C-4), 126.0 ($C_p$-A), 126.9 ($C_m$-C), 127.3 (C-5), 128.2 ($C_o$-B), 128.8 ($C_m$-A), 138.9 ($C_i$-A), 139.1 ($C_i$-B), 146.0 ($C_p$-B), 147.1 ($C_p$-C), 148.2 (C-3), 148.7 ($C_i$-C), 152.8 (C-3′). MS (70 eV) $m/z$ (%): 427 (100, M+), 305 (6), 345 (10), 77 (12). Anal. Calcd for $C_{24}H_{18}FN_5O_2$: C, 67.44; H, 4.24; N, 16.38. Found: C, 67.48; H, 4.19; N, 16.30.

#### 4.2.3. 4-[3-(4-Chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl]-3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazole (7c)

Yellow solid, 92% yield; mp: 224 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 3309 (NH), 1669 (C=N), 1596 (C=C, Ar), 1501 and 1340 ($NO_2$). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.99 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 16.29 Hz, $J_{4a'-5'}$ = 10.75 Hz), 3.55 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 16.36 Hz, $J_{4b'-5'}$ = 10.75 Hz), 5.11 (t, 1H, H-5′, $J_{5'-4a'}$ = 10.81 Hz, $J_{5'-4b'}$ = 11.15 Hz), 7.35 (t, 1H, $H_p$-A, $J$ = 7.44 Hz), 7.44 (d, 2H, $H_o$-C, $J$ = 8.47 Hz), 7.53 (t, 2H, $H_m$-A, $J$ = 7.44 Hz), 7.65 (d, 2H, $H_m$-C, $J$ = 8.48 Hz), 7.96 (d, 2H, $H_o$-A, $J$ = 7.65 Hz), 8.08 (d, 2H, $H_o$-B, $J$ = 11.30 Hz), 8.32 (d, 2H, $H_m$-B, $J$ = 11.37 Hz), 8.65 (s, 1H, H-5). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 39.8 (C-4′), 55.2 (C-5′), 118.4 ($C_o$-A), 123.0 ($C_m$-B), 124.0 (C-4), 124.1 ($C_o$-C), 124.9 ($C_o$-B), 126.7 ($C_p$-A), 127.7 (C-5), 128.7 ($C_m$-C), 129.6 ($C_m$-A), 130.0 ($C_p$-C), 132.0 ($C_i$-C), 139.2 ($C_i$-A), 139.4 ($C_i$-B), 146.7 ($C_p$-B), 147.9 (C-3), 148.3 (C-3′). MS (70 eV) $m/z$ (%): 443 (100, M+), 305 (7), 77 (19). Anal. Calcd for $C_{24}H_{18}ClN_5O_2$: C, 64.94; H, 4.09; N, 15.78. Found: C, 64.90; H, 4.19; N, 15.88.

#### 4.2.4. 4-[3-(4-Bromophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl]-3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazole (7d)

Yellow solid, 96% yield; mp: 231 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 3296 (NH), 1676 (C=N), 1595 (C=C, Ar), 1502 and 1341 ($NO_2$). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.96 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 16.13 Hz, $J_{4a'-5'}$ = 10.13 Hz), 3.52 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 16.23 Hz, $J_{4b'-5'}$ = 10.75 Hz), 5.08 (t, 1H, H-5′, $J_{5'-4a'}$ = 10.54 Hz, $J_{5'-4b'}$ = 11.36 Hz), 7.33 (t, 1H, $H_p$-A, $J$ = 8.48 Hz), 7.51 (t, 2H, $H_m$-A, $J$ = 7.44 Hz), 7.55 (s, 2H, $H_o$-C), 7.58 (s, 2H, $H_m$-C), 7.80 (d, 2H, $H_o$-A, $J$ = 7.65 Hz), 8.05 (d, 2H, $H_o$-B, $J$ = 9.10 Hz), 8.30 (d, 2H, $H_m$-B, $J$ = 8.89 Hz), 8.63 (s, 1H, H-5). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 40.1 (C-4′), 55.7 (C-5′), 119.0 ($C_o$-A), 121.7 ($C_i$-C), 124.3 ($C_m$-B), 124.5 (C-4), 127.2 ($C_p$-A), 127.9 ($C_o$-C), 129.2 ($C_o$-B), 129.9 ($C_m$-A), 130.1 (C-5), 131.9 ($C_m$-C), 139.6 ($C_i$-A), 139.9 ($C_i$-B), 147.2 ($C_p$-B), 148.4 (C-3), 149.0 (C-3′), 149.2 ($C_p$-C). MS (70 eV) $m/z$ (%): 487 (100, M+), 33 (31), 77 (42). Anal. Calcd for $C_{24}H_{18}BrN_5O_2$: C, 59.03; H, 3.72; N, 14.34. Found: C, 59.12; H, 3.69; N, 14.44.

#### 4.2.5. 3-(4-Nitrophenyl)-1-phenyl-4-[3-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl]-1*H*-pyrazole (7e)

Yellow solid, 90% yield; mp: 207 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 3310 (NH), 1663 (C=N), 1595 (C=C, Ar), 1503 and 1337 ($NO_2$). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 3.00 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 16.20 Hz, $J_{4a'-5'}$ = 10.45 Hz), 3.55 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 16.35 Hz, $J_{4b'-5'}$ = 11.20 Hz), 5.11 (t, 1H, H-5′, $J_{5'-4a'}$ = 10.46 Hz, $J_{5'-4b'}$ = 11.33 Hz), 7.32 (t, 1H, $H_p$-A, $J$ = 7.49 Hz), 7.49 (d, 2H, $H_m$-C, $J$ = 8.15 Hz), 7.51 (t, 2H, $H_m$-A, $J$ = 7.03 Hz), 7.63 (d, 2H, $H_o$-C, $J$ = 7.44 Hz), 7.88 (d, 2H, $H_o$-A, $J$ = 7.65 Hz), 8.06 (d, 2H, $H_o$-B, $J$ = 8.49 Hz), 8.28 (d, 2H, $H_m$-B, $J$ = 8.69 Hz), 8.54 (s, 1H, H-5). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 39.6 (C-4′), 54.5 (C-5′), 118.2 ($C_o$-A), 120.0 ($C_o$-C), 122.8 ($C_m$-B), 123.8 (C-4), 124.9 ($C_o$-B), 126.0 ($C_p$-A), 127.3 ($C_p$-C), 127.4 (C-5), 128.2 ($C_m$-C), 128.9 ($C_m$-A), 132.8 ($C_i$-C), 138.9 ($C_i$-A), 139.2 ($C_i$-B), 146.6 ($C_p$-B), 147.6 (C-3), 148.9 (C-3′). MS (70 eV) $m/z$ (%): 409 (100, M+), 244 (19), 118 (17), 77 (15). Anal. Calcd for

$C_{24}H_{19}N_5O_2$: C, 70.40; H, 4.68; N, 17.10. Found: C, 70.46; H, 4.60; N, 17.20.

#### 4.2.6. 3-(4-Nitrophenyl-1-phenyl-4-[3-(4-methylphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl]-1*H*-pyrazole (7f)

Yellow solid, 91% yield; mp: 249 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 3300 (NH), 1675 (C=N), 1592 (C=C, Ar), 1506 and 1345 ($NO_2$). $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.32 (s, 3H, H–$CH_3$), 2.98 (m, 1H, H-4a′), 3.48 (m, 1H, H-4b′), 5.12 (m, 1H, H-5′), 7.17 (d, 2H, $H_o$-C, $J$ = 8.07 Hz), 7.34 (t, 1H, $H_p$-A, $J$ = 7.50 Hz), 7.51 (t, 2H, $H_m$-A, $J$ = 7.37 Hz), 7.51 (d, 2H, $H_m$-C, $J$ = 8.07 Hz), 7.87 (d, 2H, $H_o$-A, $J$ = 8.27 Hz), 8.06 (d, 2H, $H_o$-B, $J$ = 8.68 Hz), 8.27 (d, 2H, $H_m$-B, $J$ = 8.68 Hz), 8.46 (s, 1H, H-5). RMN $^{13}C$ (100 MHz, DMSO-$d_6$) $\delta$ 19.9 (C–$CH_3$), 39.7 (C-4′), 54.4 (C-5′), 118.2 ($C_o$-A), 122.9 ($C_o$-C), 123.8 ($C_m$-B), 124.8 (C-4), 124.9 ($C_o$-B), 126.5 ($C_p$-A), 127.2 (C-5), 128.4 ($C_i$-C), 129.0 ($C_p$-C), 129.6 ($C_m$-A), 137.0 ($C_m$-C), 138.9 ($C_i$-A), 139.2 ($C_i$-B), 147.6 ($C_p$-B), 149.1 (C-3), 153.0 (C-3′). MS (70 eV) $m/z$ (%): 423 (82, M+), 245 (21), 131 (61), 77 (100). Anal. Calcd for: $C_{25}H_{21}N_5O_2$: C, 70.91; H, 5.00; N, 16.54. Found: C, 70.98; H, 5.10; N, 16.52.

#### 4.2.7. 4-[3-(4-Methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl]-3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazole (7g)

Yellow solid, 93% yield; mp: 239 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 3300 (NH), 1679 (C=N), 1590 (C=C, Ar), 1504 and 1339 ($NO_2$) $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.96 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 16.13 Hz, $J_{4a'-5'}$ = 10.13 Hz), 3.45 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 16.23 Hz, $J_{4b'-5'}$ = 10.75 Hz), 3.78 (s, 3H, H–$OCH_3$), 5.09 (t, 1H, H-5′, $J_{5'-4a'}$ = 10.54 Hz, $J_{5'-4b'}$ = 11.36 Hz), 6.92 (d, 2H, $H_m$-C, $J$ = 8.89 Hz), 7.32 (t, 1H, $H_p$-A, $J$ = 8.48 Hz), 7.49 (t, 2H, $H_m$-A, $J$ = 7.44 Hz), 7.56 (d, 2H, $H_o$-C, $J$ = 8.69 Hz), 7.85 (d, 2H, $H_o$-A, $J$ = 7.65 Hz), 8.04 (d, 2H, $H_o$-B, $J$ = 9.10 Hz), 8.25 (d, 2H, $H_m$-B, $J$ = 8.89 Hz), 8.43 (s, 1H, H-5) ppm. $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 40.0 (C-4′), 51.1 (C-5′), 53.5 (C–$OCH_3$), 113.9 ($C_m$-C), 118.4 ($C_o$-A), 123.8 ($C_m$-B), 124.1 ($C_p$-A), 124.2 (C-4), 125.8 ($C_o$-B), 126.7 (C-5), 128.9 ($C_m$-A), 130.6 ($C_o$-C), 139.2 ($C_i$-A), 139.5 ($C_i$-B), 147.3 ($C_p$-B), 149.8 (C-3), 153.2 (C-3′), 159.5 ($C_p$-C), 162.9 ($C_i$-C) ppm. MS (70 eV) $m/z$ (%): 439 (100, $M^+$), 133 (14), 77 (21). Anal. Calcd for $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.28; H, 4.86; N, 15.90.

#### 4.2.8. 4-[3-(3,4-Methylenedioxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl]-3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazole (7h)

Yellow solid, 95% yield; mp: 210 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 3298 (NH), 1680 (C=N), 1598 (C=C, Ar), 1505 and 1345 ($NO_2$) $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.94 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 16.33 Hz, $J_{4a'-5'}$ = 10.17 Hz), 3.44 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 16.34 Hz, $J_{4b'-5'}$ = 10.75 Hz), 5.09 (t, 1H, H-5′, $J_{5'-4a'}$ = 10.54 Hz, $J_{5'-4b'}$ = 11.54 Hz), 5.97 (s, 2H, H–$CH_2$), 7.06 (d, 1H, $H_m$-C, $J$ = 8.06 Hz), 7.19 (s, 1H, $H_{o'}$-C), 7.33 (t, 1H, $H_p$-A, $J$ = 7.85 Hz), 7.49 (t, 2H, $H_m$-A, $J$ = 7.45 Hz), 7.84 (d, 1H, $H_o$-C, $J$ = 8.07 Hz), 7.85 (d, 2H, $H_o$-A, $J$ = 7.65 Hz), 8.03 (d, 2H, $H_o$-B, $J$ = 8.69 Hz), 8.25 (d, 2H, $H_m$-B, $J$ = 8.68 Hz), 8.43 (s, 1H, H-5). $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 39.9 (C-4′), 54.4 (C-5′), 100.4 (C–$CH_2$), 107.4 ($C_m$-C), 118.2 ($C_o$-A), 119.4 ($C_o$-C), 122.9 ($C_m$-B), 123.7 (C-4), 124.9 ($C_{m'}$-C), 126.0 ($C_p$-A), 127.3 (C-5), 128.2 ($C_o$-B), 128.8 ($C_m$-A), 138.9 ($C_i$-A), 139.1 ($C_i$-B), 146.6 ($C_p$-B), 147.1 ($C_i$-C), 147.2 ($C_p$-C), 147.6 (C-3), 150.3 (C-3′). MS (70 eV) $m/z$ (%): 453 (100, $M^+$), 423 (10), 406 (9), 77 (22). Anal. Calcd for $C_{25}H_{19}N_5O_4$: C, 66.22; H, 4.22; N, 15.44. Found: C, 66.28; H, 4.12; N, 15.51.

#### 4.2.9. 1-Acetyl-3-(4-nitrophenyl)-5-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-4,5-dihydro-1*H*-pyrazole (8a)

Yellow solid, 94% yield; mp: 260 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 1660 (C=O, C=N), 1596 (C=C, Ar), 1502 and 1340 ($NO_2$). $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.30 (s, 3H, H–$COCH_3$), 3.06 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 17.15 Hz, $J_{4a'-5'}$ = 5.62 Hz), 3.56 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 17.32 Hz, $J_{4b'-5'}$ = 11.96 Hz), 5.24 (t, 1H, H-5′, $J_{5'-4a'}$ = 5.40 Hz, $J_{5'-4b'}$ = 12.00 Hz), 7.32 (t, 2H, $H_p$-A, $J$ = 7.04 Hz), 7.47 (t, 2H, $H_m$-A, $J$ = 7.48 Hz), 7.82 (d, 2H, $H_o$-C, $J$ = 8.89 Hz), 7.87 (d, 2H, $H_o$-A, $J$ = 8.66 Hz), 8.03 (d, 2H, Ho-B, $J$ = 8.74 Hz), 8.17 (d, 2H, $H_m$-B, $J$ = 8.65 Hz), 8.30 (d, 2H, $H_m$-C, $J$ = 8.70 Hz), 8.47 (s, 1H, H-5) ppm. $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.9 (C–$COCH_3$), 41.3 (C-4′), 52.0 (C-5′), 118.2 ($C_o$-A), 122.8 ($C_m$-C), 122.9 ($C_m$-B), 124.0 (C-4), 126.1 ($C_p$-A), 127.0 (C-5), 128.6 ($C_o$-C), 128.8 ($C_o$-B), 128.8 ($C_m$-A), 138.8 ($C_i$-A), 139.1 ($C_i$-B), 139.4 ($C_i$-C), 146.0 ($C_p$-B), 146.3 ($C_p$-C), 148.0 (C-3), 152.3 (C-3′), 165.9 (C=O) ppm. MS (70 eV) $m/z$ (%): 454 (100, $M^+$), 426 (11), 407 (11), 77 (25). Anal. Calcd for $C_{26}H_{20}N_6O_5$: C, 62.90; H, 4.06; N, 16.93. Found: C, 62.93; H, 4.03; N, 16.90.

#### 4.2.10. 1-Acetyl-3-(4-fluorophenyl)-5-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-4,5-dihydro-1*H*-pyrazole (8b)

Yellow solid, 90% yield; mp: 304 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 1659 (C=O, C=N), 1596 (C=C, Ar), 1508 and 1347 ($NO_2$). $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.30 (s, 3H, H–$COCH_3$), 3.23 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 17.78 Hz, $J_{4a'-5'}$ = 5.58 Hz), 3.70 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 17.79 Hz, $J_{4b'-5'}$ = 11.99 Hz), 5.24 (t, 1H, H-5′, $J_{5'-4a'}$ = 5.38 Hz, $J_{5'-4b'}$ = 11.58 Hz), 7.22 (m, 2H, $H_o$-C), 7.33 (t, 2H, $H_p$-A, $J$ = 7.24 Hz), 7.49 (t, 2H, $H_m$-A, $J$ = 7.03 Hz), 7.79 (m, 2H, $H_m$-C), 7.85 (d, 2H, $H_o$-A, $J$ = 8.48 Hz), 8.04 (d, 2H, $H_o$-B, $J$ = 8.69 Hz), 8.26 (d, 2H, $H_m$-B, $J$ = 8.68 Hz), 8.29 (s, 1H, H-5). $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.9 (C–$COCH_3$), 41.6 (C-4′), 51.5 (C-5′), 114.8 ($C_o$-C), 118.2 ($C_o$-A), 122.7 ($C_m$-B), 123.4 (C-4), 126.0 ($C_p$-A), 126.7 (C-5), 128.2 ($C_m$-C), 128.5 ($C_o$-B), 128.7 ($C_m$-A), 138.8 ($C_i$-A), 139.1 ($C_i$-B), 146.7 ($C_p$-B), 147.1 (C-3), 152.3 (C-3′), 161.5 ($C_p$-C), 163.9 ($C_i$-C), 167.1 (C=O). MS (70 eV) $m/z$ (%): 427 (100, $M^+$), 244 (21), 137 (21), 77 (28). Anal. Calcd for $C_{26}H_{20}FN_5O_3$: C, 66.52; H, 4.29; N, 14.92. Found: C, 66.56; H, 4.26; N, 14.88.

#### 4.2.11. 1-Acetyl-3-(4-chlorophenyl)-5-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-4,5-dihydro-1*H*-pyrazole (8c)

White solid, 91% yield; mp: 311 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 1659 (C=O, C=N), 1593 (C=C, Ar), 1508 and 1347 ($NO_2$). $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.94 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 16.15 Hz, $J_{4a'-5'}$ = 5.45 Hz), 2.98 (s, 3H, H–$COCH_3$), 3.50 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 16.80 Hz, $J_{4b'-5'}$ = 10.80 Hz), 5.15 (t, 1H, H-5′, $J_{5'-4a'}$ = 5.49 Hz, $J_{5'-4b'}$ = 11.54 Hz), 7.33 (t, 1H, $H_p$-A, $J$ = 7.48 Hz), 7.52 (d, 2H, $H_o$-C, $J$ = 8.40 Hz), 7.55 (t, 2H, $H_m$-A, $J$ = 7.48 Hz), 7.70 (d, 2H, $H_m$-C, $J$ = 8.45 Hz), 7.97 (d, 2H, $H_o$-A, $J$ = 7.65 Hz), 8.05 (d, 2H, $H_o$-B, $J$ = 8.69 Hz), 8.30 (d, 2H, $H_m$-B, $J$ = 8.60 Hz), 8.60 (s, 1H, H-5). $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.9 (C–$COCH_3$), 39.9 (C-4′), 55.4 (C-5′), 118.2 ($C_o$-A), 123.4 ($C_m$-B), 123.9 (C-4), 124.1 ($C_o$-C), 125.3 ($C_o$-B), 126.8 ($C_p$-A), 127.5 (C-5), 128.6 ($C_m$-C), 129.6 ($C_p$-C), 129.8 ($C_m$-A), 132.8 ($C_i$-C), 139.0 ($C_i$-A), 139.4 ($C_i$-B), 146.8 ($C_p$-B), 147.8 (C-3), 149.3 (C-3′), 166.8 (C=O). MS (70 eV) $m/z$ (%): 485 (100, $M^+$), 340 (22), 77 (41). Anal. Calcd for $C_{26}H_{20}ClN_5O_3$: C, 64.27; H, 4.15; N, 14.41. Found: C, 64.24; H, 4.14; N, 14.44.

#### 4.2.12. 1-Acetyl-3-(4-bromophenyl)-5-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-4,5-dihydro-1*H*-pyrazole (8d)

White solid, 96% yield; mp: 318 °C, FTIR (KBr), $\nu$ ($cm^{-1}$): 1658 (C=O, C=N), 1591 (C=C, Ar), 1500 and 1339 ($NO_2$). $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.98 (s, 3H, H–$COCH_3$), 3.21 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 17.79 Hz, $J_{4a'-5'}$ = 5.52 Hz), 3.88 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 17.99 Hz, $J_{4b'-5'}$ = 11.99 Hz), 5.76 (t, 1H, H-5′, $J_{5'-4a'}$ = 5.39 Hz, $J_{5'-4b'}$ = 13.18 Hz), 7.31 (t, 2H, $H_p$-A, $J$ = 6.83 Hz), 7.47 (t, 2H, $H_m$-A, $J$ = 7.24 Hz), 7.60 (d, 2H, $H_o$-C, $J$ = 8.48 Hz), 7.66 (d, 2H, Hm-C, $J$ = 8.68 Hz), 7.83 (d, 2H, $H_o$-A, $J$ = 8.07 Hz), 8.02 (d, 2H, $H_o$-B, $J$ = 8.89 Hz), 8.24 (d, 2H, $H_m$-B, $J$ = 8.68 Hz), 8.45 (s, 1H, H-5). $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.9 (C–$COCH_3$), 41.4 (C-4′), 51.4 (C-5′), 118.2 ($C_o$-A), 122.7 ($C_m$-B), 122.9 ($C_i$-C), 123.4 (C-4), 126.0 ($C_p$-A), 126.5 (C-5), 128.7 ($C_o$-B), 128.9 ($C_m$-A), 130.0 ($C_p$-C),

130.9 ($C_o$-C), 133.3 ($C_m$-C), 138.8 ($C_i$-A), 139.1 ($C_i$-B), 146.3 ($C_p$-B), 148.6 (C-3), 152.3 (C-3′), 174.7 (C=O). MS (70 eV) *m/z* (%): 487 (100, $M^+$), 228 (24), 182 (30), 77 (53). Anal. Calcd for $C_{26}H_{20}BrN_5O_3$: C, 58.88; H, 3.80; N, 13.20. Found: C, 58.80; H, 3.86; N, 13.24.

#### 4.2.13. 1-Acetyl-5-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-3-phenyl-4,5-dihydro-1*H*-pyrazole (8e)

White solid, 91% yield; mp: 291 °C, FTIR (KBr), *ν* ($cm^{-1}$): 1658 (C=O, C=N), 1594 (C=C, Ar), 1503 and 1339 ($NO_2$). $^1$H NMR (400 MHz, DMSO-$d_6$) *δ* 2.29 (s, 3H, H–$COCH_3$), 3.00 (m, 1H, H-4a′), 3.89 (m, 1H, H-4b′), 5.13 (m, 1H, H-5′), 7.33 (t, 1H, $H_p$-A, *J* = 7.20 Hz), 7.40 (t, 1H, $H_p$-C, *J* = 7.56 Hz), 7.42 (d, 2H, $H_m$-C, *J* = 7.62 Hz), 7.45 (t, 2H, $H_m$-A, *J* = 7.44 Hz), 7.66 (d, 2H, $H_o$-C, *J* = 8.40 Hz), 7.84 (d, 2H, $H_o$-A, *J* = 8.31 Hz), 8.04 (d, 2H, $H_o$-B, *J* = 8.68 Hz), 8.25 (d, 2H, $H_m$-B, *J* = 8.69 Hz), 8.45 (s, 1H, H-5). $^{13}$C NMR (100 MHz, DMSO-$d_6$) *δ* 20.9 (C–$COCH_3$), 41.5 (C-4′), 51.4 (C-5′), 118.2 ($C_o$-A), 119.4 ($C_o$-C), 122.8 ($C_m$-B), 123.3 ($C_m$-C), 123.5 (C-4), 125.9 ($C_p$-C), 126.1 ($C_p$-A), 126.8 (C-5), 128.3 ($C_m$-A), 128.5 ($C_o$-B), 129.3 ($C_i$-C), 138.8 ($C_i$-A), 139.1 ($C_i$-B), 146.6 ($C_p$-B), 148.6 (C-3), 153.2 (C-3′), 166.9 (C=O). MS (70 eV) *m/z* (%): 442 (21, $M^+$), 397 (100), 279 (46), 77 (32). Anal. Calcd for $C_{26}H_{21}N_5O_3$: C, 69.17; H, 4.69; N, 15.51. Found: C, 69.18; H, 4.67; N, 15.41.

#### 4.2.14. 1-Acetyl-3-(4-methylphenyl)-5-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-4,5-dihydro-1*H*-pyrazole (8f)

White solid, 90% yield; mp: 296 °C, FTIR (KBr), *ν* ($cm^{-1}$): 1658 (C=O, C=N), 1594 (C=C, Ar), 1505 and 1340 ($NO_2$). $^1$H NMR (400 MHz, DMSO-$d_6$) *δ* 2.28 (s, 3H, H–$COCH_3$), 2.34 (s, 3H, H–CH3), 3.19 (m, 1H, H-4a′), 3.86 (m, 1H, H-4b′), 5.76 (m, 1H, H-5′), 7.24 (d, 2H, $H_o$-C, *J* = 8.15 Hz), 7.32 (t, 2H, $H_p$-A, *J* = 7.23 Hz), 7.40 (d, 2H, $H_m$-C, *J* = 8.15 Hz), 7.46 (t, 2H, $H_m$-A, *J* = 7.56 Hz), 7.83 (d, 2H, $H_o$-A, *J* = 8.07 Hz), 8.03 (d, 2H, $H_o$-B, *J* = 8.69 Hz), 8.24 (d, 2H, $H_m$-B, *J* = 8.68 Hz), 8.25 (s, 1H, H-5). $^{13}$C NMR (100 MHz, DMSO-$d_6$) *δ* 20.1 (C–$CH_3$), 20.9 (C–$COCH_3$), 41.6 (C-4′), 51.3 (C-5′), 118.2 ($C_o$-A), 122.7 ($C_m$-B), 123.5 (C-4), 125.9 ($C_o$-C), 126.0 ($C_p$-A), 126.7 (C-5), 127.3 ($C_m$-C), 128.1 ($C_i$-C), 128.3 ($C_p$-C), 128.5 ($C_m$-A), 128.7 ($C_o$-B), 138.8 ($C_i$-A), 139.3 ($C_i$-B), 146.7 ($C_p$-B), 147.1 (C-3), 153.2 (C-3′), 167.1 (C=O). MS (70 eV) *m/z* (%): 465 (55, M+), 423 (100), 77 (33). Anal. Calcd for: $C_{27}H_{23}N_5O_3$: C, 69.66; H, 4.98; N, 15.04. Found: C, 69.76; H, 4.94; N, 15.14.

#### 4.2.15. 1-Acetyl-3-(4-methoxyphenyl)-5-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-4,5-dihydro-1*H*-pyrazole (8g)

White solid, 93% yield; mp: 293 °C, FTIR (KBr), *ν* ($cm^{-1}$): 1654 (C=O, C=N), 1598 (C=C, Ar), 1503 and 1338 ($NO_2$). $^1$H NMR (400 MHz, DMSO-$d_6$) *δ* 2.27 (s, 3H, H–$COCH_3$), 3.28 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 17.71 Hz, $J_{4a'-5'}$ = 5.50 Hz), 3.80 (s, 3H, H–$OCH_3$), 3.85 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 18.20 Hz, $J_{4b'-5'}$ = 13.44 Hz), 5.73 (t, 1H, H-5′, $J_{5-4a'}$ = 5.48 Hz, $J_{4b'-5'}$ = 13.02 Hz), 6.97 (d, 2H, $H_m$-C, *J* = 8.68 Hz), 7.31 (t, 2H, $H_p$-A, *J* = 7.86 Hz), 7.47 (t, 2H, $H_m$-A, *J* = 8.69 Hz), 7.66 (d, 2H, $H_o$-C, *J* = 8.89 Hz), 7.83 (d, 2H, $H_o$-A, *J* = 7.65 Hz), 8.03 (d, 2H, $H_o$-B, *J* = 8.98 Hz), 8.24 (d, 2H, $H_m$-B, *J* = 9.72 Hz), 8.25 (s, 1H, H-5). $^{13}$C NMR (100 MHz, DMSO-$d_6$) *δ* 20.9 (C–$COCH_3$), 41.6 (C-4′), 51.2 (C-5′), 54.8 (C–$OCH_3$), 113.8 ($C_m$-C), 118.2 ($C_o$-A), 122.7 ($C_m$-B), 123.5 ($C_i$-C), 123.6 (C-4), 125.9 ($C_p$-A), 126.8 (C-5), 127.5 ($C_o$-C), 128.5 ($C_o$-B), 128.7 ($C_m$-A), 138.8 ($C_i$-A), 139.1 ($C_i$-B), 146.7 ($C_p$-B), 147.1 (C-3), 152.6 (C-3′), 160.6 ($C_p$-C), 166.9 (C=O). MS (70 eV) *m/z* (%): 481 (53, $M^+$), 439 (100), 133 (15), 77 (17). Anal. Calcd for $C_{27}H_{23}N_5O_4$: C, 67.35; H, 4.81; N, 14.54. Found: C, 67.30; H, 4.88; N, 14.56.

#### 4.2.16. 1-Acetyl-3-(3,4-methylenedioxyphenyl)-5-[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-4,5-dihydro-1*H*-pyrazole (8h)

White solid, 90% yield; mp: 285 °C, FTIR (KBr), *ν* ($cm^{-1}$): 1655 (C=O, C=N), 1597 (C=C, Ar), 1508 and 1349 ($NO_2$). $^1$H NMR (400 MHz, DMSO-$d_6$) *δ* 2.26 (s, 3H, H–$COCH_3$), 3.15 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 17.78 Hz, $J_{4a'-5'}$ = 5.38 Hz), 3.83 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 16.96 Hz, $J_{4b'-5'}$ = 11.79 Hz), 5.73 (t, 1H, H-5′, $J_{5'-4a'}$ = 5.48 Hz, $J_{5'-4b'}$ = 11.68 Hz), 6.02 (s, 2H, H–$CH_2$), 6.90 (d, 1H, $H_o$-C, *J* = 8.06 Hz), 7.19 (s, 1H, $H_{o'}$-C), 7.27 (d, 1H, $H_m$-C, *J* = 8.06 Hz), 7.31 (t, 2H, $H_p$-A, *J* = 7.03 Hz), 7.47 (t, 2H, $H_m$-A, *J* = 7.24 Hz), 7.83 (d, 2H, $H_o$-A, *J* = 8.07 Hz), 8.04 (d, 2H, $H_o$-B, *J* = 8.40 Hz), 8.24 (d, 2H, Hm-B, *J* = 8.48 Hz), 8.25 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) *δ* 21.9 (C–$COCH_3$), 41.7 (C-4′), 51.4 (C-5′), 100.8 (C–$CH_2$), 107.6 ($C_m$-C), 118.2 ($C_o$-A), 121.0 ($C_o$-C), 122.7 ($C_m$-B), 123.5 (C-4), 125.1 ($C_{m'}$-C), 126.0 ($C_p$-A), 126.7 (C-5), 128.5 ($C_o$-B), 128.7 ($C_m$-A), 138.8 ($C_i$-A), 139.1 ($C_i$-B), 146.7 ($C_p$-B), 147.1 ($C_i$-C), 147.2 ($C_p$-C), 148.5 (C-3), 152.9 (C-3′), 166.5 (C=O) ppm. MS (70 eV) *m/z* (%): 496 (78, $M^+$), 453 (100), 77 (18). Anal. Calcd for $C_{27}H_{21}N_5O_5$: C, 65.45; H, 4.27; N, 14.13. Found: C, 65.55; H, 4.29; N, 14.12.

#### 4.2.17. 1-Acetyl-5-[3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-3-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole (9a)

White solid, 93% yield; mp: 239 °C, FTIR (KBr), *ν* ($cm^{-1}$): 1676 (C=O, C=N), 1597 (C=C, Ar), 1506 and 1343 ($NO_2$). $^1$H NMR (400 MHz, DMSOd$_6$) *δ* 2.35 (s, 3H, H–$COCH_3$), 3.28 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 18.89 Hz, $J_{4a'-5'}$ = 5.38 Hz), 3.95 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 17.99 Hz, $J_{4b'-5'}$ = 11.99 Hz), 5.74 (t, 1H, H-5′, $J_{5-4a'}$ = 5.27 Hz, $J_{4b'-5'}$ = 11.89 Hz), 7.30 (t, 2H, $H_p$-A, *J* = 7.44 Hz), 7.47 (t, 2H, $H_m$-A, *J* = 8.07 Hz), 7.53 (d, 2H, $H_o$-B, *J* = 8.27 Hz), 7.82 (d, 2H, $H_m$-B, *J* = 8.47 Hz), 7.88 (d, 2H, $H_o$-A, *J* = 8.09 Hz), 7.97 (d, 2H, $H_o$-C, *J* = 8.89 Hz), 8.30 (d, 2H, $H_m$-C, *J* = 8.90 Hz), 8.46 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) *δ* 21.9 (C–$COCH_3$), 41.9 (C-4′), 52.3 (C-5′), 118.2 ($C_o$-A), 123.2 (C-4), 123.8 ($C_m$-C), 126.4 ($C_p$-A), 126.9 (C-5), 127.6 ($C_o$-C), 128.6 ($C_o$-B), 129.4 ($C_m$-A), 129.8 ($C_m$-B), 131.7 ($C_p$-B), 132.8 ($C_i$-B), 139.2 ($C_i$-A), 147.9 ($C_p$-C), 148.3 (C-3), 152.3 ($C_i$-C), 152.5 (C-3′), 168.0 (C=O) ppm. MS (70 eV) *m/z* (%): 485 (61, $M^+$), 442 (100), 294 (81), 279 (65), 77 (42). Anal. Calcd for $C_{26}H_{20}ClN_5O_3$: C, 64.27; H, 4.15; N, 14.41. Found: C, 64.20; H, 4.22; N, 14.50

#### 4.2.18. 1-Acetyl-5-[3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-3-(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazole (9b)

White solid, 90% yield; mp: 234 °C, FTIR (KBr), *ν* ($cm^{-1}$): 1652 (C=O, C=N), 1600 (C=C, Ar). $^1$H NMR (400 MHz, DMSO-$d_6$) *δ* 2.31 (s, 3H, H–$COCH_3$), 3.23 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 17.89 Hz, $J_{4a'-5'}$ = 5.38 Hz), 3.89 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 17.79 Hz, $J_{4b'-5'}$ = 12.00 Hz), 5.69 (t, 1H, H-5′, $J_{5-4a'}$ = 5.17 Hz, $J_{4b'-5'}$ = 11.89 Hz), 7.28 (t, 2H, $H_p$-A, *J* = 7.44 Hz), 7.46 (t, 2H, $H_m$-A, *J* = 8.48 Hz), 7.53 (d, 2H, $H_o$-B, *J* = 8.68 Hz), 7.83 (m, 2H, $H_o$-C), 7.85 (d, 2H, $H_m$-B, *J* = 8.67 Hz), 7.89 (d, 2H, $H_o$-A, *J* = 8.68 Hz), 8.30 (m, 2H, $H_m$-C), 8.41 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) *δ* 21.8 (C–$COCH_3$), 42.2 (C-4′), 51.6 (C-5′), 115.7 ($C_m$-C), 118.2 ($C_o$-A), 123.5 (C-4), 126.3 ($C_p$-A), 126.8 (C-5), 128.6 ($C_o$-B), 128.9 ($C_o$-C), 129.4 ($C_m$-A), 129.7 ($C_m$-B), 131.7 ($C_p$-B), 132.7 ($C_i$-B), 139.2 ($C_i$-A), 148.2 (C-3), 153.0 (C-3′), 161.9 ($C_i$-C), 164.4 ($C_p$-C), 167.6 (C=O) ppm. MS (70 eV) *m/z* (%): 458 (57, $M^+$), 415 (100), 279 (42), 77 (33). Anal. Calcd for $C_{26}H_{20}ClFN_4O$: C, 68.05; H, 4.39; N, 12.21. Found: C, 68.15; H, 4.38; N, 12.31.

#### 4.2.19. 1-Acetyl-3-(chlorophenyl)-5-[3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-4,5-dihydro-1*H*-pyrazole (9c)

White solid, 93% yield; mp: 261 °C, FTIR (KBr), *ν* ($cm^{-1}$): 1648 (C=O, C=N), 1601 (C=C, Ar). $^1$H NMR (400 MHz, DMSO-$d_6$) *δ* 2.27 (s, 3H, H–$COCH_3$), 3.16 (dd, 1H, H-4a′, $J_{4a'-4b'}$ = 17.78 Hz, $J_{4a'-5'}$ = 5.58 Hz), 3.82 (dd, 1H, H-4b′, $J_{4b'-4a'}$ = 17.78 Hz, $J_{4b'-5'}$ = 11.78 Hz), 5.69 (t, 1H, H-5′, $J_{5-4a'}$ = 5.58 Hz, $J_{4b'-5'}$ = 11.78 Hz), 7.27 (t, 2H, $H_p$-A, *J* = 7.44 Hz), 7.44 (m, 2H, $H_m$-A), 7.48 (d, 2H, $H_o$-B, *J* = 9.10 Hz), 7.81 (d, 2H, $H_o$-A, *J* = 8.69 Hz), 7.72 (d, 2H, $H_m$-C, *J* = 9.10 Hz), 7.74 (d, 2H, $H_m$-B, *J* = 8.89 Hz), 8.20 (s, 1H, H-5) ppm.

$^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.9 (C–$COCH_3$), 41.4 (C-4′), 51.6 (C-5′), 118.0 ($C_o$-A), 122.6 (C-4), 126.1 ($C_p$-A), 126.6 (C-5), 127.7 ($C_o$-C), 128.0 ($C_m$-C), 128.6 ($C_o$-B), 129.2 ($C_m$-B), 129.3 ($C_p$-C), 129.6 ($C_m$-A), 129.8 ($C_i$-C), 131.4 ($C_p$-B), 132.3 ($C_i$-B), 138.9 ($C_i$-A), 148.1 (C-3), 152.1 (C-3′), 167.1 (C=O) ppm. MS (70 eV) *m*/*z* (%): 474 (63, $M^+$), 431 (100), 279 (62), 77 (95). Anal. Calcd for $C_{26}H_{20}Cl_2N_4O$: C, 65.69; H, 4.24; N, 11.79. Found: C, 65.71; H, 4.28; N, 11.84.

#### 4.2.20. 1-Acetyl-3-(4-bromophenyl)-5-[3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-4,5-dihydro-1*H*-pyrazole (9d)

White solid, 96% yield; mp: 259 °C, FTIR (KBr), *v* ($cm^{-1}$): 1646 (C=O, C=N), 1595 (C=C, Ar). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.27 (s, 3H, H–$COCH_3$), 3.16 (m, 1H, H-4a′), 3.82 (m, 1H, H-4b′), 5.69 (m, 1H, H-5′), 7.28 (t, 2H, $H_p$-A, *J* = 6.85 Hz), 7.44 (d, 2H, $H_o$-B, *J* = 8.48 Hz), 7.49 (t, 2H, $H_m$-A, *J* = 8.48 Hz), 7.60 (d, 2H, $H_o$-C, *J* = 10.54 Hz), 7.64 (d, 2H, $H_m$-C, *J* = 8.70 Hz), 7.73 (d, 2H, $H_m$-B, *J* = 8.70 Hz), 7.79 (d, 2H, $H_o$-A, *J* = 8.07 Hz), 8.19 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.9 (C–$COCH_3$), 41.3 (C-4′), 51.9 (C-5′), 118.0 ($C_o$-A), 122.3 ($C_i$-C), 122.7 (C-4), 125.6 ($C_p$-A), 126.1 (C-5), 127.2 ($C_m$-A), 127.7 ($C_m$-C), 128.9 ($C_o$-B), 129.2 ($C_m$-B), 129.4 ($C_p$-C), 130.9 ($C_o$-C), 131.4 ($C_p$-B), 132.3 ($C_i$-B), 138.9 ($C_i$-A), 148.1 (C-3), 152.2 (C-3′), 167.1 (C=O) ppm. MS (70 eV) *m*/*z* (%): 520 (64, $M^+$), 477 (100), 279 (64), 77 (37). Anal. Calcd for $C_{26}H_{20}BrClN_4O$: C, 60.07; H, 3.88; N, 10.78. Found: C, 60.14; H, 3.92; N, 10.70.

#### 4.2.21. 1-Acetyl-5-[3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-3-phenyl-4,5-dihydro-1*H*-pyrazole (9e)

White solid, 90% yield; mp: 249 °C, FTIR (KBr), *v* ($cm^{-1}$): 1651 (C=O, C=N), 1597 (C=C, Ar). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.27 (s, 3H, H–$COCH_3$), 3.17 (m, 1H, H-4a′), 3.83 (m, 1H, H-4b′), 5.69 (m, 1H, H-5′), 7.27 (m, 2H, $H_p$-A), 7.44 (m, 2H, $H_m$-A), 7.44 (m, 1H, $H_p$-C), 7.44 (m, 2H, $H_o$-B), 7.64 (m, 2H, $H_m$-C), 7.73 (m, 2H, $H_o$-C), 7.73 (m, 2H, $H_m$-B), 7.80 (d, 2H, $H_o$-A, *J* = 8.15 Hz), 8.19 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.9 (C–$COCH_3$), 41.5 (C-4′), 51.4 (C-5′), 118.0 ($C_o$-A), 122.8 ($C_m$-B), 122.9 (C-4), 125.6 ($C_o$-C), 125.8 ($C_o$-B), 126.1 ($C_p$-A), 127.7 (C-5), 128.6 ($C_p$-C), 129.2 ($C_m$-C), 129.3 ($C_m$-A), 130.9 ($C_i$-C), 131.5 ($C_p$-B), 132.3 ($C_i$-B), 138.9 ($C_i$-A), 148.1 (C-3), 153.1 (C-3′), 167.1 (C=O) ppm. MS (70 eV) *m*/*z* (%): 440 (59, $M^+$), 397 (100), 279 (64), 104 (39), 77 (52). Anal. Calcd for $C_{26}H_{21}ClN_4O$: C, 70.82; H, 4.80; N, 12.71. Found: C, 70.80; H, 4.70; N, 12.64.

#### 4.2.22. 1-Acetyl-5-[3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-3-(4-methylphenyl)-4,5-dihydro-1*H*-pyrazole (9f)

White solid, 93% yield; mp: 231 °C, FTIR (KBr), *v* ($cm^{-1}$): 1661 (C=O, C=N), 1597 (C=C, Ar). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ (s, 3H, H–$COCH_3$), 2.30 (s, 3H, H–$CH_3$), 3.22 (m, 1H, H-4a′), 3.80 (m, 1H, H-4b′), 5.82 (m, 1H, H-5′), 7.28 (d, 2H, $H_o$-C, *J* = 8.22 Hz), 7.33 (t, 2H, $H_p$-A, *J* = 7.33 Hz), 7.45 (d, 2H, $H_m$-C, *J* = 8.21 Hz), 7.46 (t, 2H, $H_m$-A, *J* = 7.56 Hz), 7.56 (d, 2H, $H_o$-B, *J* = 7.69 Hz), 7.68 (d, 2H, $H_m$-B, *J* = 7.67 Hz), 7.85 (d, 2H, $H_o$-A, *J* = 8.17 Hz), 8.42 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.9 (C–CH3), 21.2 (C–$COCH_3$), 41.6 (C-4′), 52.3 (C-5′), 118.4 ($C_o$-A), 122.8 ($C_m$-B), 124.0 (C-4), 125.5 ($C_o$-C), 126.0 ($C_p$-A), 126.8 (C-5), 127.9 ($C_m$-C), 128.0 ($C_i$-C), 129.0 ($C_p$-C), 129.5 ($C_m$-A), 129.6 ($C_o$-B), 139.1 ($C_i$-A), 139.3 ($C_i$-B), 147.2 (C-3), 147.6 ($C_p$-B), 153.3 (C-3′), 168.1 (C=O) ppm. MS (70 eV) *m*/*z* (%): 454 (100, $M^+$), 364 (62), 77 (53). Anal. Calcd for $C_{27}H_{23}ClN_4O$: C, 71.28; H, 5.10; N, 12.31. Found: C, 71.25; H, 5.15; N, 12.38.

#### 4.2.23. 1-Acetyl-5-[3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-3-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole (9g)

White solid, 92% yield; mp: 219 °C, FTIR (KBr), *v* ($cm^{-1}$): 1661 (C=O, C=N), 1596 (C=C, Ar). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.26 (s, 3H, H–$COCH_3$), 3.13 (m, 1H, H-4a′), 3.80 (m, 1H, H-4b′), 3.92 (s, 3H, H–$OCH_3$), 5.66 (m, 1H, H-5′), 6.98 (d, 2H, $H_m$-C, *J* = 10.96 Hz), 7.23 (t, 2H, $H_p$-A, *J* = 7.23 Hz), 7.43 (d, 2H, $H_o$-C, *J* = 10.96 Hz), 7.50 (d, 2H, $H_o$-B, *J* = 10.70 Hz), 7.64 (m, 2H, $H_m$-A), 7.76 (d, 2H, $H_m$-B, *J* = 10.75 Hz), 7.82 (d, 2H, $H_o$-A, *J* = 6.89 Hz), 8.17 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.9 (C–$COCH_3$), 41.6 (C-4′), 51.3 (C-5′), 55.0 (C–$OCH_3$), 113.7 ($C_m$-C), 118.0 ($C_o$-A), 122.9 ($C_p$-C), 123.6 (C-4), 125.6 ($C_p$-A), 126.0 (C-5), 127.5 ($C_o$-C), 128.6 ($C_o$-B), 129.2 ($C_m$-B), 130.2 ($C_m$-A), 131.5 ($C_p$-B), 132.3 ($C_i$-B), 138.9 ($C_i$-A), 148.1 (C-3), 152.9 (C-3′), 160.6 ($C_i$-C), 166.8 (C=O) ppm. MS (70 eV) *m*/*z* (%): 470 (100, $M^+$), 364 (52), 279 (60), 77 (80). Anal. Calcd for $C_{27}H_{23}ClN_4O_2$: C, 68.86; H, 4.92; N, 11.90. Found: C, 68.80; H, 4.96; N, 11.90.

#### 4.2.24. 1-Acetyl-3-(3,4-methylenedioxyphenyl)-5-[3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]-4,5-dihydro-1*H*-pyrazole (9h)

White solid, 89% yield; mp: 225 °C, FTIR (KBr), *v* ($cm^{-1}$): 1649 (C=O, C=N), 1599 (C=C, Ar). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 2.29 (s, 3H, H–$COCH_3$), 3.17 (m, 1H, H-$4_{a'}$), 3.83 (m, 1H, H-$4_{b'}$), 5.65 (m, 1H, H-5′), 6.09 (s, 2H, H–$CH_2$), 6.68 (d, 2H, $H_o$-C, *J* = 7.85 Hz), 7.21 (d, 2H, $H_m$-C, *J* = 7.44 Hz), 7.30 (t, 2H, $H_p$-A, *J* = 7.03 Hz), 7.45 (s, 1H, $H_{o'}$-C), 7.47 (t, 2H, $H_m$-A, *J* = 7.24 Hz), 7.53 (d, 2H, $H_o$-B, *J* = 7.86 Hz), 7.82 (d, 2H, $H_m$-B, *J* = 7.86 Hz), 7.88 (d, 2H, $H_o$-A, *J* = 7.65 Hz), 8.37 (s, 1H, H-5) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 20.9 (C–$COCH_3$), 41.3 (C-4′), 51.9 (C-5′), 101.5 (C–$CH_2$), 108.3 ($C_o$-C), 118.2 ($C_o$-A), 121.8 ($C_m$-C), 123.6 (C-4), 126.3 ($C_p$-A), 126.7 (C-5), 128.6 ($C_o$-B), 129.4 ($C_m$-A), 129.7 ($C_m$-B), 131.7 ($C_p$-B), 132.7 ($C_i$-B), 139.2 ($C_i$-A), 145.3 ($C_{m'}$-C), 147.7 ($C_i$-C), 148.2 (C-3), 149.0 ($C_p$-C), 153.6 (C-3′), 167.5 (C=O) ppm. MS (70 eV) *m*/*z* (%): 484 (86, $M^+$), 442 (100), 294 (25), 77 (20). Anal. Calcd for $C_{27}H_{21}ClN_4O_3$: C, 66.87; H, 4.36; N, 11.55. Found: C, 66.80; H, 4.36; N, 11.58.

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