

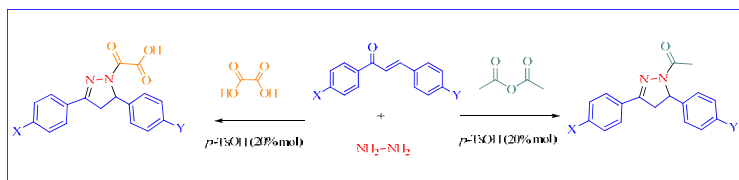
SYNTHESIS OF SOME NEW *N*-ACETYLATED PYRAZOLINE DERIVATIVES VIA THE EFFICIENT ONE-POT REACTION BY USING *p*-TOLUENESULFONIC ACID**

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A series of a new class of *N*-acetylated pyrazoline derivatives were synthesized by treatment of chalcones with hydrazine hydrate and acetic anhydride or oxalic acid in the presence of the catalytic amount of *p*-toluenesulfonic acid in ethanol. All synthesized products were characterized by FT-IR, ¹H, and ¹³C NMR spectral data and elemental analyses. Some advantages of this protocol are a simple work-up procedure, time-consuming reaction and good to high yields.



INTRODUCTION

Heterocyclic compounds, especially *N*-substituted 4, 5-dihydro-1*H*-pyrazoles, have found much interest because of their pharmacological activities and medicinal properties.¹⁻⁷ Among the existing several *N*-substituted 4, 5-dihydro-1*H*-pyrazole derivatives, and *N*-acetyl pyrazole have received considerable interests from the fields of medicinal and agricultural chemistry because of their broad range of biological activities.⁸⁻¹⁷ Also, they have a meaningful role as a precursor for the formation of other pyrazoline based heterocycles, such as nicotinonitrile,¹⁸ indoxacarb,¹⁹ carbonylhydrazide²⁰ and pyrimidine.²¹ *N*-Acetylated pyrazoline derivatives were found to display various pharmaceutical properties. For example, compound **A** has been reported for treating Alzheimer's disease,²² compound **B** show anticancer activity,²³ compound **C** displayed insecticidal activity²⁴ and compound **D** turned out to be fungicidal and insecticidal agent²⁵ (Fig. 1).

N-Acetylated pyrazolines have been previously achieved from the reaction of corresponding chalcones with hydrazine hydrate and glacial acetic acid in the presence of a variety of acidic catalysts such as fly-ash-H₂SO₄,²⁶ fly-ash-PTS,²⁷ SiO₂-H₂SO₄²⁸ and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD).²⁹ However, many of these mentioned methods suffer from disadvantages such as harsh reaction conditions, unsatisfactory yields, prolonged reaction times, cumbersome work-up procedures, and high cost. Therefore, the development of new methods for the synthesis of these products is a great goal for organic chemists and pharmacists. Although there are many reports for the preparation of *N*-acetylated 4, 5-dihydro-1*H*-pyrazole derivatives the literature survey reveals that there is no information available for the preparation of *N*-(oxo)acetic acid 4, 5-dihydro-1*H*-pyrazole derivatives.

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** Supplementary information on <http://web.icf.ro/rrech/> or <http://revroum.lew.ro>

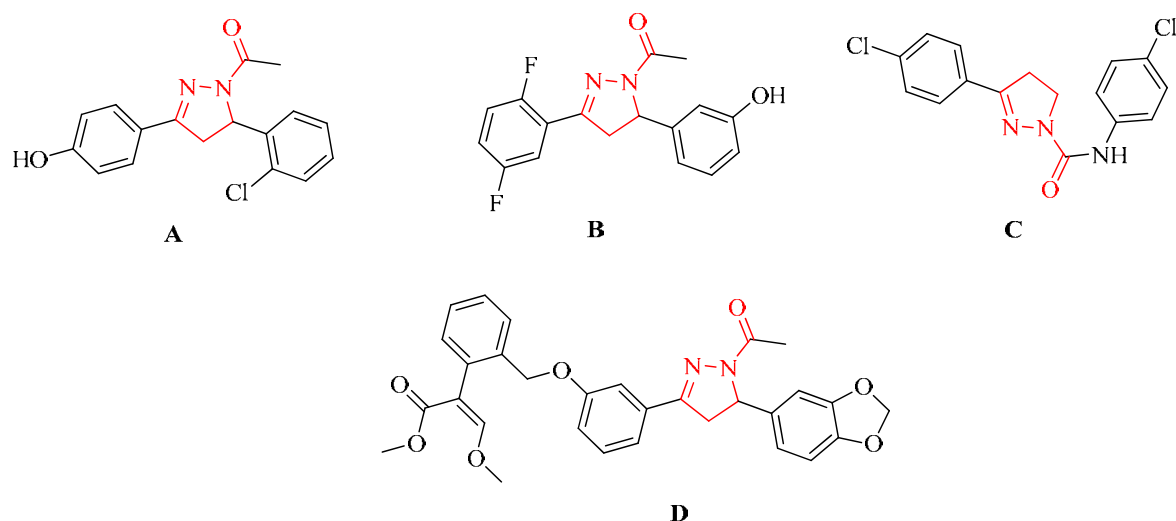
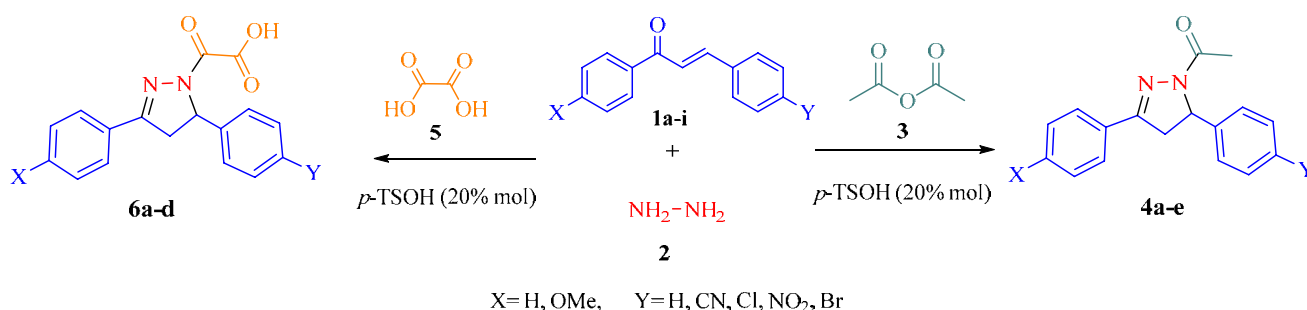


Fig. 1 – Some biological active compounds containing pyrazoline moiety.



Scheme 1 – Preparation of N-acetylated pyrazoline derivatives.

As a strong organic acid catalyst, *p*-Toluene-sulfonic acid (*p*-TsOH) catalyzes many organic reactions and serves as a proton source.³⁰⁻³⁴ In addition, *p*-TsOH is one of the few strong acids that are solid and safe; hence, it is conveniently weighed and handled. In the present study, the authors took efforts to synthesize *N*-acetylated pyrazoline derivatives (**4a-e** and **6a-d**) by cyclization of chalcones **1** with hydrazine hydrate **2** and acetic anhydride **3** or oxalic acid **5** in the presence of the catalytic amount of *p*-TsOH (Scheme 1). All the products were characterized by comparing their spectra and physical data with those reported in the literature.

RESULTS AND DISCUSSION

First, to find optimum conditions, the reaction of chalcone **1e**, hydrazine hydrate, and acetic anhydride in the presence of the *p*-TsOH as a catalyst was selected as a model reaction. The reaction was investigated by different amounts of

p-TsOH as catalysts (10, 15, 20, and 25 mol %) at different temperatures (25, 50, and 78 °C). The obtained results (Table 1) showed that optimal conditions were 20 mol % of *p*-TsOH at 78 °C (Table 1, entry 11). Also, increasing the amount of catalyst did not improve the results.

Next, various chalcones were used in the reactions that led to the related products **4a-e** in high yields (Table 2, entries 1 to 5). In order to study the scope and limitation of this reaction, various chalcone derivatives were reacted with hydrazine hydrate and oxalic acid in the presence of the *p*-TsOH (20 mol%) as the catalyst to obtain new compounds **6a-d**. To our knowledge, there is no information available for the synthesis of *N*-acetylated pyrazoline derivatives **6a-d** (Table 2, entries 6 to 9). As shown in Table 2, reactions with substituted chalcones, including electron-donating or electron-withdrawing substituents, generated the desired products in good to high yields.

The structures of all the prepared compounds were confirmed using FT-IR, ¹H, ¹³C NMR, and elemental analyses.

Table 1

Optimization conditions for preparation of 1-acetyl-5-(4-bromophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazole from chalcone (1 mmol), hydrazine hydrate (2 mmol), and acetic anhydride (1 mmol) in the presence of different amounts of *p*-TsOH as a catalyst in different temperatures and ethanol as a solvent

Entry	Amount of catalyst (mol%)	Temperature (°C)	Time (min)	Yield (%) ^a
1	10	25	150	-
2	15	25	120	Trace
3	20	25	120	25
4	25	25	120	42
5	10	50	120	33
6	15	50	90	45
7	20	50	75	63
8	25	50	65	74
9	10	Reflux in EtOH	75	52
10	15	Reflux in EtOH	65	67
11	20	Reflux in EtOH	60	91
12	25	Reflux in EtOH	60	91
13	20	Reflux in Toluene	60	83
14	25	Reflux in Toluene	60	86

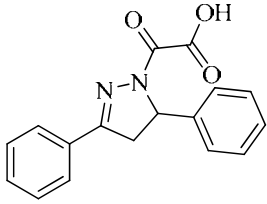
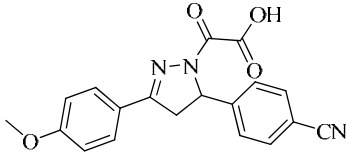
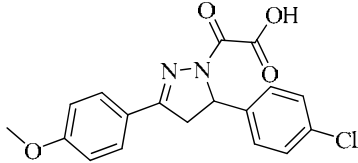
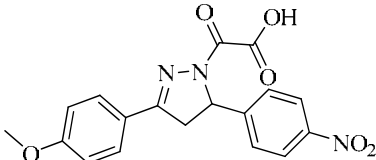
^a Yields refer to the isolated pure product

Table 2

Synthesis of N-acetylated pyrazoline derivatives using chalcone (1 mmol), hydrazine hydrate (2 mmol), and acetic anhydride (1 mmol) or oxalic acid (1 mmol) in the presence amounts of *p*-TsOH (20 mol %) as a catalyst in EtOH at different temperatures

Entry	Compound	Structure	Yield (%) ^a	Time	Mp (°C) _{Ref}
1	4a		85	70	122-123 ²⁹
2	4b		82	85	134-135 ²⁹
3	4c		87	60	116-118
4	4d		94	60	164-166 ²⁶
5	4e		91	60	177-179

Table 2 (continued)

6	6a		77	90	147-149
7	6b		84	90	161-163
8	6c		79	75	155-158
9	6d		85	60	173-175

^a Yields refer to the isolated pure product.

The FT-IR spectrum of **6b** displays three sharp absorption bands at 2230, 1665 and 1641 cm^{-1} for the nitrile, carbonyl, and C=N groups, respectively. The ^1H NMR spectrum of **6b** in CDCl_3 at 25 °C exhibits one sharp singlet at about 3.84 ppm for the methoxy groups. The diastereotopic protons of the CH_2 groups appear as a two doublet of doublet signals at about 3.61 ($^2J_{\text{HH}} = 17.6$ Hz and $^3J_{\text{HH}} = 8.8$ Hz) and 3.90 ppm ($^2J_{\text{HH}} = 17.2$ Hz and $^3J_{\text{HH}} = 9.6$ Hz) in ^1H NMR spectrum due to the presence of chiral centers in compound **6b**. The proton of the CH group appears as one doublet of doublet signal at about 5.28 ppm (i.e., $^3J_{\text{HH}} = 9.6$ Hz and $^3J_{\text{HH}} = 8.8$ Hz). The proton of the OH group appears as a single signal at about 5.99 ppm. Also, four doublet signals appeared at about 7.09, 7.72, 7.83, and 7.93 ppm that are assigned to aromatic protons. The ^{13}C NMR spectrum of **6b** exhibited a signal at about 41.2 ppm for the CH_2 group, a signal at about 55.9 ppm for the OCH_3

group, a signal at about 60.9 ppm for the CH group, two signal at about 159.7 and 162.6 ppm for the carbonyl group. Other signals are at about 110.1, 111.9, 119.4, 123.1, 126.0, 158.7, 118.9, 130.3, 133.1 and 155.6 ppm for the other carbons.

EXPERIMENTAL

1. Materials and methods

All the chemicals and solvents for synthesis were purchased from Sigma Aldrich. The uncorrected melting points were measured by an Electrothermal 9100 apparatus (UK). The FT-IR spectra were recorded on an FT-IR Bruker Vector 22 spectrometer. The ^1H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz Ultrashield Advance DRX spectrometer in $\text{DMSO}-d_6$ and CDCl_3 at 400.1 and 100.6 MHz, respectively. Elemental analyses were performed using a Heraeus CHN-O rapid analyzer. The spectral data for the newly synthesized compounds are presented in the supplementary data.

2. General procedure for the synthesis of N-acetyl (3, 5-diaryl-4, 5-dihydro-1H-pyrazole-1-yl) derivatives 4a-e

To a magnetically stirred solution of chalcone (2 mmol) and acetic anhydride (2 mmol, 0.204 g) and *p*-TsOH (20 mol%, 0.688g) in EtOH (10 mL), (4 mmol, 0.128 g) of hydrazine hydrate (0.2 mL) in 5 mL, EtOH was added dropwise. The mixture was allowed to stand at the reflux temperature for a relevant time. After completion of the reaction, as indicated by TLC (*n*-hexane/EtOAc, 3:1), was allowed reaction mixture to cool to room temperature and then poured onto crushed ice to obtain the crude product. The reaction product was recrystallized from ethanol.

Spectral data for the synthesis of N-acetyl (3, 5-diaryl-4, 5-dihydro-1H-pyrazole-1-yl) derivatives 4a-e

1-acetyl-3,5-diphenyl-4,5-dihydro-1H-pyrazole (4a)

White powder, m.p. 122-123 °C, Yield: 85%; IR (KBr) (ν_{\max} , cm^{-1}): 3058 ($\text{C}_{\text{sp}}^2\text{-H}$), 2926 ($\text{C}_{\text{sp}}^3\text{-H}$), 1645 (C=O), 1612 (C=N), 1494 (C=C); Anal. Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}$ (264.32): C, 77.25; H, 6.10, N, 10.60 Found: C, 77.23; H, 6.08, N, 10.57; $^1\text{H NMR}$ (400.1 MHz, CDCl_3): δ_{H} 2.45 (CH_3), 3.19 (1H, dd, $^2J_{\text{HH}} = 17.6$, $^3J_{\text{HH}} = 4.8$ Hz, CH_2), 3.78 (1H, dd, $^2J_{\text{HH}} = 17.6$, $^3J_{\text{HH}} = 12.0$ Hz, CH_2), 5.62 (1H, dd, $^3J_{\text{HH}} = 12.0$, $^3J_{\text{HH}} = 4.8$ Hz, CH), 7.25-7.28 (3H, m, CH_{Ar}), 7.28-7.36 (2H, m, CH_{Ar}), 7.44-7.46 (3H, m, CH_{Ar}), 7.76-7.78 (2H, m, CH_{Ar}); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): δ_{C} 22.0 (CH_3), 42.3 (CH_2), 59.9 (CH), 125.5, 126.5, 127.6, 128.7, 128.9 and 130.3 (6 CH_{Ar}), 131.4 and 141.8 (2Cq), 153.8 (C=N), 168.8 (C=O, ketone).

1-acetyl-3-(4-methoxyphenyl)-5-phenyl-4, 5-dihydro-1H-pyrazole (4b)

White powder, m.p. 134-135 °C, Yield: 82%; IR (KBr) (ν_{\max} , cm^{-1}): 3059 ($\text{C}_{\text{sp}}^2\text{-H}$), 2932 ($\text{C}_{\text{sp}}^3\text{-H}$), 1652 (C=O), 1613 (C=N), 1512 (C=C); Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_2$ (294.34): C, 73.45; H, 6.16, N, 9.52 Found: C, 73.47; H, 6.19, N, 9.49; $^1\text{H NMR}$ (400.1 MHz, CDCl_3): δ_{H} 2.43 (CH_3), 3.18 (1H, dd, $^2J_{\text{HH}} = 17.6$, $^3J_{\text{HH}} = 4.8$ Hz, CH_2), 3.74 (1H, dd, $^2J_{\text{HH}} = 17.6$, $^3J_{\text{HH}} = 12.0$ Hz, CH_2), 3.78 (OCH₃), 5.57 (1H, dd, $^3J_{\text{HH}} = 12.0$, $^3J_{\text{HH}} = 4.8$ Hz, CH), 6.84 (2H, d, $^3J_{\text{HH}} = 8.4$ Hz, CH_{Ar}), 7.19 (2H, d, $^3J_{\text{HH}} = 8.4$ Hz, CH_{Ar}), 7.44-7.46 (3H, m, CH_{Ar}), 7.76-7.78 (2H, m, CH_{Ar}); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): δ_{C} 22.0 (CH_3), 42.2 (CH_2), 55.2 (OCH₃), 59.4 (CH), 126.5, 126.9, 128.7 and 130.3 (4 CH_{Ar}), 131.4 and 134.1 (2Cq), 153.8 (C=N), 159.0 (C-O), 168.8 (C=O, ketone).

4-(1-acetyl-3-phenyl-4, 5-dihydro-1H-pyrazol-5-yl) benzonitrile (4c)

Cream powder, m.p. 116-118 °C, Yield: 87%; IR (KBr) (ν_{\max} , cm^{-1}): 3064 ($\text{C}_{\text{sp}}^2\text{-H}$), 2934 ($\text{C}_{\text{sp}}^3\text{-H}$), 2231 (CN), 1642 (C=O), 1609 (C=N), 1506 (C=C); Anal. Calcd for $\text{C}_{18}\text{H}_{15}\text{N}_3\text{O}$ (289.33): C, 74.72; H, 5.23, N, 14.52 Found: C, 74.75; H, 5.24, N, 14.54; $^1\text{H NMR}$ (400.1 MHz, CDCl_3): δ_{H} 2.45 (CH_3), 3.15 (1H, dd, $^2J_{\text{HH}} = 17.6$, $^3J_{\text{HH}} = 4.8$ Hz, CH_2), 3.83 (1H, dd, $^2J_{\text{HH}} = 17.6$, $^3J_{\text{HH}} = 12.0$ Hz, CH_2), 6.30 (1H, dd, $^3J_{\text{HH}} = 12.0$, $^3J_{\text{HH}} = 4.8$ Hz, CH), 7.37 (2H, d, $^3J_{\text{HH}} = 8.0$ Hz, CH_{Ar}), 7.45-7.47 (3H, m, CH_{Ar}), 7.64 (2H, d, $^3J_{\text{HH}} = 8.0$ Hz, CH_{Ar}), 7.74-7.76 (2H, m, CH_{Ar}); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): δ_{C} 21.9 (CH_3), 42.0 (CH_2), 59.6 (CH), 111.6 (Cq), 118.6 (CN), 126.5, 126.6, 128.8, 130.6 and 132.8 (6 CH_{Ar}), 146.9 (Cq), 153.7 (C=N), 169.0 (C=O, ketone).

1-acetyl-5-(4-nitrophenyl)-3-phenyl-4, 5-dihydro-1H-pyrazole (4d)

Yellow powder, m.p. 164-166 °C, Yield: 94%; IR (KBr) (ν_{\max} , cm^{-1}): 3042 ($\text{C}_{\text{sp}}^2\text{-H}$), 2940 ($\text{C}_{\text{sp}}^3\text{-H}$), 1648 (C=O),

1599 (C=N), 1441 (C=C), 1517 and 1338 (NO_2); Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3\text{O}_3$ (309.31): C, 66.01; H, 4.89, N, 13.58 Found: C, 65.99; H, 4.91, N, 13.57; $^1\text{H NMR}$ (400.1 MHz, CDCl_3): δ_{H} 2.46 (CH_3), 3.17 (1H, dd, $^2J_{\text{HH}} = 17.6$, $^3J_{\text{HH}} = 5.2$ Hz, CH_2), 3.85 (1H, dd, $^2J_{\text{HH}} = 17.6$, $^3J_{\text{HH}} = 12.0$ Hz, CH_2), 5.68 (1H, dd, $^3J_{\text{HH}} = 12.0$, $^3J_{\text{HH}} = 5.2$ Hz, CH), 7.43 (2H, d, $^3J_{\text{HH}} = 8.4$ Hz, CH_{Ar}), 7.44-7.46 (1H, m, CH_{Ar}), 7.47-7.48 (2H, m, CH_{Ar}), 7.75-7.77 (2H, m, CH_{Ar}), 8.21 (2H, d, $^3J_{\text{HH}} = 8.4$ Hz, CH_{Ar}); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): δ_{C} 21.8 (CH_3), 42.0 (CH_2), 59.4 (CH), 124.2 (Cq), 124.3, 126.6 and 126.7 (3 CH_{Ar}), 128.6 (Cq), 128.8 and 128.9 (2 CH_{Ar}), 130.7 (Cq), 148.8 (C=N), 169.0 (C=O, ketone).

1-acetyl-5-(4-bromophenyl)-3-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazole (4e)

Cream powder, m.p. 177-179 °C, Yield: 82%; IR (KBr) (ν_{\max} , cm^{-1}): 3035 ($\text{C}_{\text{sp}}^2\text{-H}$), 2942 ($\text{C}_{\text{sp}}^3\text{-H}$), 1659 (C=O), 1604 (C=N), 1515 (C=C); Anal. Calcd for $\text{C}_{18}\text{H}_{17}\text{BrN}_2\text{O}_2$ (373.24): C, 57.92; H, 4.59, N, 7.51 Found: C, 57.94; H, 4.57, N, 7.48; $^1\text{H NMR}$ (400.1 MHz, CDCl_3): δ_{H} 2.42 (CH_3), 3.10 (1H, dd, $^2J_{\text{HH}} = 17.6$, $^3J_{\text{HH}} = 4.8$ Hz, CH_2), 3.73 (1H, dd, $^2J_{\text{HH}} = 17.6$, $^3J_{\text{HH}} = 12.0$ Hz, CH_2), 3.87 (OCH₃), 5.53 (1H, dd, $^3J_{\text{HH}} = 12.0$, $^3J_{\text{HH}} = 4.8$ Hz, CH), 6.95 (2H, d, $^3J_{\text{HH}} = 8.8$ Hz, CH_{Ar}), 7.13 (2H, d, $^3J_{\text{HH}} = 8.4$ Hz, CH_{Ar}), 7.69 (2H, d, $^3J_{\text{HH}} = 8.4$ Hz, CH_{Ar}), 7.13 (2H, d, $^3J_{\text{HH}} = 8.8$ Hz, CH_{Ar}); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): δ_{C} 21.9 (CH_3), 42.2 (CH_2), 55.4 (OCH₃), 59.2 (CH), 113.9 (CH_{Ar}), 127.4 (Cq), 128.2, 129.7 and 130.8 (3 CH_{Ar}), 131.9 (Cq), 132.1 (CH_{Ar}), 153.5 (C=N), 161.4 (C-O), 168.7 (C=O, ketone).

3. General procedure for the synthesis of N-(oxo) acetic acid (3, 5-diaryl-4, 5-dihydro-1H-pyrazole-1-yl) derivatives 6a-d

To a magnetically stirred solution of chalcone (2 mmol) and oxalic acid (2 mmol, 0.180g) and *p*-TsOH (20 mol%, 0.688 g) in EtOH (10 mL), 4 mmol of hydrazine hydrate (0.2 mL) in 5 mL EtOH was added dropwise. The mixture was allowed to stand at reflux temperature for the relevant time. After completion of the reaction as indicated by TLC (*n*-hexane/EtOAc, 3:2), was allowed reaction mixture to cool to room temperature and then poured onto crushed ice to obtain the crude product. The reaction product was recrystallized from ethanol.

Spectral data for the synthesis of N-(oxo) acetic acid (3, 5-diaryl-4, 5-dihydro-1H-pyrazole-1-yl) derivatives 6a-d

(3,5-diphenyl-4,5-dihydro-1H-pyrazol-1-yl)(oxo)acetic acid (6a)

White powder, m.p. 147-149 °C, Yield: 77%; IR (KBr) (ν_{\max} , cm^{-1}): 3538 (OH), 3029 ($\text{C}_{\text{sp}}^2\text{-H}$), 2953 ($\text{C}_{\text{sp}}^3\text{-H}$), 1670 (C=O), 1653 (C=N), 1489 (C=C); Anal. Calcd for $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_3$ (294.30): C, 69.38; H, 4.79, N, 9.52 Found: C, 69.39; H, 4.78, N, 9.54; $^1\text{H NMR}$ (400.1 MHz, DMSO): δ_{H} 3.79 (1H, dd, $^2J_{\text{HH}} = 18.0$, $^3J_{\text{HH}} = 4.4$ Hz, CH_2), 4.00 (1H, dd, $^2J_{\text{HH}} = 18.0$, $^3J_{\text{HH}} = 11.6$ Hz, CH_2), 5.64 (1H, dd, $^3J_{\text{HH}} = 11.6$, $^3J_{\text{HH}} = 4.4$ Hz, CH), 6.41 (1H, s, OH), 7.25 (2H, d, $^3J_{\text{HH}} = 7.2$ Hz, CH_{Ar}), 7.32 (2H, d, $^3J_{\text{HH}} = 7.2$ Hz, CH_{Ar}), 7.37-7.42 (2H, m, CH_{Ar}), 7.44-7.46 (2H, m, CH_{Ar}), 7.73-7.77 (2H, m, CH_{Ar}); $^{13}\text{C NMR}$ (100.6 MHz, DMSO): δ_{C} 42.8 (CH_2), 59.8 (CH), 126.2, 127.3, 128.1, 129.1, 129.2 and 129.3 (6 CH_{Ar}), 129.4 and 136.5 (2Cq), 155.5 (C=N), 161.5 and 161.9 (2C=O).

[5-(4-cyanophenyl)-3-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol-1-yl] (oxo) acetic acid (6b)

White powder, m.p. 161-163 °C Yield: 84%; IR (KBr) (ν_{\max} , cm^{-1}): 3498 (OH), 3059 ($\text{C}_{\text{sp}}^2\text{-H}$), 2928 ($\text{C}_{\text{sp}}^3\text{-H}$), 2230

(CN), 1665 (C=O), 1641 (C=N), 1494 (C=C); Anal. Calcd for C₁₈H₁₈N₂O₂ (349.34): C, 65.32; H, 4.33, N, 12.03 Found: C, 65.30; H, 4.31, N, 12.05; ¹H NMR (400.1 MHz, DMSO): δ_H 3.61 (1H, dd, ²J_{HH} = 17.2, ³J_{HH} = 8.8 Hz, CH₂), 3.84 (3H, s, OCH₃), 3.90 (1H, dd, ²J_{HH} = 17.2, ³J_{HH} = 9.6 Hz, CH₂), 5.28 (1H, dd, ³J_{HH} = 9.6, ³J_{HH} = 8.8 Hz, CH), 5.99 (1H, s, OH), 7.09 (2H, d, ³J_{HH} = 8.8 Hz, CH_{Ar}), 7.72 (2H, d, ³J_{HH} = 8.4 Hz, CH_{Ar}), 7.83 (2H, d, ³J_{HH} = 8.8 Hz, CH_{Ar}), 7.93 (2H, d, ³J_{HH} = 8.4 Hz, CH_{Ar}); ¹³C NMR (100.6 MHz, DMSO): δ_C 41.2 (CH₂), 55.9 (OCH₃), 60.9 (CH), 110.1 (Cq), 111.9 (CH_{Ar}), 118.9 (CN), 119.4, 123.1 and 126.0 (3CH_{Ar}), 130.3 and 133.1 (2Cq), 155.6 (C=N), 158.7 and 159.7 (2C=O), 162.6 (C-O).

[5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol-1-yl] (oxo) acetic acid (6c)

Cream powder, m.p. 155-158 °C, Yield: 79%; IR (KBr) (ν_{max} , cm⁻¹): 3523 (OH), 3058 (C_{sp}²-H), 2929 (C_{sp}³-H), 1652 (C=O), 1601 (C=N), 1512 (C=C); Anal. Calcd for C₁₈H₁₅ClN₂O₄ (358.77): C, 60.26; H, 4.21, N, 7.81 Found: C, 60.25; H, 4.20, N, 7.83; ¹H NMR (400.1 MHz, DMSO): δ_H 3.61 (1H, dd, ²J_{HH} = 17.2, ³J_{HH} = 8.8 Hz, CH₂), 3.80 (3H, s, OCH₃), 3.90 (1H, dd, ²J_{HH} = 17.2, ³J_{HH} = 9.6 Hz, CH₂), 5.28 (1H, dd, ³J_{HH} = 9.6, ³J_{HH} = 8.8 Hz, CH), 6.76 (1H, s, OH), 7.04 (2H, d, ³J_{HH} = 8.8 Hz, CH_{Ar}), 7.77 (2H, d, ³J_{HH} = 8.8 Hz, CH_{Ar}), 7.90 (2H, d, ³J_{HH} = 8.4 Hz, CH_{Ar}), 8.04 (2H, d, ³J_{HH} = 8.4 Hz, CH_{Ar}); ¹³C NMR (100.6 MHz, DMSO): δ_C 41.2 (CH₂), 55.6 (OCH₃), 60.9 (CH), 111.9, 114.8 and 119.4 (3CH_{Ar}), 123.1 (Cq), 127.07 (CH_{Ar}), 129.4 and 133.2 (2Cq), 154.4 (C=N), 159.7 and 159.8 (2C=O), 162.7 (C-O).

[3-(4-methoxyphenyl)-5-(4-nitrophenyl)-4, 5-dihydro-1H-pyrazol-1-yl] (oxo) acetic acid (6d)

Yellow powder, m.p. 173-175 °C, Yield: 85%; IR (KBr) (ν_{max} , cm⁻¹): 3408 (OH), 3031 (C_{sp}²-H), 2924 (C_{sp}³-H), 1662 (C=O), 1604 (C=C), 1515 and 1361 (NO₂); Anal. Calcd for C₁₈H₁₅N₃O₆ (369.32): C, 58.54; H, 4.09, N, 11.38 Found: C, 58.56; H, 4.07, N, 11.35; ¹H NMR (400.1 MHz, CDCl₃): δ_H 3.12 (1H, dd, ²J_{HH} = 18.0, ³J_{HH} = 4.8 Hz, CH₂), 3.79 (1H, dd, ²J_{HH} = 18.0, ³J_{HH} = 12.0 Hz, CH₂), 3.85 (3H, s, OCH₃), 5.64 (1H, dd, ³J_{HH} = 12.0, ³J_{HH} = 4.8 Hz, CH), 6.35 (1H, s, OH), 6.95 (2H, d, ³J_{HH} = 8.8 Hz, CH_{Ar}), 7.40 (2H, d, ³J_{HH} = 8.8 Hz, CH_{Ar}), 7.68 (2H, d, ³J_{HH} = 8.8 Hz, CH_{Ar}), 8.16 (2H, d, ³J_{HH} = 8.8 Hz, CH_{Ar}); ¹³C NMR (100.6 MHz, CDCl₃): δ_C 41.2 (CH₂), 55.4 (OCH₃), 59.3 (CH), 114.2, 124.2, 126.6 and 128.3 (4CH_{Ar}), 131.0, 140.9 and 148.9 (3Cq), 153.7 (C=N), 159.5 and 161.6 (2C=O), 163.9 (C-O).

CONCLUSION

The present study was conducted to describe a convenient strategy for the preparation of some of the N-acetylde pyrazoline derivatives by reaction of chalcones with hydrazine hydrate and acetic anhydride or oxalic acid in the presence of the catalytic amount of *p*-toluenesulfonic acid in ethanol as a solvent. The simplicity of this procedure, easy separation of the products, time-consuming reaction, and good to high yields of the reaction could make this method as an alternative approach for the preparation of N-substituted (3,5-diaryl-4,5-dihydro-1H-pyrazole-1-yl) derivatives.

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