

Green synthesis of chromeno[2,3-*c*]pyrazoles and 4,4'-(arylmethylene)bis(1H-pyrazole-5-ols) via catalyst-free multicomponent reaction in magnetized distilled water

Mohammad Bakherad* , Ali Keivanloo , Mahsa Abedi Bajestani , Amin Rezaeifard 

a Faculty of Chemistry, Shahrood University of Technology, Shahrood, Iran

ABSTRACT

An eco-friendly benign catalyst-free synthesis of chromeno[2,3-*c*]pyrazoles and bis-pyrazolone derivatives has been reported using magnetized distilled water (MDW). Under the optimal condition, most chromeno[2,3-*c*]pyrazoles (5a–f) and bis-pyrazolone (7a–k) were obtained in 85–93% and 85–95% yields respectively. This process offers several advantages, including its environmentally friendly and cost-effective nature, along with a simplified workup procedure and a high yield of desired products. Additionally, the absence of catalysts minimizes the potential for undesirable side reactions and contamination, resulting in a cleaner and more efficient synthesis process.

KEYWORDS

Chromeno[2,3-*c*]pyrazole, Bis-pyrazolone, Catalyst-free, Magnetized distilled water

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INTRODUCTION

The multi-component reaction (MCR) is a chemical process where three or more reactants combine in a single step to form a product. This efficient method is widely used in organic synthesis for creating complex molecules. Multi-component reactions (MCRs) have recently attained significant importance because this addresses several constituent principles of green chemistry, such as reaction design and synthetic efficiency. Multi-component reactions have several advantages like operational atom economy, simplicity, and a decrease in the number of synthetic steps, thereby saving time and chemicals in the form of separations and purifications of intermediate compounds.^{1,2}

In recent years, chromens had a broad range of applications. They have shown different biological and pharmacological activities such as antitumor,³ anti-HIV,⁴ antibacterial,^{5–7} antifungal,⁸ and anti-inflammatory.⁹ Also, there is a considerable tendency to study pyrazole derivatives owning abundant biological activities, such as anti-viral,¹⁰ anti-inflammatory,¹¹ anti-depressant,¹² and anti-cancer activities.¹³

Bis-pyrazolone derivatives are very important compounds, for example, they exhibit gastric secretion stimulatory,¹⁴ anti-inflammatory,¹⁵ antimalarial,¹⁶ and antipyretic.¹⁷ Several reports are available for the synthesis of bis-pyrazolone derivatives using different catalysts including ceric ammonium nitrate (CAN),¹⁸ silica-bonded S-sulfonic acid,¹⁹ N-(3-silicapropryl)-N-methylimidazolium hydrogen sulfate,²⁰ heterogeneous acidic catalysts and catalyst-free conditions in water.^{21,22} These protocols, however, suffer from some disadvantages such as hard reaction conditions, and a tedious workup process.

With the general increment concern on environmental degradation, eco-friendly safe solvent-like water displays robust green chemical technology methods from the economic viewpoint. Water has many benefits, including the cleanest, cheapest, eco-friendly, non-flammable, easy work-up, and high specific heat capacity.²³ However, most chemical reactions cannot be done in water, as a solvent, since they need the presence of reagents, or catalysts. Therefore, if we can change the physical properties of water, its reactivity toward organic reagents will be altered. The change in the properties of water under the action of an applied magnetic field is just a typical case.

Since the mid-20th century, much researches about the magnetized treatment theory have been carried out, and applied in many fields.^{24–26}

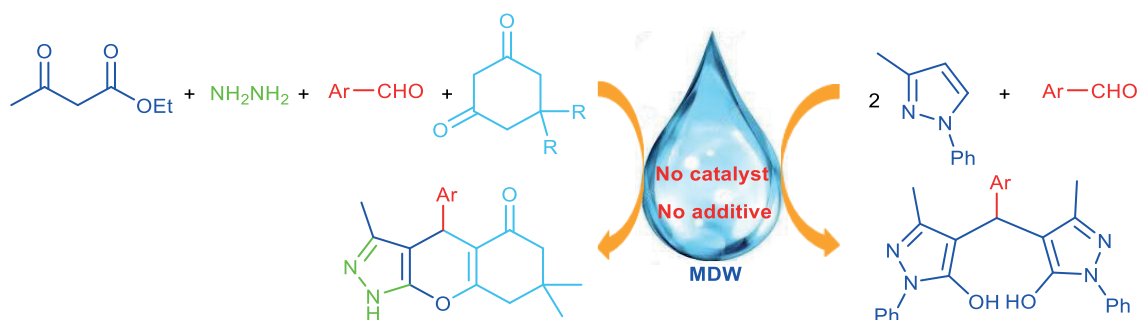
The magnetized treatment can originate the change in pH value, density, refractive index, specific heat, vaporization enthalpy, electric dipole-moment, hydrogen bond distribution, surface zeta potential, and viscosity in water.^{27–33} Water magnetization is an easy method without excessive energy consumption when a constant foreign magnet is used. Such a magnet can be installed on a previously established water tube system, resulting in no additional energy required for water magnetization. Magnetized water plays an important role in the synthesis of one-pot organic compounds. In the multi-component reactions it acts as a solvent and produces tetrahydro-benzo[*b*]pyrans,³⁴ 9-substituted-9*H*-diuracilopyrans,³⁵ pyrano[2,3-*c*]pyrazole and pyrano[4,3:5,5]pyrazolo [2,3-*d*]pyrimidine derivatives,³⁶ and 1*H*-tetrazoles and 5-substituted compounds.³⁷ Recently, Gholizadeh et al.³⁸ have described the effect of magnetized water on the oxidation reaction of phenol derivatives. Simplicity, lack of organic solvents, low cost, green, easy extraction, short reaction time, and high efficiency are among the characteristics of these reactions. In continuation of our research works focusing on the use of magnetized water as a solvent in organic synthesis,^{39,40} we wish to report a simple procedure for the preparation of chromeno[2,3-*c*]pyrazoles and bis-pyrazolones in MDW (Scheme 1).

EXPERIMENTAL

General

The materials used in the experiment were obtained from reputable sources. The chemicals and solvents were purchased from Fluka and Merck, which are two well-known companies that produce high-quality products for scientific research. The melting point of all reported compounds was determined using a digital device that can measure the temperature at which a solid substance changes into a liquid. The device was an Electrothermal model, which is a brand of digital melting point apparatus that uses a capillary tube and a heating block. The synthesized compounds' ¹H NMR and ¹³C NMR spectra were recorded using Bruker Advance II 300 NMR spectrometer. The solvent used for dissolving the compounds was dimethyl sulfoxide (DMSO), which is a polar organic solvent that can dissolve many substances. The chemical shifts (δ) were expressed in parts per million, which is a unit of measurement that indicates the relative position of a signal in an NMR spectrum compared to a reference signal. IR spectra were recorded on a device that can measure the absorption of infrared

*To whom correspondence should be addressed
Email: m.bakherad@yahoo.com



Scheme 1. Synthesis of chromeno[2,3-*c*]pyrazoles and 4,4'-(arylmethylene)bis(1*H*-pyrazole-5-ols).

radiation by molecules based on their vibrational modes. The device was a Shimadzu IR-435 grating spectrophotometer, which is a type of infrared (IR) spectrophotometer that uses a grating to disperse the radiation into different wavelengths.

Preparation of chromeno[2,3-*c*]pyrazoles (5)

Hydrazine hydrate (1 mmol), ethyl acetoacetate (1 mmol), an aldehyde (1.0 mmol), and dimedone/cyclohexanedione (1.0 mmol) were stirred at 80 °C in 3 mL of MDW. After completion of the reaction, the resulting crude product was separated and recrystallized from ethanol. The crystals were collected by filtration and dried to obtain the final product.

4-(2-Hydroxyphenyl)-3,7,7-trimethyl-7,8-dihydrochromeno[2,3-*c*]pyrazol-5(1*H*,4*H*,6*H*)-one (5a)

White powder solid (93% yield): mp, 194–196 °C; IR (ν) (KBr) cm^{-1} : 3300 (NH), 3075 (C-H Aromatic), 2800, 3000 (C-H aliphatic), 1641 (CO). ^1H NMR (300 MHz, DMSO-*d*₆) δ 0.9 (s, 3H, CH₃), 1.06 (s, 3H, CH₃), 2.07 (s, 3H, CH₃), 2.28 (s, 3H, CH₃), 2.38 (s, 2H, CH₂), 3.35 (s, 1H, OH), 5.07 (s, 1H, CH), 6.97-7.00 (m, 2H ArH), 7.09-7.10 (d, *J* = 3, 1H, ArH), 7.14-7.149 (d, *J* = 2.7 Hz, 1H, ArH), 10.42 (br, 1H, NH). ^{13}C NMR (DMSO-*d*₆, 75 MHz) δ 26.6, 27.5, 28.1, 29.6, 32.0, 50.9, 111.2, 115.7, 124.6, 126.0, 127.3, 129.6, 139.4, 150.1, 161.2, 165.2, 196.2; C₁₉H₂₀N₂O₃, (ESI) *m/z*; 324.00.

4-(3-Hydroxyphenyl)-3,7,7-trimethyl-7,8-dihydrochromeno[2,3-*c*]pyrazol-5(1*H*,4*H*,6*H*)-one (5b)

White powder solid (91% yield): mp, 110–112 °C; ^1H NMR (300 MHz, DMSO-*d*₆) δ 1.05 (s, 6H, 2CH₃), 2.32 (s, 4H, 2CH₂), 2.52 (s, 3H, CH₃), 4.18 (s, 1H, OH), 5.78 (s, 1H, CH), 6.47-6.49 (m, 1H, ArH), 6.64-6.65 (d, *J* = 2.1 Hz, 1H, ArH), 6.76 (s, 1H, ArH), 6.85-6.86 (d, *J* = 1.5 Hz, 1H, ArH), 8.682 (br, 1H, NH) ppm. ^{13}C NMR (DMSO-*d*₆, 75 MHz) δ 27.1, 28.3, 30.7, 31.5, 31.7, 47.0, 56.1, 101.4, 110.5, 114.8, 115.2, 117.4, 133.6, 137.5, 145.7, 145.8, 146.4, 165.3, 187.7, 196.6; C₁₉H₂₀N₂O₃, (ESI) *m/z*; 324.00.

4-(3-Hydroxy-4-methoxyphenyl)-3,7,7-trimethyl-7,8-dihydrochromeno[2,3-*c*]pyrazol-5(1*H*,4*H*,6*H*)-one (5c)

White powder solid (87% yield): mp, 120–122 °C; ^1H NMR (300 MHz, DMSO-*d*₆) δ 1.09 (s, 3H, CH₃), δ 1.07 (s, 3H, CH₃), 2.27 (s, 2H, CH₂), 2.33 (s, 2H, CH₂), 2.53 (s, 3H, CH₃), 3.73 (s, 3H, OCH₃), 4.20 (s, 1H, OH), 5.8 (s, 1H, CH), 6.38-6.45 (m, 1H, ArH), 6.70 (s, 1H, ArH), 6.75-6.77 (d, 1H, *J* = 2.1 Hz, ArH), 8.68 (br, 1H, NH); C₂₀H₂₂N₂O₄, (ESI) *m/z*; 354.14.

3,7,7-Trimethyl-4-(3,4,5-trimethoxyphenyl)-7,8-dihydrochromeno[2,3-*c*]pyrazol-5(1*H*,4*H*,6*H*)-one (5d)

White powder solid (90% yield): mp, 116–118 °C; IR (ν) (KBr) cm^{-1} : 3300 (NH), 3050, 3057 (C-H Aromatic), 2800, 3000 (C-H aliphatic), 1595 (CO). ^1H NMR (300 MHz, DMSO-*d*₆) δ 1.05 (s, 6H, CH₃), 2.15

(s, 4H, 2CH₂), 2.25 (s, 1H, CH₃), 3.63 (s, 9H, CH₃), δ 5.49 (s, 1H, CH), 6.36 (s, 2H, ArH), 11.92 (br, 1H, NH). ^{13}C NMR (DMSO-*d*₆, 75 MHz) δ 10.6, 30.7, 31.3, 56.0, 60.3, 104.8, 117.2, 120.6, 131.0, 138.5, 137.9, 138.5, 152.7, 181.0, 197.0; C₂₂H₂₆N₂O₅, (ESI) *m/z*; 398.18.

4-(2-Hydroxyphenyl)-3-methyl-7,8-dihydrochromeno[2,3-*c*]pyrazol-5(1*H*,4*H*,6*H*)-one (5e)

White powder solid (85% yield): mp, 238–240 °C; IR (ν) (KBr) cm^{-1} : 3300 (NH), 3050, 3075 (C-H Aromatic), 2800, 3000 (C-H aliphatic), 1645 (CO). ^1H NMR (300 MHz, DMSO-*d*₆) δ 1.67-1.76 (m, 2H, CH₂), 1.81-1.85 (t, *J* = 6.9 Hz, 2H, CH₂), 1.93-1.95 (t, *J* = 5.4 Hz, 2H, CH₂), 2.37 (s, 3H, CH₃), 3.37 (s, 1H, OH), 5.09 (s, 1H, CH), 6.94-6.97 (d, *J* = 7.8 Hz, 2H, ArH), 6.99-7.00 (d, *J* = 3.9 Hz, 1H, ArH), 7.08-7.10 (m, 1H, ArH), 7.12-7.14 (m, 1H, ArH), 10.48 (s, 1H, NH). ^{13}C NMR (DMSO-*d*₆, 75 MHz) δ 20.7, 20.8, 25.8, 27.7, 37.1, 112.4, 115.7, 124.7, 126.2, 127.3, 128.8, 150.0, 167.0, 172.1, 196.4; C₁₇H₁₆N₂O₃, (ESI) *m/z*; 296.12.

3-Methyl-4-*p*-tolyl-7,8-dihydrochromeno[2,3-*c*]pyrazol-5(1*H*,4*H*,6*H*)-one (5f)

White powder solid (80% yield): mp, 192–194 °C; ^1H NMR (300 MHz, DMSO-*d*₆) δ 1.84-1.92 (m, 2H, CH₂), 2.36-2.40 (t, *J* = 6.6 Hz, 2H, CH₂), 2.42-2.45 (t, *J* = 6.6 Hz, 2H, CH₂), 2.98 (s, 3H, CH₃), 4.28 (s, 1H, CH), 5.72 (s, 1H, CH), 6.86-6.86 (d, *J* = 1.5 Hz, 2H, ArH), 6.93-6.96 (d, *J* = 8.9 Hz, 1H, ArH), 7.01-7.03 (d, *J* = 6 Hz, 1H, ArH), 7.07-7.09 (d, *J* = 6 Hz, 1H, ArH), 9.97 (s, 1H, NH) ppm. ^{13}C NMR (DMSO-*d*₆, 75 MHz) δ 20.1, 21.0, 32.3, 35.3, 37.1, 60.5, 100.4, 116.3, 128.0, 128.3, 128.4, 128.7, 134.4, 142.5, 167.6, 169.4, 189.8, 195.8; C₁₈H₁₈N₂O₂, (ESI) *m/z*; 295.14.

Preparation of bis-pyrazolones (7)

A mixture of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (2.0 mmol), and an aldehyde (1.0 mmol), were stirred at 80 °C in 3 mL of MDW. At the end of the reaction, the resulting solid was separated by simple filtration and recrystallized from ethanol.

4-(2,4-dichlorophenyl)(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methyl)-3-methyl-1-phenyl-1*H*-pyrazol-5-ol (7c)

White powder solid (85% yield): mp, 227–229 °C; ^1H NMR (300 MHz, DMSO-*d*₆) δ 2.29 (s, 6H, 2CH₃), 5.11 (s, 1H, CH), 7.24-7.29 (t, 3H, *J* = 6, ArH), 7.41-7.48 (m, 5H, ArH), 7.570-7.577 (t, 1H, *J* = 1 Hz, ArH), 7.70 (s, 1H, CH, ArH), 7.72-7.73 (d, 2H, *J* = 4.5, ArH), 7.75-7.78 (d, 1H, *J* = 3, ArH), 12.61 (s, 1H, OH), 13.83 (s, 1H, OH).

4-((5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)(2-methoxyphenyl)methyl)-3-methyl-1-phenyl-1*H*-pyrazol-5-ol (7i)

White powder solid (85% yield): mp, 209–211 °C; ^1H NMR (300 MHz, DMSO-*d*₆) δ 2.29 (s, 6H, 2CH₃), 3.38 (s, 3H, OCH₃), 5.20 (s, 1H, CH), 6.86-6.91 (m, 1H, ArH), 6.94-6.97 (m, 1H, ArH), 7.26-7.28 (t, 1H, *J* =

2Hz, ArH), 7.42–7.48 (t, 5H, $J = 4.5$, ArH), 7.61–7.63 (d, 2H, $J = 3$, ArH), 7.70–7.73 (d, 4H, $J = 3$, ArH), 12.64 (s, 1H, OH), 14.39 (s, 1H, OH).

RESULTS AND DISCUSSION

MDW was prepared similarly to a previous method reported in a scientific paper.³⁶ The test tube containing distilled water (3 mL) was put in a magnetic field (0.8 T) for 15 minutes. This exposed the water molecules to a solid magnetic force that could affect their properties and behavior. Subsequently, the prepared MDW was used for the reaction.

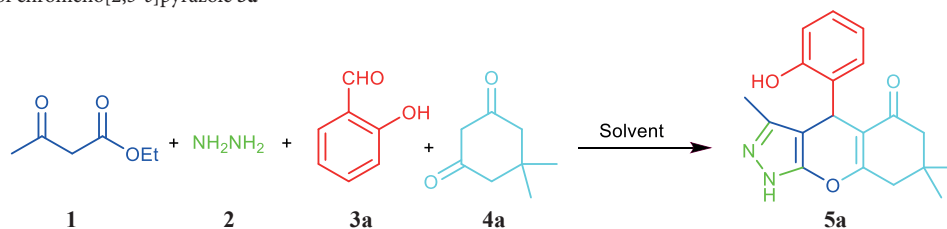
The evaluation of various solvents and catalysts for the preparation of chromeno[2,3-*c*]pyrazole **5a** is described in Table 1. First, the reaction was carried out without a catalyst in the solvents such as H₂O, MeOH, EtOH, CH₃CN, and DMF (Table 1). We observed the superior solvent was H₂O (Table 1, entry 1). Then, different catalysts such as *p*-toluenesulfonic acid (PTSA), CuCl₂, CuSO₄, CuO, MnO₂, MnCl₂, Zn(OAc)₂, ZnO, SnCl₂, and SbCl₃ in water were used to increase the reaction yield. According to Table 1, a higher reaction yield was obtained with the PTSA catalyst (Table 1, entry 6). Interestingly, when the multi-component reaction was carried out in the absence of a catalyst in MDW, an excellent yield (93%) was obtained (Table 1, entry 16). When the reaction was performed at various temperatures ranging from 60 °C to 90 °C; an excellent reaction yield (93%) was obtained at 80 °C. Increasing the reaction temperature, and the reaction time did not affect the reaction yield (Table 1, entries 18, and 19 respectively). According to Table 1, decreasing the water magnetization time

resulted in the low formation of chromeno[2,3-*c*]pyrazole **5a** (Table 1, entry 20). However, high product formation was not observed with increasing the water magnetization time (Table 1, entry 21).

Upon establishing the optimized reaction conditions, the methodology was extended by utilizing different substrates to access desired novel chromeno[2,3-*c*]pyrazoles (Table 2). According to Table 2, the reactions of various aldehydes, led to chromeno[2,3-*c*]pyrazoles **5** in high-to-excellent yields (80–93%). Moreover, a bulky aldehyde 3,4,5-trimethoxybenzaldehyde afforded the chromeno[2,3-*c*]pyrazole **5d** an excellent yield (Table 2, entry 4).

Toledo *et al.*⁴¹ have demonstrated the effect of an exterior magnetic field on the physical and chemical properties of water *via* a theoretical and experimental method. They have explained that the being of competition among the intra- and inter-molecular hydrogen bond lattices in water, diminish the powerful intra-cluster hydrogen bonds, breaks the big clusters, and forms the smaller ones with stronger inter-cluster hydrogen bonds. Thus, the numeral of hydrogen bonds between the MDW molecules and the reacting molecules enhanced. In addition, recently, we described the synthesis of 9-substituted-9*H*-diuracilopyrans from the reaction of barbituric acids with aldehydes in MDW as a solvent.³⁵ Based on the obtained results, we proved that the MDW causes more attractive forces between the aldehydes and barbituric acid molecules and, hence, enhances the interactions between them, leading to an increase in the reaction rate and chemical reactivity

Table 1. Optimization of chromeno[2,3-*c*]pyrazole **5a**



| Entry | Solvent | Catalyst | Temperature (°C) | Yield ^b (%) |
|-----------------|--------------------|----------------------|------------------|------------------------|
| 1 | H ₂ O | - | 80 | 45 |
| 2 | MeOH | - | Reflux | 20 |
| 3 | EtOH | - | Reflux | 23 |
| 4 | CH ₃ CN | - | Reflux | 12 |
| 5 | DMF | - | 90 | 15 |
| 6 | H ₂ O | PTSA | 80 | 75 |
| 7 | H ₂ O | CuCl ₂ | 80 | 50 |
| 8 | H ₂ O | CuSO ₄ | 80 | 68 |
| 9 | H ₂ O | CuO | 80 | 46 |
| 10 | H ₂ O | MnO ₂ | 80 | 40 |
| 11 | H ₂ O | MnCl ₂ | 80 | 58 |
| 12 | H ₂ O | Zn(OAc) ₂ | 80 | 60 |
| 13 | H ₂ O | ZnO | 80 | 64 |
| 14 | H ₂ O | SnCl ₂ | 80 | 40 |
| 15 | H ₂ O | SbCl ₃ | 80 | 70 |
| 16 | MDW | - | 80 | 93 |
| 17 | MDW | - | 60 | 76 |
| 18 | MDW | - | 90 | 92 |
| 19 ^c | MDW | - | 90 | 93 |
| 20 ^d | MDW | - | 90 | 70 |
| 21 ^e | MDW | - | 90 | 94 |

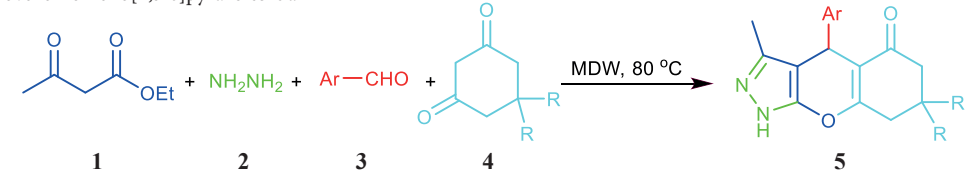
^a Reaction conditions: Ethyl acetoacetate **1** (1 mmol), hydrazine (1 mmol), 2-hydroxybenzaldehyde **3a** (1.0 mmol), dimedone **4a** (1 mmol), reaction time (2 h), solvent (3 mL), magnetization time (15 min).

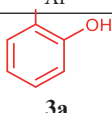
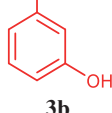
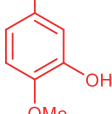
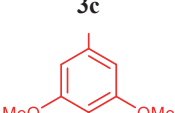
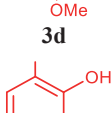
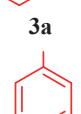
^b Isolated yield.

^c Reaction time (4 h).

^d Water magnetization time (10 min).

^e Water magnetization time (20 min).

Table 2. Synthesis of novel chromeno[2,3-*c*]pyrazoles^a **5a-f**


| Entry | Ar | R | Product | Time (min) | Yield ^b (%) | m.p. (°C) |
|-------|---|----|---------|------------|------------------------|-----------|
| 1 |  | Me | 5a | 120 | 93 | 194-196 |
| 2 |  | Me | 5b | 45 | 91 | 110-112 |
| 3 |  | Me | 5c | 45 | 87 | 120-122 |
| 4 |  | Me | 5d | 60 | 90 | 116-118 |
| 5 |  | H | 5e | 60 | 85 | 238-240 |
| 6 |  | H | 5f | 60 | 80 | 192-194 |

^a Reaction conditions: Ethyl acetoacetate **1** (1 mmol), hydrazine (1 mmol), an aldehyde **3** (1.0 mmol), dikedone/1,3-cyclohexanedione **4** (1 mmol), MDW (3 mL), magnetization time (15 min).

^b Isolated yield.

at the molecular level. Therefore, we believe that the hydrogen bonds between molecules of MDW and molecules of the substrates and intermediates involved in a reaction are responsible for the reaction activation. The Plausible mechanism for the synthesis of chromeno[2,3-*c*]pyrazoles **5** from ethyl acetoacetate, hydrazine, an aldehyde, and 1,3-diketone **4** in MDW is shown in Scheme 2.

The synthesis of chromeno[2,3-*c*]pyrazole **5** was successfully achieved through a well-defined five-step reaction sequence. The initial step involved the condensation of ethyl acetoacetate **I** and hydrazine **II**, resulting in the formation of pyrazolone **III**. Subsequently, the pyrazolone **III** ring system was converted to its corresponding enolate **IV** in the presence of magnetized distilled water (MDW), which played a crucial role in promoting enolate formation. Also, MDW plays a major role in its promoting activity for the formation of intermediate **V**, which is readily prepared in situ by the Knoevenagel condensation of aldehyde **3** with the highly active CH acidic diketone **4**. Finally, the Michael-type addition of 3-methyl-1*H*-pyrazol-5(4*H*)-one **IV** to intermediate **V** followed by cyclization and tautomerization yielded chromeno[2,3-*c*]pyrazoles **5**.

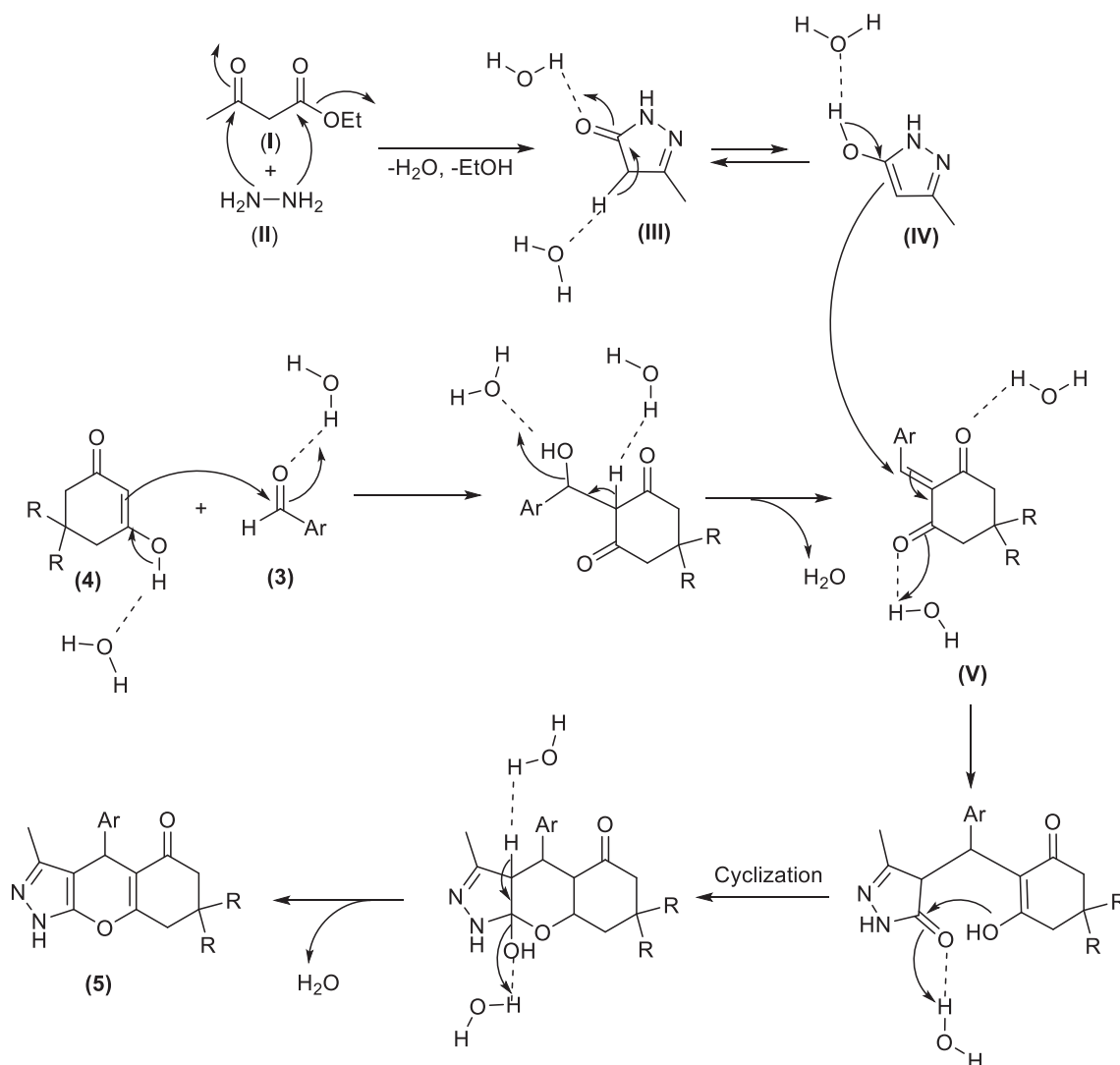
The results have shown the use of MDW as a suitable solvent for the preparation of chromeno[2,3-*c*]pyrazole derivatives. Therefore, we investigated the synthesis of bis-pyrazolone derivatives from the reaction of an aldehyde **3** with 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one **6** in MDW (Table 3). As shown in Table 3, different aldehydes underwent the reaction to give the corresponding 4,4'-

(aryl methylene)bis(1*H*-pyrazole-5-ols) in high to excellent yields. Aldehydes with electron receptor groups including NO₂, F, and Cl provided the corresponding bis-pyrazolones in excellent yields (Table 3, entries 2–7). However, the yield of the product was slightly decreased with 4-methyl benzaldehyde, 2-methoxy benzaldehyde, 4-methoxy benzaldehyde, and 2-hydroxy benzaldehyde (Table 3, entries 8–11). In this reaction, the Knoevenagel condensation takes place between pyrazole (nucleophile) and aldehyde (electrophile). Therefore, electron donating groups on aldehyde reduce the electrophilic property of aldehyde and as a result, the reaction yield decreases.

Table 4 compares the efficiency of MDW as a green solvent with some reported methods in the bis-pyrazolones **7** syntheses. As the table shows, this method has high efficiency in the synthesis of products **7**.

CONCLUSIONS

In conclusion, this study demonstrates a successful catalyst-free, green synthesis of chromeno[2,3-*c*]pyrazoles and bis-pyrazolone derivatives using magnetized distilled water as a solvent. The newly developed method utilizing MDW as the solvent, without the need for a catalyst, demonstrated remarkable results. At a temperature of 80 °C, the reaction yielded 85–95% of the desired products within a time frame of 75–120 minutes. This approach exhibits favorable results in terms of both yield and reaction time compared to alternative methods. The information presented in the Table 4, suggests



Scheme 2. A plausible mechanism for synthesis of chromeno[2,3-*c*]pyrazoles 5.

that the employment of MDW as a solvent offers an efficient and environmentally friendly approach for synthesizing bis-pyrazolone compounds. This method proves to be competitive, if not superior, in terms of yield and reaction time when compared to most other reported methods. Furthermore, it provides a greener alternative to methods involving the use of catalysts or less environmentally friendly solvents like ethanol. Moreover, the high reaction yields and reduced energy consumption further highlight the potential of this technique for widespread adoption in the field.

SUPPLEMENTARY MATERIAL

Supplementary information for this article is provided in the online supplement.

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ORCID IDS

Mohammad Bakherad: <https://orcid.org/0000-0003-3139-2249>

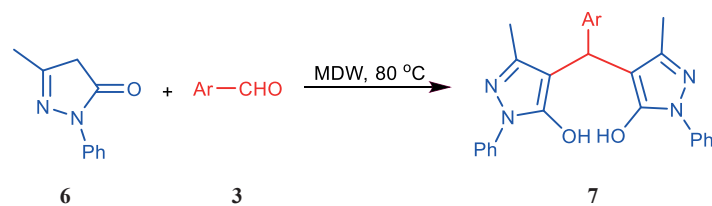
Ali Keivanloo: <https://orcid.org/0000-0003-1430-7399>








Mahsa Abedi Bajestani: <https://orcid.org/0009-0004-7115-9948>

Amin Rezaeifard: <https://orcid.org/0000-0003-2323-9498>

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Table 3. Bis-pyrazolone derivatives 7^a

| Entry | Ar | Product | Time (min) | Yield ^b (%) | mp. (°C) | mp. (°C) ^{Ref.} |
|-------|--|---------|------------|------------------------|----------|--------------------------|
| 1 |  3f | 7a | 75 | 90 | 168-170 | 171-173 ¹⁹ |
| 2 |  3g | 7b | 60 | 90 | 181-183 | 181-183 ²¹ |
| 3 |  3h | 7c | 85 | 82 | 227-229 | 228-230 ⁴² |
| 4 |  3i | 7d | 60 | 92 | 200-202 | 199-201 ²² |
| 5 |  3j | 7e | 90 | 91 | 181-183 | 183-185 ²² |
| 6 |  3k | 7f | 75 | 93 | 145-147 | 146-148 ²² |
| 7 |  3l | 7g | 75 | 95 | 224-226 | 225-227 ²¹ |
| 8 |  3e | 7h | 120 | 88 | 200-202 | 198-200 ²² |
| 9 |  3m | 7i | 120 | 85 | 209-211 | 210-212 ⁴³ |
| 10 |  3n | 7j | 120 | 86 | 174-176 | 173-175 ²² |
| 11 |  3a | 7k | 90 | 87 | 226-228 | 227-229 ²¹ |

^a Reaction conditions: Ethyl acetoacetate **1** (1 mmol), hydrazine (1 mmol), an aldehyde **3** (1.0 mmol), dimedone/1,3-cyclohexanedion **4** (1 mmol), MDW (3 mL), magnetization time (15 min).

^b Isolated yield.

Table 4. Comparison between this work and the priorly report for the preparation of bis-pyrazolones 7.

| Entry | Catalyst | Reaction conditions | Time | Yield (%) ^{Ref.} |
|-------|---|--------------------------|------------|---------------------------|
| 1 | Silica-bonded S-sulfonic acid | EtOH, Reflux | 1-4 h | 75-90 ¹⁹ |
| 2 | Sulfuric acid ([3-(3-silicapropyl)sulfanyl]propyl ester | EtOH, Reflux | 2-4 h | 74-90 ²¹ |
| 3 | Silica-bonded Ionic Liquid | EtOH, Reflux | 2-4.5 h | 77-90 ²⁰ |
| 4 | Catalyst-free | H ₂ O, Reflux | 6-8 h | 72-84 ²² |
| 5 | CAN | H ₂ O, r.t | 10-25 min | 88-94 ¹⁸ |
| 6 | Guanidine hydrochloride | H ₂ O, Reflux | 30-60 min | 85-92 ⁴⁴ |
| 7 | Zirconium@guanine@MCM-41 | EtOH, Reflux | 10-60 min | 83-99 ⁴⁵ |
| 8 | Sulfonated nanohydroxyapatite | Solvent-free, 80 °C | 2-10 min | 80-90 ⁴² |
| 9 | CuFe ₂ O ₄ | Solvent-free, 80 °C | 2-25 min | 89-98 ⁴⁶ |
| 10 | Catalyst-free | MDW, 80 °C | 75-120 min | 85-95 [This work] |

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