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ARTICLE

Zirconia Nanoparticles Catalyzed Multi-Component Synthesis of Functionalized Chromene-pyarazolone Derivatives

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ABSTRACT

The compounds **4a-m** (functionalized chromene phenyl pyarazolone derivatives) were synthesized using ultrafine zirconia nanoparticles (ZrO_2 NPs) by multi-component approach in water-ethanol as green solvent. Zirconia nanoparticles gave good catalytic activity for first four cycles of synthesized product. The structural and morphological characterizations of the as-prepared ZrO_2 nanoparticles were performed by using X-ray diffraction, Fourier transform infrared spectroscopy, energy dispersive X-ray microanalysis (EDS) spectroscopy and Ultraviolet visible (UV-visible) absorption spectroscopy. The morphological property revealed the formation of nanoscale particles. In this investigation we gave emphasis on the eco-friendly synthesis of chromene-phenyl pyrazolones derivatives using ZrO_2 nanoparticles and water-ethanol. The expected results reveals the applicability of tuneable catalytic activity, reaction time and the reusability of ZrO_2 nanoparticles even after several cycles.

KEYWORDS

ZrO_2 nanoparticles, Green solvent, Multi-component, Chromene phenyl pyarazolones.

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INTRODUCTION

The chromene scaffold is a central part of many biologically active compounds with potential medicinal use as antitumor [1], antimicrobial [2], antitrypanosomalagents [3], antimicrobial, antibiofilm activities [4], potential NF-κB inhibitors [5], in molluscicidal activity [6], antioxidant [7], antifungal [8], antiprotozoal activity [9]. Now days, multi-component reactions (MCRs) are accepted worldwide as an important tool for the synthesis of various products and intermediates in medicinal and combinatorial chemistry [10,11].

These reactions avoid time consuming and multistep process [12,13], have been proven to be graceful and rapid way to shows advantage of atom economy and high selectivity [14]. The condensation reaction of active methylene group with aldehyde function of 3-formyl chromene was studied by different workers [15] but these studies has some limitations such as use of hazardous acid or base catalyst, longer heating

period, low productivity and synthesis required multi-step process [16-18]. To the best of our literature survey, there is no efficient general multi-component protocol for the synthesis of chromene-phenyl pyrazolones derivatives using ZrO_2 nanoparticle (NPs) in green solvent with very short reaction time. The use of ZrO_2 NPs could be more effective due to their reactivity and large surface area. Being a dielectric material, ZrO_2 has a stable tetragonal phase structure in the temperature range of 25-1000 °C. The conductivity of this pure ZrO_2 material is only 10^{-7} s/cm at 1000 °C, which is close to the conductivity of insulating material [19]. The present work is an effort in which ZrO_2 NPs in water-ethanol found that best catalyst solvent combination for the synthesis of 3-methyl-4-[(4-oxo-4*H*-chromen-3-yl)-methylene]-1-phenyl-1*H*-pyrazol-5(4*H*)-ones (**Scheme-I**). To explore the catalytic activity of ZrO_2 NPs in elementary organic transformations are available in literature [20,21]. This is the first time attempt for the synthesis of reported chromene pyarazolone derivatives by multi-component single route. Thus we wish to report, a simple and efficient protocol for the synthesis of chromene pyarazolone derivatives by using ZrO_2 NPs as a heterogeneous catalyst in water-ethanol as solvent (**Scheme-I**).

EXPERIMENTAL

The chemicals with 99.9 % purity playing important role in the present synthesis are ethyl acetoacetate, phenyl hydrazine, chromene and catalyst ZrO_2 NPs were purchased from Sigma-Aldrich. An appropriate molar proportion of starting materials was taken and the protocols of standard techniques were followed for the synthesis of multi-component synthesis of functionalized chromene-pyarazolone derivatives using zirconia nanoparticles. Melting points of synthesized product were recorded on OptiMELT digital melting point apparatus and were uncorrected. The elemental analysis was performed on a Perkin Elmer 2400 series II elemental CHN analyzer. All the products were well characterized and comparison of their reported spectral data [16-18]. Spectral data for the entire synthesized product (**4a-4m**) as depicted in table are shown in supplementary data as a supporting data.

General procedure for the synthesis of compounds (4a-m): A mixture of 4-oxo-4*H*-benzopyran-3-carbaldehydes (**1**) (1 mmol), phenyl hydrazine (**2**) (1 mmol), ethyl acetoacetate (**3**) (1 mmol) and ZrO_2 NPs (10 mol %) in 4 mL ethanol water (4:1) was stirred at 60-70 °C for 5-7 min until the reaction mixture solidified. The progress of the reaction was monitored by TLC. After completion of reaction, the solvent was removed under reduced pressure; crude product was stirred with 4-6 mL methanol at 60-70 °C for 5 min followed by the simple filtration to remove catalyst out by simple filtration. Then methanol was removed under reduced pressure and the solid compound was purified by recrystallization from absolute ethanol to give product with an excellent yield (**4a**) (97 %).

Procedure of reusability of catalyst: The recovered catalyst from the reaction mixture during the synthesis of chromene pyrazolones derivative was then washed with hot methanol (14 mL) followed by hot ethanol (6 mL) and finally dried well and reused for subsequent runs. The catalytic activity of ZrO_2 NPs remains unchanged even after 8th cycles.

X-ray diffraction: The X-ray diffraction (XRD) patterns was characterized by Philips X'Pert Pro monochromatized diffractometer Cu-K_α radiation (λ = 1.54056 Å). By X-ray diffraction pattern (Fig. 1), we observed high intensity peak (103) at assigned at 2θ = 30.5. (112) and (101) reflections are present at 2θ = 51.02 and 59.31 respectively. All the reflections are indexed to the characteristic planes of a major tetragonal phase in ZrO_2 crystal system (t-ZrO_2, space group P21/a, JCPDS card No. 37-1484 and 88-1007) no extra peak was observed corresponding to monoclinic plane. A clear broad peak in powder X-ray diffraction confirmed the formation of nano-sized particles of ZrO_2. The crystallite sizes was estimated from the Debye–Scherrer equation $D = 0.9\lambda/\beta\cos\theta$; where λ is the wavelength of Cu-K_α radiation (1.54056 Å) and β is the full width of the (h k l) peak at the diffracting angle 2θ. The mean crystallite size was estimated between 20 and 30 nm.

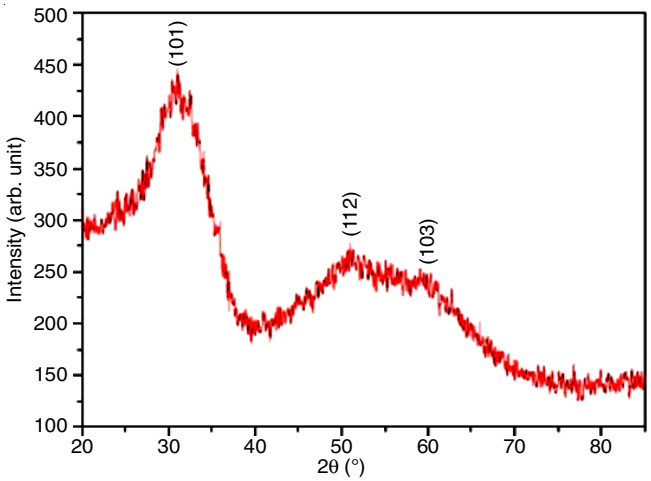
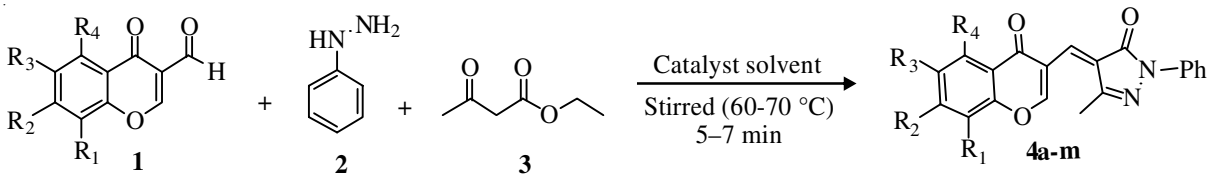


Fig. 1. Powder XRD of ZrO_2 NPs after 8th cycle

UV-visible spectroscopy: In Fig. 2 the UV-visible spectra of pure ZrO_2 NPs and ZrO_2 NPs after 8th cycle were recorded on Scinco UV-visible scanning spectrometer (ModelS-4100) with the wavelength λ = about 260 nm (Fig. 2). UV near-band edge (NBE) emission of ZrO_2 were observed at range between 458-465 nm which was equivalent to band gap of 4.76 eV. The electronic band structure of ZrO_2 is strongly influenced by the hybridization of Zr-4*d* orbital and O-2*p* orbital [22]. The interaction of chromene-pyarazolone derivatives with



Scheme-I: Synthesis of 3-methyl-4-[(4-oxo-4H-chromen-3-yl)-methylene]-1-phenyl-1H-pyrazol-5(4H)-ones

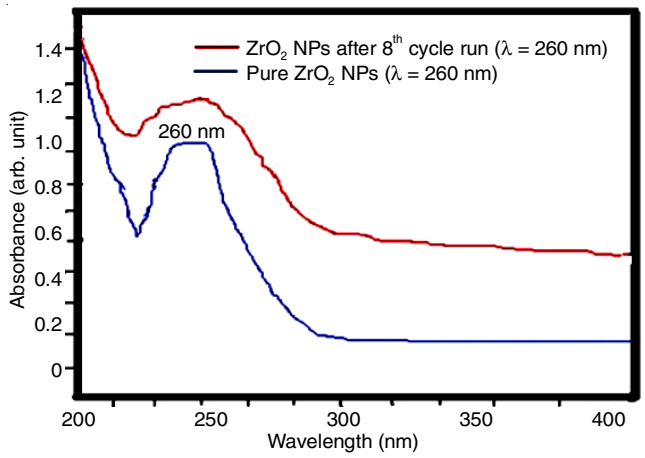


Fig. 2. UV-Visible spectra of pure ZrO_2 NPs and after 8th cycle

ZrO_2 NPs has noticeable effect in its band structure as revealed by UV-visible spectroscopy.

FT-IR: Fourier transform infrared spectra were recorded on a Perkin-Elmer FT Spectrophotometer in KBr disc (Fig. 3). The distinctive band around 3375.1 cm^{-1} can be seen which indicated the transmittance due to O–H absorptions. 944.1 cm^{-1} and a broad band near 1645.4 cm^{-1} which are associated with the O–H modes of chemisorbed water and/or terminated hydroxides at the surface. The intense absorbance band in FT-IR spectrum were observed in range between 496-490 cm^{-1} and 450-445 cm^{-1} which were attributed to the Zr-O stretching vibrations.

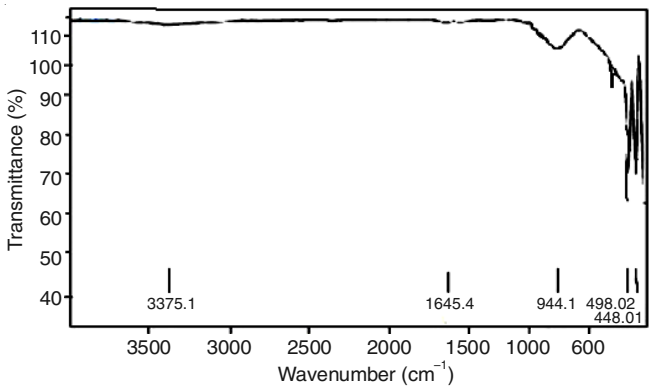


Fig. 3. FT-IR spectra of pure ZrO_2 NPs

^{1}H NMR: The nuclear magnetic resonance spectroscopy of crystalline phases is a powerful alternative technique for materials characterization that probes the atomic structure, complementing diffraction analysis and microscopy methods. The structures of the crystalline phases present in monoclinic and tetragonal ZrO_2 compounds were deduced from their ^{1}H NMR spectra recorded on Varian 300 MHz spectrophotometer in $CDCl_3$.

Spectral characterization data of compound 4a-m:

3-Methyl-4-[(5,8-dichloro-4-oxo-4H-chromen-3-yl)-methylene]-1-phenyl-1H-pyrazol-5(4H)-one (4a): Light red crystals. Yield: 97 %. m.p.: 291-293 °C. IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 697 (C-Cl); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH).7.18-7.98 (m, 5H; aromatic), 7.1 (d,1H; aromatic O-substituted -Cl), 7.5 (d,1H; aromatic O-substituted -Cl), ES-MS *m/z* (%): 241.95 M^{+1}. Anal. calcd. (%) for $C_{20}H_{12}N_2O_3Cl_2$; C, 60.70; H, 3.03; N, 7.02. Found: C, 60.63; H, 3.13; N, 6.98.

3-Methyl-4-[(6-methyl-4-oxo-4H-chromen-3-yl)-methylene]-1-phenyl-1H-pyrazol-5(4H)-one (4b): Orange red crystals. Yield: 84 %; m.p.: 239-241 °C. IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar- H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, ^{1}H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH), 7.18-7.98 (m, 5H; aromatic), 7.6 (d, 1H; aromatic), 7.65 (d, 1H; aromatic), 7.4 (s, 1H; aromatic), 2.3 (s, 3H; H_3C-Ar), ES-MS *m/z* (%): 344.11 M^{+1}. Anal. calcd. (%) for $C_{21}H_{16}N_2O_3$; C, 73.24; H, 4.68; N, 8.13. Found: C, 73.17; H, 4.73; N, 8.03.

4-[(6-Bromo-4-oxo-4H-chromen-3-yl)methylene]-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (4c): Red crystals; Yield: 90 %; m.p.: 234-235 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar- H), 1795 (C=O pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 759 (C-Cl); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH), 7.18-7.98 (m, 5H; aromatic), 7.1 (d, 1H; aromatic), 7.7 (d, 1H; aromatic O-substituted -Br), 7.9 (s, 1H; aromatic O-substituted -Br), MS (EI): *m/z* (%): 408.01 M^{+1}. Anal. calcd. (%) for $C_{20}H_{13}N_2O_3Br$; C, 58.70; H, 3.20; N, 6.85. Found: C, 58.62; H, 3.27; N, 6.77

4-[(6-Chloro-7-methyl-4-oxo-4H-chromen-3-yl)-methylene]-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (4d): Red crystals; Yield: 95 %; m.p.: 252-254 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 687 (O-substituted methyl and –Cl group). 2885 (aliphatic C-H str.); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH), 7.18-7.98 (m, 5H; aromatic), 7.10 (s, 1H; aromatic), 7.52 (s, 1H; aromatic O-substituted -Cl), 2.3 (s, 3H; C_3H-Ar), MS (EI): *m/z* (%): 378.07 M^{+1}. Anal. calcd. (%) for $C_{21}H_{15}N_2O_3Cl$; C, 66.58; H, 3.99; N, 7.40. Found: C, 66.51; H, 4.03; N, 7.31.

4-[(6,7-Dichloro-4-oxo-4H-chromen-3-yl)methylene]-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (4e): Orange red crystals; Yield: 94 %; m.p.: 267-269 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 697 (o-substituted –Cl group); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH).7.18-7.98 (m, 5H; aromatic), 7.3 (s, 1H; aromatic O-substituted -Cl), 7.5 (s, 1H; aromatic O-substituted -Cl), MS (EI): *m/z* (%): 398.02M^{+1}. Anal. calcd. (%) for $C_{20}H_{22}N_2O_3Cl_2$; C, 60.17; H, 3.03; N, 7.02. Found: C, 60.01; H, 3.11; N, 6.98.

3-Methyl-4-[(6,7-dimethyl-4-oxo-4H-chromen-3-yl)methylene]-1-phenyl-1H-pyrazol-5(4H)-one (4f): Orange red crystals; Yield: 81 %; m.p.: 249-251 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 697

(o-substituted –Cl group); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH).7.18-7.98 (m, 5H; aromatic), 7.0 (s, 1H; aromatic), 7.3 (s, 1H; aromatic), 2.3 (s, 3H; H_3C-Ar), 2.3 (s, 3H; HC_3-Ar), MS (EI): *m/z* (%): 358.13M^{+1}. Anal. calcd. (%) for $C_{22}H_{18}N_2O_3$; C, 73.73; H, 5.06; N, 7.82. Found: C, 73.68; H, 5.13; N, 7.76.

3-Methyl-4-[(8-chloro-4-oxo-4H-chromen-3-yl)-methylene]-1-phenyl-1H-pyrazol-5(4H)-one (4g): Orange red crystals; Yield: 89 %; Orange red crystals; m.p.: 219-221 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 697 (o-substituted –Cl group); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH).7.18-7.98 (m, 5H; aromatic), 7.6 (d, 1H; aromatic O-substituted -Cl), 7.2 (d, 1H; aromatic), 7.9 (m, 1H; aromatic), MS (EI): *m/z* (%):364.06 M^{+1}. Anal. calcd. (%) for $C_{20}H_{13}N_2O_3Cl$; C, 65.85; H, 3.59; N, 7.68.Found: C, 65.79; H, 3.66; N, 7.62.

3-Methyl-4-[(6-chloro-4-oxo-4H-chromen-3-yl)-methylene]-1-phenyl-1H-pyrazol-5(4H)-one (4h): Orange red crystals; Yield: 89 %; m.p.: 235-237 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 697 (o-substituted –Cl group); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH).7.18-7.98 (m, 5H; aromatic), 8.0 (s, 1H; aromatic O-substituted -Cl), 7.8 (d, 1H; aromatic O-substituted -Cl), 7.6 (d, 1H; aromatic), MS (EI): *m/z* (%): 364.06M^{+1}. Anal. calcd. (%) for $C_{20}H_{13}N_2O_3Cl$; C, 65.85; H, 3.59; N, 7.68. Found: C, 65.79; H, 3.65; N, 7.61.

3-Methyl-4-[(6,8-dichloro-4-oxo-4H-chromen-3-yl)methylene]-1-phenyl-1H-pyrazol-5(4H)-one (4i): Orange red crystals; Yield: 92 %; m.p.: 292-293 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 697 (o-substituted –Cl group); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH).7.18-7.98 (m, 5H; aromatic), 7.8 (s, 1H; aromatic O-substituted -Cl), 7.9 (s, 1H; aromatic O-substituted -Cl), MS (EI): *m/z* (%): 398.02M^{+1}. Anal. calcd. (%) for $C_{20}H_{12}N_2O_3Cl_2$; C, 60.17; H, 3.03.N, 7.02. Found: C, 60. 06; H, 3.12; N, 6.98.

3-Methyl-4-[(7-methyl-4-oxo-4H-chromen-3-yl)-methylene]-1-phenyl-1H-pyrazol-5(4H)-one (4j): Orange red crystals; Yield: 84 %; m.p.: 198-201 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 697 (o-substituted –Cl group); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH).7.18-7.98 (m, 5H; aromatic), 7.1 (s, 1H; aromatic), 6.9 (d, 1H; aromatic), 7.6 (d, 1H; aromatic), 2.3 (s, 3H; CH_3-Ar), MS (EI): *m/z* (%): 344.11M^{+1}. Anal. calcd. (%) for $C_{21}H_{16}N_2O_3$; C, 73.24; H, 4.68; N, 8.13. Found: C, 73.17; H, 4.73; N, 8.07.

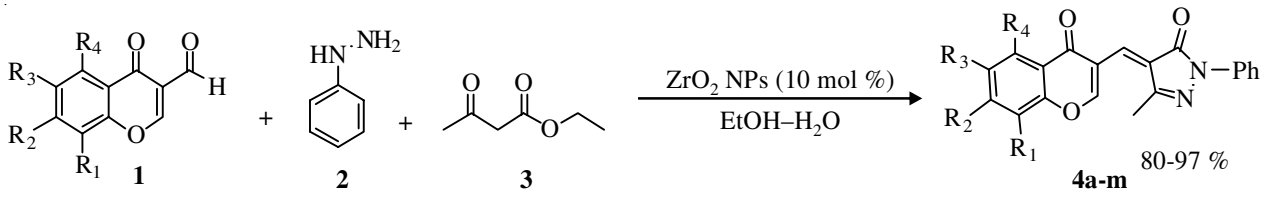
3-Methyl-4-[(5,7-dimethyl-4-oxo-4H-chromen-3-yl)-methylene]-1-phenyl-1H-pyrazol-5(4H)-one (4k): Orange red crystals; Yield: 80 %; m.p.: 214-215 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 697 (o-substituted –Cl group); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH).7.18-7.98 (m, 5H; aromatic), 6.8 (s, 1H; aromatic), 2.3 (s, 3H; CH_3-Ar), 2.4 (s, 3H; CH_3-Ar), MS (EI): *m/z* (%): 358.13 M^{+1}. Anal. calcd. (%) for $C_{22}H_{18}N_2O_3$; C, 73.73; H, 5.06; N, 7.82. Found: C, 73.67; H, 5.13; N, 7.75.

3-Methyl-4-[(6,8-dimethyl-4-oxo-4H-chromen-3-yl)-methylene]-1-phenyl-1H-pyrazol-5(4H)-one (4l): Orange red crystals; Yield: 82 %; m.p.: 280-283 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 697 (o-substituted –Cl group); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH).7.18-7.98 (m, 5H; aromatic), 7.2 (s, 1H; aromatic), 7.1 (s, 1H; aromatic), 2.1 (s, 3H; CH_3-Ar), 2.3 (s, 3H; CH_3-Ar), MS (EI): *m/z* (%): 358.13M^{+1}. Anal. calcd. (%) for $C_{22}H_{18}N_2O_3$; C, 73.73; H, 5.06; N, 7.82. Found: C, 73.65; H, 5.14; N, 7.76.

3-Methyl-4-[(4-oxo-4H-chromen-3-yl) methylene]-1-phenyl-1H-pyrazol-5(4H)-one (4m): Orange red crystals; Yield: 86 %; m.p.: 229-231 °C; IR (KBr, ν_{max}, cm^{-1}): 3065 (=C-H, Ar-H), 1795 (C=O, pyrazolinyl), 1689 (C=N, pyrazolinyl), 1665 (C=O, chromone), 1463 (γ-pyrone), 697 (o-substituted –Cl group); ^{1}H NMR (300 Mz, $CDCl_3$): δ = 2.3 (s, 3H, –CH_3; pyrazolinyl), 6.7 (s, 1H, -CH-O; chromone moiety), 7.4 (s, 1H, -CH=CH).7.18-7.98 (m, 5H; aromatic), 7.45-8.10 (m, 4H; aromatic), MS (EI): *m/z* (%): 330.1M^{+1}. Anal. calcd. (%) for $C_{20}H_{14}N_2O_3$; C, 72.72; H, 4.27; N, 8.48. Found: C, 72.63; H, 4.33; N, 8.37.

RESULTS AND DISCUSSION

Keeping focus on multicomponent green approach, we choose ZrO_2 NPs for the optimization reaction condition with various solvent (Table-1). In ethanol, good yield of product was obtained (Table-1, entry 9), on this result, if we used water in ethanol as the ethanol-water (4:1) an excellent yield was obtained in 10 mol % ZrO_2 NPs within 5 min (Table-1, entry 12).While, increasing or decreasing amount of ethanol in a set of water, the yield of product was reduced (Table-1, entries 10, 11, 14, 15) in different proportion of catalyst. This is due to the surface area of the NPs being more active in polar-protic solvents and presence of oxygen vacancies, which are responsible for stability and higher surface activity [23]. Further we focus on significant effect of time and amount of catalyst on yield of reaction, the yield of product was fall down by decreasing time of reaction, while no significant change was observed by increasing the time of reaction (Table-1, entry 12). Further we changed amount of catalyst, less than 10 mol % or greater than 10 mole % no significant yield was obtained (Table-1, entries 11, 13). The yield of product was decreases while decreasing amount of ethanol in ethanol-water solvent (Table-1, entries13-15). Thus, all examples were tested reasonably well to the excellent yields in ethanol water (4:1) with 10 mol % of catalyst (Table-2) (**Scheme-II**). The catalyst



Scheme-II: Yields in ethanol water (4:1) with 10 mol % of catalyst

TABLE-1
SCREENING OF CATALYST WITH SOLVENTS, REACTION TIME AND YIELD FOR THE SYNTHESIS OF COMPOUND **4a**

Entry	Catalyst (10 mol %)	Solvent	Time (min)	Yield (%)[a]
1	Without	Solvent free	120	00
2	ZrO_2 NPs	Solvent free	60	30
3	ZrO_2 NPs	H_2O	40	58
4	ZrO_2 NPs	CH_3CN	30	50
5	ZrO_2 NPs	DCM	30	40
6	ZrO_2 NPs	DMF	30	48
7	ZrO_2 NPs	THF	30	40
8	ZrO_2 NPs	MeOH	12	60
9	ZrO_2 NPs	EtOH	7	73
10	ZrO_2 NPs	EtOH:H_2O (6:1)	7	78
11	ZrO_2 NPs (5 mol %)	EtOH:H_2O (4:1)	10	76
12	ZrO_2 NPs	EtOH:H_2O (4:1)	3, 5, 7	60, 97, 97
13	ZrO_2 NPs (15 mol %)	EtOH:H_2O (4:1)	7	96
14	ZrO_2 NPs	EtOH:H_2O (2:1)	10	68
15	ZrO_2 NPs	EtOH:H_2O (1:1)	10	56

[a]Isolated yield; Reaction conditions: Substituted 4-oxo-4H-benzopyran-3-carbaldehydes (4-oxo-4H-chromene-3-carbaldehyde) 1 (1 mmol), phenyl hydrazine 2 (1 mmol), ethyl acetoacetate 3 (1 mmol) and ZrO_2 NPs (10 mol %) in ethanol-water (4-1) was stirred at room temperature and reflux.

TABLE-2
ZrO_2 NPs CATALYZED SYNTHESIS OF CHROMENE-PYARAZOLONE DERIVATIVES

Product	R_1	R_2	R_3	R_4	Time (min)	Yield (%)[a]	m.p. (°C)
4a	Cl	H	H	Cl	5	97	291-293
4b	H	H	CH_3	H	7	84	239-241
4c	H	H	Br	H	7	90	234-235
4d	H	CH_3	Cl	H	7	95	252-254
4e	H	Cl	Cl	H	5	94	267-269
4f	H	CH_3	CH_3	H	7	81	249-251
4g	Cl	H	H	H	7	89	219-221
4h	H	H	Cl	H	7	89	235-237
4i	Cl	H	Cl	H	5	92	292-293
4j	H	CH_3	H	H	7	84	198-201
4k	H	CH_3	H	CH_3	7	80	214-215
4l	CH_3	H	CH_3	H	7	82	280-283
4m	H	H	H	H	7	88	229-231

[a]Isolated yield; Reaction conditions: All the reaction was carried out in equimolar amounts of each compound in 4 mL of water-ethanol, stirred at 60-70 °C.

was investigated by checking its reusability, after each cycle, the ZrO_2 NPs were recovered by centrifugation, washed with hot methanol, dried and reused for successive reactions. First four cycles gave better yield and then gradually decreases (Fig. 4) and which is characterized before used in the reaction by X-ray diffraction, UV-Visible and FT-IR spectroscopy. The important feature for these catalysts is; surface of catalyst

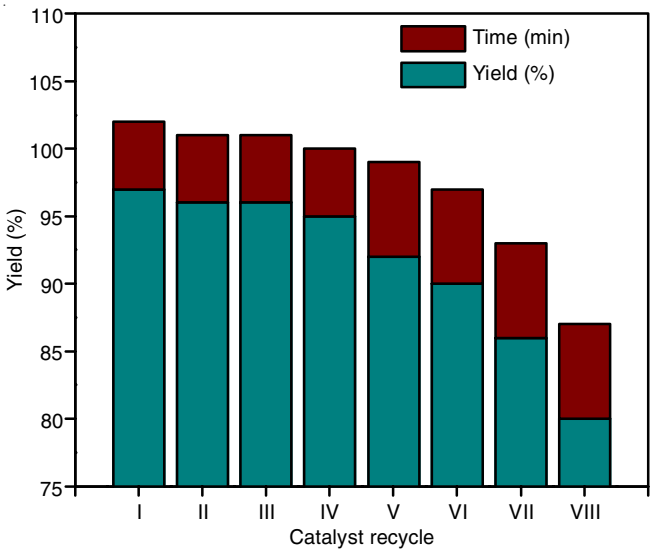
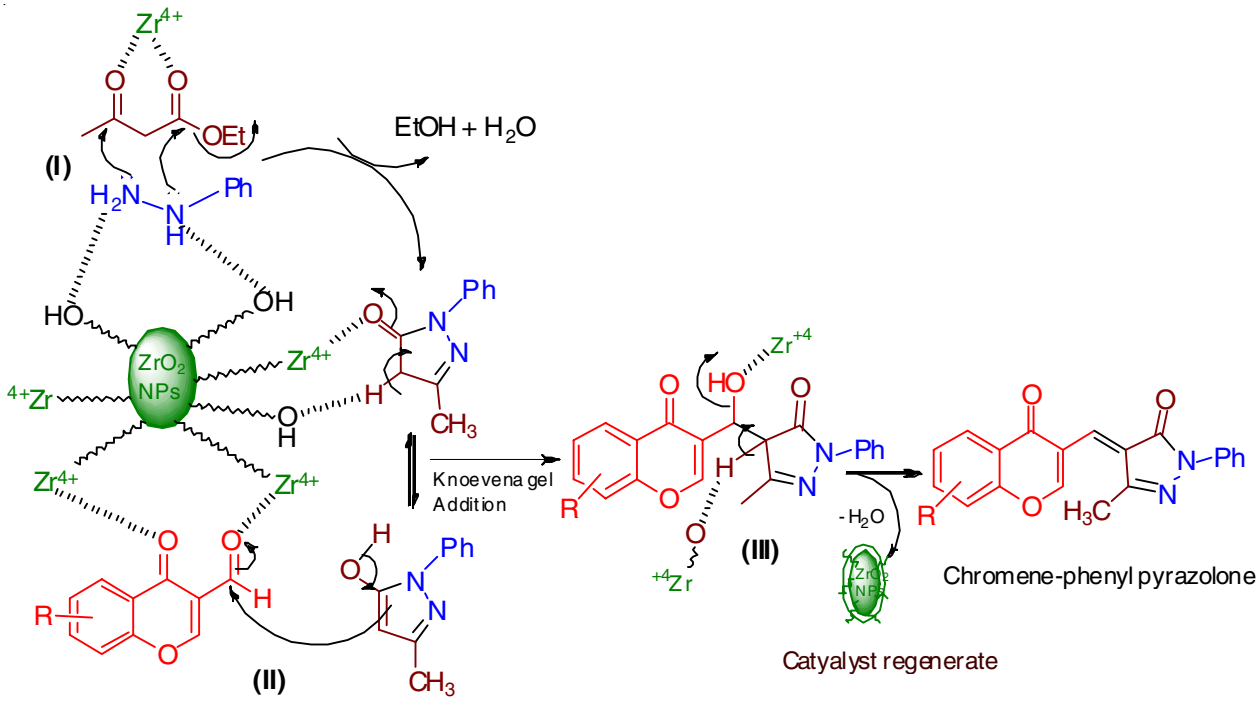


Fig. 4. Reusability of ZrO_2 NPs for the synthesis of chromene-pyarazolones as a model reaction

contains active hydroxyl, oxide groups and Zr^{4+} act as Lewis acids which are well reported [24]. The active hydroxide and oxide of nanoparticles plays an important role for cyclization and condensation reaction because of act as both function acid as well as base [25] showing with possible mechanism for the synthesis of chromene-pyrazolones has been described *via* Knoevenagel addition reaction using ZrO_2 NPs as catalyst (**Scheme-III**). Finally the structures of the compounds **4** were confirmed by spectral data. For example, in the IR spectrum, it gave a peak at 1795 cm^{-1} due to (C=O) and 1689 cm^{-1} due to (C=N) of pyrazolinyl moiety. The ^1H NMR spectrum of compound gave two singlet at 7.4 δ (s, 1H, -CH=C-) and 6.7 δ (s, 1H, -HC-O-) due to chromone moiety and one singlet at 2.3δ (s, 3H, $-CH_3$). The mechanistic path: cyclization and condensation between chromene carbaldehyde, hydrazine and ethyl acetoacetate were shown in **Scheme-III**.

Conclusion

In the present investigation, chromene-pyarazolone derivatives were successfully synthesized by simple stirring condition using ZrO_2 NPs catalyst *via* multi-component reaction in water ethanol. With the (103), (112) and (101) reflections, XRD pattern confirmed the formation of nano-sized tetragonal ZrO_2 NPs with no extra peak corresponding to monoclinic plane. FT-IR spectra was analyzed for the O–H modes and Zr–O stretching vibrations in pure ZrO_2 NPs. UV-visible spectra of ZrO_2 NPs reveal a band gap value of 4.76 eV. Results revealed that the catalytic activity of ZrO_2 NPs first 4th cycles was considered to be very good. In summary, it can be concluded that the ZrO_2 NPs and water-ethanol used to the preparation of chromene-phenyl pyrazolones is an eco-



Scheme-III: Possible mechanism of chromene-pyrazolone derivatives using of ZrO_2 NPs

friendly, readily available solvent and inexpensive. It was found that the reactions afforded very good yields under simple stirred conditions.

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