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ARTICLE

# KF/clinoptilolite nanoparticles as a novel catalyst for the green synthesis of chromens using three component reactions of 4-hydroxycoumarins: Study of antioxidant activity

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In this research, the green synthesis of chromen derivatives in good yields is described via three-component reactions of 4-hydroxycumarine, aldehydes or ketones, and methyl ketones in the presence of KF/clinoptilolite nanoparticles (KF/CP-NPs) under solvent-free conditions at 50°C in low time. The present methodology suggests some advantages such as low reaction time, easy and simple procedure, green method, inexpensive catalyst, high yield of product, and existence of different substrates for performing these reactions. In addition, it should be mentioned that antioxidant activity was studied for some prepared compounds, such as **4a–4d,** by DPPH radical trapping and reducing potential tests of ferric ion and then comparing results with TBHQ and BHT as synthetic antioxidants. In this study, compounds **4c** was shown to have moderate DPPH radical trapping, and compounds **4b** and **4d** displayed good reducing power of ferric ion.

KEYWORDS

aldehyde, chromenes, DPPH radical trapping, ferric ion, ketones, KF/clinoptilolite nanoparticles

## 1 | INTRODUCTION

Multicomponent reactions are very significant in organic synthesis because of the creation of carbon–carbon and carbon–hetero atom bonds in one pot.[1–3] Some advantages of these reactions include easy and clean procedures, producing of high yield bond formation, consuming of low time and energy, and low costs.[4] In the past few years, chemists have been informed about the environmental conditions and about performing the reaction in green conditions. Therefore, they have attempted to develop new synthetic procedures, reaction conditions, and materials that decrease the dangers to persons and the environment. Organic solvents are hazardous because they are frequently volatile liquids and are regularly used. Therefore, in recent years, performing organic reactions under solvent-free conditions is of interest because of high yields, easy separation of product and catalyst, low costs, mild reaction conditions, and low pollution.[5–7] The chemistry of heterocyclic compounds has been studied in several fields, such as natural products, biologically active agrochemicals, pharmaceutical agents, and organic materials.[8] Chromenes are important heterocycles with a broad range of biological activities,[9–14] such as anticancer, anti-inflammatory, antimicrobial, and antihyperglycemic activities, along with the properties of antineurodegenerative disorders such as Alzheimer's, Parkinson disease, and many more.[15–20] Pyrano[3,2-c]chromen-5(4*H*)-ones are the promising class of oxygen-containing heterocyclic compounds that have a diversity of biologically active products and have been shown to a broad series of biological activities.[21] Therefore, the synthesis of the pyrano[3,2-c]chromen-5(4*H*)-ones is very important in organic synthesis. Some methods have been developed for the synthesis of pyrano[3,2- c]chromen-5(4*H*)-ones.[22]

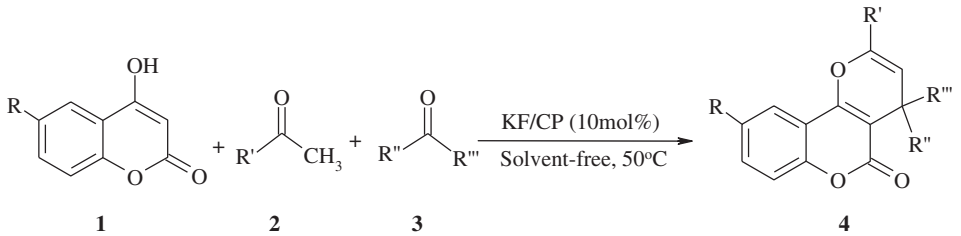
However, these methods have problems such as relatively long reaction time, difficult reaction conditions, high reaction temperature, using toxic catalysts, and an organic solvent. As a result, a new and efficient, environmentally benign practical procedure and operational simplicity method should be used for the synthesis of pyrano[3,2-c] chromen-5(4*H*)-ones. Compounds, mainly because of their redox properties and chemical structure, demonstrate antioxidant activity and have chief roles as middle metals chelators, filling singlet and triplet oxygen molecules, besides the negative effect of free radicals. Many of diseases such as cardiovascular, inflammatory bowel syndrome, cancer, aging, atherosclerosis, and Alzheimer's disease could be prevented or decreased by employing of these compounds.[23–27] Recently, medicinal chemists, food chemists, and biologists have investigated and tested the new and efficient procedure for the synthesis of antioxidant compounds as a protecting tactic against these diseases.

KF/CP, which is used as a new natural and economical solid base, has been synthesized from putting potassium fluoride on clinoptilolite as a new natural and inexpensive solid base system.[28–36] Clinoptilolite is a natural zeolite with a high internal surface area. It is precious because of its high replacing capability of cations, mainly for $K^+$. Therefore, more free fluoride anions act as a good base. In contrast, the preparation of clinoptilolite (KF/CP) is very easy without the need for any preactivation.[23–25] Here, we report a facile catalyst and green one-pot synthesis of pyrano[3,2-c] chromen-5(4*H*)-ones via three-component reaction of 4-hydroxycumarine, aldehydes or ketones, and methyl ketones under solvent-free conditions at 50°C (Table 1).

## 2 | RESULTS AND DISCUSSION

The first step in these reactions is optimization of the reaction conditions. For this reason, we selected the reaction between 4-hydroxycumarine **1**, acetophenone **2a,** and benzaldehyde **3a** as a model. To achieve the best conditions for generating chromen derivatives **4a**, we changed the solvent, catalyst, amount of catalyst, and temperature until the best outcome is achieved. The reaction was tested without a catalyst and demonstrated that these reactions have a very low yield without catalyst. Several catalysts, for example, CM-ZnO, CuO-NPs, KF/CP-NPs, ZnO-NPs, and $TiO_2$-NPs, were tested to achieve the best catalyst (Table 2). In addition, some solvents, such as $CH_2Cl_2$, $CH_3CN$, $H_2O$, and toluene, and solvent-free conditions were examined to select the best solvent for these reactions. Different temperatures were tested for the model reaction, and the results are shown in the Table 2.

**TABLE 1** Synthesis of pyrano[3,2-c]chromen-5(4*H*)-ones derivatives




**1** **2** **3** **4**

| Entry | R | R′ | R″ | R‴ | Product (4) | Time (min) | Yield[a] (%) |
|---|---|---|---|---|---|---|---|
| **1** | H | Ph | Ph | H | **4a** | 25 | 90 |
| **2** | H | Ph | 4-me-$C_6H_4$ | H | **4b** | 20 | 87 |
| **3** | H | Ph | 3,4-$OCH_2OC_6H_3$ | H | **4c** | 20 | 95 |
| **4** | H | Ph | 4-$NO_2$-$C_6H_4$ | H | **4d** | 15 | 92 |
| **5** | H | 4-MeO-$C_6H_4$ | Ph | H | **4e** | 20 | 70 |
| **6** | H | 4-Br-$C_6H_4$ | Ph | H | **4f** | 15 | 75 |
| **7** | H | 4-cl-$C_6H_4$ | 4-cl-$C_6H_4$ | H | **4 g** | 15 | 98 |
| **8** | H | 4-me-$C_6H_4$ | 4-cl-$C_6H_4$ | H | **4 h** | 25 | 95 |
| **9** | H | Ph | Ph | Me | **4i** | 30 | 85 |
| **10** | H | Me | Ph | H | **4j** | 10 | 90 |
| **11** | Me | Ph | Ph | H | **4 k** | 25 | 95 |
| **12** | Me | Ph | 4-me-$C_6H_4$ | H | **4 L** | 20 | 90 |
| **13** | H | 4-Br-$C_6H_4$ | 3-MeO-$C_6H_4$ | H | **4 m** | 18 | 87 |
| **14** | H | 4-Br-$C_6H_4$ | 4-EtO-$C_6H_4$ | H | **4n** | 18 | 90 |
| **15** | H | Et | Ph | Me | **4o** | 15 | 70 |
| **16** | H | $^t$Bu | 4-MeO-$C_6H_4$ | H | **4p** | 35 | 78 |

[a]Isolated yields

**TABLE 2** Effect of solvent, catalyst, and temperature on the formation of Compound **4a**

| Entry | Catalyst | Solvent | Temp. | Yield (%) |
|---|---|---|---|---|
| 1 | ----- | $CH_2Cl_2$ | r.t. | 5 |
| 2 | ----- | $H_2O$ | r.t. | ----- |
| 3 | ----- | $H_2O$ | 50 | ----- |
| 4 | ----- | $H_2O$ | 80 | ----- |
| 5 | ----- | $CH_3CN$ | r.t. | ----- |
| 6 | ----- | $CH_3CN$ | 50 | 10 |
| 7 | ----- | Toluene | r.t. | 10 |
| 8 | ----- | Toluene | 50 | ----- |
| 9 | ----- | Toluene | 90 | 15 |
| 10 | | Solvent-free | r.t. | ---- |
| **11** | | **Solvent-free** | **50** | **10** |
| 12 | | Solvent-free | 90 | 10 |
| 13 | KF/CP (NPs) | $CH_2Cl_2$ | r.t. | 45 |
| 14 | KF/CP (NPs) | $H_2O$ | r.t. | 68 |
| 15 | KF/CP (NPs) | $H_2O$ | 50 | 75 |
| 16 | KF/CP (NPs) | $CH_3CN$ | r.t. | 65 |
| 17 | KF/CP (NPs) | $CH_3CN$ | 50 | 78 |
| 18 | KF/CP (NPs) | $CH_3CN$ | 80 | 80 |
| 19 | KF/CP (NPs) | Toluene | r.t. | 56 |
| 20 | KF/CP (NPs) | Toluene | 50 | 68 |
| 21 | KF/CP (NPs) | Toluene | 80 | 70 |
| 22 | KF/CP (NPs) | Solvent-free | r.t. | 80 |
| **23** | **KF/CP (NPs)** | **Solvent-free** | **50** | **90** |
| 24 | KF/CP (NPs) | Solvent-free | 80 | 92 |
| 25 | ZnO-NPs | $H_2O$ | r.t. | 35 |
| 26 | ZnO-NPs | $H_2O$ | 50 | 47 |
| 27 | ZnO-NPs | $CH_3CN$ | 50 | 65 |
| 28 | ZnO-NPs | Solvent-free | r.t. | 58 |
| **29** | **ZnO-NPs** | **Solvent-free** | **50** | **75** |
| 30 | ZnO-NPs | Solvent-free | 80 | 78 |
| 31 | $TiO_2$-NPs | $CH_2Cl_2$ | r.t. | 40 |
| 32 | $TiO_2$-NPs | $H_2O$ | 50 | 75 |
| 33 | $TiO_2$-NPs | Toluene | 50 | 68 |
| 34 | $TiO_2$-NPs | $CH_3CN$ | 50 | 75 |
| **35** | **$TiO_2$-NPs** | **Solvent-free** | **50** | **80** |
| 36 | $TiO_2$-NPs | Solvent-free | 80 | 80 |
| 37 | $Fe_3O_4$-MNPs | $H_2O$ | 50 | 65 |
| 38 | $Fe_3O_4$-MNPs | $CH_3CN$ | 50 | 78 |
| 39 | $Fe_3O_4$-MNPs | Toluene | 50 | 75 |
| **40** | **$Fe_3O_4$-MNPs** | **Solvent-free** | **50** | **82** |
| **41** | $Fe_3O_4$-MNPs | Solvent-free | 80 | 85 |
| 42 | CuO-NPs | $H_2O$ | 50 | 30 |
| 43 | CuO-NPs | $CH_3CN$ | 50 | 48 |
| 44 | CuO-NPs | Toluene | 50 | 65 |
| **45** | **CuO-NPs** | **Solvent-free** | **50** | **70** |
| 46 | CuO-NPs | Solvent-free | 80 | 70 |

As shown in the Table 2, in the solvent-free conditions, products have high yield than other solvents. For the $CH_3CN$ and toluene, products have similar yield to solvent-free conditions, but both solvents are organic and toxic. Of the

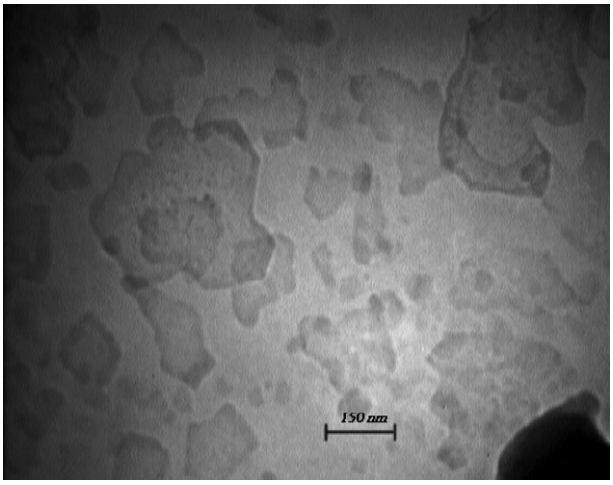



**FIGURE 1** SEM image of KF/CP NPs[37]

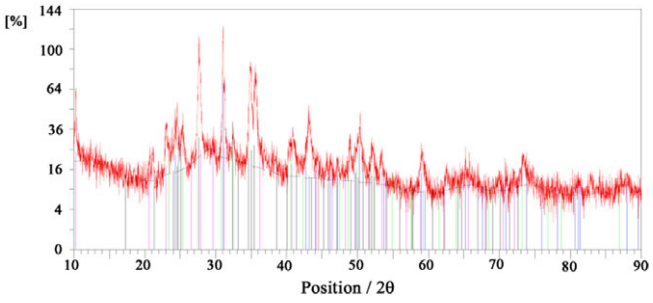



**FIGURE 2** XRD spectra of KF/CP NPs[37]

catalysts, KF/CP NPs is the best catalyst for these reactions. KF/CP-NPs are a basic catalyst that can be prepared very easily according to the reported article.[37] The morphology of synthesized KF/CP-NPs was assessed by scanning electron microscopy images (SEM) as seen in Figure 1.

X-ray diffraction patterns (XRD) were used to calculate the size of prepared KF/CP-NPs (Figure 2). The average crystallite size (D) for KF/CP-NPs was calculated based on the peak with the strongest intensity using Debye–Scherrer's equation ($D = K\lambda/\beta cos\theta$), where $D$ is the grain size, β is full width at half-maximum or half width (FWHM) in radians, $h$ is the position of the maximum of diffraction peak, $K$ is the so-called shape factor (0.89), θ is Bragg's diffraction angle, and λ is the X-ray wavelength used (1.5406 A° for $CuK_\alpha$). Particle size of KF/CP has been found to be 41 nm.

The amount of catalyst is changed from 10 to 25%. When the amount of catalyst is increased from 10 to 25%, the yield of the reaction did not show any considerable increase. Consequently, 10% (w/w) of KF/CP-NPs was selected as the optimum amount. According to results, the optimum conditions for the formation of compound **4a** are 10 mol% KF/CP-NPs as a catalyst, 50°C temperature, and solvent-free conditions. These conditions are tested for other reactions that are shown in Table 1.

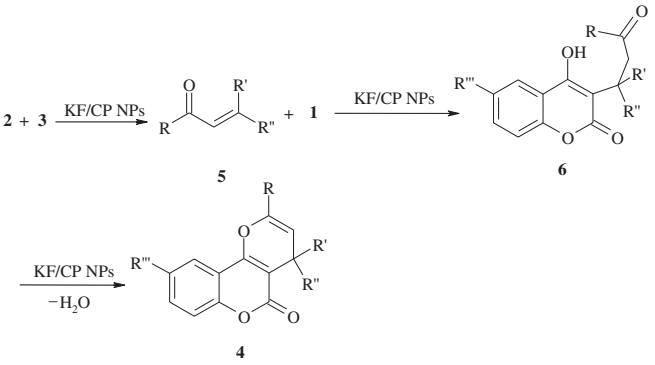
Reusability is one of the significant properties of this catalyst. After the reaction was complete, ethyl acetate is poured in the mixture of reactions, and the catalyst is

**TABLE 3** Reuse of KF/CP-NPs for the synthesis of **4a**

| | Cycle | | | | |
|---|---|---|---|---|---|
| | **1** | **2** | **3** | **4** | **5** |
| Yield (%) | 90 | 90 | 90 | 87 | 87 |

separated by filtration. The catalyst is then washed with ethyl acetate, air-dried, and used directly under the same conditions without further purification. It was shown that the catalyst could be used for five runs without a considerable decrease in the yield of product and its catalytic activity (Table 3).

The structures of compounds **4a–p** were confirmed by $^{1}$H NMR, $^{13}$C NMR, mass, and IR spectra, which are in agreement with the proposed structures. For example, the $^{1}$H NMR spectrum of 4e showed one singlet for methoxy protons at δ = 3.87 ppm and two doublet at 4.72 and 5.75 ppm for methine proton, along with signals at 6.95–8.03 ppm for aromatic moiety. In addition, one signal at δ = 162.3 ppm was observed in the $^{13}$C NMR spectrum of **4e**, which was attributed to the carbonyl group. A proposed mechanism for the creation of compound **4** is showed in Scheme 1. It is conceivable that the reaction starts with the formation of hydrogen bonding between the fluoride ion of KF/CP-NPs as a basic catalyst and the proton of compound **1** and condensation with compounds **2**, giving rise to the intermediate **5**. Intermediate **5** in the presence of KF/CP-NPs reacts with compound **3** to produce intermediate **6** that undergoes cyclization to generate chromene derivatives **4**.




**SCHEME 1** Green synthetic of pyrimido [2,1-*a*] isoquinolines

## 2.1 | Antioxidant evaluations

### 2.1.1 | DPPH radical trapping activity

The DPPH radical trapping test is usually utilized to measure the power of compounds to trap free radicals and their activity as an antioxidant in foods and biological systems.[38–40] In this analysis, antioxidants, by giving hydrogen or an electron to the DPPH radical, generate the nonradical form of DPPH that reduces the absorbance of DPPH at 517 nm.[38,41] Figure 3 shows the DPPH trapping activity of **4a-4d** from 200 to 1,000 ppm concentrations compared to synthetic antioxidants (BHT and TBHQ). The results demonstrated that structure and concentration were effective factors for the DPPH scavenging activity ($p < 0.05$) (Figure 3). In general, the power of free radical trapping activity of 4a-4d was attained TBHQ>BHT > 4c > 4b > 4a > 4d, respectively that weak than to BHT and TBHQ. In all samples, free radical trapping activity was enhanced by increasing the concentration so that the power of free radical scavenging increased from 200 to 1,000 ppm concentrations. For example, a concentration of 1,000 ppm of **4a** had 12.3% inhibition, while 200 ppm demonstrated 4.2% free radical inhibition.

### 2.1.2 | Ferric ions ($Fe^{3+}$) reducing potential (FRAP)

The reducing power of the prepared compounds was calculated by converting the amount of $Fe^{3+}$/ferricyanide complex to the $Fe^{2+}$/ferrous form at 700 nm.[38] The power of reducing for compounds **4a–4d** compared with synthetic antioxidants (BHT and TBHQ) are shown in Figure 4. If one compound has the bigger reducing power, this means a higher absorbance of the compounds. The reducing activity order of compounds **4a–4d** was as follows: TBHQ>BHT > **4d > 4b > 4c > 4a** (Figure 4). In all compounds, when the concentration was enhanced, the power of ferric ions reducing was increased. Compounds **4d** and **4b** displayed

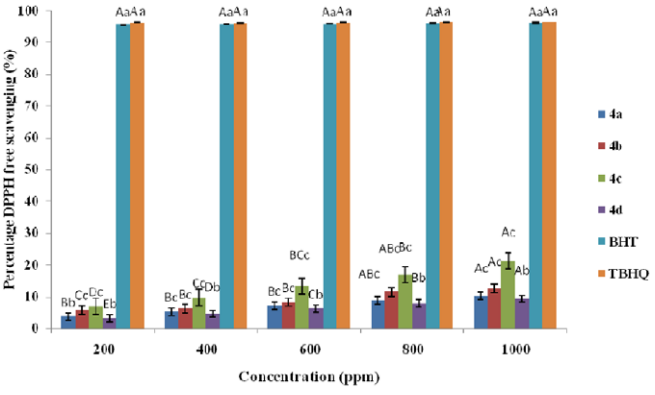



**FIGURE 3** Radical scavenging activity (RSA) of compounds **4a–4d.** Values in the same concentration followed by different letters are significantly different ($p < 0.05$)

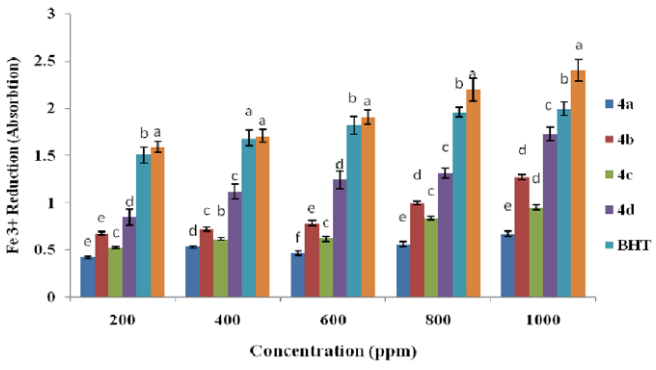



**FIGURE 4** Ferric ions ($Fe^{3+}$) reducing antioxidant power (FRAP) of compounds **4a–4d**. Values in the same concentration followed by different letters are significantly different ($p < 0.05$)

very good reducing activity compared to the standards (BHT and TBHQ). In addition, **4c** and **4a** had medium reducing activity than BHT and TBHQ. The power of these compounds in reducing is an indicator of their electron transfer.

## 3 | CONCLUSION

In conclusion, the main purpose of carrying out this work was to investigate a new method for the synthesis of chromene derivatives via three-component reaction of 4-hydroxycumarine, aldehydes or ketones, and methyl ketones under solvent-free conditions at 50°C. The main advantage of this procedure compared to some previously reported approaches was using environment-friendly synthesized KF/CP nanoparticles. The method offers other advantages, including high yields of products and easy experimental work-up procedure. In this research, antioxidant activity was investigated for some synthesized compounds, such as **4a–4d**, using the DPPH radical trapping and reducing potential tests of ferric ion and comparing results with synthetic antioxidants (TBHQ and BHT). In this study, compounds **4a–4d** demonstrated moderate DPPH radical trapping and good reducing power of ferric ion

## 4 | EXPERIMENTAL

All chemicals in this work were prepared in Fluka (Buchs, Switzerland) and were utilized without further purification. Clinoptilolite was obtained from the Afrandtooska Company in the region of Semnan. KF/CP-NPs were prepared according to literature reported.[37] Melting points were measured on an electrothermal 9,100 apparatus. Elemental analyses for C, H, and N were carried out using a Heraeus CHN–O-Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MAT 8430 spectrometer operating at an ionization potential of 70 eV. IR spectra were measured on a Shimadzu IR-460 spectrometer. $^1$H and $^{13}$C NMR spectra were measured with a BRUKER DRX-500 AVANCE spectrometer at 500.1 and 125.8 MHz, respectively. $^1$H and $^{13}$C spectra were obtained for solutions in $CDCl_3$ using TMS as internal standard or 85% $H_3PO_4$ as external standard.

### 4.1 | Preparation of nano-KF/clinoptilolite

Nano-sized natural clinoptilolite zeolite was generated by grinding in a planetary ball mill using a zirconia vial set in dry conditions with a time period of about 20 min. Then, the KF/CP-NPs catalyst was prepared according to previously reported procedure.[37] Thus, 1 g of KF was dissolved in distilled water (10 mL) and nanoclinoptilolite (9 g). The mixture was stirred for 50 min. Then, the water was evaporated at 60–70°C under reduced pressure. Moreover, the impregnated clinoptilolite was dried at 70–80°C in a vacuum drying oven for 30 hr. The resulting material was powdered using a pestle and mortar. The obtained KF/CP-NPs retained in a desiccator until required.

### 4.2 | General procedure for the synthesis of chromene derivatives 4

For example, to a stirred mixture of acetophenone **2b** (2 mmol) and 4-methyl benzaldehyde **3b** (2 mmol) in the presence of catalytic amounts of KF/CPNPs (10 mol%) under solvent-free conditions and 50°C was added 4-hydroxycumarine **1** (2 mmol) after 10 min. The reaction mixture was stirred for 10 min. After completion of the reaction (monitored by TLC), 15 mL $H_2O$ was poured in the mixture of reactions. The reaction mixture was filtered, and the solid residue was washed by ethyl acetate to remove the catalyst. By evaporating solvent compounds, **4b** was separated. These compounds are purified by $Et_2O$.

**2,4-Diphenylpyrano[3,2-c]chromen-5(4H)-one (4a):** Pale yellow powder; mp 172–174°C, yield: 0.63 g (90%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1720, 1,695, 1,587, 1,457, 1,328, 1,129 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 4.52 (1H, d, $^3J_{HH}$ = 4.2 Hz, CH), 5.78 (1 H, d, $^3J_{HH}$ = 4.3 Hz, CH), 7.08 (2 H, t, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.16 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.23 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.35 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.42 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.47 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.52 (1 H, t, $^3J_{HH}$ = 7.7 Hz, CH), 7.58 (2 H, d, $^3J_{HH}$ = 7.7 Hz, 2 CH), 7.72 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 8.04 (1 H, d, $^3J_{HH}$ = 7.7 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 37.2 (CH), 103.6 (CH), 104.0 (C), 115.2 (C), 116.5 (CH), 123.2 (CH), 124.8 (CH), 125.2 (CH), 127.4 (2 CH), 128.6 (2CH), 129.2 (2CH), 129.6 (2CH), 130.2 (CH), 132.3 (CH), 132.9 (C), 143.5 (C), 146.8 (C), 153.2 (C), 156.2 (C), 161.5 (C=O) ppm. Anal. calcd for $C_{24}H_{16}O_3$: C, 81.80; H, 4.58. Found: C, 81.65; H, 4.43. MS, *m/z* (%): 352 ($M^+$, 15), 275 (68), 144 (56), 77 (100).

**2-Phenyl-4-p-tolylpyrano[3,2-c]chromen-5(4H)-one (4b)**: white powder; mp 183–185°C, yield: 0.64 g (87%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1725, 1,689, 1,568, 1,487, 1,356, 1,295, 1,137 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 2.28 (3H, s, Me), 4.62 (1 H, d, $^3J_{HH}$ = 4.8 Hz, CH), 5.78 (1 H, d, $^3J_{HH}$ = 4.8 Hz, CH), 7.05 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.12 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.32 (1 H, t, $^3J_{HH}$ = 7.7 Hz, CH), 7.41 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.45 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.48 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.52 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.62 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.76 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 23.4 (Me), 43.2 (CH), 103.5 (CH), 104.2 (C), 116.3 (C), 116.7 (CH), 123.4 (CH), 125.2 (CH), 127.2 (2 CH), 128.4 (2 CH), 129.2 (2CH), 129.6 (2CH), 130.4 (CH), 132.3 (CH), 133.2 (C), 138.2 (C), 139.7 (C), 149.3 (C), 155.4 (C), 156.4 (C), 161.7 (C=O) ppm. MS, *m/z* (%): 366 ($M^+$, 20), 351 (52), 275 (100). Anal. calcd for $C_{25}H_{18}O_3$: C, 81.95; H, 4.95. Found: C, 81.72; H, 4.83.

**4-(Benzo[d][1,3]dioxol-5-yl)-2-phenylpyrano[3,2-c]chromen-5(4H)-one (4c):** White powder; mp 175–177°C, yield: 0.75 g (95%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1727, 1,693, 1,587, 1,468, 1,378, 1,295, 1,129 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 4.73 (1 H, d, $^3J_{HH}$ = 5.2 Hz, CH), 5.68 (1 H, d, $^3J_{HH}$ = 5.2 Hz, CH), 5.87 (1 H, d, $^3J_{HH}$ = 1.6 Hz, CH), 5.92 (1 H, d, $^3J_{HH}$ = 1.6 Hz, CH), 6.82 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 6.95 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.12 (2 H, t, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.18 (1 H, s, CH), 7.37 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.42 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.48 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.53 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.63 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.75 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 48.3 (CH), 101.2 ($CH_2$), 103.7 (CH), 104.3 (C), 109.5 (CH), 110.3 (CH), 116.5 (C), 116.8 (CH), 122.3 (CH), 124.5 (CH), 125.3 (CH), 128.2 (2 CH), 128.9 (2CH), 130.2 (CH), 132.3 (CH), 133.4 (C), 135.3 (C), 147.2 (C), 149.3 (C), 150.6 (C), 155.6 (C), 156.5 (C), 161.3 (C=O) ppm. MS, *m/z* (%): 396 (M$^+$, 15), 275 (100), 189 (68). Anal. calcd for $C_{25}H_{16}O_5$: C, 75.75; H, 4.07. Found: C, 75.87; H, 4.23.

**4-(4-Nitrophenyl)-2-phenylpyrano[3,2-c]chromen-5(4H)-one (4d)**: Yellow powder; mp 227–229°C, yield: 0.73 g (92%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1726, 1,695, 1,596, 1,485, 1,378, 1,284, 1,135 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 4.68 (1 H, d, $^3J_{HH}$ = 4.5 Hz, CH), 5.83 (1 H, d, $^3J_{HH}$ = 4.5 Hz, CH), 7.07 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.35 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.42 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.48 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.52 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.58 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.68 (2 H, d, $^3J_{HH}$ = 7.8 Hz, 2 CH), 7.76 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.87 (2 H, d, $^3J_{HH}$ = 7.8 Hz, 2 CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 46.8 (CH), 103.6 (CH), 104.3 (C), 116.5 (C), 117.2 (CH), 123.9 (2 CH), 124.3 (CH), 125.5 (CH), 128.5 (2 CH), 129.3 (2CH), 129.8 (2CH), 130.6 (CH), 132.5 (CH), 133.4 (C), 147.2 (C), 148.5 (C), 149.2 (C), 155.4 (C), 156.5 (C), 161.8 (C=O) ppm. MS, *m/z* (%): 397 (M+, 10), 350 (45), 275 (100). Anal. calcd for $C_{24}H_{15}NO_5$: C, 72.54; H, 3.80. Found: C, 72.76; H, 3.94.

**4-(4-methoxyphenyl)-2-phenylpyrano[3,2-c]chromen-5(4H)-one (4e)**: Pale yellow powder; mp 157–159°C, yield: 0.51 g (70%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1727, 1,690, 1,582, 1,487, 1,375, 1,283, 1,129 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 3.87 (3H, s, Me), 4.65 (1 H, d, $^3J_{HH}$ = 5.6 Hz, CH), 5.83 (1 H, d, $^3J_{HH}$ = 5.6 Hz, CH), 7.12 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.23 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.34 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.38 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.42 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.48 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.54 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.62 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.78 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 48.2 (CH), 55.6 (MeO), 103.6 (CH), 104.5 (C), 114.3 (2 CH), 116.5 (C), 116.8 (CH), 124.3 (CH), 125.5 (CH), 127.4 (C), 127.9 (CH), 128.3 (2CH), 128.7 (2CH), 129.6 (2 CH), 132.5 (CH), 142.3 (C), 149.5 (C), 155.2 (C), 156.3 (C), 159.7(C), 162.2 (C=O) ppm. MS, *m/z* (%): 382 (M$^+$, 15), 289 (93), 31 (100). Anal. calcd for $C_{25}H_{18}O_4$: C, 78.52; H, 4.74. Found: C, 78.67; H, 4.86.

**2-(4-Bromophenyl)-4-phenylpyrano[3,2-c]chromen-5(4H)-one (4f):** White powder; mp 198–200°C, yield: 0.65 g (75%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1725, 1,689, 1,568, 1,456, 1,386, 1,295, 1,137 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 4.83 (1 H, d, $^3J_{HH}$ = 5.8 Hz, CH), 5.92 (1 H, d, $^3J_{HH}$ = 5.8 Hz, CH), 7.15 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.25 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.36 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.42 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.46 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.52 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.56 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.65 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.84 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 48.4 (CH), 103.7 (CH), 104.6 (C), 116.7 (C), 116.9 (CH), 123.6 (C), 124.2 (CH), 125.3 (CH), 127.4 (CH), 128.5 (2CH), 128.9 (2CH), 129.3 (2 CH), 131.8 (2 CH), 132.2 (CH), 132.5 (C), 142.3 (C), 149.8 (C), 155.4 (C), 156.5 (C), 161.4 (C=O) ppm. MS, *m/z* (%): 431 (M$^+$, 15), 156 (100), 77 (68). Anal. calcd for $C_{24}H_{15}BrO_3$: C, 66.84; H, 3.51. Found: C, 66.96; H, 3.63.

**2,4-Bis(4-chlorophenyl)pyrano[3,2-c]chromen-5(4H)-one (4g)**: Pale yellow powder; mp 236–238°C, yield: 0.82 g (98%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1727, 1,695, 1,578, 1,468, 1,392, 1,278, 1,153 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 5.02 (1 H, d, $^3J_{HH}$ = 4.6 Hz, CH), 5.87 (1 H, d, $^3J_{HH}$ = 4.6 Hz, CH), 7.16 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.22 (2 H, d, $^3J_{HH}$ = 7.7 Hz, 2 CH), 7.37 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.43 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.48 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.56 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.65 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.78 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 48.3 (CH), 104.2 (CH), 104.8 (C), 116.3 (C), 116.5 (CH), 124.2 (CH), 125.6 (CH), 128.6 (2 CH), 129.2 (2 CH), 130.2 (2CH), 132.3 (CH), 132.6 (C), 132.8 (C), 134.3 (C), 140.2 (C), 149.2 (C), 155.4 (C), 156.7 (C), 161.2 (C=O) ppm. MS, *m/z* (%): 421 (M+, 10), 310 (58), 111 (100), 77 (64). Anal. calcd for $C_{24}H_{14}Cl_2O_3$: C, 68.43; H, 3.35. Found: C, 68.62; H, 3.49.

**4-(4-Chlorophenyl)-2-p-tolylpyrano[3,2-c]chromen-5(4H)-one (4h):** Pale yellow powder; mp 223–225°C, yield: 0.76 g (95%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1725, 1,687, 1,564, 1,476, 1,387, 1,297, 1,164 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 2.35 (3 H, s, Me), 5.06 (1 H, d, $^3J_{HH}$ = 4.8 Hz, CH), 5.93 (1 H, d, $^3J_{HH}$ = 4.8 Hz, CH), 7.15 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.25 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.35 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.39 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH),7.44 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.52 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.64 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.75 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 21.4 (Me), 48.5 (CH), 104.3 (CH), 105.2 (C), 116.4 (C), 116.7 (CH), 124.3 (CH), 125.7 (CH), 126.2 (2 CH), 128.8 (2 CH), 129.3 (2CH), 129.7 (2 CH),

131.8 (C), 132.2 (CH), 132.6 (C), 136.7 (C), 140.2 (C), 150.3 (C), 155.4 (C), 156.7 (C), 161.3 (C=O) ppm. MS, *m/z* (%): 400 ($M^+$, 10), 365 (68), 91 (100), 77 (68). Anal. calcd for $C_{25}H_{17}ClO_3$: C, 74.91; H, 4.27. Found: C, 74.75; H, 4.16.

**4-Methyl-2,4-diphenylpyrano[3,2-c]chromen-5(4H)-one (4i):** white powder; mp 181–182°C, yield: 0.62 g (85%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1726, 1,695, 1,578, 1,475, 1,386, 1,284, 1,165 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 1.65 (3 H, s, Me), 6.22 (1 H, s, CH), 7.15 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.23 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.28 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.35 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.39 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.45 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.52 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.58 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.63 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.75 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 28.3 (Me), 51.3 (C), 107.5 (C), 108.6 (CH), 116.4 (CH), 124.3 (CH), 125.6 (CH), 127.2 (CH), 128.2 (2 CH), 129.4 (2CH), 129.8 (2CH), 130.2 (2CH), 130.8 (CH), 132.2 (CH), 133.4 (C), 142.3 (C), 149.3 (C), 155.3 (C), 156.3 (C), 161.2 (C=O) ppm. MS, *m/z* (%): 366 ($M^+$, 15), 296 (86), 77 (100). Anal. calcd for $C_{25}H_{18}O_3$: C, 81.95; H, 4.95. Found: C, 81.78; H, 4.76.

**2-Methyl-4-phenylpyrano[3,2-c]chromen-5(4H)-one (4j):** pale yellow powder; mp 134–136°C, yield: 0.62 g (90%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1728, 1,698, 1,594, 1,489, 1,387, 1,289, 1,158 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 1.87 (3 H, s, Me), 4.86 (1 H, d, $^3J_{HH}$ = 4.6 Hz, CH), 5.85 (1 H, d, $^3J_{HH}$ = 4.6 Hz, CH), 7.13 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.25 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.36 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.42 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.49 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.56 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.68 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 19.2 (Me), 46.7 (C), 100.3 (CH), 103.5 (C), 116.5 (C), 117.4 (CH), 124.2 (CH), 125.3 (CH), 127.2 (CH), 128.2 (2CH), 129.5 (2CH), 131.8 (CH), 141.3 (C), 148.2 (C), 156.2 (C), 157.4 (C), 161.5 (C=O) ppm. Anal. calcd for $C_{19}H_{14}O_3$: C, 78.61; H, 4.86. Found: C, 78.76; H, 4.98. MS, *m/z* (%): 290 ($M^+$, 10), 213 (86), 77 (100).

**9-Methyl-2,4-diphenylpyrano[3,2-c]chromen-5(4H)-one (4k):** white powder; mp 217–219°C, yield: 0.69 g (95%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1732, 1,697, 1,586, 1,476, 1,358, 1,292, 1,162 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 2.36 (3 H, s, Me), 4.94 (1H, d, $^3J_{HH}$ = 4.8 Hz, CH), 5.83 (1 H, d, $^3J_{HH}$ = 4.8 Hz, CH), 7.05 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.15 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.23 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.29 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.32 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.39 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.45 (1 H, s, CH), 7.53 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.63 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 22.3 (Me), 48.6 (C), 104.2 (CH), 104.6 (C), 116.5 (C), 120.3 (CH), 126.3 (CH), 127.4 (CH), 128.3 (2 CH), 128.8 (2 CH), 129.2 (2 CH), 129.8 (2 CH), 130.4 (CH), 133.6 (C), 134.2 (CH), 134.2 (C), 142.3 (C), 150.2 (C), 151.2 (C), 157.3 (C), 162.4 (C=O) ppm. Anal. calcd for $C_{25}H_{18}O_3$: C, 81.95; H, 4.95. Found: C, 81.83; H, 4.82. MS, *m/z* (%): 366 ($M^+$, 15), 296 (84), 77 (100).

**9-Methyl-2-phenyl-4-p-tolylpyrano[3,2-c]chromen-5(4H)-one (4l)**: white powder; mp 209–211°C, yield: 0.69 g (90%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1726, 1,695, 1,587, 1,483, 1,376, 1,285, 1,197 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 2.26 (3H, s, Me), 2.35 (3 H, s, Me), 4.78 (1 H, d, $^3J_{HH}$ = 5.3 Hz, CH), 5.62 (1 H, d, $^3J_{HH}$ = 5.3 Hz, CH), 7.04 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.09 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.16 (2 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.22 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH), 7.42 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.47 (1 H, s, CH), 7.53 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.64 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.76 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 21.3 (Me), 22.5 (Me), 47.8 (CH), 103.8 (CH), 104.3 (C), 116.4 (C), 120.4 (CH), 126.2 (CH), 127.2 (2 CH), 128.3 (2 CH), 128.8 (2 CH), 129.3 (2CH), 130.5 (CH), 133.6 (C), 133.8 (CH), 134.2 (C), 138.3 (C), 139.2 (C), 149.5 (C), 150.7 (C), 157.2 (C), 162.3 (C=O) ppm. MS, *m/z* (%): 380 (M+, 10), 365 (65), 303 (28), 289 (100). Anal. calcd for $C_{26}H_{20}O_3$: C, 82.08; H, 5.30. Found: C, 82.27; H, 5.42.

**2-(4-bromophenyl)-4-(4-methoxyphenyl)pyrano[3,2-c]chromen-5(4H)-one (4m):** Pale yellow powder; mp 156–158°C, yield: 0.80 g (87%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1728, 1,692, 1,578, 1,483, 1,395, 1,294, 1,176 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 3.87 (3 H, s, MeO), 4.85 (1 H, d, $^3J_{HH}$ = 5.3 Hz, CH), 5.74 (1 H, d, $^3J_{HH}$ = 5.3 Hz, CH), 6.94 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.18 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.22 (1 H, s, CH), 7.32 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH),7.37 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.42 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.48 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.54 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.62 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.75 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 49.5 (Me), 55.6 (MeO), 103.8 (CH), 104.6 (C), 115.3 (CH), 116.3 (C), 116.8 (CH), 118.6 (CH), 121.3 (CH), 122.4 (CH), 123.2 (C), 124.3 (CH), 125.5 (CH), 128.8 (2 CH), 131.5 (2 CH), 132.2 (CH), 132.8 (C), 144.2 (C), 149.3 (C), 155.2 (C), 156.2 (C), 159.3 (C), 162.2 (C=O) ppm. MS, *m/z* (%): 461 ($M^+$, 10), 156 (100), 77 (82). Anal. calcd for $C_{25}H_{17}BrO_4$: C, 65.09; H, 3.71. Found: C, 65.23; H, 3.85.

**2-(4-bromophenyl)-4-(4-ethoxyphenyl)pyrano[3,2-c]chromen-5(4H)-one (4n):** Pale yellow powder; mp 154–156°C, yield: 0.86 g (90%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1725, 1,695, 1,583, 1,487, 1,368, 1,257, 1,184 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 1.38 (3 H, t, $^3J_{HH}$ = 7.3 Hz, Me), 4.23 (2 H, q, $^3J_{HH}$ = 7.3 Hz, $CH_2O$), 4.67 (1 H, d, $^3J_{HH}$ = 4.8 Hz, CH), 5.84 (1 H, d, $^3J_{HH}$ = 4.8 Hz, CH), 6.95 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.15 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.37 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH),7.42 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.54 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.59 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.64 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.75 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 14.2 (Me), 18.6 (CH), 63.2 ($CH_2O$),

103.6 (CH), 104.2 (C), 115.6 (2 CH), 116.4 (C), 117.2 (CH), 123.2 (C), 124.3 (CH), 125.6 (CH), 129.2 (2 CH), 130.4 (2 CH), 131.4 (2 CH), 131.8 (CH), 132.6 (C), 133.5 (C), 149.8 (C), 155.3 (C), 156.4 (C), 159.5 (C), 162.4 (C=O) ppm. MS, *m/z* (%): 475 ($M^+$, 10), 430 (86), 77 (82), 45 (100). Anal. calcd for $C_{26}H_{19}BrO_4$: C, 65.70; H, 4.03. Found: C, 65.84; H, 4.18.

**2,4-dimethyl-4-phenylpyrano[3,2-c]chromen-5(4H)-one (4o):** white powder; mp 143–145°C, yield: 0.49 g (78%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1726, 1,692, 1,586, 1,487, 1,378, 1,282, 1,173 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 1.38 (3 H, t, $^3J_{HH}$ = 7.3 Hz, Me), 1.68 (3 H, s, Me), 2.23 (2 H, m, $CH_2$), 5.36 (1 H, s, CH), 7.16 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.25 (2 H, t, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.32 (2 H, d, $^3J_{HH}$ = 7.5 Hz, 2 CH), 7.37 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.42 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.48 (1 H, t, $^3J_{HH}$ = 7.5 Hz, CH), 7.63 (1 H, d, $^3J_{HH}$ = 7.5 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 11.2 (Me), 28.2 (Me), 31.4 (Me), 43.5 (C), 101.2 (C), 115.4 (C), 116.2 (CH), 119.3 (CH), 123.2 (CH), 124.5 (CH), 126.7 (2 CH), 127.2 (CH), 129.7 (2 CH), 132.2 (CH), 141.6 (C), 153.3 (C), 155.5 (C), 156.2 (C), 160.8 (C=O) ppm. MS, *m/z* (%): 318 ($M^+$, 10), 241 (86), 77 (100). Anal. calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 79.37; H, 5.86.

**4-(4-methoxyphenyl)-2-tert-butylpyrano[3,2-c]chromen-5(4H)-one (4p)**: Pale brown powder; mp 162–164°C, yield: 0.56 g (78%). IR (KBr) ($\nu_{max}$/cm$^{-1}$): 1725, 1,693, 1,585, 1,476, 1,378, 1,289, 1,134 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ 1.26 (9H, s, $Me_3C$), 3.75 (3 H, s, MeO), 4.73 (1 H, d, $^3J_{HH}$ = 5.4 Hz, CH), 5.76 (1 H, d, $^3J_{HH}$ = 5.4 Hz, CH), 6.94 (2 H, d, $^3J_{HH}$ = 7.7 Hz, 2 CH), 7.12 (2 H, d, $^3J_{HH}$ = 7.7 Hz, 2 CH), 7.34 (2 H, d, $^3J_{HH}$ = 7.6 Hz, 2 CH), 7.38 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.42 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH), 7.54 (1 H, t, $^3J_{HH}$ = 7.6 Hz, CH), 7.76 (1 H, d, $^3J_{HH}$ = 7.6 Hz, CH) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 31.2 ($Me_3C$), 34.2 ($Me_3C$), 35.6 (CH), 55.6 (MeO), 95.4 (CH), 101.3 (C), 114.6 (2 CH), 115.4 (C), 117.5 (CH), 125.2 (CH), 126.4 (CH), 127.5 (2 CH), 128.6 (C), 132.2 (CH), 155.2 (C), 156.3 (C), 158.2 (C), 159.6 (C), 163.4 (C=O) ppm. MS, *m/z* (%): 362 ($M^+$, 10), 305 (84), 57 (100), Anal. calcd for $C_{23}H_{22}O_4$: C, 76.22; H, 6.12. Found: C, 76.34; H, 6.25.

### 4.3 | DPPH radical scavenging test

Some derivatives of synthesized chromene derivatives, such as **4a–4d,** are tested as antioxidants. Antioxidant activity of this compounds was measured by the DPPH (2, 2-Diphenyl-1-picrylhydrazyl) radical trapping test, consistent with the method reported by Shimada et al.[41] Different concentrations of **4a–4d** (200–1,000 ppm) were added to an identical volume of methanolic solution of DPPH (1 mM). The mixtures were combined and then placed in a dark room. After 30 min, absorbance of the mixture was measured. The maximum absorbance of the mixture was 517 nm at room temperature. Compounds **4a-4d** were replaced with 3 mL methanol in the control sample. Butylated hydroxytoluene (BHT) and 2-tert-butylhydroquinone (TBHQ) were used as standard controls. The DPPH operation is computed using the following formula:[43]

$$I = [(AB\text{-}AS)/AB] \times 100$$

where I = DPPH inhibition (%), AB = absorbance of control sample (0 min), and AS = absorbance of an examined sample at the end of the reaction (after 30 min).

### 4.4 | Reducing power experiment

The power of **4a-4d** to reduce iron (III) was guessed using the Yildirim et al.[42] procedure. The compounds **4a-4d** (1 mL) were mixed with 2.5 mL of phosphate buffer (0.2 M, pH 6.6) and 2.5 mL of potassium ferricyanide ($K_3Fe[CN]_6$; 10 g/L) and stirred for 30 min at 50°C. After that, 2.5 mL of trichloroacetic acid (10% w/v) was added to the solution and centrifuged for 10 min. Finally, 2.5 mL of the supernatant was combined with 2.5 mL of distilled water and 0.5 mL $FeCl_3$ (1 g/L). The absorbance of samples was calculated at 700 nm. Higher absorbance means were attributed to higher reducing power.

#### 4.4.1 | Statistical study

Each measurement was performed thrice. The data were analyzed by running one way analysis of variance (ANOVA) utilizing SPSS software version 18.0. A one-way ANOVA was used to evaluate difference in the mean value of samples and control. All mean separations were performed using Duncan multiple range examination, with an importance level of 95% ($p < 0.05$).

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