One-pot and green synthesis 1*H*-pyrazolo[1,2-*b*] phthalazine-5,10-dione and dihydropyrano[3,2-*c*] chromene derivatives by Fe3O4@SiO2-imine/ phenoxy-Cu(II) as an efficient and reusable catalyst

Milad Nesarvand[1] · **Davood Azarifar**[1] · **Hakimeh Ebrahimiasl**[1]

Abstract

In the current study, magnetite-silica core–shell nanoparticles modified with Cu-salen complex (Fe_3O_4@SiO_2-imine/phenoxy-Cu(II)) was utilized as a heterogeneous catalyst for the one-pot multicomponent synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione and dihydropyrano[3,2-*c*]chromene derivatives under solvent-free conditions, without using any harmful organic reagents/solvent. The current synthetic protocol demonstrates that the reactions proceeds to completing step, leading to the successful synthesis of high purity compounds. Advantages of this method include easy purification, reusability of the catalyst, green and mild procedure and synthesis of new derivatives in high yields within short reaction time.

Keywords Green chemistry · Magnetic nanoparticles · 1H-pyrazolo[1,2-b]phthalazine-5,10-dione · dihydropyrano[3,2-c]chromene

Introduction

The synthesis of new heterocyclic compounds is of paramount importance, because of their abundance, pharmaceutical and industrial applications [1]. So far, many methods have been proposed to synthesize these compounds. In the last two decades, multi-component reactions (MCRs) have become a powerful, rapid and efficient approach for the synthesis of heterocyclic compounds [2–7]. The utilization of MCRs offers several advantages such as increased reaction rate,

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✉ Hakimeh Ebrahimiasl
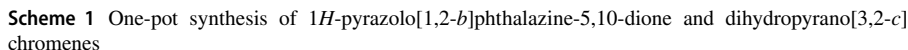 h_ebrahimiasl64@yahoo.com

  Davood Azarifar
  azarifar@basu.ac.ir

1 Department of Organic Chemistry, Faculty of Chemistry, Bu-Ali Sina University, 6517838683 Hamedan, Iran

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reduction of time, high atom economy and avoidance of complicated purification processes. These benefits make MCRs a considerable method for the synthesis of complex heterocyclic compounds [8]. One the key driving forces of the MCRs is the utilization of heterogeneous recyclable catalysts, that very recently, the efforts have been directed to surface and structural modification of the heterogeneous catalysts by using the recent trends in the nanoarchitecture [9–16].

1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione and dihydropyrano[3,2-*c*]chromene derivatives are two crucial classes of heterocycles for which several synthetic methods have been developed for the synthesis of their derivatives. Their biological and pharmacological properties and thus, their clinical applications are the notable reasons for the interest in these compounds [17–23]. Anti-convulsant, vasorelaxant, cardiotonic, antipyretic, anti-inflammatory, anticancer, antifungal and antibacterial activities are some examples of biological properties of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives [24–27]. Also, dihydropyrano[3,2-*c*]chromenes are well known for anti-anaphylactic, antitumor, antimicrobial, anti-tuberculosis agents, analgesic, anti-cancer and anticoagulant activities [28–31]. Owing to all the above-mentioned importance and applications of these compounds, it is of primary importance to find the superior synthesis approaches for them by scientists. So far, innumerable approaches have been proposed by researchers for the manufacture of these compounds, among which there is a commonly employed strategy which consists of one-pot three-component reaction. This reaction has been studied with different catalysts and conditions. As an illustration, in 2019, 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione was synthesized by Pati et al. using CuO nanoparticles as a reusable catalyst under solvent-free conditions [32]. Piltan et al. in 2017, synthesized 1*H*-pyrazolo[1,2-*b*] phthalazine-5,10-dione using the ZrO_2 nanoparticles as a catalyst, at 100 °C and under solvent-free conditions [2–7]. In 2019, dihydropyrano[3,2-*c*]chromenes derivatives were synthesized by Hallaoui et al. using $Co_3(PO_4)_2$ as a catalyst at 80 °C. This reaction was performed in a mixture of water/ethanol (4:1) [33]. In another research work, Sharma et al. in 2018, reported the new derivatives of dihydropyrano[3,2-*c*]chromenes at 80 °C in the presence of [Bmim] Sac as a non-toxic and green ionic liquid in aqueous media [34]. In the last few decades, magnetic nanoparticles (MNPs) have attracted a lot of attention as sustainable and efficient catalysts for multi-component reactions (MCRs) due to their features such as large surface to volume ratio, high thermal stability, chemical stability, easy magnetic separation and high potential of recyclability.

Given the fact that we have recently introduced Copper-based Schiff Base Complex Immobilized on Core-shell $Fe_3O_4@SiO_2$ as a magnetically recyclable and highly efficient nanocatalyst for green synthesis of 2-amino-4*H*-chromene derivatives [35], in this article, we have presented another important application of $Fe_3O_4@SiO_2$-Imine/Phenoxy-Cu(II) catalyst as an efficient, low price, safe, catalytic performance and magnetic powerful solid acid catalyst for one-pot synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione and dihydropyrano[3,2-*c*]chromenes. The schematic illustration of the synthesis route is exhibited in Scheme 1.

Scheme 1 One-pot synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione and dihydropyrano[3,2-*c*] chromenes

Experimental

Chemicals and instruments

All chemicals were purchased from Merck and Fluka Companies. ^{1}H NMR and ^{13}C NMR spectra were measured on a spectrometer at 250, 400, 300, 90 MHz and 62.5, 100, 75 MHz, respectively, in DMSO-d_6. Fourier transform infrared (FT-IR) spectra were obtained using the Shimadzu 435-U-04 FT spectrophotometer from KBr pellets. Melting points were recorded on a BUCHI 510 apparatus in open capillary tubes.

Preparation of Fe$_3$O$_4$–SiO$_2$–(CH$_2$)$_3$–1,3-Phenylenediamine-Schiff base Complex of Cu(II)

Magnetic Fe$_3$O$_4$ nanoparticles were synthesized via co-precipitation of solutions containing Fe^{3+} and Fe^{2+} ions [36]. FeCl$_3$·6H$_2$O (11.3 g, 0.0418 mol) and FeCl$_2$·4H$_2$O (5.648 g, 0.0209 mol) were dissolved in 100 ml of deionized water. The mixture was stirred at 85 °C for 30 min, and then 25 ml of ammonia (28% aqueous solution) was added rapidly to the reaction mixture. The reaction was stirred for another 30 min at 85 °C. Then, the black Fe$_3$O$_4$ nanoparticles were separated with an external magnet. They were washed with distilled water followed by EtOH and dried

at 80 °C in an oven. Then, 1.0 g of the MNPs was dispersed in a mixture of 80 ml of deionized water, 20 ml of EtOH and 2.0 ml of ammonia (28 wt%), and then 2.0 mL of tetraethyl orthosilicate (TEOS) was added to the mixture and stirred at 50 °C for 2 h. The core–shell MNPs ($Fe_3O_4@SiO_2$ MNPs) were separated using a magnet and washed with deionized water, EtOH, and then dried in an oven [37]. In the following, $Fe_3O_4@SiO_2$–functionalized Cl was synthesized via surface reaction of $Fe_3O_4@SiO_2$ using (3-chloropropyl) triethoxysilane as the silylation agent. 1.0 g of $Fe_3O_4@SiO_2$ and 50.0 ml of toluene were mixed into a 250 ml round flask. Then, (3 Chloropropyl)triethoxysilane (2.0 ml) was added to the mixture and refluxed at 110 °C with stirring for 12 h. In the end, $Fe_3O_4@SiO_2@Cl$ MNPs were separated by a magnet and washed with toluene and EtOH several times. Finally, the product was dried in an oven. Then, for Synthesis of $Fe_3O_4@SiO_2$–$(CH_2)_3$–NH–$(3-NH_2C_6H_4)$ MNPs,1, 3-phenylenediamine (1.3 g, 0.012 mol) and a few drops of triethylamine as a base were dissolved in ethanol (70 ml). Then $Fe_3O_4@SiO_2$–$(CH_2)_3$–Cl (1 g) was added to the mixture and dispersed (15 min). The resulting mixture was refluxed in N_2 for 24 h. After refluxing, the final precipitate was separated with a magnet, washed several times with ethanol and dried at room temperature. For the synthesis of $Fe_3O_4@SiO_2$- iminomethyl/phenol,at First, $Fe_3O_4@SiO_2$–$(CH_2)_3$–NH–$(3-NH_2C_6H_4)$ nanoparticles (1 g) was dispersed in 50 ml of methanol (15 min) and refluxed. Then, salicylaldehyde (2.93 g, 24 mmol) was dissolved in ethanol (30 ml) and added dropwise to the nanoparticles using a decanter funnel. The reaction mixture was refluxed for 24 h and the product was separated using a magnet, washed several times with ethanol, and dried in an oven. Finally, 1 g from the previously synthesized nanoparticles was dispersed in 50 ml ethanol (15 min). Then 5% (w/v) solution of $Cu(OAc)_2$ in ethanol (5 ml) was added dropwise to the previous mixture and the resulting mixture was refluxed for 48 h. After the reaction completed, the product was separated using the magnet, washed with 50 ml ethanol and water to remove the remaining unreacted materials and dried in an oven. The resulted $Fe_3O_4@SiO_2$-imine/phenoxy-Cu(II) magnetic nanoparticles (MNPs) were characterized by various techniques including SEM, TEM, XRD, XPS, EDX, VSM, FT-IR and ICP [35].

General procedure for the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives

Under the optimum reaction conditions, phthalhydrazide (1 mmol), malononitrile (1 mmol), aldehyde (1 mmol) and the catalyst (0.02 g) were added to a test tube. The mixture was stirred magnetically and heated at 80 °C under solvent-free conditions. After completion of the reaction (judged by the TLC (n-hexane/ethyl acetate 10:3)), 10 ml of hot ethanol was added to the reaction mixture and the catalyst was separated using an external magnet. Then, 20 ml of distilled water was added to the reaction mixture and precipitated product isolated by filtration. The product was washed with NaOH (0.5 mol) to produce a pure product. The product was characterized using physical and spectroscopic data (FTIR, NMR and MS).

General procedure for the synthesis of dihydropyrano[3,2-*c*]chromene derivatives

Under the optimum reaction conditions, 4-hydroxycoumarin (1 mmol), malononitrile (1 mmol), aldehyde (1 mmol) and 0.03 g catalyst were added to a test tube. The mixture was stirred magnetically and heated at 90 °C under solvent-free conditions. After completion of the reaction (by the TLC (n-hexane/ethyl acetate 7:4)), 10 ml of hot ethanol was added to the reaction mixture and the catalyst separated using an external magnet. Then, 20 ml distilled water was added to the reaction mixture and precipitated product isolated by filtration. The product was washed with NaOH (0.5 mol) to produce a pure product. The product was characterized using physical and spectroscopic data (FT-IR, NMR and MS).

Analytical data of selected products

3-amino-5,10-dioxo-1-phenyl-5,10-dihydro-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carbonitrile (4a) Yellow solid; mp 249–251 °C. FT-IR (KBr, cm^{-1}): 3361, 3260, 2197, 1682, 1660. ^{1}H NMR (90 MHz, DMSO-d$_6$, δ ppm): 6.12 (s, 1H, CH), 7.31–7.87 (m, 9H, Ar–H), 8.29 (t, 2H, NH$_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$, δ ppm): 61.4, 62.9, 116.2, 126.5, 126.6, 127.3, 128.1, 128.5, 128.6, 128.7, 133.6, 134.7, 138.4, 150.6, 153.7, 156.5 ppm.

    3-amino-1-(naphthalen-1-yl)-5,10-dioxo-5,10-dihydro-1*H*-pyrazolo[1,2-*b*] phthalazine-2-carbonitrile (4b) Yellow solid; mp 275–276 °C. FT-IR (KBr, cm^{-1}): 3365, 3260, 2192, 1682, 1655. ^{1}H NMR (300 MHz, DMSO-d$_6$, δ ppm): 6.27 (s, 1H, CH), 7.50–8.28 (m, 11H, Ar–H), 8.29 (t, 2H, NH$_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$, δ ppm): 61.3, 63.2, 116.0, 124.2, 125.0, 125.1, 126.3, 126.6, 126.9, 127.5, 127.7, 127.9, 128.4, 128.7, 128.9, 132.8, 132.9, 133.6, 134.5, 135.8, 150.7, 153.8, 156.7 ppm.

    3-amino-1-(naphthalen-2-yl)-5,10-dioxo-5,10-dihydro-1*H*-pyrazolo[1,2-*b*] phthalazine-2-carbonitrile (4c) Yellow solid; mp 265–269 °C. FT-IR (KBr, cm^{-1}): 3367, 3258, 2192, 1682, 1655. ^{1}H NMR (250 MHz, DMSO-d$_6$, δ ppm): 6.27 (s, 1H, CH), 7.51–8.13 (m, 11H, Ar–H), 8.25 (t, 2H, NH$_2$).

    3-amino-1-(2,4-dichlorophenyl)-5,10-dioxo-5,10-dihydro-1*H*-pyrazolo[1,2-*b*] phthalazine-2-carbonitrile (4d) Yellow solid; mp 230–234 °C. FT-IR (KBr, cm^{-1}): 3370, 3260, 2204, 1676, 1632, 698. ^{1}H NMR (90 MHz, DMSO-d$_6$, δ ppm): 6.35 (s, 1H, CH), 7.43–7.90 (m, 7H, Ar–H), 8.45 (t, 2H, NH$_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$, δ ppm): 59.7, 60.6, 116.1, 125.5, 127.2, 127.9, 128.7, 128.7, 128.8, 129.3, 129.7, 132.7, 133.0, 134.0, 134.3, 135.0, 151.3, 154.1, 157.2 ppm.

    3-amino-1-(4-chloro-3-nitrophenyl)-5,10-dioxo-5,10-dihydro-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carbonitrile (4e) Yellow solid; mp 262–264 °C. FT-IR (KBr, cm^{-1}): 3364, 3299, 2190, 1682, 1662, 1567, 1383, 693. ^{1}H NMR (250 MHz, DMSO-d$_6$, δ ppm): 6.24 (s, 1H, CH), 7.78–8.18 (m, 7H, Ar–H), 8.29 (t, 2H, NH$_2$). ^{13}C NMR (62 MHz, DMSO-d$_6$, δ ppm): 60.5, 62.0, 116.2, 124.1, 124.8, 127.1, 127.6, 128.8, 129.5, 132.0, 132.7, 134.2, 135.0, 140.3, 148.4, 151.5, 154.2, 157.2. MS: m/z: 395, 239, 217, 187, 162, 130, 104, 76, 50 [M+H]$^+$.

3-amino-5,10-dioxo-1-(3,4,5-trimethoxyphenyl)-5,10-dihydro-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carbonitrile (4f) Yellow solid; mp 253–256 °C. FT-IR (KBr, cm^{-1}): 3372, 3295, 2841, 2185, 1681, 1658. ^{1}H NMR (300 MHz, DMSO-d$_6$, δ ppm): 3.32–3.75 (s, 9H, OCH$_3$), 6.11 (s, 1H, CH), 6.73–8.26 (m, 6H, Ar–H), 8.27 (t, 2H, NH$_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$, δ ppm): 56.0, 59.8, 61.2, 63.3, 104.1, 116.2, 126.7, 127.2, 128.7, 128.8, 133.7, 134.1, 134.5, 137.3, 150.6, 152.8, 153.9, 156.6 ppm.

3-amino-1-(4-methoxyphenyl)-5,10-dioxo-5,10-dihydro-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carbonitrile (4 g) Yellow solid; mp 239–241 °C. FT-IR (KBr, cm^{-1}): 3376, 3266, 2197, 1677, 1661. ^{1}H NMR (300 MHz, DMSO-d$_6$, δ ppm): 3.73 (s, 3H, OCH$_3$), 6.07 (s, 1H, CH), 6.89–8.24 (m, 8H, Ar–H), 8.36 (t, 2H, NH$_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$, δ ppm): 55.1, 61.3, 62.6, 113.9, 116.2, 126.5, 127.1, 128.5, 128.6, 130.2, 133.1, 134.6, 150.6, 153.4, 156.6, 159.1 ppm.

3-amino-5,10-dioxo-1-(p-tolyl)-5,10-dihydro-1*H*-pyrazolo[1,2-*b*]phthalazine-2-carbonitrile (4 h) Yellow solid; mp 253–255 °C. FT-IR (KBr, cm^{-1}): 3366, 3263, 3036, 2197, 1682, 1658. ^{1}H NMR (90 MHz, DMSO-d$_6$, δ ppm): 2.31 (s, 3H, CH$_3$), 6.11 (s, 1H, CH), 7.09–7.83 (m, 8H, Ar–H), 8.32 (t, 2H, NH$_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$, δ ppm): 61.5, 62.8, 116.0, 126.6, 126.7, 127.3, 128.5, 129.2, 133.6, 134.6, 135.3, 137.5, 150.4, 153.6, 156.6 ppm.

2-amino-4-(4-chloro-3-nitrophenyl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (5b) Cream solid; mp 252–258 °C. FT-IR (KBr, cm^{-1}): 3392, 3319, 2198, 1694, 1530, 1380, 1255. ^{1}H NMR (250 MHz, DMSO-d$_6$, δ ppm): 4.65 (s, 1H, CH), 7.45–7.85 (m, 7H, Ar–H), 8.02 (t, 2H, NH$_2$). ^{13}C NMR (62 MHz, DMSO-d$_6$, δ ppm): 36.4, 57.0, 102.7, 113.4, 116.9, 119.3, 123.0, 123.7, 125.0, 131.8, 133.5, 133.7, 144.8, 148.2, 152.7, 154.5, 158.5, 160.0. MS: m/z: 395, 378, 348, 295, 282, 239, 120, 92, 66 [M + H]$^+$.

2-amino-4-(naphthalen-1-yl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (5c) Cream solid; mp 259–264 °C. FT-IR (KBr, cm^{-1}): 3311, 2188, 1696, 1255. ^{1}H NMR (250 MHz, DMSO-d$_6$, δ ppm): 5.45 (s, 1H, CH), 7.36–7.95 (m, 11H, Ar–H), 8.42 (t, 2H, NH$_2$). ^{13}C NMR (62 MHz, DMSO-d$_6$, δ ppm): 31.9, 59.0, 105.0, 113.3, 117.0, 119.6, 122.9, 123.8, 125.1, 126.3, 126.5, 127.9, 128.9, 131.4, 133.3, 133.7, 141.1, 152.5, 154.2, 158.3, 160.0.

2-amino-4-(4-hydroxyphenyl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (5e) Cream solid; mp 264–266 °C. FT-IR (KBr, cm^{-1}): 3407, 3286, 3218, 2196, 1696, 1215. ^{1}H NMR (300 MHz, DMSO-d$_6$, δ ppm): 4.31 (s, 1H, CH), 6.66–7.86 (m, 8H, Ar–H), 7.88 (t, 2H, NH$_2$), 9.34 (s, 1H, OH).

2-amino-4-(2,4-dichlorophenyl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (5f) Cream solid; mp 254–256 °C. FT-IR (KBr, cm^{-1}): 3296, 3160, 2200, 1716, 1258. ^{1}H NMR (400 MHz, DMSO-d$_6$, δ ppm): 4.98 (s, 1H, CH), 7.35–7.90 (m, 7H, Ar–H), 7.92 (t, 2H, NH$_2$). ^{13}C NMR (100 MHz, DMSO-d$_6$, δ ppm): 39.9, 56.4, 102.9, 113.3, 117.1, 119.1, 123.0, 125.2, 128.3, 129.3, 132.5, 132.8, 133.6, 139.9, 152.7, 154.6, 156.5, 158.6, 159.9.

2-amino-4-(2-chlorophenyl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (5 g) Cream solid; mp 265–268 °C. FT-IR (KBr, cm^{-1}): 3284, 3179, 2200, 1709, 1259. ^{1}H NMR (400 MHz, DMSO-d$_6$, δ ppm): 4.99 (s, 1H, CH), 6.81–7.90 (m, 8H, Ar–H), 7.92 (t, 2H, NH$_2$). ^{13}C NMR (100 MHz, DMSO-d$_6$, δ ppm): 36.4,

56.6, 103.1, 112.8, 116.5, 118.6, 122.5, 122.8, 124.6, 128.2, 129.0, 130.6, 132.7, 133.0, 152.1, 153.9, 158.0, 159.3.

2-amino-4-(3-bromophenyl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (5 h) Cream solid; mp 272–276 °C. FT-IR (KBr, cm^{-1}): 3380, 3292, 2195, 1716, 1258. ^{1}H NMR (400 MHz, DMSO-d$_6$, δ ppm): 5.00 (s, 1H, CH), 7.17–7.91 (m, 8H, Ar–H),7.93 (t, 2H, NH$_2$). ^{13}C NMR (100 MHz, DMSO-d$_6$, δ ppm): 36.9, 57.1, 103.6, 113.3, 117.0, 119.2, 123.0,123.4, 125.1, 128.8, 129.3, 131.1, 133.2, 133.8, 142.4, 152.6, 154.4, 158.4, 159.5, 159.8.

Result and discussion

In this work, Fe$_3$O$_4$@SiO$_2$-imine/phenoxy-Cu(II) was synthesized as an efficient and recyclable catalyst for the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione and dihydropyrano[3,2-*c*]chromenes derivatives. For synthesis of the catalyst, the Fe$_3$O$_4$ nanoparticles were first prepared via the co-precipitation method, in which the silica was utilized as a protecting shell to coat the Fe$_3$O$_4$ nanoparticles and form a core–shell structure (Fe$_3$O$_4$@SiO$_2$), the nanoparticles of which were coated by (3-chloropropyl)triethoxysilane, yielding the Fe$_3$O$_4$@SiO$_2$–(CH$_2$)$_3$-Cl MNPs. In the next step, the Fe$_3$O$_4$@SiO$_2$–(CH$_2$)$_3$-Cl nanoparticles were reacted with 1,3-phenylenediamine to yield the Fe$_3$O$_4$@SiO$_2$–(CH$_2$)$_3$–NH–(3-NH$_2$C$_6$H$_4$) nanoparticles. Conversion of the Fe$_3$O$_4$@SiO$_2$–(CH$_2$)$_3$–NH–(3-NH$_2$C$_6$H$_4$) nanoparticles into Fe$_3$O$_4$@SiO$_2$-Iminomethyl/phenol was accomplished via the reaction of Fe$_3$O$_4$@SiO$_2$–(CH$_2$)$_3$–NH–(3-NH$_2$C$_6$H$_4$) nanoparticles with salicylaldehyde. Ultimately, Fe$_3$O$_4$@SiO$_2$-imine/phenoxy-Cu (II) was synthesized by dispersing the material in Cu(OAc)$_2$ solution [35].

To check the catalytic activity of Fe$_3$O$_4$@SiO$_2$-imine/phenoxy-Cu(II) in the one-pot synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione the reaction of phthalhydrazide, malononitrile and aldehyde was selected as a model reaction. The reaction conditions, including solvent, temperature and different amount of catalyst, were optimized and listed in Table 1. Based on these data, no reaction progress was observed in the absence of a catalyst and 25 mg of the catalyst was a suitable amount for this reaction. Then, a variety of temperatures were monitored in the model reaction, by which the highest yield of product was achieved at 80 °C. Additionally, various solvents were also employed to study the reaction. Therefore, The best result for the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives can be obtained by using 20 mg of catalyst, solvent-free conditions and a temperature of 80 °C.

This reaction was studied under the optimum condition for different aromatic aldehydes with different electron-withdrawing and electron-donating groups and the results were presented in Table 2. In this work, it was concluded that the reaction could proceed much better when utilizing an aldehyde of the electron-withdrawing group.

A schematic illustration of a feasible mechanism for the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives by using Fe$_3$O$_4$@SiO$_2$-imine/phenoxy-Cu(II) catalyst, is presented in Scheme 2. Initially, the activation

Table 1 Effect of conditions in the synthesis of *H*1-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives in the presence of Fe_3O_4@SiO_2-Imine/Phenoxy-Cu(II)[a]
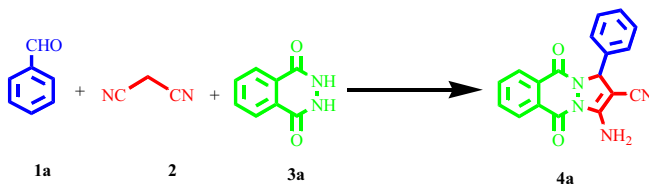
Entry	Catalyst (mg)	Solvent	Temperature (°C)	Time (min)[b]	Yield (%)[c]
1	No catalyst	Solvent-free	r.t	90	Trace
2	10	Solvent-free	80	50	66
3	**20**	**Solvent-free**	**80**	**20**	**92**
4	30	Solvent-free	80	35	88
5	20	Water	r.t	100	28
6	20	Acetonitrile	r.t	80	Trace
7	20	Ethanol	Reflux	60	55
8	20	Ethanol: water	Reflux	60	66
9	20	Water	Reflux	70	40
10	20	Acetone	Reflux	95	40
11	20	Toluene	Reflux	80	50
12	20	Solvent-free	50	40	50
13	20	Solvent-free	60	34	68
14	20	Solvent-free	70	25	79
15[d]	20	Solvent-free	80	30	35
16[e]	20	Solvent-free	80	120	28
17[f]	20	Solvent-free	80	50	68

[a]Reaction conditions: phthalhydrazide (1 mmol), malononitrile (1 mmol), benzaldehyde (1 mmol), solvent (5 mL)

[b] Reaction progress monitored by TLC

[c] Isolated pure yield
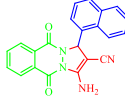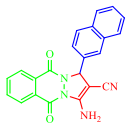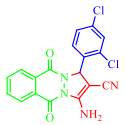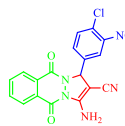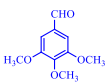
[d] Fe_3O_4 nanoparticles were used as the catalyst

[e] Fe_3O_4@SiO_2 nanoparticles were used as the catalyst

[f]Fe_3O_4@SiO_2-Iminomethyl/Phenol nanoparticles were used as the catalyst

of C–H bond in malononitrile by the catalyst (as a Lewis acid catalyst) leads to the attack of malononitrile on the activated carbonyl group of aldehyde. Knoevenagel condensation reaction between malononitrile and aldehyde was followed by dehydration to provide the intermediate (b). Then, the michael addition between Intermediate b and phthalhydrazide, forms intermediate (c). Then intramolecular cyclization and tautomerization in presence of the catalyst give 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione.

Table 2 Fe$_3$O$_4$@SiO$_2$-Imine/Phenoxy-Cu(II) catalyzed synthesis of H1-pyrazolo[1,2-b]phthalazine-5,10-diones under solvent-free condition**s**

Entry	Substrate	Products	Time (min.)	Yield (%)[a]	M.p (°C)	
					Found	Reported[Ref]
4a			20	92	249–251	249–251[1]
4b			15	95	275–276	275–277[2]
4c			16	91	265–269	267–269[1]
4d			15	92	230–234	231–232[1]
4e			14	96	262–264	–
4f			23	88	253–256	253–255[8]
4 g			22	89	239–241	240–242[17–21]
4 h			20	90	253–255	253–255[1]

[a]Isolated yields

After the successful synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones, we evaluated the catalytic activity of Fe$_3$O$_4$@SiO$_2$-imine/phenoxy-Cu(II) for the synthesis of dihydropyrano[3,2-c]chromene derivatives. For this purpose, the reaction of aldehyde (1 mmol), malononitrile (1 mmol) and 4-hydroxycoumarin (1 mmol) were applied as a model, and diverse solvents, temperature and catalyst content were used to optimize the reaction (Table 3). The best result for this
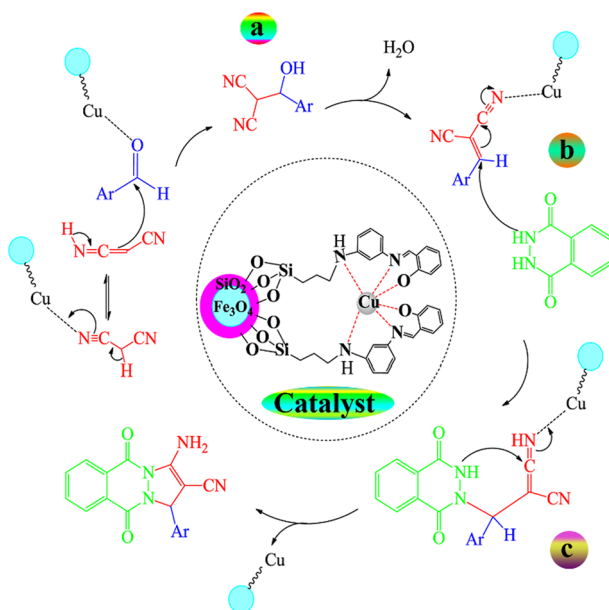
Scheme 2 Proposed mechanism for synthesis of 1*H*- pyrazolo[1,2-*b*]phthalazine-5,10-diones

reaction can be obtained by using 30 mg of catalyst, solvent-free conditions and a temperature of 90 °C.

After optimizing the reaction parameters, the catalyst was investigated on different aromatic aldehydes with different electron-withdrawing and electron-donating groups and the results are presented in Table 4. In this work, it was concluded that the reaction could proceed more efficiently when utilizing an aldehyde possessing an electron-withdrawing group.

Scheme 3 shows the probable mechanism for one-pot synthesis of dihydropyrano[3,2-*c*]chromene derivatives by using $Fe_3O_4@SiO_2$-imine/phenoxy-Cu(II) as a Lewis acid catalyst. Based on this mechanism, the activation of C–H bond in malononitrile by the catalyst leads to the attack of malononitrile on an activated carbonyl group of aldehyde. Knoevenagel condensation reaction between malononitrile and aldehyde followed by dehydration to provide the intermediate (b). Michael addition between Intermediate b and 4-hydroxycoumarin further forms the intermediate (d). Then, the intramolecular cyclization and tautomerization in presence of the catalyst results in dihydropyrano[3,2-*c*]chromene.

The model reaction was also used to assess the reusability of the catalyst. For this purpose, after which the reaction was completed, the separated catalyst was washed several times with water and hot ethanol, dried and reused in the next cycle. Figure 1 exhibits the results (FT-IR,TEM,XRD of reused catalyst in the

Table 3 Effect of conditions in the synthesis of dihydropyrano[3,2-*c*]chromene derivatives in the presence of Fe_3O_4@SiO_2-Imine/Phenoxy-Cu(II)[a]
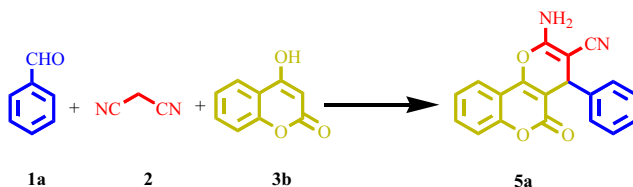
Entry	Catalyst (mg)	Solvent	Temperature (°C)	Time (min)[b]	Yield (%)[c]
1	No catalyst	Solvent-free	90	80	15
2	10	Solvent-free	90	40	68
3	20	Solvent-free	90	35	80
4	**30**	**Solvent-free**	**90**	**17**	**95**
5	50	Solvent-free	90	20	89
6	30	Solvent-free	70	30	75
7	30	Solvent-free	80	25	86
8	30	Solvent-free	100	20	85
9	30	Chloroform	Reflux	70	38
10	30	Ethyl acetate	Reflux	70	16
11	30	Toluene	Reflux	80	24
12	30	Water	r.t	100	24
13	30	Ethanol	r.t	110	34
14	30	Dichloromethane	r.t	80	20
15	30	Water	50	90	35
16	30	Water	Reflux	60	48
17	30	Ethanol	Reflux	70	55
18[d]	30	Solvent-free	90	50	40
19[e]	30	Solvent-free	90	80	20
20[f]	30	Solvent-free	90	35	65

[a]Reaction conditions: 4-hydroxycoumarin (1 mmol), malononitrile (1 mmol), benzaldehyde (1 mmol), solvent (5 mL)

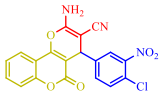[b]Reaction progress monitored by TLC

[c]Isolated pure yield
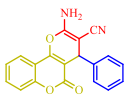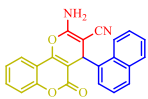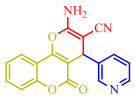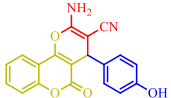
[d]Fe_3O_4 nanoparticles were used as the catalyst

[e]Fe_3O_4@SiO_2 nanoparticles were used as the catalyst

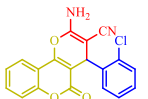[f]Fe_3O_4@SiO_2-Iminomethyl/Phenol nanoparticles were used as the catalyst

fifth run), confirming the recyclability of the catalyst. Hot-filtration test also indicated that the catalyst has no leaching in each cycle.

Table 4 Fe$_3$O$_4$@SiO$_2$-Imine/Phenoxy-Cu(II) catalyzed synthesis of dihydropyrano[3,2-*c*]chromene under solvent-free conditions

Entry	Substrate	Products	Time (min.)	Yield (%)[a]	M.p (°C)	
					Found	Reported[Ref]
5a			17	95	255–258	256–258[22]
5b			15	96	252–258	–
5c			17	93	259–264	–
5d			21	88	255–258	255–257[23]
5e			24	89	264–266	263–265[22]
5f			17	92	254–256	253–255[22]
5 g			18	92	265–268	261–263[22]
5 h			18	90	272–276	276–278[24, 25]

[a] Isolated yields

   Our method is advantageous to other methods from viewpoint of the shorter reaction time and higher yield of production with an insignificant fraction of the side products. This method compared with other methods shown in Table 5.

Conclusion

The application of Fe$_3$O$_4$@SiO$_2$-imine/phenoxy-Cu(II) as a catalyst shows a highly efficient catalytic activity for the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione and dihydropyrano[3,2-*c*]chromene derivatives due to the presence of Cu species in the catalyst which act as Lewis acid. The newly synthesized derivatives
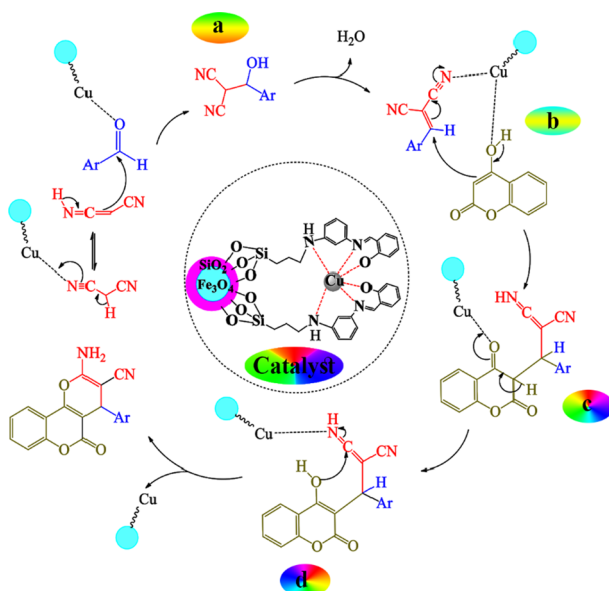
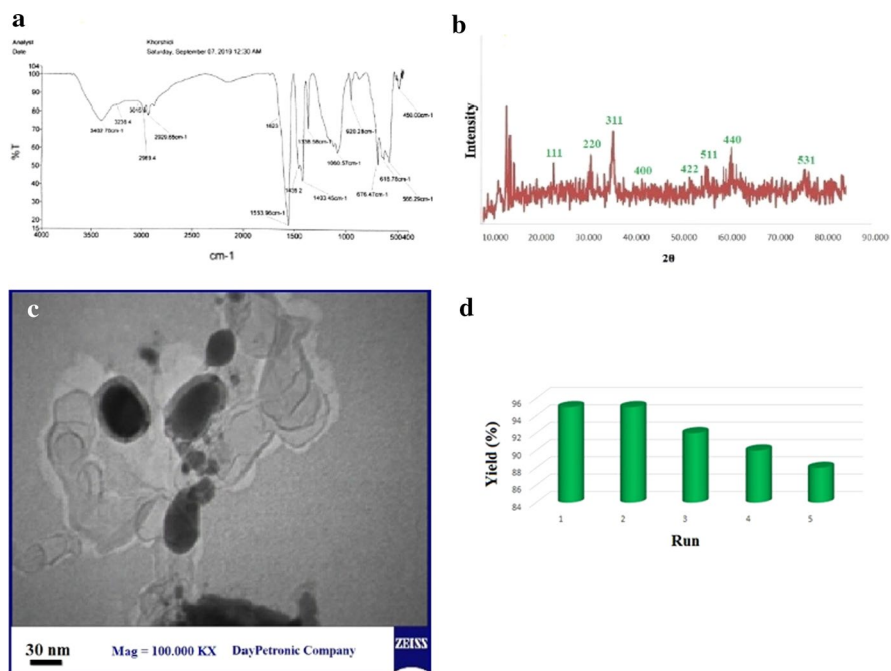**Scheme 3.** Proposed mechanism for synthesis of dihydropyrano[3,2-*c*]chromene

Fig. 1 image of the FT-IR (**a**),XRD (**b**), TEM(**c**) of reused catalyst and, recyclability of the Fe$_3$O$_4$@ SiO$_2$-imine/phenoxy-Cu(II) (**d**)

Table 5 Compared this method with reported methods

Entry	Catalyst	Conditions	Product	Time (min)	Yield (%)	References
1	β-Cyclodextrin	H_2O–EtOH (4:1), 100 °C	4a	150	93	[26]
2	CuI- NP_S	Solvent-free, 70 °C	4a	27	91	[38]
3	p-TSA (30 mol%)	[Bmim]Br, 100 °C	4a	180	94	[39]
4	Et_3N (20 mol%)	EtOH, 50 °C, ultrasound	4a	60	90	[40]
5	ZrO_2- NPs	Solvent-free, 100 °C	4a	40	91	[41]
6	AL-KIT-6	EtOH, 60 °C	4a	240	93	[42]
7	**Fe_3O_4@SiO_2-Imine/Phenoxy-Cu(II)**	**Solvent-free, 80 °C**	**4a**	**20**	**92**	present work
8	Nano-Al_2O_3	EtOH, r.t	5a	300	80	[43]
9	Nano-Al(OH)$_3$	EtOH, reflux	5a	120	71	[44]
10	Fe_3O_4/SiO_2/Met	H_2O/EtOH (1:1), reflux	5a	60	85	[45]
11	$H_6P_2W_{18}O_{62}$·18H_2O	H_2O-EtOH, reflux	5a	30	89	[46]
12	MgO/H_2O	EtOH, reflux	5a	32	89	[47]
3	(S)-Proline	H_2O-EtOH, reflux	5a	180	72	[48]
14	Ni@Imine-Li$^+$-MMT	Solvent-free, 100 °C	5a	18	93	[49]
15	**Fe_3O_4@SiO_2-Imine/Phenoxy-Cu(II)**	**Solvent-free, 90 °C**	**5a**	**17**	**95**	present work

were analyzed and their structure was corroborated. The main advantages of this work are facile reaction workup, recyclability and reusability of the catalyst, low catalyst loading, short reaction times and considerable yield of the product. Briefly, our method is advantageous to other methods from viewpoint of the shorter reaction time and higher yield of production with an insignificant fraction of the side products.

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