Nickel ferrite nanocrystalline as a green and recyclable catalyst for the synthesis of Spiro-oxindole-chromene

S H Oktavia, A H Cahyana and R T Yunarti

Department of Chemistry, Faculty of Mathematics and Natural Sciences (FMIPA), Universitas Indonesia, Depok 16424, Indonesia

Corresponding author’s email: herrykim@ui.ac.id

Abstract. A separable NiFe$_2$O$_4$ nanocrystalline catalyst was synthesized via a simple co-precipitation method. The catalytic activity of this heterogenous catalyst was investigated to synthesize Spiro-oxindole-chromene derivates via Knoevenagel condensation, and Michael addition reaction under conventional heating condition. The catalyst showed a prominent catalytic activity in a good yield (86.74 %). This easily separated catalyst could be recycled efficiently for four cycles without significant loss of its activity. Furthermore, the products were investigated for the antioxidant activity using DPPH method. The IC$_{50}$ of the compounds was found to be 182.3 ppm. The use of catalysts has been proven a simple, efficient and environmentally friendly reaction. Based on the results, it is known that the reaction could not be achieved without the presence of NiFe$_2$O$_4$ catalyst.

Keywords: NiFe$_2$O$_4$, nanocrystalline, Spiro-oxindole-chromene, antioxidant

1. Introduction
In recent years, the synthesis of magnetic nano-sized has been an interesting objects of catalyst research because of low cost in producing, environmentally friendly, efficient, and recyclable. The nanosized properties are able to maximize contact between reactants and catalyst to improve the catalytic activity. The use of catalysts could be easily separated by external magnet is one of the most promising strategies that make it a useful class of heterogeneous catalysts, because the catalyst could be used for several times [1]. Specifically, nano-sized iron oxide-based magnet such as magnetic (Fe$_3$O$_4$) and maghemite ($\gamma$-Fe$_3$O$_4$) have previously been explored as the catalyst, as well as supporting catalyst in several organic reactions [2]. Another oxide, spinel ferrite (MFe$_2$O$_4$; M = Ni, Zn, Mn, and Co) has received much attention because for its application as catalyst. Well-dispersed spinel ferrite is slightly toxic and poisonous accompanied by a high specific surface area. These two compounds not only greatly improve the dispersion and interface structure of bimetal oxide, but also adjust the selectivity, acidity, and durability. Therefore, spinel ferrite catalyst has an amazing synergistic effect to the reaction because of these two kinds of metal on it [3].

Among various spinel ferrite nano-sized that is currently being developed is nickel ferrite NiFe$_2$O$_4$. This nano-sized possesses an inverse spinel structure, that is, all Ni$^{2+}$ ions are in the octahedral site and Fe$^{3+}$ ions are evenly distributed in the tetrahedral and the octahedral sites. NiFe$_2$O$_4$ nano-sized shows ferrimagnetic properties from anti-parallel magnetic moment pairs between the magnetic moment of Fe$^{3+}$ ion in tetrahedral site and magnetic moment of Ni$^{2+}$ and Fe$^{3+}$ ion in octahedral site [4]. An inverse
spinel structure from NiFe$_2$O$_4$ is an important soft magnetic material with moderate saturation magnetization, remarkable thermal stability, high magneto crystalline anisotropy, high electrical resistivity, chemical stability, and mechanical hardness [5]. NiFe$_2$O$_4$ nano-sized has been extensively investigated and showed a better catalytic for organic reactions such as the synthesis of pyridine 2-alkoxy-3-arylimidazo[1,2-α]pyridines [6], 1,4-dihydropyranol[2,3-c]pyrazole [7], spiro[indole-3,2’-pyrrole]-2,5’(1H,1’H)-diones [8], substituted 4H-chromene [9], etc. In this current study, NiFe$_2$O$_4$ nanocrystalline was used for the first time to synthesize the Spiro-oxindole-chromene via multicomponent reaction and the compounds are characterized by TLC, FT-IR and LC-MS/MS, tested for antioxidant activity.

2. Materials and method

All the materials were purchased from Merck and Sigma-Aldrich. Fourier Transform Infrared Spectroscopy (FTIR) was performed by using Shimadzu 8400 spectrometer with KBr background. X-Ray Diffraction patterns were recorded using a Malvern Analytical X-ray diffractometer. Images of Scanning Electron Micrograph (SEM) were obtained with a Sigma Zeiss Microscope. The nanocrystalline elemental analysis was performed using Dispersive Energy X-ray (ZX) Spectroscopy recorded on Amatek. Mass spectrum (MS) was carried out by LC-MS/MS (Waters). The product was monitored by TLC.

2.1. General procedure for NiFe$_2$O$_4$ nanocrystalline synthesis

NiFe$_2$O$_4$ was prepared using a modified co-precipitation method from the previous study by Heravi et al. Fe(NO$_3$)$_3$.6H$_2$O (6 mmol) and Ni(NO$_3$)$_2$.6H$_2$O (3 mmol) were dissolved in 25 mL of deionized water and stirred for 30 min at room temperature. The pH was controlled at 10 by adding 0.5 M NaOH dropwise and the brown precipitation formed. Thereafter, the precipitation was washed for several times until pH 7 with deionized water, and dried for 12 h at 70 °C. It was then calcined at 660 °C for 2 h [7].

2.2. General Procedure for Spiro-oxindole-chromene synthesis

A mixture of isatin (0.1 mmol), malononitrile (0.1 mmol), 8-hydroxyquinoline (0.1 mmol), and the presence of NiFe$_2$O$_4$ catalyst in ethanol as a solvent. The mixture was stirred and heated to 70 °C. The reaction was recorded by TLC and an external magnetic field was used to separate the catalyst. The mixture was recrystallized with hot ethanol and cold water.

2.3. Antioxidant activity test

The antioxidant assay procedure was determined using 1,1-diphenyl-2-picrylhydrazyl (DPPH•) based on the procedure of Subbareddy and Sumanthi [10]. Briefly, 2 mL of Spiro-oxindole-chromene with various concentrations (0, 50, 100, 150, 200 and 250 ppm) were prepared by dissolving the stock solution (0.0125 g compound in 25 mL ethanol) which was mixed into 2 mL of 0.1 mM DPPH solution and incubated in the dark chamber for 30 min at room temperature. Then, the absorbance of incubated sample was determined at 517 nm by UV-Vis spectroscopy. The free radical scavenging activity was calculated by the equation:

\[
\% \text{ Inhibition} = \frac{[AC - AS/AC]}{AC} \times 100
\]

where AC is the absorption of DPPH solution and AS is the absorption of the sample solution. Moreover, the IC$_{50}$ value was determined for the sample.

2.4. Spectral data of the compound

2’-amino-2-oxospiro[indoline-3,4’-pyrano[3,2-h]quinoline]-3’carbonitrile
Color: red solid. Melting point: 209.4–209.8 °C. Rf: 4 cm. LC-MS/MS [M+H]+= m/z 341.10 (Rt 7.97). IR (KBr): t_max = 3319.63, 3203.90, 2199.43, 1614.48, 1473.67, 1380.12, 1115.86, 758.05.

3. Results and discussion

3.1. Characterization of NiFe2O4 nanocrystalline

The FTIR spectrum of NiFe2O4 nanocrystalline is shown in figure 1a. FTIR analysis shows two characteristics peak of NiFe2O4 at 408.92663 cm\(^{-1}\) which could be assigned to metal vibration of Ni-O bonds and 614.35424 cm\(^{-1}\) could be assigned to vibration of Fe-O bonds. The bands at 3495.16448 cm\(^{-1}\) and 1579.76805 cm\(^{-1}\) could be assigned to the stretching and bonding of O-H group [11].

XRD analysis of NiFe2O4 nanocrystalline is shown in figure 1b. The XRD patterns of NiFe2O4 nanocrystalline showed peaks at 30.30°; 35.71°; 37.32°; 43.34°; 53.90°; 57.48°; 63.04°. These indicate that NiFe2O4 nanocrystalline structure is cubic spinel (JCPDS: 01-074-2081). However, there is a small percentage of α-Fe2O3 (33.16°) associated with NiFe2O4 was detected by XRD, it’s because of thermal treatment [12]. The crystalline size of NiFe2O4 was calculated using Debye-Scherrer equation (D=K.λ/β.cosθ), based on the peak intensity in the XRD analysis. The crystalline size of NiFe2O4 nanocrystalline was found 23.56 nm.

Figure 2a and figure 2b show the SEM-EDX analysis of NiFe2O4 nanocrystalline. SEM-EDX analysis was used to evaluate NiFe2O4 nanocrystalline composition. According to the result of SEM-EDX, it could be seen that the comparison of Ni, Fe and O in NiFe2O4 nanocrystalline is suitable with the previous study that is 1:2:4 [13] (table 1).

3.2. Synthesis of Spiro-oxindole-chromene using NiFe2O4 nanocrystalline

The amount of catalyst becomes the main parameter in obtaining the optimal condition for multicomponent reaction between isatin (0.1 mmol), malononitrile (0.1 mmol), and 8-hydroxyquinoline (0.1 mmol) in figure 3. From the result of the calculation, it was found that by using 6% (mol) the amount of catalyst gave the optimal result for complete reaction in 4 h and result of 87.84% in 10 mL ethanol as a solvent and heated at 70 °C. It was discovered that no yield increase noted when the reaction was conducted with the 8 and 10% (mol) amount of catalyst. NiFe2O4 nanocrystalline is considered as an efficient catalyst in organic reaction.

Figure 1. (a) FT-IR spectrum and (b) XRD patterns of NiFe2O4 nanocrystalline.
Figure 2. (a) SEM-EDX patterns and (b) Morphology of NiFe$_2$O$_4$ nanocrystalline.

Table 1. EDX of NiFe$_2$O$_4$ nanocrystalline.

| Element | wt%  | at%  |
|---------|------|------|
| NiK     | 24.94| 15.28|
| FeK     | 51.47| 32.67|
| OK      | 23.60| 52.28|

Figure 3. Reaction of Spiro-oxindole-chromene.

Table 2 shows that there was no product was obtained in the absence of the catalyst (table 2) indicating that the catalyst plays a necessary role in the reaction. Raising the amount of the catalyst increased the yield of the product even after the optimum amount of the yield decreased. The amount of 6 mol% catalyst gives the highest yield, so the amount of 6 mol% catalyst is used as a reference for further synthesis. Ni is the important active component because of its high Lewis acidity that would lead to the reaction to be more readily achievable [14]. Composition of catalyst is generally affecting the catalytic activity. In the case of ferrite, the activity of catalyst depends on several parameters, namely particle size, redox properties of metal ions, and their distribution between the tetrahedral site and octahedral site of the cubic spinel lattice. The octahedral site takes a significant part in catalyst because the octahedral site is exposed on the surface. In addition, metal ions at octahedral site are located at a greater distance therefore they could interact freely with the reactant molecules [15]. The second parameter is the effect of reaction time (2, 4 and 6 h) on the yield product. The reaction was carried out at 70 °C with the amount of 6 mol % catalyst in 10 mL ethanol as the solvent. The optimal time for the
reaction is 4 h, the increase of time decreases the yield of product. The third parameter is the effect of temperature (r.t °C, 50 °C, 70 °C) on the yield product. The reaction was carried out at 70 °C with the amount of 6 mol% catalyst in 10 mL ethanol as the solvent for 4 h.

This catalyst is stable, which could be proven by comparing the fresh and reused NiFe₂O₄ nanocrystalline. The proposed mechanism of the reaction using NiFe₂O₄ nanocrystalline as a catalyst is likely to follow the Knoevenagel Reaction involving the evident coupling of aldehyde (isatin) with active methylene (malononitrile), and also Michael addition of intermediate gives the target product. The mechanism of reaction is shown in figure 4.

The use of heterogeneously catalyzed reaction has an advantage of the reuse possibility. The recyclable of NiFe₂O₄ nanocrystalline catalyst was also investigated using the optimized reaction conditions. The recyclable of the catalyst was tested by running 4 reactions using the same catalyst. The yield indicated that there was no significant change in yield by using the same catalyst for several times as shown in figure 5.

Based on the figure 5, there are no significant change in % yield after the catalyst used for 4 times for synthesis. But, the decline in catalytic ability can be occurred due to several factors, such as agglomeration of particles which will reduce the surface area, thereby reducing the catalyst performance. Besides, the activity of the catalys will decrease along with the use of the catalyst. This can be caused by the deactivation of the catalyst. Some of the causes of the catalyst deactivation in this case are (1) poisoning (2) contamination, and solid-state diffusion.

The XRD spectra in figure 6 show that the typical peaks of NiFe₂O₄ still appears although some peaks have decreased, such as the peaks at 37.32° and 53.90° which is the peaks of NiFe₂O₄. It can be concluded that the NiFe₂O₄ plays the role in catalyzing the organic reaction, even though there is a small percentage of α-Fe₂O₃.

3.3. Antioxidant activity

The antioxidant activity was carried out using the 1,1-diphenyl-2-picrylhydrazyl (DPPH•) assay. The activity of the compounds was compared with 8-hydroxyquinoline as a precursor. The IC₅₀ value was obtained using the regression analysis between concentration and % inhibition (figure 7a and figure 7b). The result showed that Spiro-oxindole-chromene has a lower IC₅₀ (182.3 ppm) than 8-hydroxyquinoline as a precursor (32.73 ppm).

| Entry | Catalyst (% mol) | Temperature (°C) | Time (hour) | Yield (%) |
|-------|------------------|------------------|-------------|-----------|
| 1     | 0                | 70               | 4           | Trace     |
| 2     | 2.5              | 70               | 4           | Trace     |
| 3     | 5                | 70               | 4           | 75.57     |
| 4     | 7.5              | 70               | 4           | 86.74     |
| 5     | 10               | 70               | 4           | 81.74     |
| 6     | 7.5              | r.t.             | 4           | Trace     |
| 7     | 7.5              | 50               | 4           | Trace     |
| 8     | 7.5              | 70               | 2           | 51.62     |
| 9     | 7.5              | 70               | 6           | 62.93     |
Figure 4. Mechanism reaction of Spiro-oxindole-chromene by NiFe$_2$O$_4$ nanocrystalline.

Figure 5. Recyclability catalyst test result in the synthesis of Spiro-oxindole-chromene.
4. Conclusion

A simple, efficient and environmentally friendly NiFe$_2$O$_4$ nanocrystalline had been synthesized using a simple co-precipitation method as a catalyst in the multicomponent reaction of an isatin, malononitrile, and 8-hydroxyquinoline. The recyclable property of catalyst is the most important property to green chemistry principle. The synthesized compound also has a good antioxidant activity with IC$_{50}$ 261.48 ppm.

Acknowledgments

This work was financially supported by Universitas Indonesia under research grant PITTA A with grant contract number NBK-0432/UN2.R3.1/HKP.05.00/2019.
References
[1] Wang D and Astruc D 2014 Chem. Rev. 114 6949-85
[2] Karimi B and Farhangi E 2011 Chem. Eur. J. 17 6056-60
[3] Luo L et al. 2015 Catal. Sci. Technol. 5 3159-65
[4] Hajalilou A, Hashim M, Ebrahimim-Kahrizsangi R, Kamari H M and Sarami N 2014 Ceram. Int. 40 5881-7
[5] Wang J et al. 2009 J. Alloys Compd. 479 791-6
[6] Payra S, Saha A and Banerjee S 2016 RSC Adv. 6 52495-9
[7] Heravi M R P and Morsalie N 2018 Iran. Chem. Commun. 6 87-96
[8] Meghyasi R, Safaei-Ghomi J and Sharif M A 2016 J. Chem. Res. 40 397-9
[9] Ahankar H, Ramazani A, Slepokura K, Lis T and Joo S W 2018 Turk. J. Chem. 42 719-34
[10] Subbareddy C V, Sundarrajnan S, Mohanapriya A, Subashini R and Shannugam S 2018 J. Mol. Liq. 251 296-307
[11] Moghaddam F M, Tavakoli G and Rezvani H R 2014 Appl. Organomet. Chem. 28 750-5
[12] Gotic M, Czako-Nagy I, Popovic S and Music S 2010 Philos. Mag. Lett. 78 193-201
[13] Naik K M and Sampath S 2018 Electrochim. Acta 292 268-75
[14] Li Q, Wang X, Yu Y, Chen Y and Dai L 2016 Tetrahedron 72 8358-63
[15] Goyal A, Bansal S and Singhal S 2014 Int. J. Hydrogen Energ. 39 4895-908