An efficient one-pot multi-component synthesis of spirooxindoles using $Fe_3O_4/g-C_3N_4$ nanocomposite as a green and reusable catalyst in aqueous media

Fatemeh Kamali, Farhad Shirini

 PII:
 S0022-2860(20)31967-0

 DOI:
 https://doi.org/10.1016/j.molstruc.2020.129654

 Reference:
 MOLSTR 129654



To appear in: Journal of Molecular Structure

Received date:	2 June 2020
Revised date:	5 November 2020
Accepted date:	21 November 2020

Please cite this article as: Fatemeh Kamali, Farhad Shirini, An efficient one-pot multicomponent synthesis of spirooxindoles using $Fe_3O_4/g-C_3N_4$ nanocomposite as a green and reusable catalyst in aqueous media, *Journal of Molecular Structure* (2020), doi: https://doi.org/10.1016/j.molstruc.2020.129654

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier B.V.

An efficient one-pot multi-component synthesis of spirooxindoles using Fe₃O₄/g-C₃N₄ nanocomposite as a green and reusable catalyst in aqueous media

Fatemeh Kamali and Farhad Shirini*

Department of Chemistry, College of Science, University of Guilan, Rasht, 41335-19141, Iran E-mail address: shirini@guilan.ac.ir, Tel/Fax: +98 131 3233262

Highlights:

- ✓ Introduction of $Fe_3O_4/g-C_3N_4$ nanocomposite as an efficient magnetic nanocatalyst.
- ✓ Application of $Fe_3O_4/g-C_3N_4$ in the promotion of the synthesis of spirooxindoles.
- ✓ Simple and easy experimental procedure.
- ✓ Availability and reusability of the catalyst.
- ✓ Use of water as an eco-friendly solvent.

Abstract

In this study, an efficacious method is described for the synthesis of spirooxindole derivatives using Fe_3O_4/g - C_3N_4 as a green catalyst. This is a one-pot three-component condensation in water as a clean and environmentally favorable media. The present procedure proposes various remarkable privileges such as mild reaction conditions, simple work-up procedure and environment friendly. Moreover, the catalyst used is easily recovered by the external magnetic field and reused without significant deterioration in catalytic activity after at least six times.

Keywords: Spirooxindoles, magnetic nanocomposite, water, reusable, catalyst, Fe₃O₄/g-C₃N₄.

1. Introduction

Green chemistry as a powerful tool plays momentous role in various research fields such as synthetic organic, biomedical, industrial chemistry, etc. [1-2]. An important step in the successful development of green chemistry is the design of highely efficiently and inexpensive synthetic methods, and therefore requires short and efficacious synthetic sequences for this purpose.

MCRs employ a minimum of three reactants or reaction centers, and most of the contents from the starting materials are combined to provide collection of complex scaffolds from the easily available precursors in a simple one-pot procedure [3-6]. Based on this, these types of reactions comply with the principles of green chemistry by saving time and energy, while containing the high atom-economy, quick and simple implementation. Therefore, there is increasing interest in multicomponent reactions to rapidly build versatile scaffolds [7-8]. Newly execution of MCRs in water as reaction medium has engrossed extremely attention, because water is an inexpensive, safe, and environmentally mild solvent. Sometimes it exhibits higher reactivity and selectivity compared to other conventional organic solvents owing to its strong hydrogen bonding ability [9-10].

In the last years, the spiro [4*H*-pyran] derivatives have attracted notable attention in organic synthesis. The spirooxindole system is the core structure of diversity of natural alkaloieds. Moreover, they have momentous medicinal properties including anticancer [11], antioxidant [12], antimicrobial [13], antifungal [14], anti HIV [15] and antitubercular activities [16]. Due to the aforesaid properties a variety of methods using diverse types of catalysts have been reported in the literature for the procurement of these types of compounds [17-20].

On the other hand, we have observed a drastic growth of interest in materials with graphitelike structures, such as graphene (G) and graphene oxide (GO), because of their unparalleled

attributes including large surface area and hexagonal array of carbon atoms in graphite sheets which are ideal for strong interactions with other molecules [21-30].

As a new two dimensional graphite analogue, graphitic carbon nitride $(g-C_3N_4)$ have absorbed much regard in research fields [31-33]. Friendly polymeric nature of $g-C_3N_4$ assures enough flexibility of the structure, which can serve as a host matrix of distinguished compatibility to different inorganic nanoparticles [34-36]. Further, procurement of $g-C_3N_4$ can be simply performed by thermal condensation of low-cost nitrogen rich precursors, and therefore, it is economic and environmentally [37]. However, a significant impediment which has limited the further expansion of $g-C_3N_4$ in the field of catalysis is difficulty of its separation from reaction mixture due to its very dispersive nature.

Recently, magnetic nano particles (MNPs) have imbibed striking attention in the area of chemical research due to their inimitable applications such as their utilization for drug delivery systems [38], cell separation [39], magnetic resonance imaging [40], cancer treatments through hyperthermia [41] and protein separation [42].

According to the above, preparation of magnetically separable nanocomposites based on g- C_3N_4 would enable their simple separation from the solution with an external magnet. Magnetic substance, Fe₃O₄ will not only raise the recycling rate, but also the catalytic activity of the intelligent material. The Fe₃O₄/g-C₃N₄ nanocomposite is g-C₃N₄ sheets decorated by Fe₃O₄ nanoparticles.

As a part of our program in the development of expedient methods and regarding to unique physicochemical characteristics of graphitic carbon nitride $(g-C_3N_4)$ such as its excellent thermal and chemical stability, low cost, non-toxicity, and "earth-abundant" nature, herein, we have introduced a facile and benign protocol for the synthesis of spirooxindoles using Fe₃O₄/*g*-C₃N₄ nanocomposite as catalyst. For this purpose, at the first step pure *g*-C₃N₄ was fabricated *via* one-step polymerization of melamine as a cheap feedstock without any organic

solvents. Then Fe_3O_4/g - C_3N_4 nanocomposite was synthesized by decoration of graphitic carbon nitride nanosheets with Fe_3O_4 nanoparticles. In the next step, considering the principles of green chemistry, the synthesis of spirooxindoles as biologically important compounds using MCRs in the presence of Fe_3O_4/g - C_3N_4 nanocomposite as a reusable and environmentally benign catalyst in water as a green solvent was investigated. Based on our knowledge , Fe_3O_4/g - C_3N_4 nanocomposite has been relatively less explored as a catalyst in organic synthesis.

2. Experimental

2.1 Chemicals and apparatus

Chemicals were purchased from Fluka (Buchs, Switzerland), Merck (Darmstadt, Germany) and Sigma-Aldrich (Steinheim, Germany) Chemical Companies. The purity determination of the substrate and reaction monitoring were accompanied by thin-layer chromatography (TLC) on a silica gel polygram SILG/UV 254 plate. The products were separated and purified by different chromatographic techniques and were identified by the comparison of their IR, NMR and refractive index with those reported for the authentic samples. All yields refer to the isolated products. The IR spectra were run on a Perkin–Elmer bio-spectrometer. The ¹H NMR and ¹³C NMR (250 MHz) were run on a Bruker Avance DPX-300 FTNMR spectrometer (d in ppm). Melting points were recorded on a Bu⁻ chi B-545 apparatus in open capillary tubes. A Philips PW1840 diffractometer with Cu K_a radiation was used to record the X-ray patterns of the synthesized nanoparticles. Scanning electron microscope images were obtained with LEO 1430 VP. Thermogravimetric analysis (TGA) was carried out on a T.A model Q600 instrument. The magnetic properties were determined using vibrating sample magnetometry (VSM; Lake Shore 7200 at 300 KVsm).

2.2 Catalyst preparation

2.2.1 Preparation of $g-C_3N_4$

Graphitic carbon nitride (g-C₃N₄) was prepared through a facile calcination of melamine in air. In detail, 2.0 grams of melamine was weighted and put into an alumina crucible with a loose cover. Then this powder was heated to 250 °C from room temperature in a muffle furnace at a heating rate of 5 °C/min. The temperature was then enhanced to 550 °C with a heating rate of 10 °C/min and maintained at this temperature for another 2 h. Then, yellow *g*-C₃N₄ sample was cooled to room temperature [43].

2.2.2 Preparation of Fe_3O_4/g - C_3N_4

0.125 g g-C₃N₄ powder was dispersed in 250 mL of ethanol/water (1:1) and ultrasonicated for 5 h at ambient temperature. After that, FeCl₃.6H₂O (1.838 g) and FeCl₂.4H₂O (0.703 g) were dissolved in the solution using sonication for 2 h. In the next step, 10 mL of ammonia solution (NH₄OH) was rapidly injected into the reaction mixture. The suspension was then transmitted into a 100 mL Teflon-lined stainless steel autoclave and held at 100 °C for 1 h. After cooling to room temperature, black precipitates were collected after being washed with ethanol and water repeatedly. In the end, the gained precipitate was dried in an oven at 60 °C for 10 h [44].

2.3 Catalytic activity

2.3.1 General procedure for the preparation of spirooxindole derivatives

A mixture of isatin (1 mmol), malononitrile (1 mmol), C–H activated acid compound (1 mmol) and Fe₃O₄/*g*-C₃N₄ (0.025 g) in H₂O (5 mL) at 80 °C was stirred for the appropriate time [TLC: *n*-hexane: ethyl acetate (5:4)]. After completion of the reaction, the mixture was cooled to room temperature and filtered off, ethanol (10 mL) was added and the catalyst was removed using an external magnet. Evaporation of the solvent from mixture gave the solid

residue which recrystallized from EtOH to afford the pure product. Finally $Fe_3O_4/g-C_3N_4$ washed with H₂O and ethanol and be used for the next run.

2.4 Spectroscopic data of the selected compounds

2-Amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3carbonitrile (4c):

FT-IR (KBr, cm⁻¹) v_{max} : 3372, 3310, 3180, 3141, 2927, 2192, 1722, 1683, 1604, 1469, 1348, 1224, 1056; ¹H NMR (250 MHz, DMSO- d_6): δ (ppm): 0.98 (s, 6H), 2.10 (s, 2H), 2.4 (s, 2H), 6.77-7.19 (m, 4H Ar-H and 2H NH₂), 10.37 (s, 1H, NH); ¹³C NMR (62.9 MHz, DMSO- d_6): δ (ppm): 27.4, 28.0, 32.3, 47.2, 50.4, 57.9, 109.7, 111.2, 117.7, 122.4, 123.4, 128.5, 134.8, 142.4, 152, 159.4, 164.5, 178.4, 195.3.

2'-Amino-7',7'-dimethyl-2,5'-dioxo-5',6',7',8'-tetrahydro-2H-spiro[acenaphthylene-1,4'chromene]-3'-carbonitrile (4m):

FT-IR (KBr, cm⁻¹) v_{max} : 3350, 3275, 3144, 2910, 2180, 1714, 1668, 1598, 1475; ¹H NMR (250 MHz, DMSO- d_6): δ (ppm): 1.00 (s, 6H), 2.06 (s, 2H), 2.60 (s, 2H), 7.33-8.26 (m, 6H Ar-H and 2H NH₂); ¹³C NMR (62.9 MHz, DMSO- d_6): δ (ppm): 27.6, 27.9, 32.5, 50.1, 51.4, 58.4, 112.4, 117.9, 120.2, 121.8. 125.0, 128.9, 129.3, 130.2, 131.9, 132.6, 140.9, 143.6, 159.2, 165.0, 195.8, 204.0.

3. Results and discussion

As we have mentioned previously, the focus of this article is on the preparation of Fe_3O_4/g - C_3N_4 nanocomposite as a green catalyst (Scheme 1) and its applicability in the acceleration of the synthesis of spirooxindoles as a model organic reaction.

3.1 Characterization of Fe_3O_4/g - C_3N_4

3.1.1 FT-IR study

FT-IR spectrum of g-C₃N₄ (Fig. 1b), displayed characteristic absorption at 1640 cm⁻¹ because of the heterocyclic C=N stretching vibration bond. The peaks centered at 1240, 1323, 1409

and 1546 cm⁻¹ are ascribable to the C–N stretching of tri-s-triazine [44]. The sharp peak centered at 809 cm⁻¹ is a characteristic breathing mode of the triazine unit [36]. The broad band around 3000-3300 cm⁻¹ region is attributed to the stretching vibration modes of residual N-H components, associated with uncondensed amino groups. In the case of Fe₃O₄-MNPs (Fig. 1c) represented characteristic absorption at 564 and 443 cm⁻¹ due to the Fe–O–Fe vibration related to the magnetite phase [33]. In addition, FT-IR spectrum of Fe₃O₄/g-C₃N₄ nanocomposite (Fig. 1d) showed the successful formation of Fe₃O₄/g-C₃N₄ nanocomposite. It can be clearly seen that the essential characteristic peaks of *g*-C₃N₄ and Fe₃O₄ emerge in the spectrum of Fe₃O₄/g-C₃N₄ nanocomposite. Howere, the spectrum of Fe₃O₄/g-C₃N₄ nanocomposite shows the broad band around 3400 cm⁻¹ which is assigned to the O–H stretching vibrations of adsorbed H₂O molecules caused the absorption band to appear at 1640 cm⁻¹.

3.1.2 XRD study

Figure 2 showed the XRD patterns of Fe₃O₄ nanoparticles, pure *g*-C₃N₄ and Fe₃O₄/*g*-C₃N₄ nanocomposite. In XRD pattern of Fe₃O₄ nanoparticles (Fig. 2a) diffraction peaks with 2 θ at 30°, 35.6°, 43.2°, 53.7°, 57.2° and 62.5° are seen which affirm the structure of the magnetite Fe₃O₄ (JCPDS card no. 79-0418). From the Fig. 2b, it can be observed that the *g*-C₃N₄ sample has two distinct peaks at 12.9° and 27.6°, which can be indexed to the hexagonal phase of graphitic C₃N₄ (JCPDS 87-1526). The sharp and intense diffraction peak at 2 θ = 27.6° which is attributed to the (002) planes of graphitic structures. The minor peak at 12.9° relates to the hole-to-hole arrays of tri-*s*-triazine units. The Fe₃O₄/g-C₃N₄ nanocomposite had the peaks corresponding Fe₃O₄ and g-C₃N₄, indicting Fe₃O₄ were successfully deposited on g-C₃N₄ surface. As can be seen in Fig. 2c, the diffraction peak (002) is a characteristic peak

of g-C₃N₄ that was present in the pattern of the Fe₃O₄/g-C₃N₄ nanocomposite. It was also seen that the crystal phase of Fe₃O₄ did not change after hybridization with g-C₃N₄.

3.1.3 SEM study

SEM images were utilized to investigate the morphology of the catalyst. Figure 3 showed the image of Fe_3O_4/g - C_3N_4 nanocomposite with different diameter. Pursuant to the Fig. 3a, *g*- C_3N_4 has the layered structure which after combining with Fe₃O₄, the nanoparticles are sparsely distributed on the surface of *g*- C_3N_4 nanosheets, resulting in the formation of a heterostructure. Also from the enlarge image of Fe₃O₄/*g*- C_3N_4 (Fig. 3b) it was observed that Fe₃O₄ nanoparticles have well covered the surface of *g*- C_3N_4 and their average size is about 15-30 nm.

3.1.4 TGA study

TGA was used to determine the content of Fe₃O₄ nanoparticles on *g*-C₃N₄ nanosheets. Figure 4 shows TGA curves of pure *g*-C₃N₄ and the Fe₃O₄/*g*-C₃N₄ nanocomposite. As shown in Fig. 4a, when the temperature is higher than 550 °C, the sublimation or decomposition of *g*-C₃N₄ occurred and the decomposition of *g*-C₃N₄ is completed at about 650 °C which is attributed to the burning of g-C₃N₄. It is evident that, pure *g*-C₃N₄ is stable up to 550 °C. As can be seen for Fe₃O₄/*g*-C₃N₄ nanocomposite (Fig. 4b) the weight loss in the range 460-550 °C was observed, which could be ascribed to loss of the *g*-C₃N₄. Because of the oxidation and decomposition of *g*-C₃N₄ in the Fe₃O₄/*g*-C₃N₄ nanocomposite the stability of the nanocomposite was decreased. The degradation of the Fe₃O₄/*g*-C₃N₄. This indicated that there was a tight contact between Fe₃O₄ and *g*-C₃N₄. According to the mass loss in Fe₃O₄/*g*-C₃N₄ nanocomposite was decreased. The degradation of the Fe₃O₄/*g*-C₃N₄ manocomposite was was a tight contact between Fe₃O₄ and *g*-C₃N₄. According to the mass loss in Fe₃O₄/*g*-C₃N₄ nanocomposite was a tight contact between Fe₃O₄ Nps and *g*-C₃N₄ in the Fe₃O₄/*g*-C₃N₄ nanocomposite was decreased.

3.1.5 VSM study

The magnetization hysteresis for the Fe₃O₄ nanoparticles and Fe₃O₄/g-C₃N₄ nanocomposite are shown in Fig. 5. The saturation magnetization (*Ms*) of Fe₃O₄ nanoparticles (curve a) was about 77.8 emu/g, which decreased to 39.5 emu/g for Fe₃O₄/g-C₃N₄ nanocomposite (curve b). This decrease could be attributed to the wide existence of g-C₃N₄ in the structure of the Fe₃O₄/g-C₃N₄ nanocomposite that has a shielding effect. Such magnetizations clearly reveal that the Fe₃O₄/g-C₃N₄ nanocomposite possesses excellent magnetic sensitivity and the synthesized nanocomposite could be simply separated with the help of an external magnet.

3.2 Application of Fe₃O₄/g-C₃N₄

In continuance of our interest on the application of ecofriendly catalysts for extension of effectual and green benign synthetic methodologies, herein we desire to report one-pot synthesis of spirooxindole derivatives using $Fe_3O_4/g-C_3N_4$ as an efficient and reusable catalyst. First of all and in an optimized procedure, the condensation of isatin, malononitrile and dimedone was checked as a model in the attendance of varying amounts of the catalyst under different conditions in various solvents (*n*-Hexane, CHCl₃, CH₃CN, EtOH and H₂O) and also in the absence of solvent. The obtained results showed that the reaction using 0.025 g Fe₃O₄/g-C₃N₄ as the catalyst in H₂O at 80 °C proceeded with the highest yield (Table 1). On the basis of our prior optimized conditions, the activity of the catalyst was then investigated in the one-pot three component reaction of various C-H activated acid compounds with isatin and malononitrile. As observed in Table 2, the reaction of isatin/5flouroisatin with other C–H activated acid compounds (1,3-cyclohexanedione, α/β naphthol, 4-hydroxycoumarin, ethyl acetoacetate, barbituric acid) and malononitrile also afforded the desirable products in good yields. Therewith, we have performed cyclocondensation with cyclohexane-1,3-dione, dimedone and 4-hydroxycoumarin, malononitril, and

acenaphthenequinone instead of isatin, and the corresponding products were obtained in good yields under similar reaction conditions (Table 2, entries 12–14).

To understand the reaction mechanism, for the synthesis of the spirooxindoles, we have envisioned a rough approach by combining the theoretical aspects (Scheme 2). The increased reaction rate by Fe_3O_4/g - C_3N_4 was consistent with the double-activation of this catalyst. At the first step, Fe_3O_4 can activate the carbonyl group of isatin making it more susceptible to nucleophilic attacks. Also, hydrogen bonding interactions between the amine groups of the catalyst and the isatin may play an important role in activation of carbonyl group of isatin. As well as, the triazine rings may lead to efficient deprotonation of the malononitrile. Therefore, the methylene anion should be able to covalently interact with the carbonyl group of the isatin to formation of the Knoevenagel intermediate (1). It seems that formation of hydrogen bonding with the amino groups of Fe_3O_4/g - C_3N_4 , brings activated isatin and methylene anion into close proximity and thereby increasing the reactivity of the reaction. Then dimedone converts to enole form after tautomerisation and attacks to the Knoevenagel intermediate as Michael acceptor to give (II) which is also promoted by Fe_3O_4/g - C_3N_4 . Finally, the target products are formed *via* an intramolecular cyclization (III).

The reusability of the catalyst was tested in the reaction of isatin with malononitrile and dimedone under the optimized reaction conditions as shown in Fig. 6. After completion of the reaction, ethanol was added and the catalyst was simply separated by attaching an external magnet and washed with H₂O and ethanol, dried under vacuum and reused in a subsequent reaction. It was found that Fe_3O_4/g -C₃N₄ could be used for six successive runs without a noticeable decrease in its activity. The morphology of the catalyst was investigated by SEM (Fig. 7) and it showed the same shape before use and after six reuses in the model reaction.

To presentation the privileges of the above mentioned method, we further compared the efficiency of the prepared catalyst with some of those reported in the literature, for the

reaction of isatin, malononitrile and dimedone (Table 3). Albeit all of the mentioned catalysts are appropriate for certain synthetic conditions, but most of them suffer from one or more disadvantages such as long reaction times, low yields, use of toxic catalyst, boring work-up procedure and high catalyst loading. Moreover, in most of the reported methods, catalysts are not recyclable. So the use of $Fe_3O_4/g-C_3N_4$ leads to an improved protocol in terms of compatibility with environment, reaction times, yields of the products and the amounts of the catalyst compared with the other catalysts.

4. Conclusions

In conclusion, a substantial and convenient technique for the synthesis of spirooxindole derivatives has been developed *via* one-pot three-component reaction in the presence of $Fe_3O_4/g-C_3N_4$ nanocomposite. The catalyst can be recovered and reused at least six times without loss of activity. The uses of water, absence of tedious separation techniques, mild reaction conditions, and simple procedure are the other notable features of this protocol which make it a beneficial and noteworthy process for the synthesis of spirooxindoles as biologically attractive compounds.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Credit author statement

Introduction of a reusable catalyst for the synthesis of spirooxindole derivatives, high yields of the products and easy and simple procedure are the main advantaged of this article make it be a good candidate for publication in J. Mol. Structure. It should be emphasize that the submission is original, not under consideration for publication elsewhere, and that all authors are aware of the submission and agree to its publication.

Acknowledgements

We are thankful to the University of Guilan Research Council for the partial support of this work.

References

- A. Ivanković, A. Dronjić, A. M. Bevanda, S. Talić, Int J Sustain Green Energy, 2017, 6, 39-48.
- [2] K. Alfonsi, J. Colberg, P. J. Dunn, T. Fevig, S. Jennings, T. A. Johnson, H. P. Kleine, C. Knight, M. A. Nagy, D. A. Perry, M. Stefaniak, *Green Chem.* 2008, 10, 31-36.
- [3] (a) J. Zhu, H. Bienayme, Multicomponent Reactions; Eds.; Wiely-VCH:Weinheim, 2005;
 (b) B. Ganem, Acc. Chem. Res. 2009, 42, 463-472. (c) A. Domling, I. Ugi, Angew. Chem. Int. Ed. 2000, 39, 3169-3210.
- [4] R. C. Cioc, E. Ruijter, R. V. Orru, Green Chem. 2014, 16, 2958-2975.
- [5] I. A. Ibarra, A. Islas-Jácome, E. González-Zamora, Org. Biomol. Chem. 2018, 16, 1402-1418.
- [6] S. Zhi, X. Ma, W. Zhang, Org. Biomol. Chem. 2019, 17, 7632-7650.
- [7] P. Slobbe, E. Ruijter, R. V. Orru, *MedChemComm.* 2012, 3, 1189-1218.
- [8] Gh. Mohammadi Ziarani, R. Moradi, T. Ahmadi, N. Lashgari, RSC Adv. 2018, 8, 12069-12103
- [9] M. C. Pirrung, K. D. Sarma, J. Am. Chem. Soc. 2004, 126, 444-445.
- [10] D. Paprocki, A. Madej, D. Koszelewski, A. Brodzka, R. Ostaszewski, *Front. Chem.***2018**, 6, 502.

- [11] K. Ding, Y. Lu, Z. Nikolovska-Coleska, S. Qiu, Y. Ding, W. Gao, J. Stuckey, K. Krajewski, P. P. Roller, Y. Tomita, D. A. Parrish, J. Am. Chem. Soc. 2005, 127, 10130–10131.
- [12] S. Mathusalini, T. Arasakumar, K. Lakshmi, C. H. Lin, P. S. Mohan, M. G. Ramnath, R. Thirugnanasampandan, *New J Chem*, **2016**, 40, 5164-5169.
- [13] H. Ramadoss, D. Saravanan, S. P. Sudhan, S. S. Mansoor, *Der Pharmacia Lettre* 2016, 8, 25-29.
- [14] A. H. Abdel-Rahman, E. M. Keshk, M. A. Hanna, S. M. El-Bady, *Bioorg. Med. Chem.*2004, 12, 2483-2488.
- [15] G. Kumari, M. Modi, S. K. Gupta, R. K. Singh, *Eur. J. Med. Chem.* 2011, 46, 1181-1188.
- [16] V. V. Vintonyak, K. Warburg, H. Kruse, S. Grimme, K. Hübel, D. Rauh, H. Waldmann, Angew. Chem. Int. Ed. Engl. 2010, 49, 5902-5905.
- [17] B. M. Rao, G. Niranjan Reddy, T. Vijaikumar Reddy, B. L. A. Prabhavathi Devi, R. B. N. Prasad, J. S. Yadav, B. V. Subba Reddy, *Tetrahedron Lett.* 2013, 54, 2466-2471.
- [18] K. Rad-Moghadam, L. Youseftabar-Miri, Tetrahedron 2011, 67, 5693-5699.
- [19] Y. B. Wagh, Y. A. Tayade, S. A. Padvi, B. S. Patil, N. B. Patil, D. S. Dalal, *Chin. Chem. Lett.* 2015, 26, 1273-1277.
- [20] Y. Li, H. Chen, D. Shi, S. Ji, J. Comb. Chem. 2010, 12, 231-237.
- [21] Y. Shao, J. Wang, H. Wu, J. Liu, I. A. Aksay, Y. Lina, *Electroanalysis* 2010, 22, 1027-1036.
- [22] K. Chaudhary, K. Prakash, D. T. Masram, Appl. Surf. Sci. 2020, 509, 144902.
- [23] K. Prakash, K. Chaudhary, D. T. Masram, Appl. Catal., A. 2020, 593, 117411.
- [24] D. Yadav, S. K. Awasthi, New J Chem. 2020, 44, 1320-1325.
- [25] D. Yadav, S. K. Awasthi, Dalton Trans. 2020, 49, 179-186.

- [26] D. Yadav, S. K. Awasthi, Green Chem. 2020. DOI: 10.1039/D0GC01469A.
- [27] N.K.M. Subodh, K. Chaudhary, G. Kumar, D. T. Masram, ACS Omega 2018, 3, 16377-16385.
- [28] K. Prakash, D. T. Masram, *Dalton Trans.* 2020, 49, 1007-1010.
- [29] K. Chaudhary, K. Prakash, N. K. Mogha, D. T. Masram. Arab. J. Chem. 2020, 13, 4869-4881.
- [30] G. Kumar, N. K. Mogha, M. Kumar, D. T. Masram, Dalton Trans. 2020, 49, 1963-1974.
- [31] S. Patnaik, S. Martha, K. M. Parida, *RSC Adv.* **2016**, 6, 46929-46951.
- [32] Z. Zhao, Y. Sun, F. Dong, *Nanoscale* **2015**, 7, 15-37.
- [33] T. He, Y. Wu, C. Jiang, Z. Chen, Y. Wang, G. Liu, Z. fXu, G. Ning, X. Chen, Y. Zhao, *PloS one*, **2020**, 15, e0237389.
- [34] Y. Zhang, D. M. Ligthart, X. Y. Quek, L. Gao, E. J. Hensen, Int. J. Hydrog. Energy.
 2014, 39, 11537-11546.
- [35] S. Samanta, S. Martha, K. Parida, ChemCatChem. 2014, 6, 1453-1462.
- [36] H. Li, Y. Xu, H. Sitinamaluwa, K. Wasalathilake, D. Galpaya, C. Yan, *Chinese J. Catal.***2017**, 38, 1006-1010.
- [37] J. Zhu, P. Xiao, H. Li, S. A. C. Carabineiro, ACS Appl. Mater. Interfaces. 2014, 6, 16449-16465.
- [38] P. Sharma, S. Rana, K. C. Barick, C. Kumar, H. G. Salunked, P. A. Hassan, New J Chem. 2014, 38, 5500-5508.
- [39] Y. Jing, L. R. Moore, P. S. Williams, J. J. Chalmers, S. S. Farag, B. Bolwell, M. Zborowski, *Biotechnol. Bioeng.* 2007, 96, 1139-1154.
- [40] L. Zeng, W. Ren, L. Xiang, J. Zheng, B. Chen, A. Wu, Nanoscale 2013, 5, 2107-2113.
- [41] Y. M. Huh, Y. W. Jun, H. T. Song, S. Kim, J. S. Choi, J. H. Lee, S. Yoon, K. S. Kim, J. S. Shin, J. S. Suh, J. Cheon, J. Am. Chem. Soc. 2005, 127, 12387-12391.

- [42] H. Gu, K. Xu, C. Xu, B. Xu, Chem. Commun. 2006, 941-949.
- [43] E. Rafiee, M. Khodayari, Chinese J. Catal. 2017, 38, 458-468.
- [44] X. Jia, R. Dai, Y. Sun, H. Song, X. Wu, J. Mater. Sci: Mater. Electron. 2016, 27, 3791-3798.
- [45] S. Riyaz, A. Naidu, K. P. Dubey, Lett. Org. Chem. 2012, 9, 101-105.
- [46] Z. G. Mohammadi, M. N. Hosseini, N. Lashgari, A. Badiei, M. Amanlou, R. Bazl, J. Nanostructures. 2013, 2, 489-500.
- [47] Z. Karimi-Jaberi, A. Fereydoonnezhad, Iranian Chem. Commun. 2017, 5, 407-416.
- [48] M. T. Maghsoodlou, R. Heydari, F. Mohamadpour, M. Lashkari, Iranian J. Chem. Chem. Engin. 2017, 36, 31-38.
- [49] G. Shanthi, G. Subbulakshmi, P. T. Perumal, Tetrahedron 2007, 63, 2057-2063.
- [50] G. D. Wang, X. N. Zhang, Z. H. Zhang, J. Heterocycl. Chem. 2013, 50, 61-65.
- [51] Y. Li, H. Chen, C. Shi, D. Shi, S. Ji, J. Comb. Chem. 2010, 12, 231-237.
- [52] M. Dabiri, M. Bahramnejad, M. Baghbanzadeh, Tetrahedron 2009, 65, 9443-9447.
- [53] A. Hasaninejad, N. Golzar, M. Beyrati, A. Zare, M. M. Doroodmand, J. Mol. Catal. A: Chem. 2013, 372, 137-150.
- [54] M. N. Elinson, F. V. Ryzhkov, T. A. Zaimovskaya, M. P. Egorov, *Monatsh. Chem.*2016, 147, 755-760.
- [55] A. R. Karimi, M. Sourinia, Z. Dalirnasab, M. Karimi, Can. J. Chem. 2015, 93, 546-549.
- [56] N. Azizi, S. Dezfooli, M. M. Hashemi, J. Mol. Liq. 2014, 194, 62-67.
- [57] B. Karmakar, A. Nayak, J. Banerji, Tetrahedron Lett. 2012, 53, 5004-5007.
- [58] A. Mobinikhaledi, N. Foroughifar, M. A. Bodaghi Fard, Synth. Commun. 2011, 41, 441-450.

[59] S. L. Zhu, S. J. Ji, Y. Zhang, Tetrahedron 2007, 63, 9365-9372.

- [60] F. Mohamadpour, M. T. Maghsoodlou, R. Heydari, M. Lashkari, *Res. Chem. Intermed.***2016**, 42, 7841-7853.
- [61] M. Kidwai, A. Jain, V. Nemaysh, R. Kumar, P. M. Luthra, *Med. Chem. Res.* 2013, 22, 2717-2723.
- [62] V. Y. Mortikov, Y. M. Litvinov, A. A. Shestopalov, L. A. Rodinovskaya, A. M. Shestopalov, *Russ Chem Bull Int Ed.* 2008, 57, 2373-2380.
- [63] D. R. Chandam, A. G. Mulik, D. R. Patil, M. B. Deshmukh, *Res. Chem. Intermed.* 2016, 42, 1411-1423.
- [64] L. Moradi, Z. Ataei, Z. Zahraei, J. Iran. Chem. Soc. 2019, 16, 1273-1281.
- [65] L. Moradi, Z. Ataei, Green Chem. Lett. Rev. 2017, 10, 380-386.

OUTRO

Scheme, Figure and Table Captions

Scheme 1. Preparation of $Fe_3O_4/g-C_3N_4$.

Scheme 2. Plausible mechanism for the formation of spirooxindole derivatives in the presence of Fe₃O₄/g-C₃N₄.

Fig. 1. FT-IR spectra of Melamine (a), g-C₃N₄ (b), Fe₃O₄ (c) and Fe₃O₄/g-C₃N₄ (d).

Fig. 2. XRD pattern of Fe₃O₄ (a), g-C₃N₄ (b) and Fe₃O₄/g-C₃N₄ (c).

Fig.3. SEM images of Fe₃O₄/*g*-C₃N₄.

Fig. 4. TGA curves of g-C₃N₄ (a) and Fe₃O₄/g-C₃N₄ (b).

Fig.5. VSM pattern of Fe_3O_4 (a) and Fe_3O_4/g -C₃N₄ (b).

Fig. 6. Recycling of the catalyst in the synthesis of spirooxindoles.

Fig 7 The SEM image of the recycled catalyst after 6 reaction runs in the synthesis of spirooxindoles.

Table 1. The effect of temperature, amounts of the catalyst and solvent on the synthesis of spirooxindoles.

Table 2. The synthesis of spirooxindole derivatives in the presence of Fe₃O₄/g-C₃N₄.

Table 3. Comparison of the results obtained in the presence of $Fe_3O_4/g-C_3N_4$ with other catalysts reported in the literature in the synthesis 2-amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile (4c).



Scheme 1. Preparation of $Fe_3O_4/g-C_3N_4$.

out



Scheme 2. Plausible mechanism for the formation of spirooxindole derivatives in the presence of Fe_3O_4/g - C_3N_4 .





Fig. 2 XRD pattern of Fe_3O_4 (a), $g-C_3N_4$ (b) and $Fe_3O_4/g-C_3N_4$ (c).



Fig.3 SEM images of $Fe_3O_4/g-C_3N_4$.









Fig.6. Recycling of the catalyst in the synthesis of spirooxindoles.



Fig 7. The SEM image of the recycled catalyst after 6 reaction runs in the synthesis of spirooxindoles.

Entry	Solvent	Temperature(°C)	Catalyst loading (g)	Time (min)	Yield (%) ^a
1	Solvent-free	r.t.		120	Trace
2	Solvent-free	70		100	Trace
3	<i>n</i> -Hexane	reflux	0.03	80	Trace
4	CHCl ₃	reflux	0.03	80	Trace
5	CH ₃ CN	70	0.03	70	48
6	EtOH	60	0.025	60	65
7	H ₂ O	70	0.02	50	77
8	H ₂ O	80	0.025	15	94

Table 1. The effect of temperature, amounts of the catalyst and solvent on the synthesis of spirooxindoles.

^aIsolated yields



Table 2. The synthesis of spirooxindole derivatives in the presence of $Fe_3O_4/g-C_3N_4$.

6	OH OH O O	$F \xrightarrow{H_2N}_{NC} O \xrightarrow{NC}_{N} O \xrightarrow{NC}_{H} O \xrightarrow{H_2N}_{H} O \xrightarrow$	20	91	>300	>300 ^[47]
7	OH	H ₂ N NC NC H 4g	30	89	245-247	243-245 ^[48]
8	ОН	$ \begin{array}{c} H_2N \\ NC \\ H O \\ H O \\ 4h \end{array} $	35	85	234-236	236 ^[49]
9	O O OMe	$H_2N \to O \to OMe$ $H_2N \to O \to OMe$ $H_1 \to O \to OMe$ $H_1 \to O \to OMe$	38	87	280-282	280-281 ^[50]
10	O O OEt	$H_2N \to O$ $NC \to OEt$ H_4	35	85	263-264	258-260 ^[51]
11		$H_2N \to O \to H$ $NC \to NH \to O$ H H H	40	87	274-276	271-274 ^[47]
12			40	90	246-248	245-247 ^[52]
13		H ₂ N NC O O O O O O	25	94	263-265	260-262 ^[52]



Reaction conditions: C–H activated acid compounds (1 mmol), isatins/acenaphthenequinone (1mmol), malononitrile (1 mmol), catalyst (0.025 g), and H₂O (5 mL); reactions conducted at 80 $^{\circ}$ C.

Rieror

Table 3. Comparison of the results obtained in the presence of $Fe_3O_4/g-C_3N_4$ with other catalysts reported in the literature in the synthesis 2-amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile (**4c**).

Entry	Catalyst	Conditions	Time (min)	Yield (%) ^[ref.]
1	NaOAc (0.3 mmol)	25°C/grinding	15	95 ^[54]
2	SSA-MNPs (0.1 g)	H ₂ O: EtOH/ Ultrasound, 60 °C	80	95 ^[55]
3	Urea:ChCl (0.5 mL)	80°C	60	95 ^[56]
4	NC MgO (15 mol %)	80°C/H ₂ O	120	95 ^[57]
5	InCl ₃ (10 mol %)	CH ₃ CN/Reflux	90	75 ^[49]
6	TBAB (10 mol %)	Solvent-free/100°C	40	90 ^[58]
7	TEBA (20 mol %)	60°C/H ₂ O	120	94 ^[59]
8	Cu(OAc) ₂ . H ₂ O (15 mol %)	Solvent-free/80 °C	240	86 ^[60]
9	I ₂ (10 mol %)	50°C/H ₂ O	60	80 ^[61]
10	NEt ₃	EtOH/Reflux	30	83 ^[62]
11	Oxalic acid dihydrate: proline (LTTM) (5 ml)	r.t.	30	94 ^[63]
12	SnO ₂ NPs (0.03 g)	EtOH/r.t.	8	96 ^[64]
13	CuO NPs (0.003 g)	EtOH/r.t.	8	98 ^[65]
14	Fe ₃ O ₄ /g-C ₃ N ₄ (0.025 g)	80°C/H ₂ O	15	94 ^[This work]

Graphical abstract

