

Fe₃O₄ nanoparticles as a recyclable catalyst in the conversion of indole to isatin

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ABSTRACT

Oxidation reaction of indole to isatin was performed in the presence of Fe₃O₄ nanoparticles (as catalyst) and commercial grade perhydrol (as oxidant). Magnetite nanoparticles were synthesized via chemical precipitation method and characterized by XRD and TEM techniques. The efficiency of reaction was obtained from GC analysis of the mixture. The catalyst was easily separated from the reaction mixture (after completion or before each injection) by using a magnetic field of 1.4 T. The recycled catalyst maintained activity for successive runs.

Keywords: Isatin, Fe₃O₄, Nanoparticle, Oxidation, Catalyst.

1. INTRODUCTION

Indoles have been topics of research interest for over a century. The most versatile method for preparation of indoles was first reported in 1883 by Fischer. Isatins as the oxidation products of indoles, on the other hand, serve as precursors to many biologically active compounds [1]. Direct oxidation of indoles is a common method, and much research has been carried out to develop practical methods which would be applicable to various indoles [2]. For example, Parrick and co-workers developed a synthetic methodology for isatins from indoles, using *N*-bromosuccinimide to promote their oxidation to yield 3, 3-dibromooxindoles that were subsequently hydrolyzed to the desired isatins [3, 4]. In an alternative methodology, 4 and 6-substituted-2-oxin-

doles, obtained from *O*-nitroaryl-malonates, were converted to 3,3-dibromooxindoles by reaction with pyridinium perbromide. These intermediates were hydrolyzed to the corresponding isatins. This method is limited to substrates with moderate to strongly electron withdrawing groups (otherwise bromination of the aromatic ring occurs) [5]. The usual oxidation of indoles, however, suffers from drawbacks such as need for a large excess of metal oxidant and lack of control on the progress of reaction which yields a mixture of products. Since the metal residues are environmentally undesirable and often cause problems during reaction and work-up, development of selective indole oxidations requiring only a catalytic amount of metal reagent in combination with an

appropriate stoichiometric oxidant is a great challenge.

The use of nanosized magnetic particles in the manufacture of fine chemicals, on the other hand, has attracted increasing attention, owing to the special features such as large surface area, high number of surface active sites, unique electrical and magnetic properties, selectivity, stability and above all, reusability, which are most sought after in green chemistry, drug delivery and biosensors [6, 7].

In continuation of our recent interest to the chemistry of indoles [8-10], hereby we report efficient application of magnetite nanoparticles as the catalyst for conversion of indole to isatin.

2. EXPERIMENTAL

2.1 Reagents and Materials

All materials were purchased from Merck and used without further purification. Fe_3O_4 magnetic nanoparticles were synthesized by using a five-necked reactor. A stock solution of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (10.4 g), $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (4.0 g) and HCl (1.7 mL, 12 mol L^{-1}) in 50 mL of deionized water which was degassed with nitrogen gas for 20 min

before use, added dropwise (by using a dropping funnel connected to one neck) into 500 mL of degassed NaOH solution (1.5 mol L^{-1}) at 80 °C during 30 min. Central neck was connected to a home-made condenser allowing circulation of cold water to prevent vaporization of solution. A glassware stirrer rotating at 1000 rpm, was passed through the condenser and central neck. Third neck was used to sparge nitrogen gas during the synthesis. The other necks were used for temperature monitoring and sampling. After completion, the obtained Fe_3O_4 nanoparticles were separated from the reaction medium by a magnetic field (1.4 T strength), and washed with 500 mL deionized water four times. The obtained nanoparticles were characterized by using XRD and TEM.

2.2 Characterization

Fig. 1 shows the XRD pattern of the synthesized magnetic nanoparticles, which is matched well with library patterns (JCPDS No. 19-629), indicating that the sample has a cubic crystal system.

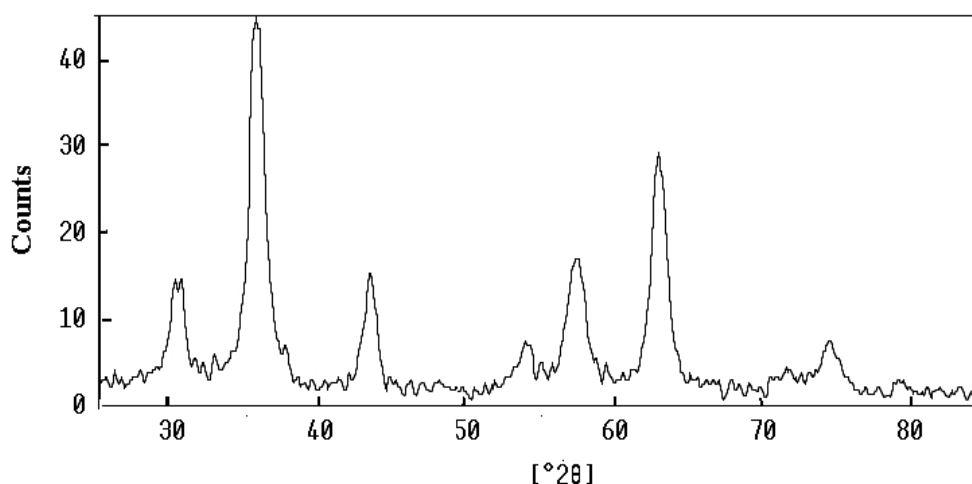


Fig. 1. XRD pattern of synthesized Fe_3O_4 nanoparticles.

TEM image of the prepared nanoparticles was obtained as shown in Fig. 2. Fe_3O_4 surface morphology analysis

demonstrated the agglomeration of many ultrafine particles with diameter of about 40 nm.

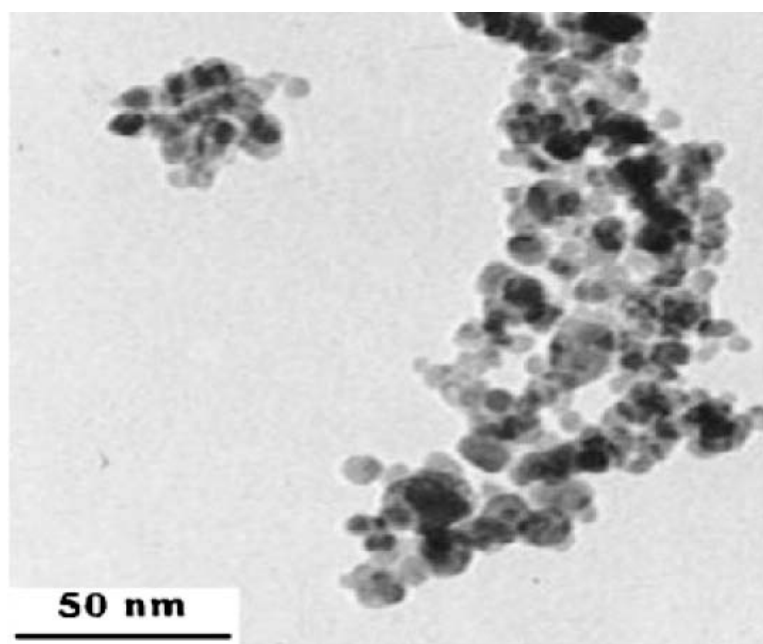


Fig. 2. TEM image of the synthesized Fe_3O_4 nanoparticles.

Evaluations of product mixtures were carried out using a Varian CP-3800 Gas Chromatograph (split/splitless injector, CP Sil 8CB column, FID assembly). X-ray powder diffraction (XRD) measurements were performed using a Philips diffractometer of X'pert Company with mono chromatized $\text{Cu } k_\alpha$ radiation. The samples were characterized with a transition electron microscope (TEM) from the Hitachi Company (H-800, Japan). Ultra-sonication was performed in a TECNO-GAZ Tecna 3 ultrasonic cleaner with a frequency of 50-60 KHz and a normal power of 250 W.

2.3 Reaction conditions

Fe_3O_4 nanoparticles (0.10g) were added to a solution of indole (1 mmol) in MeNO_2 (5mL) and the reaction mixture was sonicated at 35 °C. During sonication, perhydrol was added dropwise (excess) until completion of the reaction as was monitored by GC. Sampling was performed every 10 min. by injecting the supernatant liquid obtained from application of a 1.4 T magnetic field to the reaction mixture.

3. RESULTS AND DISCUSSION

First of all, the reaction conditions were optimized. The optimized details are summarized in Scheme 1.

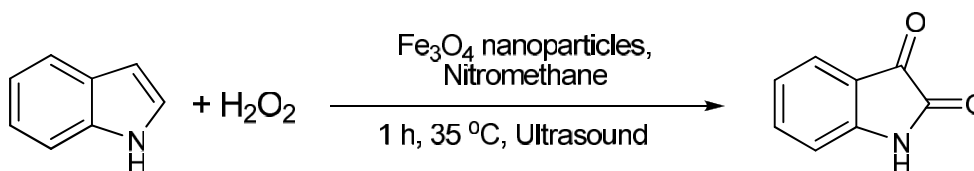


Fig. 3. Optimized conditions of the reaction.

To examine the influence of the catalyst loading, the reaction was carried out in different loadings and the

progress of the reaction was monitored by GLC technique. Nitromethane was used as internal standard. Increase in

the corresponding isatin peak areas was selected as a measure of reaction progress. The optimum loading of the catalyst was found to be 0.10 g per mmol of indole. Solvent screening

experiments showed (Table 1) that the yield was solvent dependent and nitromethane resulted into the best yield (70%).

Table 1 Effect of solvents on the yield of isatin.

Entry ^(a)	Solvent	Time (h)	Yield ^(b) (%)
1	CH ₃ OH	1	15
2	C ₂ H ₅ OH	1	17
3	CH ₃ CN	1	42
4	CH ₃ Cl	1	35
5	CH ₃ NO ₂	1	70

^(a) The reaction was carried out according to general experimental procedure.

^(b) The yield based on GC analysis.

Effect of the catalyst type on the reaction yield was also studied. A comparison was made between Fe₃O₄ nanoparticles, commercial magnetite granules and ferric chloride hydrate. Among the tested materials as catalyst, laboratory synthesized Fe₃O₄ nanoparticles was found to be superior to others. Another purpose of this study was to investigate the recovery of the

magnetite nanoparticles catalyst after use. It was found that the separated catalyst by using a magnetic field can be reused at least for four times without any considerable decay in its catalytic performance. However, some more reaction time is needed after each use for the same product achievements (Fig. 3).

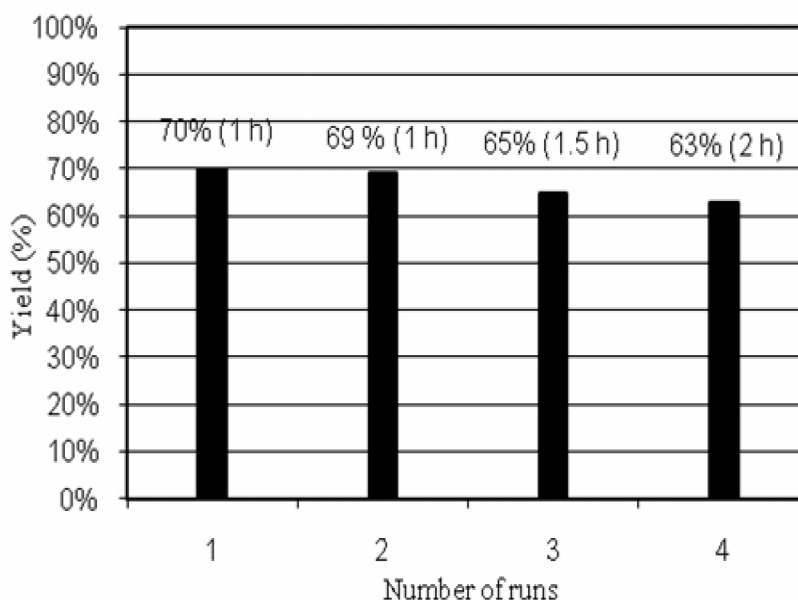


Fig. 4. The reuse of Fe₃O₄ nanoparticles in successive runs.

4. CONCLUSION

An efficient method for oxidation of indole to isatin based on the magnetite nanoparticles as catalyst has been

developed. Some of the main advantages of the present protocol are mild reaction conditions, selectivity toward isatin as the oxidation product and easy

recycling of the catalyst. The method can also be employed for oxidation of other heterocycles that are currently under investigation in our research laboratory.

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REFERENCES

- [1] M. Bandini, A. Eichholzer, *Angew. Chem. Int. Ed.*, 48, 9608 (2009).
- [2] R. J. Sundberg, *The Chemistry of Indoles* (Academic press, New York, 1996).
- [3] J. Parrick, A. Yahya, Y. Jin, *Tetrahedron Lett.*, 25, 3099 (1984).
- [4] J. Parrick, A. Yahya, A. S. Ijaz, J. Yizun, *J. Chem. Soc., Perkin Trans.*, 1, 1989 (2009).
- [5] E. A. Kraynack, J. E. Dalgard, F. C. A. Gaeta, *Tetrahedron Lett.*, 39, 7679 (1998).
- [6] D. L. Leslie-Pelecky, R. D. Rieke, *Chem. Mater.*, 8, 1770 (1996).
- [7] D. W. Elliott, W. X. Zhang, *Env. Sci. Tech.*, 35, 4922 (2001).
- [8] A. Khorshidi, *Ultrason. Sono-chem.*, 19, 570 (2012).
- [9] A. Khorshidi, K. Tabatabaeian, *J. Serb. Chem. Soc.*, 76 (10), 1346 (2011).
- [10] A. Khorshidi, K. Tabatabaeian, *J. Mol. Cat. A: Chemical*, 344, 128 (2011).

نانو ذرات Fe_2O_3 به عنوان کاتالیزور قابلیت بازیافت در تبدیل ایندول به ایزاتین

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چکیده:

واکنش اکسایش ایندول به ایزاتین در حضور نانو ذرات Fe_2O_3 به عنوان کاتالیزور و پرهیدرول تجارتي به عنوان اکسنده انجام گردید. نانو ذرات مغناطیسی از طریق روش رسوبدهی شیمیایی سنتز شده و توسط تکنیک‌های XRD و TEM مشخصه یابی شدند. کارایی واکنش از آنالیز GC مخلوط واکنش بدست آمد. کاتالیزور به آسانی از مخلوط واکنش (بعد از کامل شدن یا قبل از هر تزریق) توسط یک آهن ربا با میدان مغناطیسی ۱.۴ تسلا تفکیک گردید. فعالیت کاتالیزور جدا شده برای مراحل متوالی حفظ شده است.

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