

Novel nanomagnetic material with dimethylamino tag: a selective and recyclable catalyst for the reaction of malononitrile, aryl aldehydes and dimedone

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ABSTRACT

A novel nanomagnetic material with a dimethylamino tag namely nano-Fe₃O₄@SiO₂@R-NMe₂ ([NFSRN]) was produced, and characterized by EDS, FT-IR, VSM, FE-SEM, XRD and TGA analyses. Then, it was applied as a highly effective and magnetically recyclable catalyst for the one-pot multi-component reaction of malononitrile, arylaldehydes and dimedone. Interestingly, in most entries, among the possible products which can be produced from the reactants, only 2-amino-tetrahydrobenzo[*b*]pyrans were obtained in high yields and relatively short times, and no other product was obtained.

Keywords: *Nanomagnetic catalyst, Nano-Fe₃O₄@SiO₂@R-NMe₂ ([NFSRN]), 2-Amino-tetrahydrobenzo[*b*]pyran, Multi-component reaction.*

1. Introduction

Nanomagnetic materials have a wide range of applications in medicinal and industrial fields. Among the nanomagnetic cores, nano-Fe₃O₄ has unique properties, e.g., thermal and chemical stability, appropriate magnetic property, easy recycling, low toxicity, simple functionalization and large specific surface area [1,2]. Magnetic nanomaterials have been utilized for bioanalysis [3], energy conversion [4], drug delivery [5], control of enzyme function [6], in MRI [7] and energy storage paper supercapacitors [8]. Catalytic activity has also been reported for these materials [9-15].

Multi-component reaction (MCR) is a beneficial way for production of various complex molecules; the benefits of MCRs are well described in the literature [16-19].

The heterocycles bearing pyran core are of great importance in pharmacological and biological studies. Some of their activities include antitumor [20], antioxidant [21], antifungal [22], antimicrobial [23], antibacterial [24] and anti-Parkinson [25] properties.

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Moreover, they have been used as potential biodegradable agrochemicals [26], cosmetics [27], pigments [27] and photoactive materials [28]. 2-Amino-tetrahydrobenzo[*b*]pyrans can produce through the one-pot multi-component reaction of malononitrile, arylaldehydes and dimedone using a catalyst [29-37].

We have produced a novel nanomagnetic material (containing a dimethylamino tag) namely nano-Fe₃O₄@SiO₂@R-NMe₂ ([NFSRN]) and identified it by EDS (energy-dispersive X-ray spectroscopy), FT-IR, VSM (vibrating sample magnetometry), FE-SEM (field emission scanning electron microscopy), XRD (X-ray diffraction) and TGA (thermal gravimetric analysis) methods. Then, we have tested the catalytic performance of [NFSRN] for the synthesis of 2-amino-tetrahydrobenzo[*b*]pyrans from malononitrile, arylaldehydes and dimedone.

2. Experimental

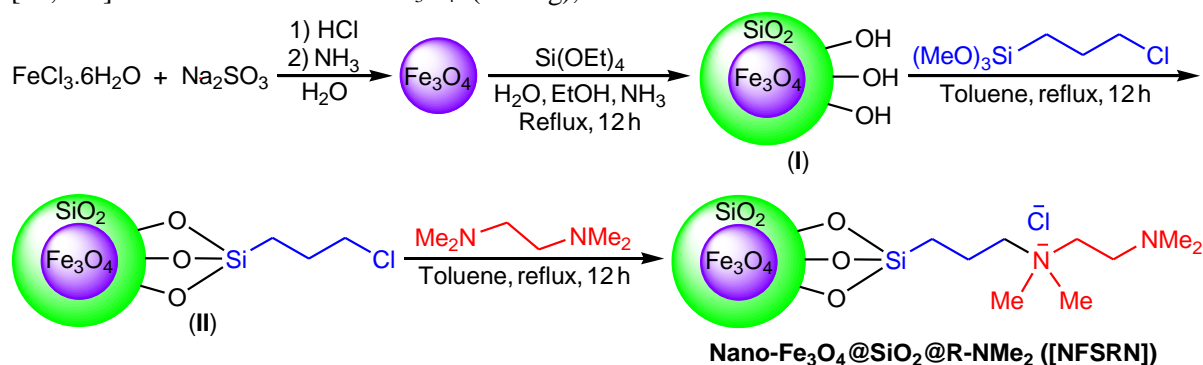
2.1. Chemicals and instruments

The chemicals were bought from Merck, Fluka and Iranian Chemical Companies. Silica gel SIL G/UV 254 plates were utilized for thin layer chromatography (TLC). Melting points were measured using a Buchi B-545 device. A Shimadzu IR-60 device was applied for

running FT-IR spectra. ^1H and ^{13}C NMR spectra were recorded by a Bruker Avance DPX FT-NMR spectrometer. EDS was achieved by a SAMx-EDS instrument. A MIRA3TESCAN-XMU instrument was utilized to obtain FE-SEM micrographs. VSM analysis was accomplished by a MDK device (Meghnatis Daghigh Kavir). XRD pattern was acquired using an apparatus model X'Pert PRO MPD, PANalytical, the Netherlands (Cu $K\alpha$ radiation, $\lambda=1.5408$). TGA was done by a Bahr STA-504 instrument at 25-600 °C in argon atmosphere (temperature increase rate was 10 °C.min $^{-1}$).

2.2. Preparation of [NFSRN]

The reported procedure was used to synthesize nano- Fe_3O_4 [38, 39]. A mixture of nano- Fe_3O_4 (0.50 g),



Scheme 1. The preparation of [NFSRN].

2.3. General procedure for the synthesis of 2-amino-tetrahydrobenzo[b]pyrans

A mixture of malononitrile (0.28 mmol, 0.019 g), aldehyde (0.25 mmol), dimedone (0.25 mmol, 0.07 g) and [NFSRN] (0.01 g) in EtOH (2 ml) was stirred and refluxed. After consuming the reactants (as observed by TLC), the solvent (EtOH) was evaporated, EtOAc (10 ml) was added, and stirred for 2 min under reflux conditions; the catalyst was separated magnetically from the hot solution, washed by EtOAc, and dried (the product is soluble in hot EtOAc; however, the catalyst is not soluble in this solvent). EtOAc of the remained solution was evaporated, and the residue was recrystallized from EtOH (95%) to give the pure product. Selected spectral data and original spectrums of the products have been given in supplementary information.

3. Result and Discussion

3.1. The catalyst characterization

[NFSRN] was synthesized according to **Scheme 1**, and characterized by EDS, FT-IR, VSM, FE-SEM, XRD and TGA analyses.

$\text{Si}(\text{OEt})_4$ (1.5 ml), H_2O (10 ml), EtOH (40 ml) and NH_3 solution (1.5 ml) was stirred for 12 h under reflux conditions, cooled to room temperature, centrifuged, decanted and dried to furnish **I** [39,40]. Afterward, (3-chloropropyl)trimethoxysilane (0.92 ml, 5 mmol) and **I** in dry toluene (40 ml) were stirred and refluxed under nitrogen gas for 12 h, cooled to room temperature, centrifuged, decanted, washed by dry toluene (twice) and Et_2O , and dried to afford **II** [39]. N,N,N',N' -Tetramethylethylenediamine (0.75 ml, 5 mmol) was added to **II** in toluene (30 ml), and stirred in reflux conditions for 12 h; the precipitate was isolated by centrifuging and decanting, washed by toluene, and dried to obtain [NFSRN] (**Scheme 1**).

The nanomaterial has iron, oxygen, silicon, carbon, nitrogen and chlorine elements in its structure; the EDS analysis approved this subject (**Fig. 1**).

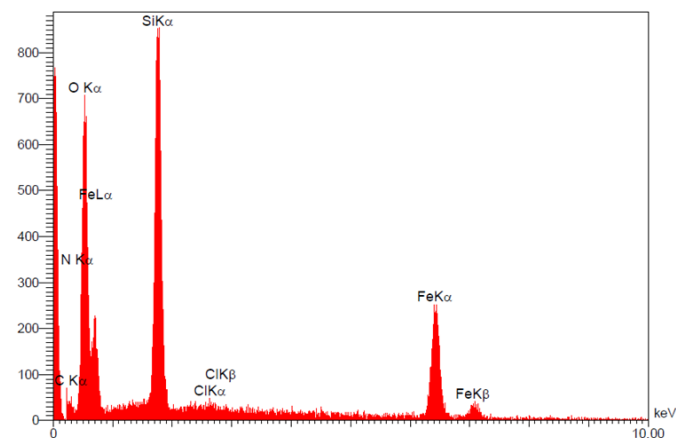


Fig. 1. The EDS spectrum of nano- Fe_3O_4 @ SiO_2 @R-NMe $_2$.

In the FT-IR spectrum (**Fig. 2**), the peak observed at 466 cm^{-1} is related to rocking of Si–O bond. Symmetric and asymmetric stretching vibrations of Si–O–Si were seen at 801 and 1097 cm^{-1} , respectively. The peak appeared at 1641 cm^{-1} and corresponds to O–H bending of Si–OH. Fe–O bond gave a peak at ~584 cm^{-1} . The peak

pertaining to stretching vibration of C–H was observed at 2926 cm^{-1} . The broad peak at $\sim 3000\text{-}3700\text{ cm}^{-1}$

belongs to stretching of OH groups on SiO_2 surface. The literature data approved the commentaries [18, 39].

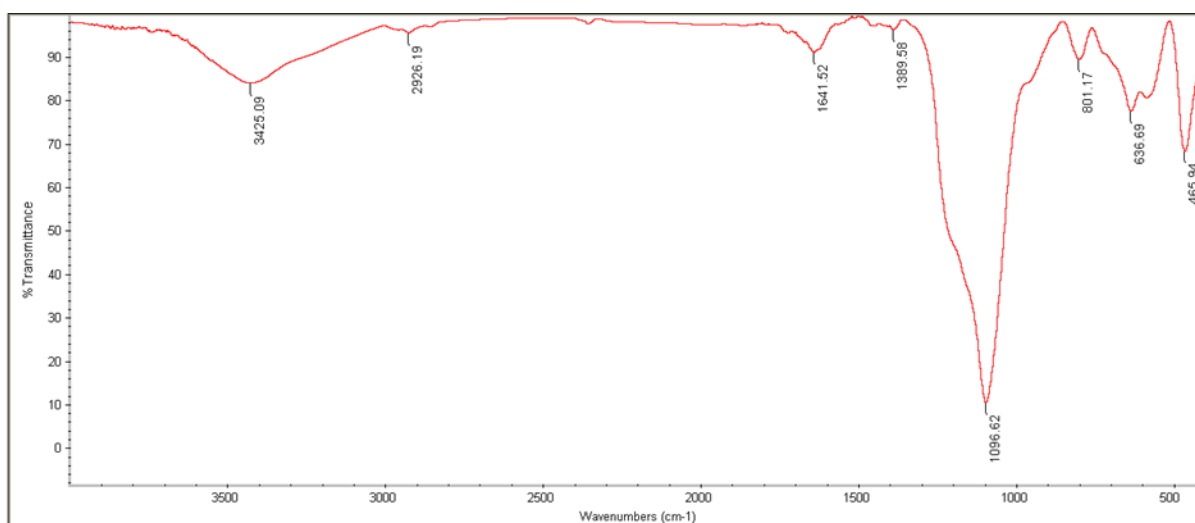


Fig. 2. The FT-IR spectrum of [NFSRN].

Fig. 3 represents a VSM diagram of [NFSRN]. The reported saturation magnetization (M_S) of the applied Fe_3O_4 for the catalyst synthesis was 52 emu.g^{-1} [39]; but, M_S of the catalyst was 37 emu.g^{-1} . The decrease in M_S can be attributed to coating silica on the Fe_3O_4 nanoparticles, and the organic moieties immobilized on the silica surface. Nevertheless, a suitable magnetic property was observed for [NFSRN], and it could be readily isolated from the reaction mixture by an external magnet.

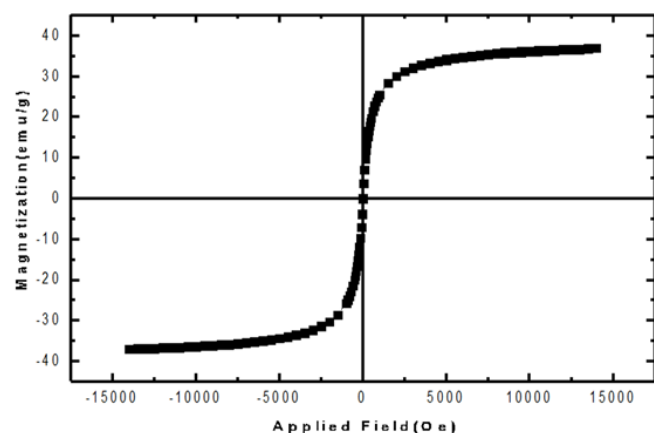


Fig. 3. The VSM diagram of [NFSRN].

The sizes and morphologies of the particles were characterized by FE-SEM (**Fig. 4**). The obtained micrographs demonstrated that the particles sizes of [NFSRN] are less than 100 nm, i.e., it is a nanomaterial; moreover, the nanoparticles have crystalline and amorphous forms.

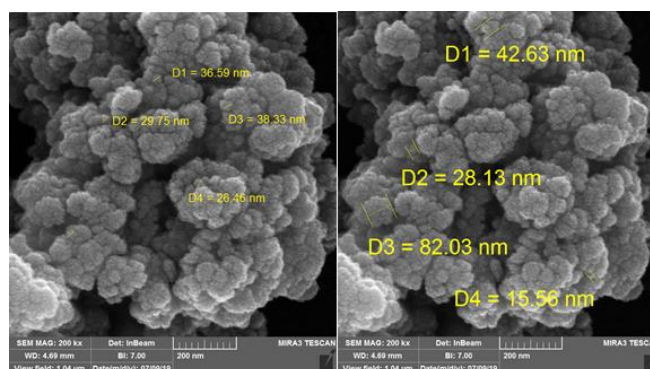


Fig. 4. The FE-SEM micrographs of [NFSRN].

In the XRD pattern of [NFSRN] (**Fig. 5**), some sharp diffraction lines (at $2\theta \approx 18.3, 30.5, 35.9, 43.8, 54.0, 57.7, 63.2, 74.9^\circ$) and two broad peaks (at $2\theta \approx 19.9\text{-}27.6^\circ$ and $48.9\text{-}52.1^\circ$) were observed. These results confirmed that the nanoparticles are in both crystalline and amorphous forms; the literature verified this consequence [18, 41].

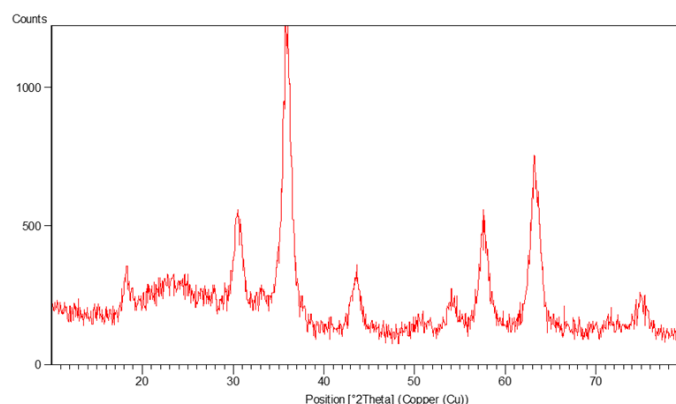


Fig. 5. The XRD pattern of [NFSRN].

Thermal gravimetric (TG), derivative thermal gravimetric (DTG) and differential thermal analysis (DTA) were used for studying thermal stability of [NFSRN] (**Fig. 6**). Three steps weight losses were observed for [NFSRN]: (i) below 175 °C, which can be due to vaporizing the adsorbed solvents on the catalyst surface, (ii) at ~175-410 °C, which can be due to decomposition of the organic groups bonded to the silica surface, and (iii) at ~410-600 °C, which may be because of condensing of the silanol groups. The literature data confirmed these commentaries [18].

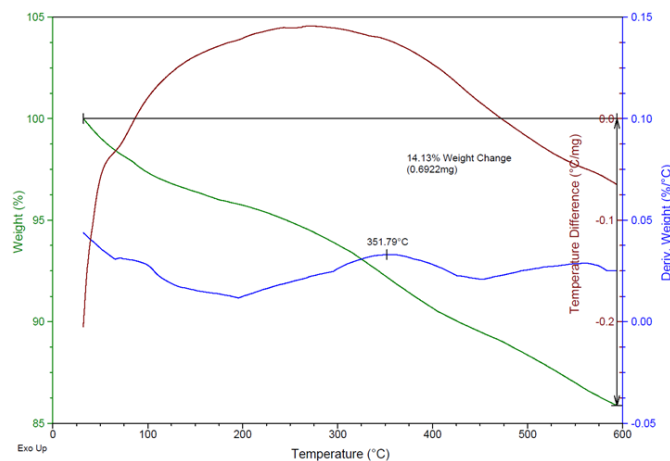
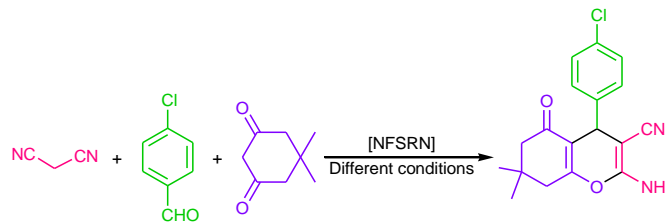


Fig. 6. The TG, DTG and DTA curves of [NFSRN].

3.2. Application of [NFSRN] as catalyst for the reaction of malononitrile, arylaldehydes and dimedone

At the outset, the reaction of malononitrile (0.28 mmol), 4-chlorobenzaldehyde (0.25 mmol) and dimedone (0.25 mmol) was selected as a model to produce 2-amino-tetrahydrobenzo[*b*]pyran **2** (**Scheme 2**), and the influence of the catalyst amount, temperature and solvent on the reaction was investigated; the results are shown in **Table 1**. Based on **Table 1**, the best results were acquired when the reaction was accomplished using 0.01 g of [NFSRN] in ethanol under reflux conditions (**Table 1**, entry 2). Increment of the catalyst amount up to 0.012 g caused the formation of byproducts besides the desired 2-amino-tetrahydrobenzo[*b*]pyran (the main product) and decreased the main product yield to 61% (**Table 1**, entry 4). Performing the reaction using 0.008 g of [NFSRN] gave 78% of the main product; in these conditions, some of the starting materials remained unreacted, and a few amount of a byproduct was produced (**Table 1**, entry 3). When the reaction was carried out in the presence of 0.01 g of the nanomagnetic catalyst at 70 °C, byproducts were not obtained; but, some of the unreacted starting materials were observed (**Table 1**, entry 1). Thus, the amount of [NFSRN] was an essential factor for the reaction selectivity. Among the used solvents, EtOH

afforded the highest yield (**Table 1**, entries 2 and 5-8); and the yield was moderate when the reaction was performed under solvent-free conditions (**Table 1**, entry 9). In other solvents and solvent-free conditions, both unreacted starting materials and byproducts were observed (**Table 1**, entries 5-9).



Scheme 2. The model reaction.

Table 1. Influence of the catalyst amount, temperature and solvent on the model reaction

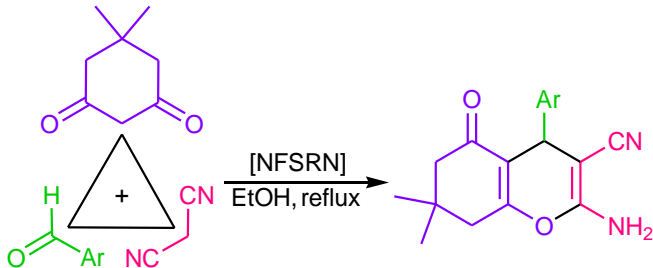
Entry	The catalyst amount (g)	Solvent (2 mL)	Temp. (°C)	Time (h)	Yield (%)
1	0.01	EtOH	70	4	92
2	0.01	EtOH	Reflux	4	97
3	0.008	EtOH	Reflux	5	78
4	0.012	EtOH	Reflux	4	61
5	0.01	EtOAc	Reflux	4	48
6	0.01	MeCN	Reflux	4	37
7	0.01	H ₂ O	Reflux	5	84
8	0.01	THF	Reflux	4	32
9	0.01	-	80	1	76

To appraise the scope and effectiveness of [NFSRN] for producing 2-amino-tetrahydrobenzo[*b*]pyrans, the reaction was tested in the presence of different arylaldehydes; the results are given in **Table 2**. As **Table 2** shows, benzaldehyde and aromatic aldehydes bearing halogen (chloro, fluoro and bromo), electron-attracting (nitro) and electron-releasing (methoxy and methyl) substituents on para, meta or ortho afforded high yields of the products in reasonable reaction times. Moreover, the arylaldehydes containing two substituents gave good results (**Table 2**, entries 3 and 11). Most of the used aldehydes afforded only the main product (the corresponding 2-amino-tetrahydrobenzo[*b*]pyran) without any byproducts (**Table 2**, compounds **2**, **3**, **5**, **7**, **8**, **9**, **10** and **12**); however, in the case of the other utilized aldehydes, a few amounts of byproducts were synthesized beside the

main products (compounds **1**, **4**, **6** and **11**) {according to the literature [42,43], two byproducts can be produced from malononitrile, arylaldehydes and dimedone, apart from 2-amino-tetrahydrobenzo[*b*]pyrans (**Scheme 3**).

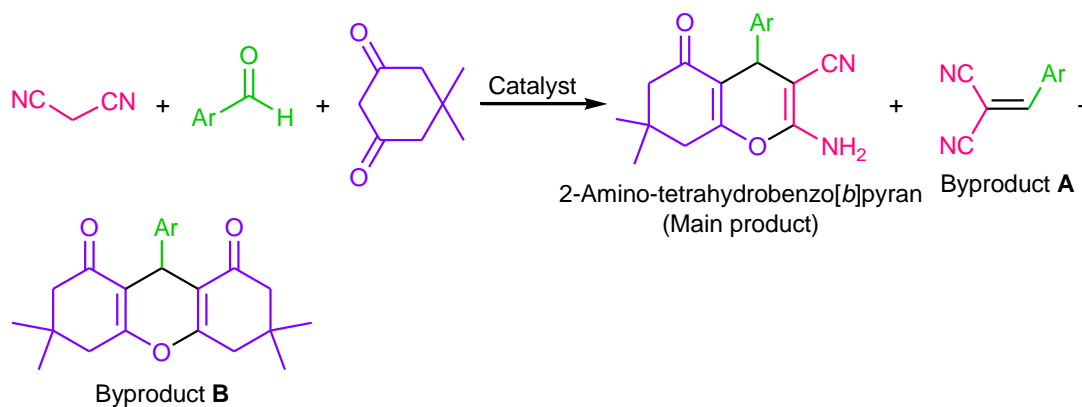
Considering the obtained results, we can say that [NFSRN] was a highly efficacious, general, and highly selective catalyst for the preparation of 2-amino-tetrahydrobenzo[*b*]pyrans.

Table 2. The preparation 2-amino-tetrahydrobenzo[*b*]pyran derivatives catalyzed by [NFSRN].



Compd. No.	Ar	Time (h)	Yield ^a (%)	M.p. (°C) [lit.]
1	C ₆ H ₅	3	92	232-234 (232-233) [31]
2	4-ClC ₆ H ₄	4	97	213-215 ((212-214) [31]
3	2,4-Cl ₂ C ₆ H ₃	2.5	96	181-183 (186-188) [29]
4	4-FC ₆ H ₄	2	93	196-198 (198-200) [34]
5	4-BrC ₆ H ₄	1.5	95	201-203 (199-200) [33]
6	2-BrC ₆ H ₄	3	86	160-161 (151-153) [44]
7	4-NO ₂ C ₆ H ₄	2	98	181-183 (179-182) [35]
8	3-NO ₂ C ₆ H ₄	4	98	204-206 (206-208) [35]
9	2-NO ₂ C ₆ H ₄	2	87	183-185 (180-183) [35]
10	3-CH ₃ OC ₆ H ₄	4	92	198-200 (195-197) [37]
11	3,4-(CH ₃ O) ₂ C ₆ H ₃	4	89	183-185 (184-185) [29]
12	4-CH ₃ C ₆ H ₄	4	94	217-219 (215-218) [35]

a) Isolated yield of the main product.



Scheme 3. The possible products which can produce from malononitrile, arylaldehydes and dimedone.

For examining recyclability of the catalyst, the reaction of malononitrile, dimedone and 4-nitrobenzaldehyde was chosen; [NFSRN] was recycled according to the

procedure mentioned in the experimental section. The nanomagnetic catalyst was reused for three times without decrement in its catalytic activity (**Fig. 7**, runs 2-4); nevertheless, the reaction time increased up to 3 h,

and the yield slightly decreased (86%) in fourth recycling (Fig. 7, run 5).

[NFSRN] has a basic tag (NMe_2); based on this and the literature [31], a plausible mechanism was proposed for the reaction (Scheme 4). The catalyst roles, which have been obviously displayed in the mechanism, include: (i) proton abstracting and production of nucleophiles in steps 1, 3 and 5, (ii) proton abstracting for removal of H_2O in step 2, and (iii) help to tautomerization in steps 4 and 6.

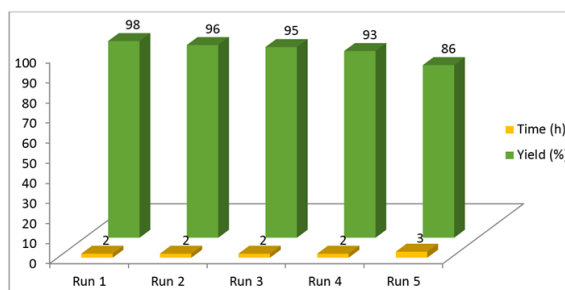
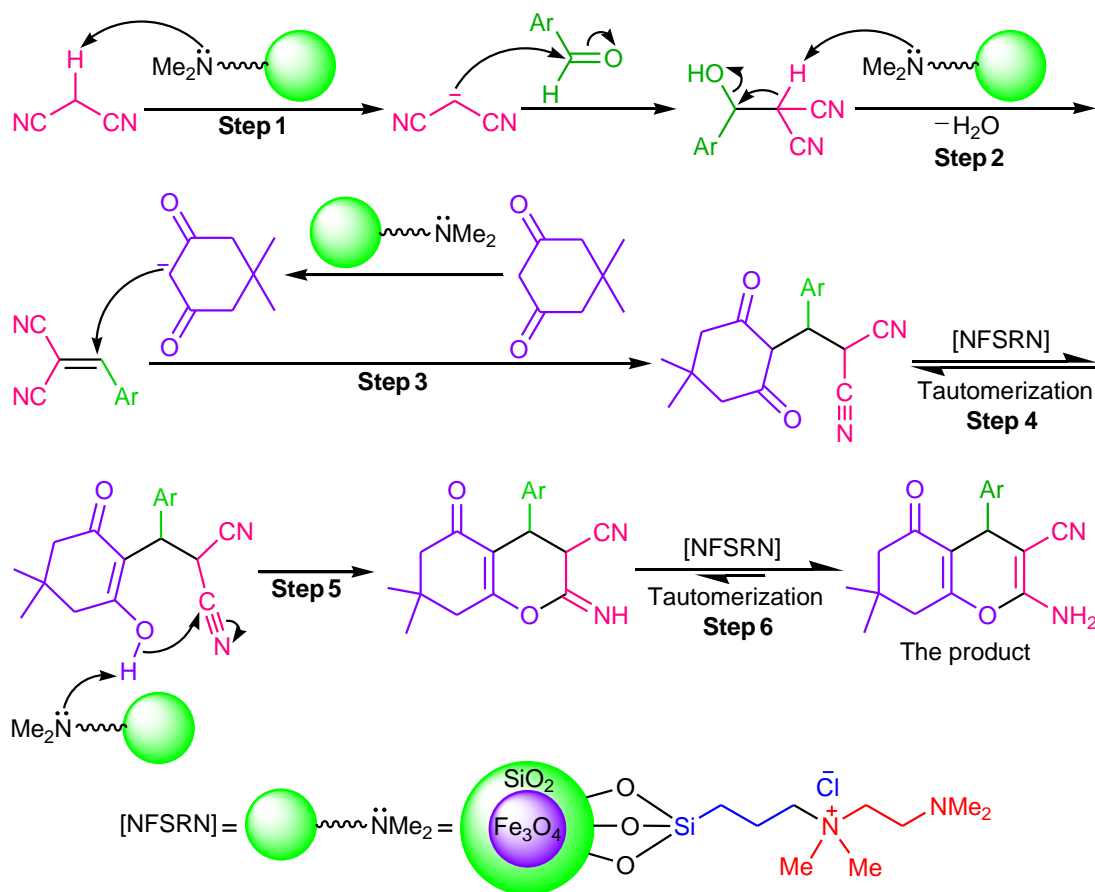


Fig. 7. Recyclability test of the catalyst.



Scheme 4. The proposed mechanism.

4. Conclusions

In summary, we have prepared a novel nanomagnetic material, and applied it as a catalyst for the synthesis of 2-amino-tetrahydrobenzo[*b*]pyrans. The advantages of this synthesis include wide scope, efficacy, high selectivity, magnetic recyclability of the catalyst and simple purification of the products.

Acknowledgements

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References

- [1] Y. Wei, B. Han, X. Hu, Y. Lin, X. Wang, X. Deng, *Procedia Eng.* 27 (2012) 632-637.
- [2] J. Sun, S. Zhou, P. Hou, Y. Yang, J. Weng, X. Li, M. Li, *J. Biomed. Mater. Res. A* 80 (2007) 333-341.
- [3] M. Ahmadi, H. Elmongy, T. Madrakian, M. Abdel-Rehim, *Anal. Chim. Acta* 958 (2017) 1-21.
- [4] H.-p. Feng, L. Tang, G.-m. Zeng, Y. Zhou, Y.-c. Deng, X. Ren, B. Song, C. Liang, M.-y. Wei, J.-f. Yu, *Adv. Colloid Interface Sci.* 267 (2019) 26-46.
- [5] B. K. Purushothaman, M. Harsha S, P. U. Maheswari, K. M. M. S. Begum, *J. Drug Deliv. Sci. Technol.* 52 (2019) 509-520.
- [6] A. Majouga, M. Sokolsky-Papkov, A. Kuznetsov, D. Lebedev, M. Efremova, E. Beloglazkina, P. Rudakovskaya,

- M. Veselov, N. Zyk, Y. Golovin, N. Klyachko, A. Kabanov, *Colloids Surf. B: Biointerfaces* 125 (2015) 104-109.
- [7] R. S. García, S. Stafford, Y. K. Gun'ko, *Appl. Sci.* 8 (2018) 172.
- [8] C. Pereira, R. S. Costa, L. Lopes, B. Bachiller-Baeza, I. Rodríguez-Ramos, A. Guerrero-Ruiz, P. B. Tavares, C. Freire, A. M. Pereira, *Nanoscale* 10 (2018) 12820-12840.
- [9] J. Kothandapani, S. S. Ganesan, *Curr. Org. Chem.* 23 (2019) 313-334.
- [10] F. Tamaddon, D. Arab, E. Ahmadi-AhmadAbadi, *Carbohydr. Polym.* 229 (2020) 115471.
- [11] B. B. F. Mirjalili, R. Araqia, S. A. Mohajeri, *Iran. J. Catal.* 9 (2019) 11-19.
- [12] R. Kordnezhadian, M. Shekouhy, A. Khalafi-Nezhad, *New J. Chem.* 43 (2019) 18559-18570.
- [13] M. M. Dutta, H. Talukdar, P. Phukan, *Dalton Trans.* 48 (2019) 16041-16052.
- [14] Z. Kheilkordi, G. Mohammadi Ziarani, A. Badiei, H. Vojoudi, *Iran. J. Catal.* 10 (2020) 65-70.
- [15] M. Torabi, M. Yarie, M. A. Zolfigol, *Appl. Organomet. Chem.* 33 (2019) e4933.
- [16] H. R. Safaei, T. Khastkhoda, M. Shekouhy, *ChemistrySelect* 3 (2018) 6273-6278.
- [17] Z. Abshirini, A. Kohzadian, Z. paryav, A. Zare, *Iran. J. Catal.* 9 (2019) 251-257.
- [18] A. Zare, A. Kohzadian, Z. Abshirini, S. S. Sajadikhah, J. Phipps, M. Benamarad, M. H. Beyzavi, *New J. Chem.* 43 (2019) 2247-2257.
- [19] A. Kakavand Ghalenoei, M. Bakherad, A. Keivanloo, *Iran. J. Catal.* 9 (2019) 293-303.
- [20] F. W. Perrella, S. F. Chen, D. L. Behrens, R. F. Kaltenbach, S. P. Seitz, *J. Med. Chem.* 37 (1994) 2232-2237.
- [21] Y. Wang, S.-Y. Mo, S.-J. Wang, S. Li, Y.-C. Yang, J.-G. Shi, *Org. Lett.* 7 (2005) 1675-1678.
- [22] R. Schiller, L. Tichotová, J. Pavlík, V. Buchta, B. Melichar, I. Votruba, J. Kuneš, M. Špulák, M. Pour, *Bioorg. Med. Chem. Lett.* 20 (2010) 7358-7360.
- [23] H. Hussain, S. Aziz, B. Schulz, K. Krohn, *Nat. Prod. Commun.* 6 (2011) 841-843.
- [24] R. R. Kumar, S. Perumal, P. Senthilkumar, P. Yogeewari, D. Sriram, *Bioorg. Med. Chem. Lett.* 17 (2007) 6459-6462.
- [25] L. Bonsignore, G. Loy, D. Secci, A. Calignano, *Eur. J. Med. Chem.* 28 (1993) 517-520.
- [26] G. Sabitha, K. Arundhathi, K. Sudhakar, B. S. Sastry, J. S. Yadav, *Synth. Comm.* 39 (2009) 433-442.
- [27] G. P. Ellis, *The Chemistry of Heterocyclic Compounds, Chromenes, Chromanes and Chromones*; A. Weissberger, E. C. Taylor (Eds.); John Wiley: New York, NY, USA (1977), pp. 11-139.
- [28] D. Armetso, W. M. Horspool, N. Martin, A. Ramos, C. Seoane, *J. Org. Chem.* 54 (1989) 3069-3072.
- [29] H. R. Saadati-Moshtaghin, F. Mohammadi Zonoz, *Res. Chem. Intermed.* 44 (2018) 2195-2213.
- [30] L. Khazdooz, A. Zarei, T. Ahmadi, H. Aghaei, L. Golestanifar, N. Sheikhan, *Res. Chem. Intermed.* 44 (2018) 93-115.
- [31] F. Ataiea, A. Davoodnia, A. Khojastehnezhad, *Polycycl. Aromat. Compd.*, in press, doi: 10.1080/10406638.2019.1622137.
- [32] M. Hajjami, F. Gholamian, R. H. E. Hudson, A. M. Sanati, *Catal. Lett.* 149 (2019) 228-247.
- [33] S. Nemouchi, R. Boulcina, B. Carboni, A. Debache, C. R. Chim. 15 (2012) 394-397.
- [34] H. Hu, F. Qiu, A. Ying, J. Yang, H. Meng, *Int. J. Mol. Sci.* 15 (2014) 6897-6909.
- [35] S. Rostamnia, A. Morsali, *Inorg. Chim. Acta* 411 (2014) 113-118.
- [36] M. Shahabi Nejad, H. Sheibani, *Catal. Lett.* 148 (2018) 125-133.
- [37] M. Esmaeilpour, J. Javidi, F. Dehghani, F. Nowroozi Dodeji, *RSC Adv.* 5 (2015) 26625-26633.
- [38] S. Qu, H. Yang, D. Ren, S. Kan, G. Zou, D. Liand, M. Li, *J. Colloid Interface Sci.* 215 (1999) 190-192.
- [39] M. A. Zolfigol, R. Ayazi-Nasrabadi, S. Baghery, *Appl. Organomet. Chem.* 30 (2016) 273-281.
- [40] Y. H. Deng, C. C. Wang, J. H. Hu, W. L. Yang, S. K. Fu, *Colloids Surf. A* 262 (2005) 87-93.
- [41] A. Zare, R. Khanivar, N. Irannejad-Gheshlaghchaei, M. H. Beyzavi, *ChemistrySelect* 4 (2019) 3953-3960.
- [42] A. Zanon, S. Chaemchuen, F. Verpoort, *Catal. Lett.* 147 (2017) 2410-2420.
- [43] B. Zeynizadeh, S. Rahimi, A. Hallaj, *Curr. Org. Synth.* 16 (2019) 939-947.
- [44] M. Nasr-Esfahani, T. Abdizadeh, *J. Nanosci. Nanotechnol.* 13 (2013) 5004-5011.