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Fe₃O₄@SiO₂-PEG/en is a Useful and Effective Nanocatalyst for One-pot Synthesis of 1-Amidoalkyl-2-naphthol Derivatives under Solvent-free Conditions

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This study investigated the catalytic role of Fe₃O₄@SiO₂-PEG/en nanoparticles in the synthesis of 1-amidoalkyl-2-naphthols by using the multicomponent one-shell reaction between different aldehydes with 2-naphthol and acetamide under solvent-free conditions, at a temperature of 90 degrees of Celsius. In addition, a comparison was made with existing methods. Recent studies show the important features of this heterogeneous catalyst, such as mild reaction conditions, simple operation, non-toxicity, low waste, short reaction time, high product yield, and the ability to reuse the catalyst. These features make this catalytic method efficient in terms of economics and benefits.

Keywords: 1-Amidoalkyl-2-naphthol derivatives, Fe₃O₄@SiO₂-PEG/en nanocatalysts, Three-component reaction, One-pot synthesis, Solvent-free conditions

INTRODUCTION

Oxazines as precursors for the preparation of 1-amidoalkyl-2-naphthols are present in several biologically important natural products and drugs, such as some nucleoside antibiotics and HIV protease inhibitors like ritonavir and lopinavir [1-3]. Until today, various catalysts have been used for the synthesis of amidoalkyl naphthols, for example, 1-butyl-3-methyl imidazolium hydrogen sulfate ([bmim][HSO₄]) [4], N-(4-sulfonic acid) butyl triethyl ammonium hydrogen sulfate ([TEBSA][HSO₄]) [5], thiamine hydrochloride (VB₁) [6], wet-cyanuric chloride (wet-TCT) [7], P₂O₅ [8], H₃PW₁₂O₅ [9], 2,4,6-trichloro-1,3,5-triazine (TCT) [10], copper para toluene sulfonate (CPTS) [11], phosphoric acid molybdate deposited on silica [12], methane sulfonic acid (MSA) [13], Ph₃CCl [14], oxalic acid [15], and supported ionic liquid phase (SILP) [16]. However, some of the mentioned methods face some

challenges, including the use of toxic, acidic, expensive catalysts, long reaction times, and low product efficiency.

Recently, the attention of scientists and researchers has been focused on technological approaches to prevent pollution and design processes that minimize the use of hazardous chemicals and organic solvents. Though, homogeneous catalysts in organic reactions have high efficiency [17-20], low thermal and chemical stability [21] are significant issues, and their recovery from the reaction mixture is generally difficult. To solve this problem, heterogeneous catalysts, for example antimony (III) acetate [22], Ag nanoparticles [23], nano-graphene oxide [24], and nano-Ni [25], are used instead of homogeneous catalysts. The easiest way for this purpose is to establish homogeneous catalysts on environmentally friendly materials [26-30]. Today, magnetite nanoparticles have been widely used due to their unique properties like high surface area, low toxicity, biocompatibility, and recyclability [31-36]. Magnetic separation makes recovery of the catalyst from the reaction mixture by an external magnetic field much simpler than centrifugation and filtration [37].

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Due to the importance of amidoalkyl naphthols and the heterogeneous catalyst ability of $\text{Fe}_3\text{O}_4@\text{SiO}_2/(\text{CH}_2)_3\text{-en-SO}_3\text{H}/\text{H}_2\text{SO}_4$ nanoparticles in organic reactions, we reported a new method for the synthesis of these compounds with the presence of this catalyst and solvent-free conditions.

EXPERIMENTAL

Materials and Instrumentation

All materials were purchased from Sigma-Aldrich and Merck. Magnetic property was determined at room temperature on VSM (Hot Desert Magnetism Company of Iran). TEM measurements were performed with a Zeiss EM10C microscope at 100 kV. Using the Zeiss-Sigma VP instrument, SEM and EDS analyses were made for the morphology and elemental analysis of the synthesized nanocatalysts. XRD analysis was studied using a PANalytical X'Pert Pro X-ray diffractometer. FT-IR spectrum was recorded with a Shimadzu IRPrestige-21 spectrometer and samples were analysed using KBr disc. Melting points were determined with an Electro thermal 9100 apparatus. IR spectra were recorded with a Shimadzu IR-470 spectrometer. ^1H and ^{13}C NMR spectra were recorded on Broker DRX-400 Advance spectrometer for solutions in d_6 -DMSO using TMS as an internal standard.

Preparation of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PEG/en}$

PEG-300 (3 mmol) and sodium hydride (3 mmol) were poured in 20 ml toluene at 0 °C under an inert atmosphere. Then the mixture was stirred for one hour at 60 °C, 1.0 g of $\text{Fe}_3\text{O}_4@\text{SiO}_2/(\text{CH}_2)_3\text{-Cl}$ [31] was added to 50 mL of toluene and stirred under reflux conditions for 12 h. The obtained magnetic nanoparticles were washed with ethanol and acetone and dried at 60 °C. 1.0 g of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PEG}$ was dispersed in 100 ml of toluene for 20 min with ultrasonic radiation. Then, 2 ml of (3-chloropropyl) triethoxysilane was added to the reaction mixture and refluxed for 12 h, the resulting $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PEG/Cl}$ was washed with ethanol and dried at 60 °C. 5 ml of ethylenediamine was added to

$\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PEG/Cl}$ (1.0 g) in 100 ml of acetonitrile, the reaction mixture was stirred for 12 h under reflux conditions. The reaction mixture was cooled, the formed magnetic nanoparticles were separated with a magnet, washed with ethanol and, dried under a temperature of 60 °C [38].

General Method of Preparing 1-Amidoalkyl-2-naphthols

A mixture of aldehydes (1 mmol), 2-naphthol (1 mmol), acetamide (1.2 mmol), and $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-PEG/en}$ magnetic nanoparticles (0.03 g) at 90 °C was heated without solvent. After completion of the reaction based on TLC analysis (n-hexane/ethyl acetate, 5:2), the mixture was filtered, the filtered one was washed with water, and the product was isolated. The crude product was recrystallized from ethanol to obtain pure 1-amidoalkyl-2-naphthol derivatives in 80-96% yield.

Selected Spectroscopic Data

N-(5-ethyl-2-hydroxyphenyl) (2-hydroxynaphthalen-1-yl) methyl acetamide. m.p. = 208-210 °C; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) KBr: 3347, 3321, 1635, Anal. Calcd. for $\text{C}_{21}\text{H}_{21}\text{NO}_3$: C, 75.22; H, 6.26; N, 4.17, found: C.75.10; H. 6.18; N. 4.14%; ^1H NMR (400 MHz, DMSO- d_6): δ 1.3 (3H, t, CH_3), 2.6 (2H, q, CH_3), 2.2 (3H, s, CH_3), 5.79 (1H, s, CH), 5.0 (2H, broad s, OH), 6.16 (1H, d, CH), 7.04-7.74 (9H, m, ArH). 8.00 (1H, NH), ^{13}C NMR (100.6 MHz, DMSO- d_6): δ 13.2. (CH_3), 23.6 (CH_3), 32.7 (CH_2), 48.5. (CH), 112.1, 115.3, 118.7, 119.6, 121.0, 122.0, 123.9, 126.3, 128.3, 129.2, 129.4, 130.1, 133.0, 143.0, 151.8, 152.1, 173.0.

N-(2-hydroxynaphthalen-1-yl) (3-hydroxyphenyl) methyl acetamide. m.p. = 212-214 °C; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) KBr, 3310, 3314, 1620, Anal. Calcd. for $\text{C}_{19}\text{H}_{17}\text{NO}_3$: C, 74.26; H, 5.53; N, 4.56; found: C. 74.50; H. 5.24; N. 4.39%, ^1H NMR (400 MHz, DMSO- d_6): δ 2.02 (3H, s, CH_3), 5.0 (2H, broad s, OH), 6.06 (1H, s, CH), 6.84-7.46 (10H, m, ArH). 8.21 (1H, NH), ^{13}C NMR (100 MHz, DMSO- d_6): δ 23.6. (CH_3), 48.5. (CH), 48.5. (CH), 115.5, 118.7, 122.6, 126.0, 123.9, 126.3,

128.3, 129.1, 129.6, 130.5, 133.7, 144.0, 14% .0, 152.8, 153.1, 175.03.

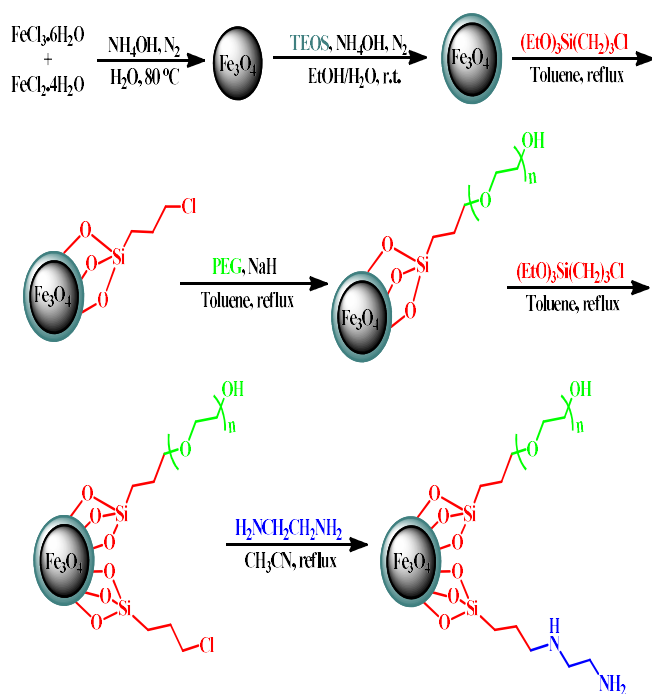
RESULTS AND DISCUSSION

The preparation method of polyethylene glycol/ethylene diamine phase transfer catalyst with nanomagnetic support (Fe₃O₄@SiO₂-PEG/en) is shown below (Scheme 1).

As stated above, physical and chemical techniques such as FT-IR, SEM, EDS, TEM, XRD, and VSM were used to characterize the Fe₃O₄@SiO₂-PEG/en magnetic nanocatalyst Figs. 1 to 5.

To obtain optimal conditions, the reaction of 2-naphthol (1 mmol), 4-nitrobenzaldehyde (1 mmol), and acetamide (1.2 mmol) was performed under different conditions with diverse amounts of magnetic nanocatalyst Fe₃O₄@SiO₂-PEG/en.

To compare the activity of Fe₃O₄@SiO₂-PEG/en magnetic nanocatalysts with other catalysts, the reaction was carried out with other catalysts at temperature 90 °C for



Scheme 1. The preparation method

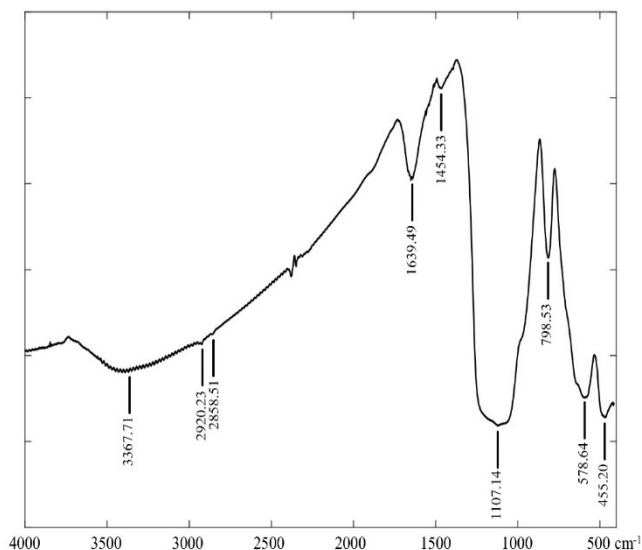


Fig. 1. FT-IR spectrum of the catalyst.

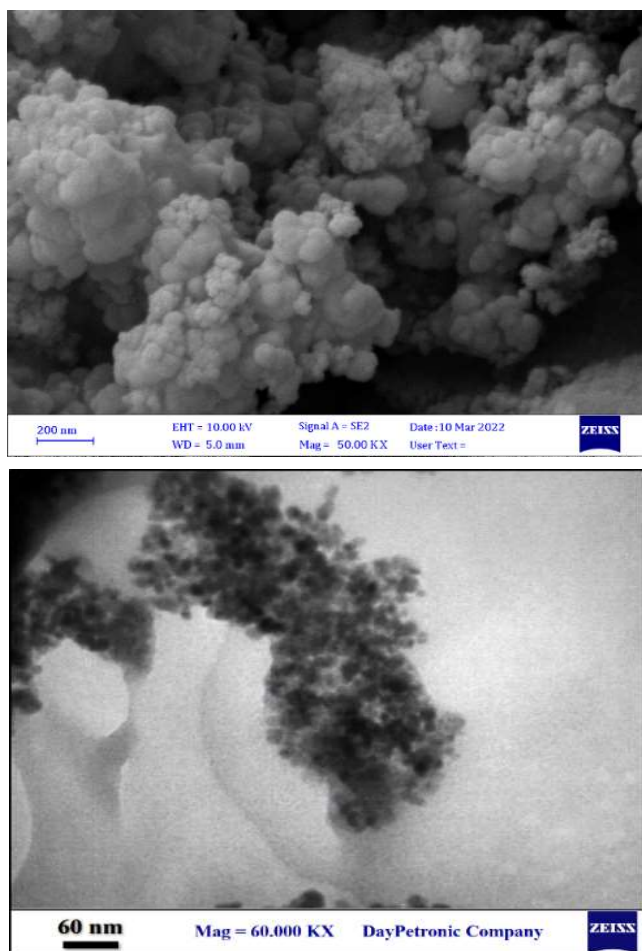


Fig. 2. SEM (left) and TEM (right) images of the catalyst.

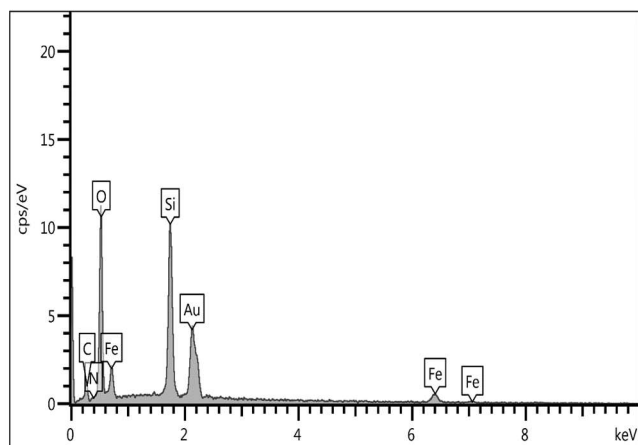
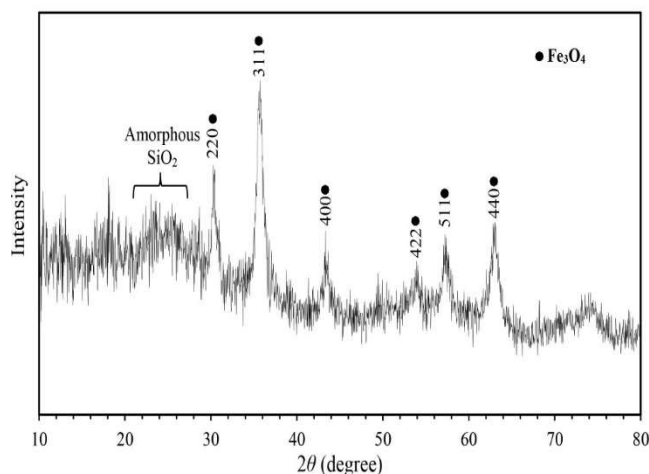
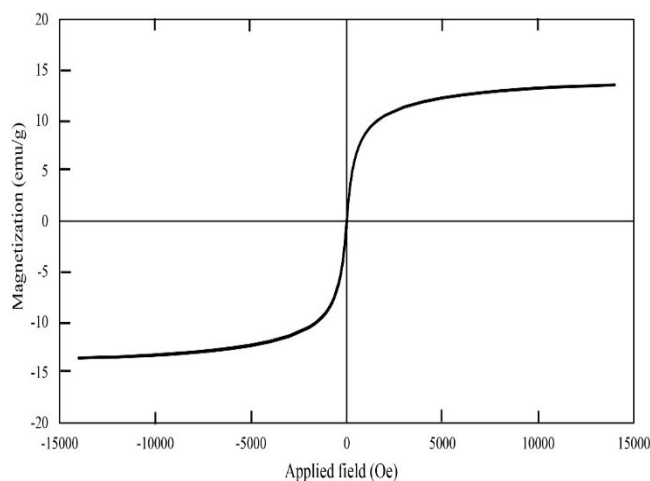

Fig. 3. EDS spectrum of the catalyst.

Fig. 4. XRD pattern of the catalyst.

Fig. 5. Magnetization vs. applied magnetic field for the catalyst.

Table 1. Evaluation of the Activity of Different Catalysts for the Synthesis of 1-Amidoalkyl-2-naphthols

| Entry | Catalyst | Time (min) | Yield (%) |
|-------|---|------------|-----------|
| 1 | - | 15 | 25 |
| 2 | Ce(SO ₄) ₂ | 15 | 25 |
| 3 | I ₂ | 15 | 30 |
| 4 | K- 10 clay | 15 | 40 |
| 5 | K ₅ CoW ₁₂ O ₄₀ .3H ₂ O | 15 | 50 |
| 6 | FeCl ₃ .SiO ₂ | 15 | 55 |
| 7 | HClO ₄ -SiO ₂ | 15 | 65 |
| 8 | NaHSO ₄ .H ₂ O | 15 | 65 |
| 9 | Al(H ₂ PO ₄) ₃ | 15 | 70 |
| 10 | p-TSA | 15 | 55 |
| 11 | Sulfamic acid | 15 | 60 |
| 12 | Silica sulfuric acid | 15 | 65 |
| 13 | Silver NPs | 15 | 80 |
| 14 | Antimony(III) acetate | 15 | 85 |
| 15 | nano-graphene oxide | 15 | 95 |
| 16 | nano-Fe ₃ O ₄ @SiO ₂ -PEG/en | 15 | 95 |

15 min in solvent-free conditions. The results can be seen in Table 1. According to the table, this catalyst is an effective and useful green catalyst for the synthesis of 1-amidoalkyl-2-naphthols.

To optimize the amount of catalyst, the reaction between 2-naphthol, 4-nitrobenzaldehyde, and acetamide was performed at 90 °C for 15 min in solvent-free conditions using different amounts of Fe₃O₄@SiO₂-PEG/en nanocatalyst (Table 2). The amount of 0.03 g nanocatalyst Fe₃O₄@SiO₂-PEG/en showed the best efficiency in 15 min (Table 2, entry 4).

The response of the model was investigated in several solvents (Table 3). Based on the results, different solvents affect the reaction efficiency. Solvents required more time

and did not have acceptable efficiency; the best results are obtained in free solvent conditions (Table 3, entry 5).

To optimize the temperature, the model reaction, *i.e.*, the reaction of 2-naphthol, 4-nitrobenzaldehyde, and acetamide,

Table 2. Optimization of Nano-Fe₃O₄@SiO₂-PEG/en Amount for the Synthesis of 1-Amidoalkyl-2-naphthols

| Entry | Catalyst (g) | Time (min) | Yield (%) |
|-------|--------------|------------|-----------|
| 1 | - | 15 | 0 |
| 2 | 0.07 | 15 | 65 |
| 3 | 0.01 | 15 | 84 |
| 4 | 0.03 | 15 | 96 |
| 5 | 0.05 | 15 | 95 |

Table 3. The Effect of the Solvent on the Synthesis of 1-Amidoalkyl-2-naphthols by Fe₃O₄@SiO₂-PEG/en

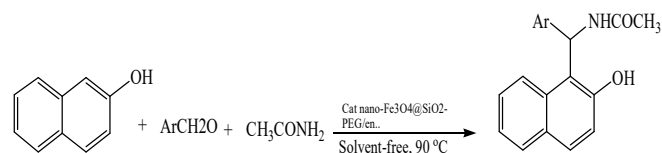
| Entry | Solvent | Time (min) | Yield (%) |
|-------|-------------------|------------|-----------|
| 1 | H ₂ O | 60 | 10 |
| 2 | EtOH | 60 | 30 |
| 3 | EtOAc | 60 | 25 |
| 4 | CHCl ₃ | 60 | 10 |
| 5 | Neat | 10 | 96 |

Table 4. Optimizing the Temperature Using 0.03 g of Nano-Fe₃O₄@SiO₂-PEG/en

| Entry | Temperature (°C) | Time (min) | Yield (%) |
|-------|------------------|------------|-----------|
| 10 | 40 | 15 | 20 |
| 11 | 60 | 15 | 75 |
| 12 | 80 | 15 | 85 |
| 5 | 90 | 15 | 96 |

was performed using 0.03 g of catalyst at different temperatures (Table 4). According to Table 4, the best temperature is 90 °C in terms of reaction time and efficiency.

Scheme 2 demonstrates the optimized condition for the reaction and Table 5 lists different applied pressures for this reaction.



Scheme 2. Synthesis of 1-amidoalkyl-2-naphthols in the presence of nano-Fe₃O₄@SiO₂-PEG/en

As can be seen in Table 5, the reaction with aldehydes containing electron-withdrawing groups such as 4-nitrobenzaldehyde is performed in a shorter time than with aldehydes containing electron-donating groups.

CONCLUSION

In this study, using Fe₃O₄@SiO₂-PEG/en magnetic nanoparticles, a new method for synthesizing biologically active 1-amidoalkyl-2-naphthols from 2-naphthol, acetamide and other aldehydes without solvent were presented. Providing excellent yields for synthesis, it is both simple and inexpensive. The important features of this method are mild reaction conditions, easy operation, high performance, green aspects of operation such as avoiding dangerous organic solvents, toxic catalysts and wastes, ease of recovery, and reuse of the catalyst.

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Table 5. Reaction between 2-Naphthol, Aldehydes, and Acetamide Catalyzed by Nano-Fe₃O₄@SiO₂-PEG/en (0.03 g) at 90 °C

| Entry | Ar | Time (min) | Yields (%) | m.p. (°C) | | Ref. |
|-------|--|---------------|---------------|--------------|----------|------|
| | | | | Found | Reported | |
| 1 | 2-NO ₂ C ₆ H ₄ | 15 | 95 | 261-263 | 263-265 | [12] |
| 2 | 3-NO ₂ C ₆ H ₄ | 16 | 95 | 253-255 | 252-256 | [12] |
| 3 | 4-NO ₂ C ₆ H ₄ | 15 | 96 | 241-243 | 242-243 | [12] |
| 4 | 3-ClC ₆ H ₄ | 17 | 91 | 237-239 | 237-238 | [12] |
| 5 | 4-ClC ₆ H ₄ | 17 | 89 | 229-231 | 226-228 | [12] |
| 6 | 2-OHC ₆ H ₄ | 20 | 89 | 212-214 | 215-217 | [12] |
| 7 | 2-OH-5- CH ₂ CH ₃ C ₆ H ₄ | 20 | 91 | 207-209 | | |
| 8 | 4-OH-3-CH ₃ OC ₆ H ₄ | 20 | 87 | 212-214 | 212 | [12] |
| 9 | 4-CH ₃ C ₆ H ₄ | 22 | 80 | 210-212 | 212 | [10] |
| 10 | 2-OH-3-CH ₃ OC ₆ H ₄ | 20 | 90 | 158-160 | 157-159 | [12] |
| 11 | 4-CH ₃ CO ₂ C ₆ H ₄ | 18 | 90 | 220-222 | 220-222 | [12] |
| 12 | 4-NHCH ₃ C ₆ H ₄ | 22 | 83 | 120-122 | 121-123 | [12] |
| 13 | 3-OHC ₆ H ₄ | 20 | 90 | 211-213 | | |

REFERENCES

- [1] D. Seebach, J.L. Matthews, Chem. Commun. (2015) 1997. Y.F. Wang, T. Lzawa, S. Kobayashi, M. Ohno, J. Am. Chem. Soc. 104 (1982) 6456. John Wiley & Sons, New York, 1997.
- [2] A.Y. Shen, C.T. Tsai, C.L. Chen, Eur. J. Chem. 34 (1997) 877.
- [3] X.H. Cai, H. Guo, B. Xie, Int. J. Chem. 3 (2011) 119.
- [4] S.B. Sapkal, K.F. Shilke, B.R. Madje, B.B. Shingate, M.S. Shingare, Bull. Korean Chem. Soc. 30 (2009) 2887.
- [5] A.R. Hajipour, Y. Ghayeb, N. Sheikhan, A.E. Ruoho, Tetrahedron Lett. 50 (2009) 5649.
- [6] M. Lei, L. Ma, L. Hu, Tetrahedron Lett. 50 (2009) 6393.
- [7] Gh.H. Mahdavinia, M.A. Bigdeli, Chinese Chem. Lett. 20 (2009) 383.
- [8] G.Ch. Nandi, S. Samai, R. Kumar, M.S. Singh, Tetrahedron Lett. 50 (2009) 7220.
- [9] A. Dorehiraee, H. Khabazzadeh, K. Saidi, Arkivoc. 7 (2009) 303.
- [10] P.Z.-H. Zhang, Monatsh Chem. 140 (2009) 199.
- [11] M. Wang, Y. Liang, Monatsh Chem. (2010).
- [12] A. Zare, A.R. Hasaninejad, E. Rostami, A.R. Moosavi-Zare, M. Pishahang, E-J. Chem. 7 (2010) 1162.
- [13] V.J. Rani, M. Suresh, P. Lavanya, K.V. Vani, B. Nagarjuna, C.V. Rao, Der PharmaChemica. 2 (2010) 224.
- [14] A. Khazaei, M.A. Zolfigol, A.R. Moosavi-Zare, A. Zare, A. Parhami, A. Khalafi-Nezhad, Applide Catalysis. A; Generl. 386 (2010) 179.
- [15] S.A.M.K. Ansari, J. Sangshetti, N.D. Kokare, P.S. Wakte, D.B. Shinde, Indian J. Chem. Techn. 17 (2010) 71.

- [16] G. Rashinkar, R. Salunkhe, *J. Mol. Catal. A. Chem.* 316 (2010) 146.
- [17] G. Jenner 1995 Homogeneous catalytic reactions involving methyl formate *Appl. Catal. A. Gen.* 121 25
Schultz M. J and M. S Sigman 2006 Recent advances in homogeneous transition metal catalyzed aerobic alcohol oxidations *Tetrahedron* 62 8227.
- [18] P.R. Verma, Mandal, S.P. Gupta, B. Mukhopadhyay, *Tetrahedron Lett.* 54 (2013) 4914.
- [19] H. Kargar, M. Fallah-Mehrjardi, R. Behjatmanesh-Ardakani, K.S. Munawar, M. Ashfaq, M.N. Tahir *Inorg. Chim. Acta* 527 (2021) 120568.
- [20] C. Garkoti, J. Shabir, S. Mozumdar, *New J. Chem.* 41 (2017) 9291.
- [21] A.E.C. Collis, I.T. Horváth, *Sci. Technol.* 1 (2011) 912.
- [22] F. Hakimi, *J. Chem. Res.* 40 (2016) 489.
- [23] F. Hakimi, *J. Inorg. and Nano-Metal Chem.* 47 (2017) 994.
- [24] F. Hakimi, F. Mirjalili, M. Fallah, Mehrjardim, *Asian J. Green Chem.* 4 (2019) 183.
- [25] P.G. Kargar, C. Len, R. Luque, *Chem. Pharm.* 27 (2022) 100672.
- [26] B. Ye, S. Kim, M. Lee, M. Ezazi, H.D. Kim, G. Kwon, D.H. Lee, *RSC Adv.* 10 (2020) 16700.
- [27] P.S. Shinde, P.S. Suryawanshi, K.K. Patil, V.M. Belekar, S.A. Sankpal, S.D. Delekar, S. Jadhav, *J. Compos. Sci.* 5 (2021) 75.
- [28] S. Sayyah, M. Fallah-Mehrjardi, S.J. Saghanezhad, *Mini-Rev. Org. Chem.* 18 (2021) 11.
- [29] P.R. Sruthi, P.P. Nimmi, S.S. Babu, S. Anas, *ChemistrySelect.* 7 (2022) e202104273.
- [30] M.Z. Sarker, M.M. Rahman, H. Minami, T. Suzuki, M.A. Rahman, A. Khan, S.M. Hoque, H. Ahmad, *A Physicochem. Eng.* 647 (2022) 129044.
- [31] F. Hakimi, I. Salimi, Fallah-Mehrgardi, *Lett. in Org. Chem.* 19 (2022) 842.
- [32] F. Hakimi, E. Golrasan, *Asian J. of Green Chem.* 7 (2023) 47.
- [33] F. Hakimi, A. Sharifi, E. Golrasan, *Chem. Methodologies* 7 (2023) 489.
- [34] A. Mokkarat, S. Kruanetr, U. Sakee, *J. Mol. Struct.* 1259 (2022) 132745.
- [35] D. Shi, M. Lv, H. Tong, J. Liu, H. Cai, D. Luo, C. Ma, X. Xu, B. Wang, *J. Environ. Manage.* 303 (2022) 114238.
- [36] M. Kazemi, M. Mohammadi, *Appl. Organomet. Chem.* 34 (2020) e5400.
- [37] D. Azarifar, O. Badalkhani, Y. Abbasi, *J. Sulfur Chem.* 37 (2016) 656.
- [38] M. Fallah-Mehrjardi, M. Zare, *Polycycl. Aromat. Compd.* 43 (2023) 7355.