

ONE POT SYNTHESIS OF 1, 2, 3- TRIAZOLES AND 1,4 DIHYDROPYRIDINES CATALYZED BY NI-Fe₃O₄ NANOCATALYST

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ABSTRACT

A series of 1-substituted-4-phenyl-1H-1,2,3-triazole and 1,4 dihydropyridines were efficiently synthesized by conventional and nonconventional way by use of Ni-Fe₃O₄ Nano catalyst with good yield.

Keywords: Ni-Fe₃O₄ Nano Catalyst, 1, 2, 3- Triazoles and 1,4 Dihydropyridines.

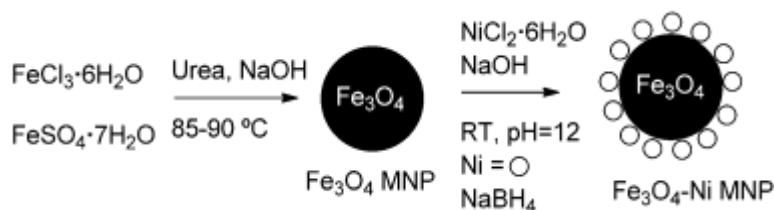
INTRODUCTION

Free nano Fe₂O₃ have been shown to be active, stable, and highly selective catalysts for various oxidations with high turnover number (TON) and excellent selectivity.¹⁻³ The reduction of nitro as well as carbonyl compounds⁴ with hydrogen-transfer reagents is a much safer and more benign process than reactions involving molecular hydrogen, metal hydrides, or soluble metals. In continuation of researcher efforts to develop protocols for green raw materials⁵⁻⁶ and heterogeneous catalysis for hydrogen transfer reactions and nano-catalysis,⁷⁻¹⁰ researcher propose to use glycerol as hydrogen donor as well as solvent in the reduction of nitro and carbonyl compounds using a new, efficient, recyclable, and in expensive ferrite-nickel magnetic-nanoparticles (Fe₃O₄-Ni mnps). Recently 1,2,3 Triazoles were readily prepared from Cu(I)-catalyzed azide-alkyne 1,3-dipolar Cycloaddition (cuaac).¹¹⁻¹² 1,2,3-triazoles have significant anti- proliferative activity against a wide variety of human cancer cell lines, including those that are multidrug resistant.¹³⁻¹⁴ Cu(II)-Clay as a novel, environmentally benign, recyclable, efficient and heterogeneous catalyst for the one pot synthesis of 1,2,3-triazoles via a three component reaction of alkyl halides, sodium azide and terminal alkynes using H₂O:etoh (1:1) mixture as solvent under ultrasonic conditions at room temperature.¹⁵

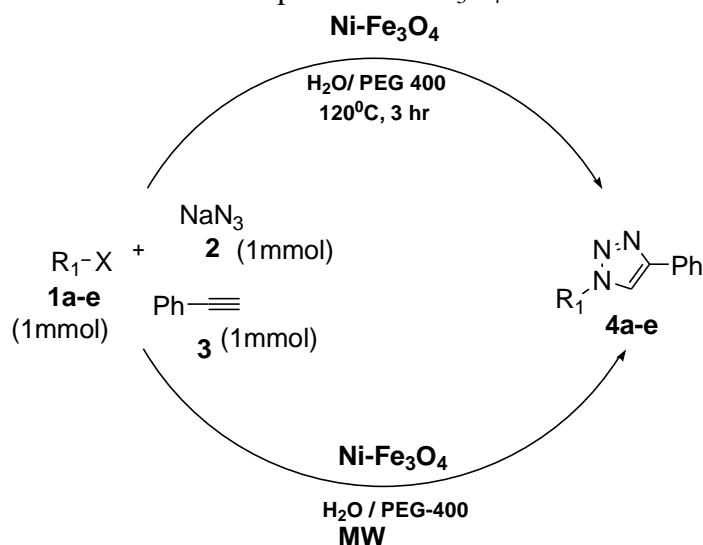
Recently 1,4-dihydropyridines prepared by direct condensation of aldehydes, malononitrile and barbituric acid in aqueous media has been reported under ultrasound irradiation,¹⁶ or catalyzed by diammonium hydrogen phosphate.¹⁷ 1,4-dihydropyridines compounds are most important classes of drug molecules and were introduced for medical use in 1911.¹⁸ They have attracted much attention due to their antiviral,¹⁹ antibiotic,²⁰ anti-inflammatory,²¹ and antitumor²²⁻²³ activities

EXPERIMENTAL

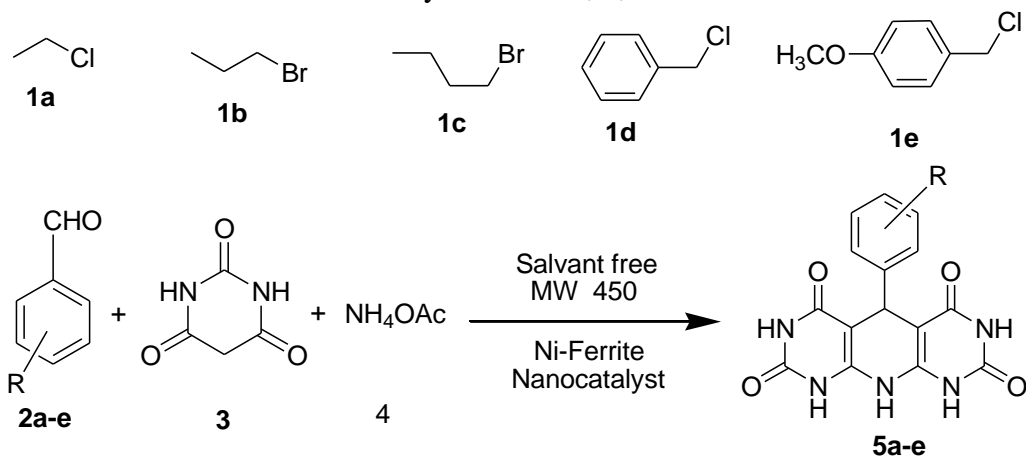
Solvents, reagents and chemicals were purchased from Aldrich, Fluka, Merck, SRL, Spectrochem and Process Chemicals generally used without further purification. IR spectra were recorded on a Perkin FT-IR spectrometer. The NMR spectra were measured with a 400 MHz Bruker Avance spectrometer at 400 and 100 MHz, for ¹H for ¹³C, respectively, in CDCl₃ solution with TMS as an internal standard. Chemical shifts are given in ppm (δ) and are referenced to the residual proton resonances of the solvents. The synthesized Fe₃O₃-Ni MNPs were characterized by several techniques such as XRD, ICP-AES, TEM, and FEG-SEM-EDS. The progress of the reaction has been monitored by thin layer chromatography.



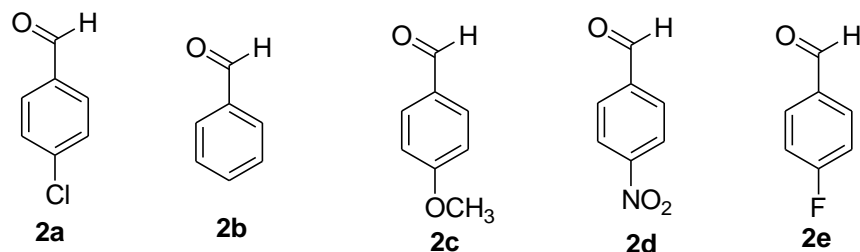
Scheme-I : Preparation of $\text{Fe}_3\text{O}_4\text{-Ni}$ MNPs



Scheme-II: Synthesis of 1, 2, 3- triazoles



Scheme-III: Synthesis of 1,4-dihydropyridines



Preparation of Ferrites/Fe₃O₄

The ferrites magnetic Nanoparticle was prepared by reported procedure. The FeCl₃·6H₂O (5.41 g) and urea (3.6 g) were dissolved in water (200 mL) at 85 to 90°C for 2 h. The solution turned to brown color. To the resultant reaction mixture cooled to room temperature was added FeSO₄·7H₂O (2.78 g) and then 0.1m NaOH until pH 10. The molar ratio FeIII to FeII in the above system was nearly 2.00. The obtained hydroxides were treated by ultrasound in the sealed flask at 30 to 35°C for 30 min. After ageing for 5 h, the obtained black powder of Fe₃O₄ was washed, and dried under vacuum.

General procedure for the synthesis of Fe₃O₄-Ni MNPs:

Ferrite magnetic nanoparticle Fe₃O₄ (2 g) and NiCl₂·6H₂O (10 wt % of nickel on ferrite) were stirred at room temperature in aqueous solution for 1 h. After impregnation, the suspension was adjusted to pH 12 by adding sodium hydroxide (0.5m) and stirred for 10 to 12 h. The solid was washed by distilled water (510 mL). The obtained metal precursors were reduced by adding an aqueous solution of 0.2m NaBH₄ drop wise under gentle stirring in an ice water bath for 30 min until no bubbles were observed in the solution. The resulting Fe₃O₃-Ni MNPs were ultrasonicated for 10 min and then washed with distilled water and subsequently with ethanol.

Synthesis of 1,2,3- triazoles catalyzed by NiFe₃O₄ catalyst by conventional method :

(4a-e)

Charged phenyl acetylene (1.5m mol), Alkyl halide/Ar-x (1.5m mole), NaN₃ (1.5 m mol), 1.46 mol % of Ni-Fe₃O₄ catalyst by using H₂O (5.0 ml) -PEG 400 (1gm) in sealed tube . Reaction mixture was heated at 150°C until the TLC analysis shows that the reaction is completion. Then reaction mixture was cooled to rt, Ni-Fe₃O₄ catalyst was isolated by an magnetic decantation, water was removed by rotary evaporation, the crude product was purified by column chromatography in 90 – 95 % yields.

Synthesis of 1, 2, 3-triazoles catalyzed by using NiFe₂O₄ catalyst by microwave irradiation : **(4a-e)**

Equimolar aliphatic and aromatic halide, sodium azide, phenyl acetylene and Ni- Fe₃O₄ catalyst in mixture of H₂O (5ml) and PEG-400 (1.g) charged in 10 ml RBF. The mixture was heated to 80°C under microwave irradiation (MW.480W) until TLC analysis shows that the reaction is complete. Then the reaction mixture was cooled to rt, Ni-Fe₃O₄ catalyst was isolated by using external permanent magnet, water was removed by rotary evaporation, the crude product was purified by column chromatography in 80-95 % yield.

4a- White solid, mp 54-56°C; IR ; 754, 805, 1040, 1455,1484, 3381 cm⁻¹ ¹H NMR (400 MHz, CDCl₃) δ: 1.33 (t , 3H,), 4.35 (q , 2H), 7.2-7.8(5H) ,7.6(s, 1H) ¹³C NMR (100 MHz, CDCl₃) δ: 15.50, 15.57, 45.23, 45.34, 119.02, 125.65, 128.06, 128.81, 129.78, 130.69, 147.74. MS (m/z): 173.9

4b. White solid, mp 62-64°C, IR: 1240, 1555, 1485, 3281 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ: 0.85-0.98 (3H, t), 1.88-1.98 (2H, m), 4.30-4.35 (2H,t), 7.26-7.84 (5H, Ar), 7.75 (1H, s). ¹³C NMR (100 MHz, CDCl₃) δ: 23.72, 29.68, 51.92, 119.52, 125.62, 128.01, 128.78, 130.70, 147.61. MS (m/z): 187.

4c. White solid, mp 48-50°C; IR: 1140, 1650, 1484, 3360 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ: 0.96 (3H, t), 1.38 (2H, sextet), 1.92 (2H, quintet), 4.39 (2H, t), 7.26-7.82 (5H, Ar), 7.74 (1H, s). ¹³C NMR (100 MHz, CDCl₃) δ: 13.57, 19.78, 32.37, 50.19, 119.48, 125.73, 128.12, 128.88, 130.79, 147.76. MS (m/z): 201.

4d. White solid, mp 126-128°C, IR: 694, 729, 768, 1049, 1076, 1223, 1358, 1466, 3121 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ: 5.23(2H, s), 7.26-7.82(10H, Ar), 7.69(1H, s). ¹³CNMR (100 MHz, CDCl₃) δ: 54.1, 119.7, 125.7, 128, 128.2, 128.7, 128.8, 129.1, 130.6, 134.7, 148.1, MS (m/z): 235.

4e. White solid, mp 132-136°C. IR: 794, 731, , 1055, 1076, 1223, 1356, 1464, 3131 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ: 5.23 (s, 2H), 6.40 (s, 1H), 7.33 (d, 2H), 7.42 (d, 2H), 7.5 (s, 1H), 6.90 (d, 2H), 6.61 (d, 2H), 3.54 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ: 58.1, 54, 112.4, 126.7, 128.9, 127, 128.2, 128.7, 127.8, 129.1, 131.5, 134.7, 156.1. MS (m/z): 235.

Table-I: Preparation of 1, 2, 3-triazoles by microwave irradiation: (4a-e)

Entry	Time (hr)	Yield (%)
4a	3.00	85
4b	2.50	75
4c	3.15	78
4d	2.30	89
4e	2.10	90

General procedure for preparation 1,4-dihydropyridines: (5a-e)

Mixture of aromatic aldehyde (5 mmol), barbituric acid (10 mmol) and ammonium acetate (8 mmol) was irradiated in microwave instrument (450 W) for a certain period of time without solvent. After completion of the reaction (monitored TLC), reaction mixture was diluted with ethyl acetate (20 mL), washed organic layer with saturated NaHCO₃ solution (3 x 15 mL) and then with brine solution. Dried organic layer over anhydrous Na₂SO₄ and concentration under reduced pressure gave crude product, recrystallized from ethanol.

5a. mp: 300°C, IR: 3661, 3175, 1682, 1633, 1458, 776 cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 10.10 (s, 1H), 3.5 (s, 1H), 5.93 (s, 1H), 7.18 (dd, J = 2.2 Hz, 2H), 7.04 (d, J = 7.8, 2H). ¹³C NMR (125 MHz, DMSO-d₆): δ 168.11, 152.12, 129.37, 127.77, 126.30, 40.49, 91.22. EI-MS (m/z): 418 (M+1).

5b. mp: 298-300°C; IR: 3054, 1700, 1676, 1606, 1405, 1507 cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 10.01 (s, 1H), 3.6 (s, 1H), 7.09 (t, 1H), 7.18 (dd, J = 2.2 Hz, 2H), 7.05 (d, J = 7.8, 2H). ¹³C NMR (125 MHz, DMSO-d₆): δ 164.40, 150.10, 130.8, 128.12, 126.30, 38.20, 79.10. EI-MS (m/z): 378 (M+1).

5c. mp: 285-286°C; IR: 3056, 1676, 1606, 1405, 1507, 776 cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 10.01 (s, 1H), 6.75 (dd, J = 2.2 Hz, 2H), 7.01 (d, J = 7.8, 2H), 3.76 (s, 3H), 3.30 (s, 1H). ¹³C NMR (125 MHz, DMSO-d₆): δ 80.10, 152.40, 40.05, 152.10, 165.20, 135.30, 115.20, 132.10, 55.40. EI-MS (m/z): 406 (M+1).

5d. mp: 270-271°C; IR: 3135, 1689, 1605, 1458, 1528, 776 cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 10.01 (s, 1H), 6.01 (s, 1H), 8.05 (dd, J = 2.2 Hz, 2H), 7.38 (d, J = 7.8, 2H), 4.40 (s, 1H). ¹³C NMR (125 MHz, DMSO-d₆): δ 81.10, 150.40, 37.05, 150, 164.20, 150.30, 145.20, 120.10. EI-MS (m/z) : 420 (M+1).

5e. mp: 255-256°C; IR: 3661, 3175, 1682, 1633, 1458, 776 cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 10.01 (s, 1H), 6.01 (s, 1H), 6.82 (dd, J = 2.2 Hz, 2H), 7.08 (d, J = 7.8, 2H), 4.43 (s, 1H). ¹³C NMR (125 MHz, DMSO-d₆): δ 81.10, 150.40, 37.05, 150, 164.20, 150.30, 145.20, 120.10. EI-MS (m/z) : 391 (M+1).

RESULTS AND DISCUSSION

In the beginning, the synthesis of $\text{Fe}_3\text{O}_4\text{-Ni}$ MNPs were prepared by the simple wet impregnation method followed by chemical reduction (**Scheme-I**) and characterized by X-ray diffraction (XRD), TOF-SIMS and transmission electron microscopy (TEM). The presence of Ni on the surface of ferrite was confirmed with time of flight secondary ion mass spectrometry (TOF-SIMS), which is the most surface sensitive (<1 nm) and widely used technique for surface characterization. The surface composition of the powder was determined from the characteristic XPS peak intensities of Ni, Fe, O and C, that is, Ni_{2p} , $\text{Fe}_{2p}^{3/2}$, O_{1s} and C_{1s} , respectively. Oxygen appears to be the most abundant element in the powder (49%) followed by carbon (33%), nickel (11%), and iron (7%). The characteristic peak of nickel (Ni 2p) is presented in Figure 1.7. The main contributions of Ni 2p_{3/2} and Ni 2p_{1/2} peaks are at 854.2 and 872.5 eV, respectively. A series of 1-ethyl-4-phenyl-1H-1, 2, 3-triazole and 1, 4 dihydropyridine were synthesized by conventional and microwave method analyzed by IR, ¹HNMR, ¹³CNMR and mass spectroscopy.

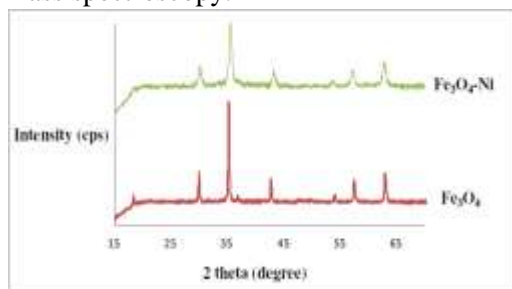


Fig.1.0 XRD pattern of the NiFe_3O_4 nanoparticles

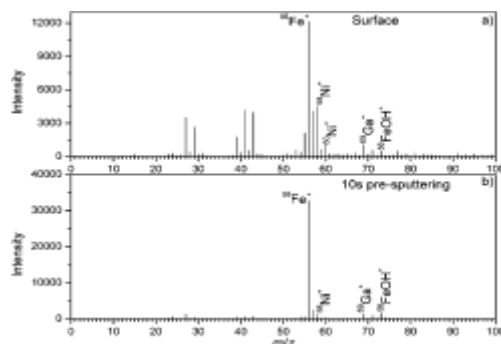


Fig.1.1 TOF-SIMS positive ion spectra (a) intact surface spectrum, (b) after pre-sputtering for 10 seconds in continues mode with Ga^+ ion beam at same impact energy of 10 keV

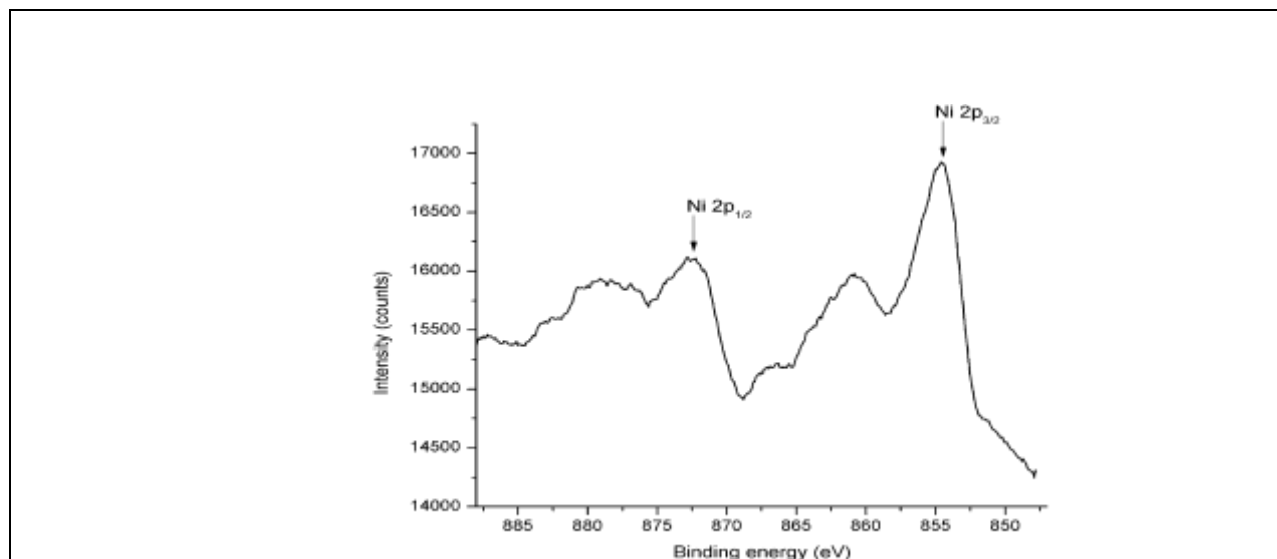


Fig.1.2 Ni_{2p} XPS line taken in FAT 22 mode with the energy step of 0.1 eV and acquisition time window of 24s

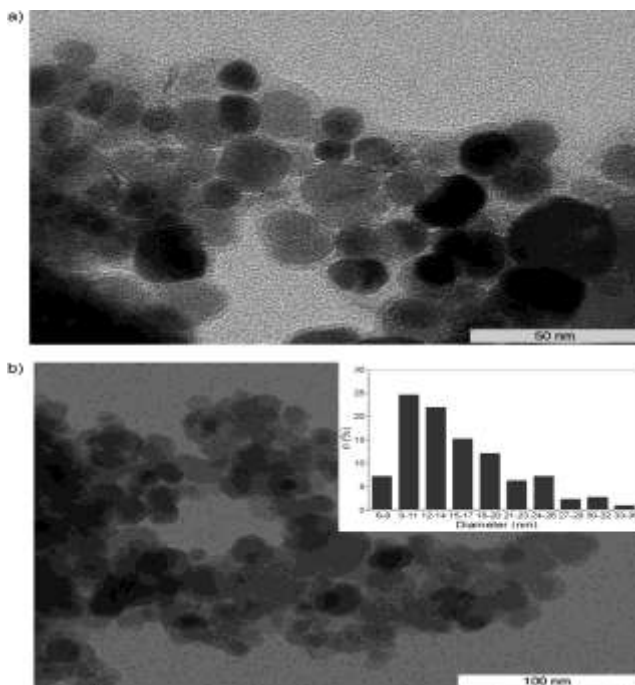


Fig.1.3 a) TEM images of Fe₃O₄Ni MNPs at different magnifications 50nm; b) 100nm showing particle size distribution; the corresponding histogram is superimposed onto image

CONCLUSION

We have reported a convenient, practical and an efficient method for the synthesis of 1-ethyl-4-phenyl-1H-1, 2, 3-triazole and 1, 4 dihydropyridine by using of Fe₃O₄-Ni MNPs by conventional and non-conventional method without use of solvent. This operationally simple procedure and provides a better scope than previously reported.

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