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Green asymmetric synthesis of binol *via* oxidative cross-coupling in the presence of chiral magnetic nano ligands

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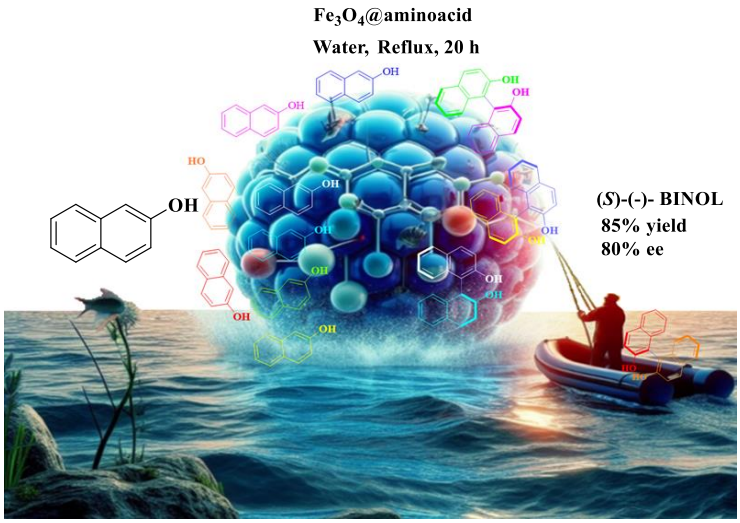
Abstract

A green synthesis method was used to prepare racemic binol for the first time, yielding up to 92% in the presence of magnetic nanoparticles Fe_3O_4 in water. Additionally, an enantioselective cross-coupling of 2-naphthols was conducted using a chiral magnetic nanoligand L-cysteine@Fe_3O_4, resulting in the preparation of the *S*-binol enantiomer with up to 85% yield and 80% enantioselectivity. The nanomagnetic particles' structure and morphology were characterized using various techniques, including energy-dispersive X-ray spectroscopy (EDAX), scanning electron microscopy (SEM), thermogravimetric analysis (TGA), differential thermal analysis (DTA), X-ray diffraction (XRD), vibrating-sample magnetometer (VSM) analysis, and Fourier-transform infrared (FT-IR) spectroscopy.



Keywords: Chiral magnetic nano ligand, cross-coupling reaction, aminoacid, Binol, green synthesis

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Introduction

Atropisomers are a series of compounds with a conformational chirality that result from hindered rotation around a single bond[1]. This property plays a critical role in enantioselective reactions catalyzed by these compounds[2]. The unique property of atropisomers has made them important tools in medicinal chemistry for developing new drugs with enhanced stereoselectivity and biological activity[3]. Due to their ability to control stereochemistry in reactions, these compounds have proven to be valuable in various fields, including natural product and pesticide synthesis [4,5]. Studying such compounds and their spatial chemistry has opened up new possibilities for designing molecules with specific chirality for synthesizing complex molecules and materials with tailored properties, making them essential tools in modern organic chemistry.

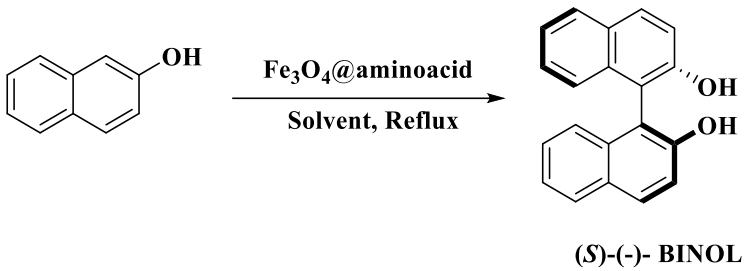
Binol (1,1'-bi-2-naphthol) is a well-known example of a compound demonstrating atropisomeric stereoisomers. Binol derivatives, derived from binaphthyl compounds, are widely used as efficient catalysts in various chemical reactions and industries [6]. finds applications in the production of chiral drugs[7,8], enantioselective recognition[9], Enantioselective fluorescent sensors[10], and antibacterial property[11]. Binol acts as a powerful chiral ligand or catalyst, facilitating the production of chiral compounds with high yield and selectivity. This makes it highly valuable in the chemical and pharmaceutical industries. Additionally, binol derivatives can be converted into other useful ligands, such as phosphoramidites[12], hydrogen phosphonates[13], binol phosphoric acid[14], and binol phosphate[15].

The synthesis of chiral binol typically involves the reaction of the 2-naphthol in the presence of a chiral ligand and transition metal[16]. The chiral ligands play a pivotal role in controlling the stereochemistry of this reaction, enabling the selective formation of the desired enantiomer of binol. Various catalytic methods exist for synthesizing biaryl compounds in organic chemistry. One prevalent approach is the Suzuki-Miyaura cross-coupling reaction, involving the coupling of an aryl halide with an arylboronic acid or boronate ester in the presence of Various catalytic methods exist for synthesizing biaryl compounds in organic chemistry[17,18]. Another popular method is the Ullmann reaction[19] entailing the direct coupling of two aryl halides with a copper catalyst. Additionally, using an oxidizing agent, the Scholl reaction can be employed for synthesizing biaryls through the oxidative coupling of phenols or arylamines[20]. Other transition metals such as nickel[21], iron[22], and palladium[18] have been explored as catalysts for biaryl synthesis , offering chemists a wide range of options for designing efficient and selective reactions to access diverse biaryl structures.

Using nanomagnetic catalysts for biaryl synthesis offers a convenient and efficient method for carrying out these reactions[23-25], with potential advantages in such catalyst recovery and reusability. One commonly used nanomagnetic catalyst is Fe_3O_4, which can be functionalized with different ligands to enhance its catalytic activity and selectivity in various reactions.

Previously, the preparation of chiral binol through oxidative coupling was reported in several works using various metal and chiral mediums. Several reports have used ferric salts for the preparation of binol derivatives however, the use of nanomagnetic Fe_3O_4 for the synthesis of racemic binols and chiral magnetic nano ligands involved Fe_3O_4 and aminoacids has not been extensively explored.

Previously, chiral binol was prepared through oxidative coupling in various works using different metals and chiral mediums[16]. While ferric salts have been used for the preparation of binol derivatives, to the best of our knowledge, the use of nanomagnetic Fe_3O_4 for synthesizing racemic binols and chiral magnetic nano ligands involving Fe_3O_4 and amino acids has not been extensively explored. Therefore, we report the preparation of chiral binol in the presence of Fe_3O_4 coated with amino acids as a chiral magnetic nano ligand for the first time (Scheme 1).

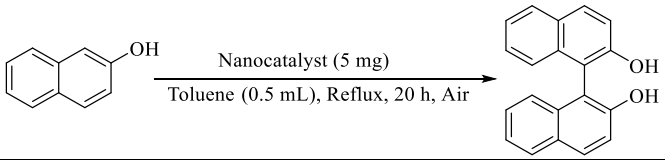


Scheme 1. This work

Results and Discussion

Initially, the cross-coupling of 2-naphthols was performed in toluene for 20 hours in the presence of various nanoparticles as catalysts. As indicated in Table 1, no product was obtained when HZSMS-5, CuO, and TiO_2 nanoparticles were used as catalysts (entries 1-3). The yield of racemic binol was low when Montmorillonite (K10), MCM-41, and Fe_3O_4@MCM-41 were used (entries 4-6). A 65% isolated yield of racemic binol was obtained when the reaction was carried out in the presence of Fe_3O_4 nanoparticles. However, when the reaction was run in the presence of Fe_3O_4@CuO, the yield of racemic binol was lower than Fe_3O_4 (entries 7 and 8). In the next step, the effect of various solvents was examined on the reaction yield (Table 2). Several solvents, such as tetrahydrofuran, dichloromethane, acetone, and nitromethane, did not produce the desired product (entries 1-4). 1,2-dichlorobenzene and chloroform resulted in partial yields (entries 5 and 6). The yield of binol was moderate using xylene derivatives, acetonitrile, and ethanol as solvents (entries 7-11). The results obtained with toluene and water were the same, so water was selected as the green solvent for this reaction (entries 12 and 13). We also investigated the effect of temperature on the reaction yield, showing higher yields at reflux temperature (entry 14). Also, the oxygen in the air is essential for the oxidation step. No product was observed when using the nitrogen atmosphere (entry 15). Additionally, the reaction was performed in the presence of different amounts of Fe_3O_4 nanoparticles, 1, 5, 10, 20, and 25 mg. Using 1 mg of Fe_3O_4 nanoparticles decreased the yield of the product. The yield of the product with 20 and 25 mg of Fe_3O_4 nanoparticles was nearly the same, yielding 90%, so 20 mg of Fe_3O_4 nanoparticles was selected as the optimum amount (not mentioned in the table).

Table 1. Influence of various nano catalysts on the model reaction

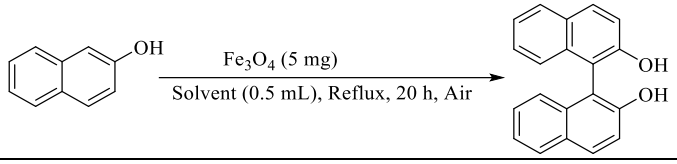


Entry [a]	Catalyst	Yield (%)[b]
1	HZSMS-5	No product
2	CuO	No product
3	TiO_2	No product
4	K10	20
5	MCM-41	10
6	MCM@Fe_3O_4	30
7	Fe_3O_4	85

8	Fe_3O_4@Cu	65
9	-	No product

[a] Reaction condition: 2-naphtole (0.1 mmol), nano catalyst (5 mg), toluene (0.5 mL), [b] isolated yields.

Table 2. Influence of various solvents on the model reaction

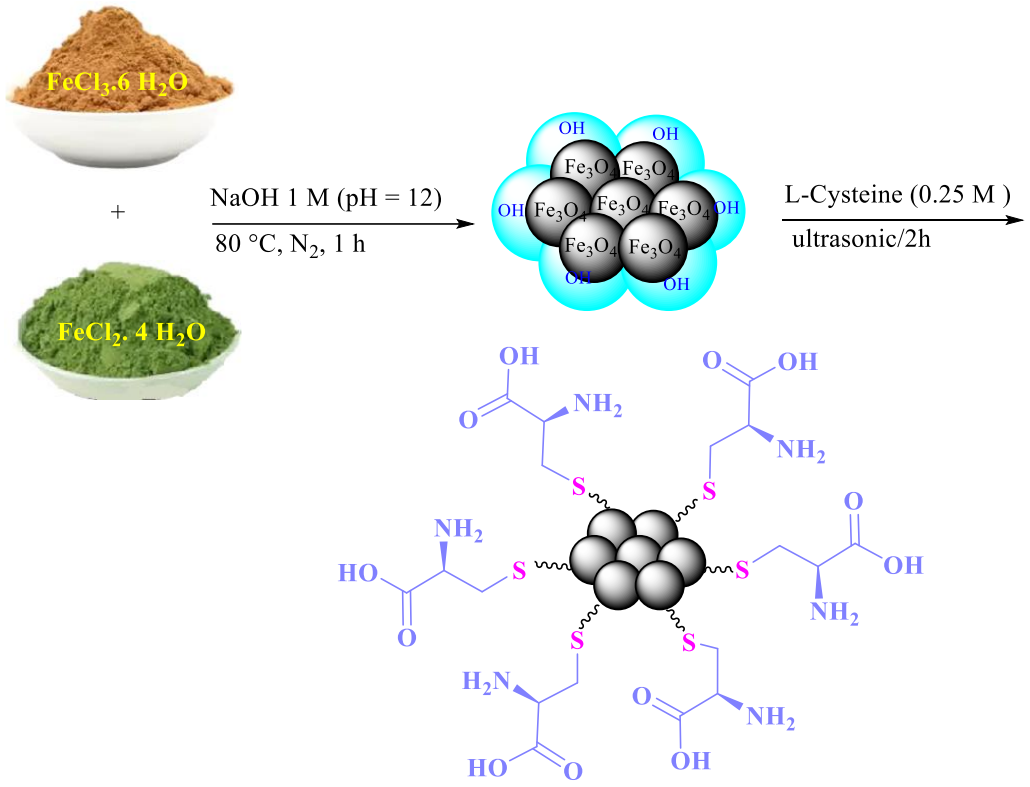


Entry[a]	Solvents	Yield (%)[b]
1	Tetrahydrofuran	No product
2	Dichloromethane	No product
3	Acetone	No product
4	Nitromethane	No product
5	1, 2-Dichlorobenzene	trace
6	Chloroform	trace
7	*o*-Xylene	40
8	*m*-Xylene	42
9	*p*-Xylene	55
10	Acetonitrile	44
11	Ethanol	75
12	Toluene	85
13	H_2O	80
14[c]	H_2O	43
15[d]	H_2O	0

[a] Reaction condition: 2-naphtole (0.1 mmol), Fe_3O_4 nanoparticles (5 mg), solvent (0.5 mL), [b] isolated yields. [c] at room temperature, [d] under nitrogen atmosphere.

The chiral amino acid-coated magnetic nanoparticles ($AA@Fe_3O_4$) were prepared as follows: First, Fe_3O_4 synthesis was initiated by coprecipitation of ferric and ferrous salts in a basic solution[26]. This was

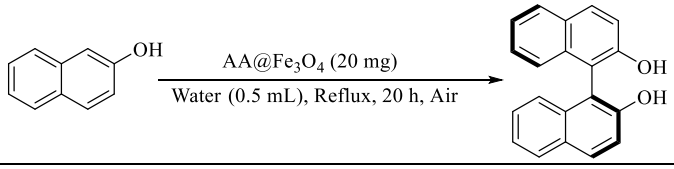
followed by immobilizing amino acids using L-proline, L-alanine, and L-cysteine on Fe_3O_4 nanoparticles (Scheme 2) [27].



Scheme 2. The preparation of Fe_3O_4 nanoparticles and L-cysteine@Fe_3O_4

The asymmetric synthesis of binol was performed under optimal conditions in the presence of chiral magnetic nano ligands. The reaction was carried out in the presence of immobilized chiral magnetic nano ligands, L-Alanine@Fe_3O_4, L-Proline@Fe_3O_4, and L-cysteine. When the reaction was checked in the presence of L-Alanine@Fe_3O_4 and L-Proline@Fe_3O_4, 72% and 65% yield and 68% and 72% enantioselectivity of *S*-binol resulted respectively. The highest yield and enantioselectivity were observed with L-cysteine@ Fe_3O_4 (85% yield and 80% ee of *S*-binol).

Table 3. Effect of chiral magnetic nano ligands on the reaction



Entry[a]	Chiral nanoligand	Yield (%)[b]	ee (%)[c]
1	L-Alanine@Fe_3O_4	72	68
2	L-Proline@Fe_3O_4	65	72
3	L-Cysteine@Fe_3O_4	85	80

[a] Reaction condition: 2-naphtole (0.1 mmol), chiral nano ligands (20 mg), water (0.5 mL), [b] isolated yields. [c]determined by HPLC using a chiral stationary phase, *S*-binol was obtained as a major enantiomer.

Conclusions

In summary, we have reported a new and green method for the synthesis of racemic binol in the presence of a recyclable catalyst $Fe_3O_4$with a high yield along with an asymmetric oxidative cross-coupling of 2-naphthols, using chiral magnetic nano ligand (L-cysteine@ Fe_3O_4) achieving an 85% yield and 80% enantioselectivity in water as the green solvent. The nano catalyst was recovered and reused five times without significant yield loss and three times for enantioselectivity.

Experimental Section

General. All chemicals were purchased from Sigma-Aldrich or Merck Chemicals. Solvents were distilled and dried before being used according to the literature procedure. Deionized water was obtained from an ultra-pure water system Elga (UK). The composition of nanoparticles was determined using a DX-2700 X-ray diffractometer with a Cu Kα X-ray source (λ = 1.542 Å) in a step scan mode with a scanning rate of 0.03° s^{-1} in the range from 10° to 80°. FT-IR (KBr) spectra were recorded on a Bruker Vector 22 FT-IR spectrophotometer. Magnetic properties of the nanoparticles were investigated using a vibrating sample magnetometer (VSM, MPMS (SQUID) XL-7, Quantum Design, USA) with an applied field between −20,000 and 20,000 Oe at 300 K. The morphology and size of the particles were recorded by scanning electron microscope (SEM) recorded by MIRA3 FEG-SEM-TESCAN that this device has a resolution of up to 1 nm and a magnification of up to 1 million times the applied voltage of 30 kv equipped with energy diffraction X-ray spectroscopy (EDX)-detectors. TGA measurement of temperature and mass changes, was determined by BAHR STA 503 with a maximum temperature of 1500 °C and speeds of 0.01-100 K/min. The ^{1}H NMR spectrum was recorded on BrukerAvIII HD- 400 MHz using TMS as the internal standard. HPLC was performed using a Shimadzu Prominence.

Preparation of Fe_3O_4 coated aminoacid (aminoacid@Fe_3O_4). Fe_3O_4 nanoparticles were synthesized by a known method (co-precipitation method)[28]. Subsequently, aminoacid was coated on the Fe_3O_4 nanoparticles to prepare aminoacid@Fe_3O_4 nanoparticles as follows: 1 g of Fe_3O_4 nanoparticles in 10 mL H_2O was dispersed for 15 min using an ultrasonic bath and 0.25 M (10 mL) of aminoacid was added and stirred for 2 h hour. Then, aminoacid@Fe_3O_4 was collected by an external magnet, washed with a mixture of water-ethanol, and dried overnight [29]. The characterization of prepared nanocatalysts were completely investigated and confiremd according the literatures (refer to Supplementary Material).

Heterogeneous catalytic procedure. In a 100 mL round-bottom flask, 2 mmol (0.29 g) of dark brown 2-naphthol powder was dissolved in 40 mL water at reflux for 15 minutes. 20 mg aminoacid@Fe_3O_4 was added and stirred for 20 hours. After completion of the reaction (monitored by TLC), The reaction mixture was cooled and Fe_3O_4@aminoacid was recovered from the reaction mixture using an external magnet, washed with 1/1 water/ethanol and stored for the next reaction. The mixture solution of the reaction was extracted by ethyl acetate three times and purified by column chromatography on silica (eluant: 3/1 of Ethyl acetate/ hexane) after solvent evaporation yielded 0.48 g of pure *S*-Binol (85% yield). (Note: the racemic procedure is the same). Mp 209-211 ºC, Optical Rotation $[a]_D^{22}$ (c = 0.6 THF) -23.8° for 80 % ee [30]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (2H, s), 7.20 (2H, d, *J* 8.3 Hz), 7.35 (1H, dt, *J* 2.76, 4.4 Hz), 7.38-7.45 (1H, m), 7.94 (1H, d, *J* 7.84 Hz), 8.02

(1H, d, *J* 8.92 Hz)[31]. HPLC (Figure 9): (Chiralcel OD-H column with 90:10 *n*-hexane:isopropanol as eluent 0.5 mL/min, 20 °C, λ 254 nm), retention times: t_{major}= 27.1 min, t_{minor}= 33.4 min [32].

The stability and preservation of catalytic activity of the nanomagnetic catalysts were evaluated by studying their recovery and reusability. The synthesis of binol was successfully performed using recycled L-Cysteine@Fe_3O_4 for the fifth time without a significant decrease in yield. However, the enantioselectivity decreased after three uses (4th time was 50 % ee).

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Supplementary Material

Supplementary material is available online - copies of the NMR, HPLC spectra and nano ligand analyses data are given in the supplementary material a file associated with this manuscript

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