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New Green, Recyclable Magnetic Nanoparticles Supported Amino Acids as Simple Heterogeneous Catalysts for Knoevenagel Condensation

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Abstract: Coumarin derivatives were synthesized using magnetically recoverable iron oxide nanoparticles supported amino acids as heterogeneous catalysts *via* one-pot multi component reaction using MW irradiation. Easy recovery of the catalyst using an external magnet, efficient recycling, and reusable without significant loss of their catalytic efficiency makes the protocol greener and sustainable.

Keywords: Knoevenagel condensation, Fe_3O_4-DA-Phe, nanocatalyst, green chemistry.

INTRODUCTION

Primary amines as catalysts in organic reactions are undoubtedly very commonly used. The first primary amine-promoted process was credibly the Knoevenagel condensation [1], which was reported more than a century ago. Several ventures in the field of amino acid catalysis are presented in the literature [2-6]. Following these significant discoveries, asymmetric amino catalysis has sophisticated amazingly in the past few years, and immense new catalysts and novel reactions appeared in the literature at an increased rate [7, 8]. The fact that chemists frequently aim to mimic nature and prepare biomimetic catalysts, whose role in asymmetric catalysis is even more surprising, as primary amino acid catalysis is of vast significance in enzyme catalysis. There has been intensive research trepidation on the expansion of surface adaption of superparamagnetic nanoparticles for their imminent applications in catalysis [9, 10].

Magnetic nanomaterials are envisaged to have a major impact in many areas, including biotechnology/ biomedicine, environmental remediation and particularly catalysis [11]. Few numbers of methods have been developed for the synthesis of high-quality Fe_3O_4 nanoparticles of various amino acid based surface modifiers such as L-Arginine-Capped Fe_3O_4 [12], Fe_3O_4–cysteine [13], functionalization of ferrite MNPs by the glutathione [14] and magnetic nanoparticle-supported proline [15] are used in catalytic reactivity. Various types of MNPs-supported dopamine with amino acid have emerged recently which include *N*-acetyl histidine [16] and biomimetic nanocatalyst Fe_2O_3-Asp-His [17]. Since easily recoverable and reuseable heterogenous catalyst is still in high demand, an impressive feature of supported magnetic nanoparticle catalyst is the ready separation using an external magnet, which achieves a simple separation of catalyst without filtration.

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Coumarin and their derivatives have attracted significant interest in recent times because of their potential biological activities such as antibacterial, anticoagulant, pesticidal, fungicidal and antimicrobial [18-22]. A notable achievement has been made by Philip Kisanga and co-workers [23] for the preparation of some substituted coumarins by Knoevenagel condensation under solvent-free conditions. Following these pioneering works, a number of other groups have reported similar approaches for these reactions under mild conditions, with different kinds of catalysts [24]. More recently nano metal oxides have been used in the synthesis of coumarin derivatives through Knoevenagel condensation [25] however, these nano metal oxides feature difficulty in separation of catalyst from reaction mixture. As a consequence, novel catalysts that can be magnetically separated are still urgently required.

As part of our ongoing research focused on the development of reusable catalysts for various organic transformations [26-29]. Here we report the preparation and characterization of a magnetically separable Fe_3O_4 functionalized with dopamine conjugated amino acid catalyst and its application for the catalytic activity of Knoevenagel condensation *via* the enamine mechanism that has an alternative in asymmetric organocatalysis. The objective is not only to easily separate the catalyst from the reactant by means of the simple application of an external magnetic field, but at the same time also, to demonstrate advances in primary amine-catalyzed enantioselective reactions.

RESULT AND DISCUSSION

The catalysts (Fe_3O_4-DA-Phe), (Fe_3O_4-DA-Val) and (Fe_3O_4-DA-Ile) were prepared by the concise route outlined in (Scheme **1**). Dopamine (DOPA) was first linked with carboxylic group of Fmoc protected amino acids via the DCC/ NHS chemistry. The dopamine moiety proved to have high affinity to the Fe_3O_4 surface. Through DOPA, the amino acids were covalently anchored on the surface of the Fe_3O_4 particles.

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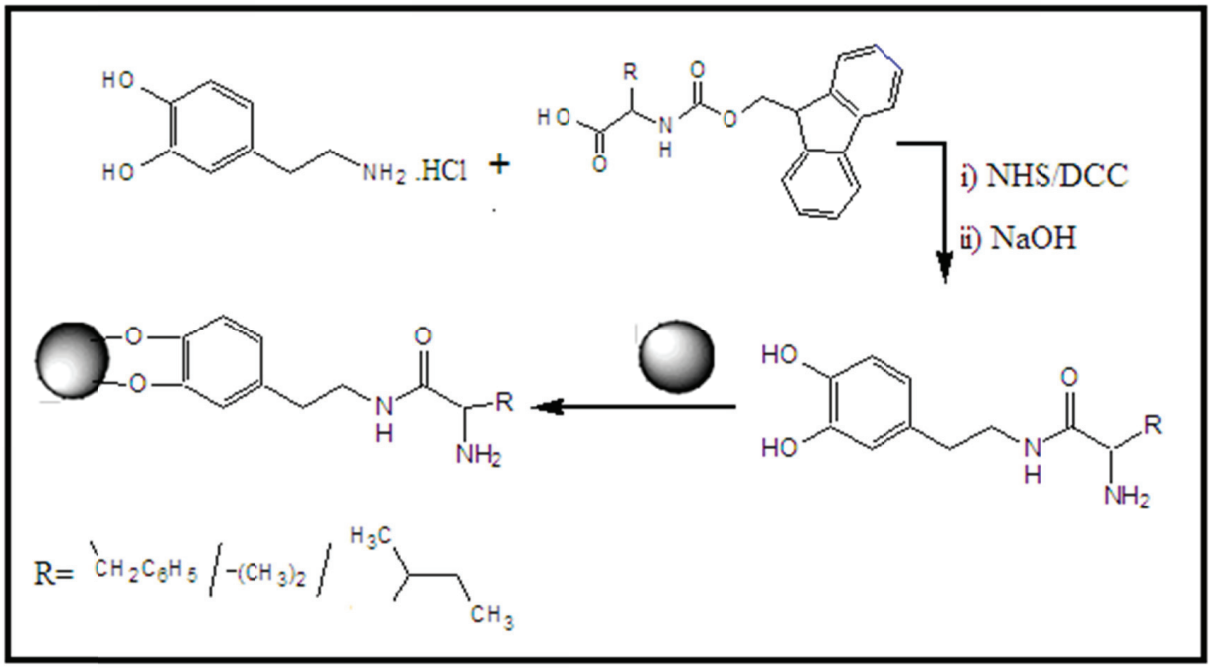


Scheme 1. Synthesis of functionalized iron oxide nanoparticle supported-amino acids ((Fe_3O_4-DA-Phe), (Fe_3O_4-DA-Val) and (Fe_3O_4-DA-Ile)).

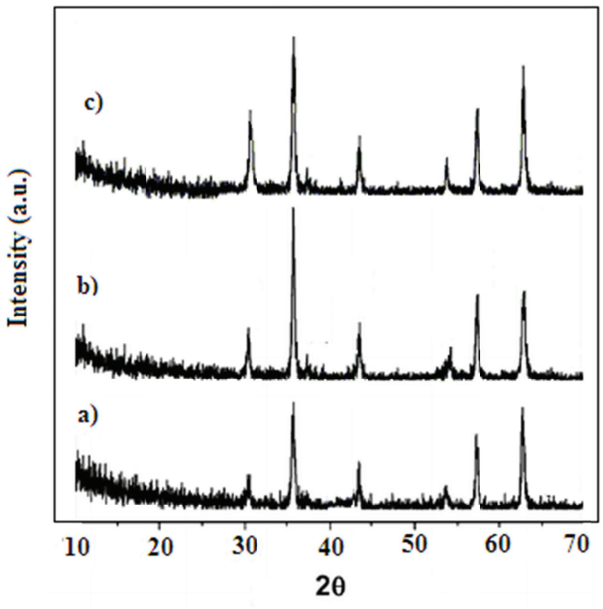


Fig. (1). XRD pattern of the a) (Fe_3O_4-DA-Phe), b) (Fe_3O_4-DA-Val) and c) (Fe_3O_4-DA-Ile)).

Catalyst Characterization

The obtained particles were analyzed by XRD to identify the crystallographic structure. The XRD pattern of nano sized catalysts ((Fe_3O_4-DA-Phe), (Fe_3O_4-DA-Val) and (Fe_3O_4-DA-Ile)) is shown in (Fig. **1**). The diffraction patterns and relative intensities of all the peaks matched well with those of magnetite (JCPDS No.19-0629). Broad XRD peaks clearly indicate the nanocrystalline nature of the material which is indicative of a cubic spinel structure of the magnetite which conforms well to the reported value [30] The average crystallite size D was calculated using the Debye–Sherrer formula $D= K \lambda /(\beta \text{ Cos } \theta)$ where *K* is Sherrer constant, λ the X ray wavelength, β the peak width of half-maximum, and θ is the Bragg diffraction angle [31]. The 2θ value to be 35.9. The crystallite size of the powder particles is calculated as about 28 nm.

The morphology of the sample was investigated with scanning electron microscopy SEM (Fig. **2**) which shows a) (Fe_3O_4-DA-Phe), b) (Fe_3O_4-DA-Val) and c) (Fe_3O_4-DA-Ile) Catalyst to be in nanostructure. These nanoparticles are generally random and not uniform.

The FTIR spectrum for the Fe_3O_4 functionalized with dopamine conjugated amino acid catalysts is shown in (Fig. **3**). In the FT-IR spectrum of Fe_3O_4-DA-Phe (**1**), the disappearance of the C=O stretching peak of the carboxylic groups of phenylalanine at 1680 cm^{-1} and the appearance of the amide peaks at 1647 and 1552 cm^{-1} clearly indicate the formation of the conjugated product. The N–H stretching bonds of the amide and OH-groups of the dopamine anchors are at around 3438 cm^{-1}. The aromatic CH stretching peaks of the dopamine and phenyl units of phenylalanine appeared at 3008 cm^{-1}. The absorption band at 764.4cm^{-1} is attributed to the Fe-O bonds and 574 cm^{-1} for Fe_3O_4. The spectral features of dopamine conjugated amino acid are observed for functionalized Fe_3O_4 by the presence of vibration bands at 1096, 1552, 1647, 3008 and 3438 cm^{-1}, respectively. These bands are absent in the spectrum of uncoated magnetite particles and confirm the presence of dopamine conjugated amine on magnetite. Similarly for Fe_3O_4-DA-Val (**2**) Bands at 1640 cm^{-1} (C=O stretching of a secondary amide), 3432cm^{-1} N–H stretching bands of the amide, 3020 cm^{-1} attributes for aromatic CH stretching and band at 2961 cm^{-1} contribute for C-H stretching. A strong absorption band at 591.8 cm^{-1} was due to the vibration of the Fe–O bond of

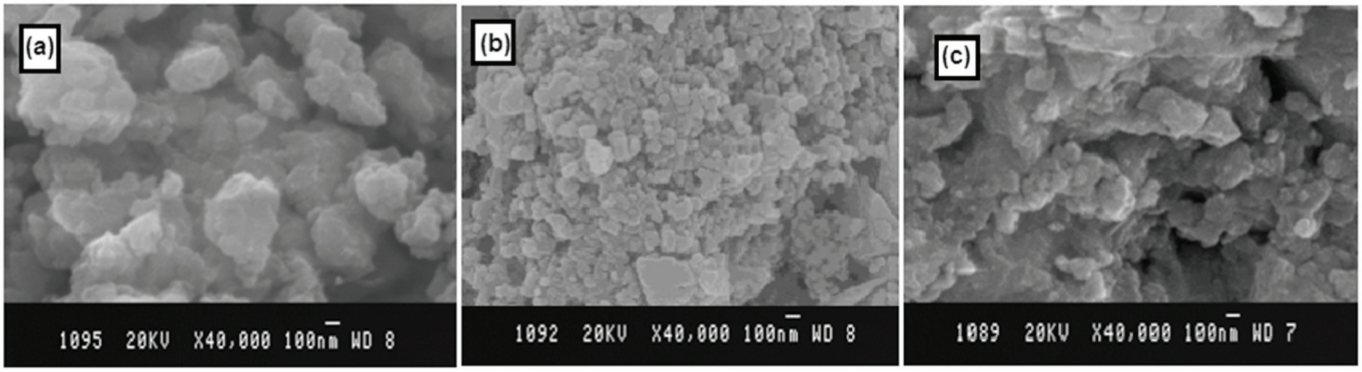


Fig (2). SEM images of synthesized a) (Fe_3O_4-DA-Phe), b) (Fe_3O_4-DA-Val) and c) (Fe_3O_4-DA-Ile).

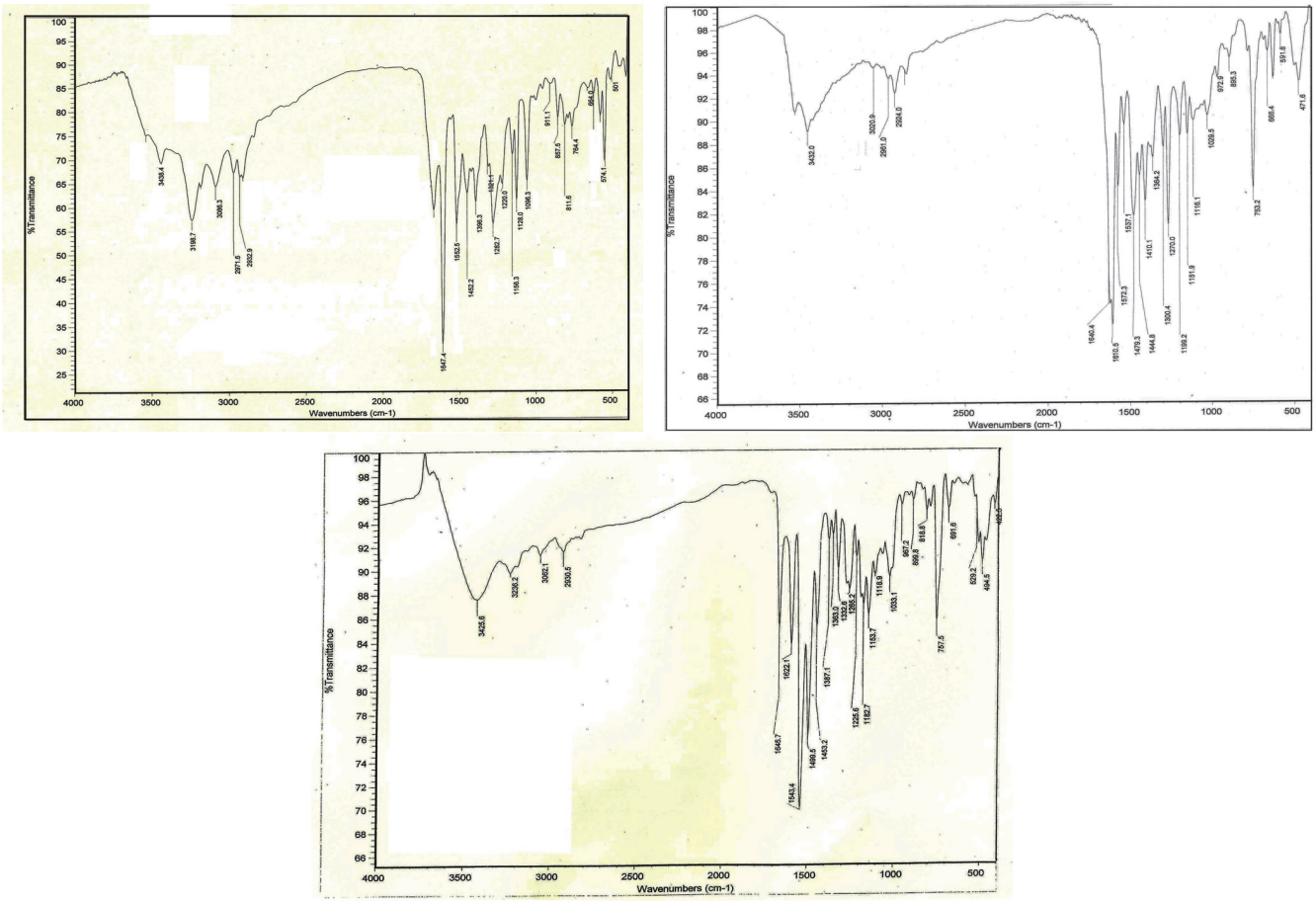


Fig. (3). IR spectra of synthesized a) (Fe_3O_4-DA-Phe), b) (Fe_3O_4-DA-Val) and c) (Fe_3O_4-DA-Ile).

to the vibration of the Fe–O bond of ferrite and the weak wide absorption at about 1029 cm^{-1} in the spectra and the vibration of C–O bond of Fe_3O_4 modified by dopamine.

In IR spectrum for Fe_3O_4-DA-Ile (**3**) bands at 1645 cm^{-1} (C=O stretching of a secondary amide), 3425 cm^{-1} N–H stretching bonds of the amide, 3062 cm^{-1} attributes to aromatic CH stretching and band at 2930 cm^{-1} contributes for C-H stretching. A strong absorption band at 592 cm^{-1} was due to the vibration of the Fe–O bond of ferrite.

To study the surface group on magnetic nanoparticles, very dilute samples were examined by ^1H NMR [32]. ^1H NMR resolved spectra of ligands bound to a paramagnetic nanocrystal are difficult to perform due to large broadening effects caused by paramagnetic properties.

Catalytic Reactivity of Fe_3O_4-DA-Phe Catalyst Through Knoevenagel Condensation

Although numerous methods in preparing coumarins by Knoevenagel condensation are known, newer methods continue to attract attention for their experimental simplicity and effectiveness. To demonstrate the reactivity of amino acids found at the surface of Fe_3O_4-DA-Phe catalyst**,** we decided

to evaluate the catalytic reactivity through Knoevenagel condensation for the synthesis of coumarin derivatives. This system was successfully applied to our previous research [25]. Thus, we have been interested in the development of method for Knoevenagel condensation that would avoid the use of added acids and bases, is easy to perform and economical for application to large scale preparations. The experimental reaction is presented in (scheme **2**).

To obtain the optimal reaction conditions, the synthesis of ethyl 2-oxo-2*H*-chromene-3-carboxylate **(3a)** was used as a model reaction. A mixture of *o*-hydroxy benzaldehyde (2 mmol), nano catalyst (15mg) and diethyl malonate (2.5 mmol) was irradiated in a microwave oven. The effect of catalysts Fe_3O_4-DA-Phe, Fe_3O_4-DA-Val and Fe_3O_4-DA-Ile was examined under microwave and thermal conditions to evaluate their capabilities. The results are summarized in (Table **1**). A control experiment was conducted in the absence of the nano catalyst; for ethyl 2-oxo- 2*H*-chromene-3-carboxylate **(3a)** the reaction did not proceed and the substrate remained unchanged, while good results were obtained in the presence of nanocatalyst.

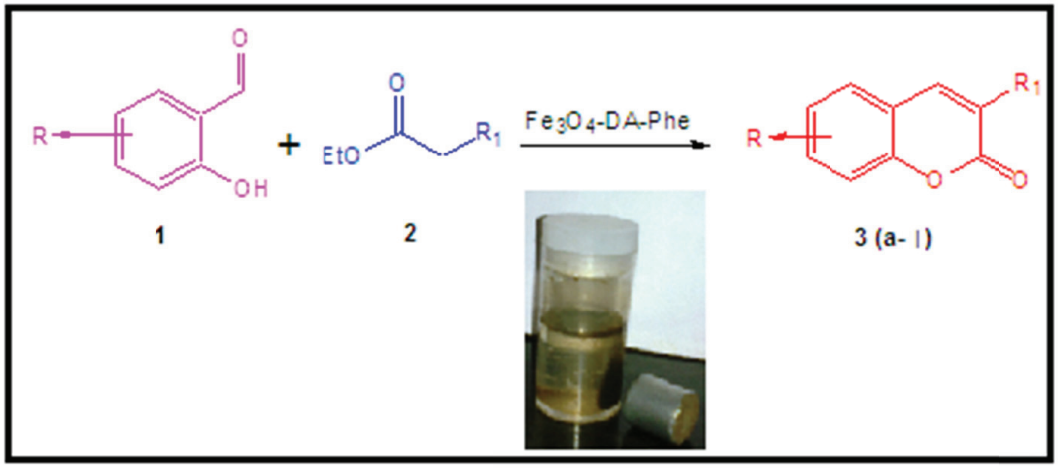
On the optimized amount of catalyst, we found that 15mg of Fe_3O_4-DA-Phe catalyst could effectively catalyze the reaction for formation of the desired product. With the inclusion of 10 mg of Fe_3O_4-DA-Phe catalyst the reaction took longer time. Using more than 20 mg of Fe_3O_4-DA-Phe catalyst has less effect on the yield and time of the reaction (Table **2**). In order to select the appropriate microwave power, the model reaction was examined at different microwave powers (100–400W) with controlled temperature (max. 140 ◦C) in the presence of Fe_3O_4-DA-Phe catalyst. The reaction was also examined at 60–140 °C under thermal conditions. Higher yield and shorter reaction time were attained at 120 °C.

Table 2. Optimization of the Fe_3O_4-DA-Phe Catalyzed Model Reaction for Synthesis of Ethyl 3-carboxylate (3a).

Entry	Catalysts (mg)	Yields(%)[a]
1	No catalyst	-
2	Fe_3O_4-DA-Phe (10 mg)	65
3	Fe_3O_4-DA-Phe (15 mg)	94[b]
4	Fe_3O_4-DA-Phe (20 mg)	75
5	Fe_3O_4-DA-Phe (15 mg)	80[c]
6	Fe_3O_4-DA-Phe (15 mg)	75[d]

a Isolated yield
b Reaction was carried out at 120 °C
c Reaction was carried out at 100 °C
d Reaction was carried out at 140 °C

To compare the efficiency of the solvent-free versus solution conditions, the reaction was examined in several solvents under microwave and thermal conditions. Thus, a mix-



Scheme 2. Synthesis of coumarins by Knoevenagel condensation using Fe_3O_4-DA-Phe.

Table 1. The effect of different catalysts (15 mg) on reaction of *o*-hydroxy benzaldehyde (2 mmol), and diethyl malonate (2.5 mmol) under microwave (MW, 300W, max.120 °C) and thermal (Δ, 100 °C) conditions.

Entry	Catalysts	Time (min)		Yield[a] (%)	
		MW	Δ	MW	Δ
1	No catalyst	--	--	---	---
2	Fe_3O_4	15	80	88	79
3	Fe_3O_4-DA-Phe	6	35	94	90
4	Fe_3O_4-DA-Val	8	60	89	80
5	Fe_3O_4-DA-Ile	12	75	89	90

Table 3. Comparative synthesis of compound 3a **using solution versus the solvent-free conditions under microwave (MW, 300W, max.120 °C').**

Entry	Solvents	Time (min)	Yield[a] (%)
		MW	MW
1	No solvent	6	94
2	DMF	10	25
3	Acetonitrile	18	20
4	Dioxane	16	30
5	Methanol	12	75
6	Ethanol	10	80

[a] isolated yield

ture of 2-hydroxy benzaldehyde (2 mmol), Fe_3O_4-DA-Phe (15mg) and *β*-dicarbonyl compound (2.5 mmol) was irradiated in microwave oven (300 W, max. 120 °C). The results are depicted in (Table **3**). As it is clear from (Table **3**), lower yields and longer reaction times were observed in solution conditions. Therefore, the solvent-free method is more efficient.

To investigate the versatility and capability of our method, the reactions of *o*-hydroxy benzaldehyde were examined with diethyl malonate compounds under both microwave conditions. As (Table **3**) indicates, the reactions proceeded efficiently and the desired products were obtained in good to excellent yields.

In order to investigate the scope of this reaction, a variety of different substituted *o*-hydroxybenzaldehydes and different 1,3-dicarbonyl compounds were subjected to this reaction (Table **4**, entries 1–12). A variety of substituted *o*-hydroxy benzaldehydes possessing a wide range of electron-donating and electron-withdrawing functional groups afforded the corresponding products in good yields. Structure of all the synthesized compounds was confirmed by IR and ^{1}H NMR and data for these compounds are shown in experimental procedure section. These spectral data matched well with those of reported samples [22-33].

The structure of ethyl 2-oxo-2*H*-chromene-3-carboxylate **(3a)**. It showed strong IR absorption bands at 1744, 1656,1614 cm^{-1} due to coumarin carbonyl, C=O (ketone) and alkene aromatic groups respectively. In its ^{1}H NMR spectrum one singlet at δ 8.7, 6.31 and 6.94 was assigned to a methyl group, olefinic proton and an aromatic proton respectively. Two aromatic protons of coumarin moiety appeared as doublets at 6.92, 7.57.

Table 4. Knoevenagel condensation of 2-hydroxy aldehydes with various β-dicarbonyl compounds in the presence of Fe_3O_4-DA-Phe catalyst under microwave (MW, 300 W, max. 130 °C) and thermal (Δ, 100 °C) conditions.

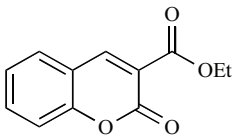
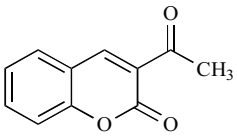
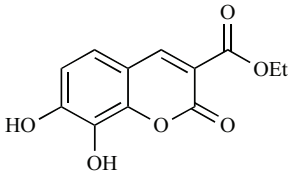
Entry	R	R[1]	Product	Time (min) Yield[a](%)		Observed	Literature
				MW	MW	M.P. (°C)	M.P. (°C)
1	H	CO_2Et	 **3a**	6	94	92	93-94 [23]
2	H	COMe	 **3b**	5	93	122	121-123 [23]
3	3-OH, 4-OH	CO_2Et	 **3c**	5	82	232	233-234 [33]

Table 4. contd….

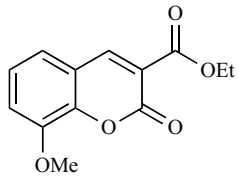
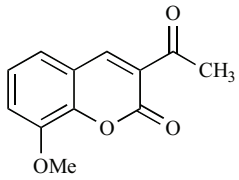
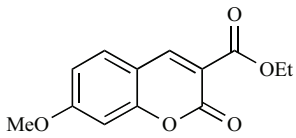
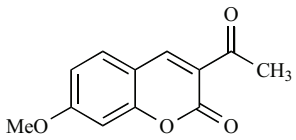
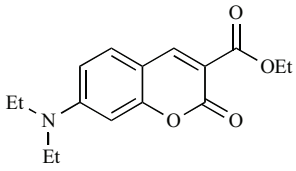
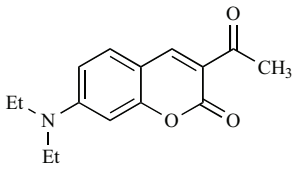
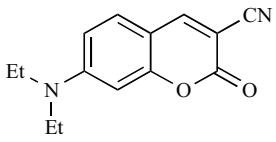
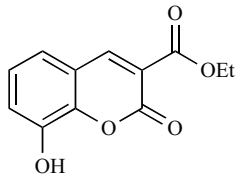
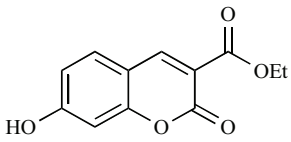
Entry	R	R^1	Product	Time (min) Yield[a](%)		Observed	Literature
				MW	MW	M.P. (°C)	MW
4	3-OMe	CO_2Et	 **3d**	8	85	89	88-90 [23]
5	3-OMe	COMe	 **3e**	8	92	175	173-174 [23]
6	4-OMe	CO_2Et	 **3f**	8	90	121-124	120-125 [23]
7	4-OMe	COMe	 **3g**	6	86	115-116	115-116 [23]
8	Et_2N	CO_2Et	 **3h**	8	89	77	77-78 [23]
9	Et_2N	COMe	 **3i**	5	94	152	151-154 [23]
10	Et_2N	CN	 **3j**	6	92	227	228-229 [23]

Table 4. contd….

Entry	R	R^1	Product	Time (min) Yield[a](%)		Observed	Literature
				MW	MW	M.P. (°C)	MW
11	3-OH	CO_2Et	 **3k**	6	65	172	174-175 [33]
12	4-OH	CO_2Et	 **3l**	7	88	167	166-167 [33]

Recovery of Catalyst

To examine applications of heterogeneous systems, since the lifetime of the catalyst and its level of reusability are significant factors, the catalyst recovered by magnetic separation from the reaction mixture of *o*-hydroxy benzaldehyde and diethyl malonate after dilution with ethyl acetate was reused as such for subsequent experiments (up to five cycles) under similar reaction conditions. The catalyst was washed with distilled water repeatedly and dried for 2–3 h under vacuum before re-use. The observed fact that yields of the product remained comparable in these experiments (Table **5**), established the recyclability and reusability of the Fe_3O_4-DA-Phe catalyst without significant loss of activity.

Table 5. Reuse of Fe_3O_4-DA-Phe catalyst.

No. of Uses	Yield (%)	Recovery of Catalyst
1	94	96
2	92	92
3	88	90
4	85	90
5	84	85

EXPERIMENTAL

Chemicals and Instruments

All chemicals (AR grade) were commercially available and used without further purification. *o*-hydroxybenzaldehydes and 1,3-dicarbonyl compounds were commercially, procured from HiMedia Laboratories Pvt. Ltd., and used without any further purification, Dopamine hydrochloride, dicyclohexylcarbodiimide (DCC) *N*-hydroxysuccinimide (NHS) and Fmoc Protected Amino Acids were purchased from Sigma–Aldrich.

The melting points of the products were determined by a Mel-Temp apparatus and were uncorrected. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates and visualization was effected with short wavelength UV light (254 nm). The IR spectra were recorded on a Shimadzu model impact 400D FT-IR Spectrophotometer using KBr pellets. ^{1}H NMR was recorded on a Bruckner AC-300F 300 MHz spectrometer in DMSO using TMS as an internal standard with ^{1}H resonance frequency of 300 MHz. The microwave oven (2.45 GHz, maximum power 300 W) used for sample preparation was a single mode microwave synthesis system (Discover, CEM, USA). Temperature was controlled by automatic adjusting of microwave power. X-ray powder diffraction (XRD) patterns were recorded using a Rigaku D/max 2550 V X-ray diffractometer with high-intensity Cu Ka radiation (k=1.54178 Å) and a graphite monochromator. A JEOL JEM 6700F field emission scanning electron microscope was used for the determination of the morphology of the particles.

General Procedure for the Synthesis of Magnetic Nanoparticles

A mixed solution of iron(II) chloride heptahydrate (0.546 g, 2.16 mmol) and iron(III) chloride hexahydrate (1.169 g, 4.32 mmol) in deionized water (5 mL) was added dropwise to sodium hydroxide solution (20 mL, 1 M) with vigorous stirring and continuous bubbling of nitrogen through the solution. The solution became blue-black in color and was left to stir for further 30 minutes. The nanoparticles were magnetically separated with an external magnet, the supernatant solution decanted, and the particles washed with deionized water until the pH of the supernatant stabilized at pH 7. Further magnetic separation, replacement of the aqueous supernatant with methanol and removal of the solvent under reduced pressure gave the Fe_3O_4 nanoparticles as a fine black powder [34].

Synthesis of 2-amino-*N*-[2-(3,4-dihydroxyphenyl)ethyl]-3-phenylpropanamide 1

2-Amino-*N*-[2-(3,4-dihydroxyphenyl)ethyl]-3-phenylpro panamide was prepared in accordance with the reported pro-

cedure [17] with slight modification. Fmoc protected phenylalanine (0.387mg, 1.0 eq.) was dissolved in $CHCl_3$ (3 mL) at 0 ºC under N_2. DCC (7 mg, 33 µmol, 1.1 eq.) was added and the solution stirred for 15 minutes at 0 ºC. NHS (4 mg, 33 µmol, 1.1 eq.) and 12.7 mg of dopamine hydro chloride (DOPA) were dissolved in a mixture solvent containing 20 mL of $CHCl_3$, 10 mL of DMF, was added and the solution stirred for 1 hour at 0 ºC and for 14 hours at RT under N_2. Solvent was removed under reduced pressure, leaving a pale brown residue. Added 50 mL aq NaOH were added to remove the Fmoc group. Swirled mixture for 30 min.

Synthesis of 2-amino-*N*-[2-(3,4-dihydroxyphenyl)ethyl]-2-methylpropanamide 2

Fmoc-protected valine (0.325mg, 1.0 eq.) was dissolved in $CHCl_3$ (3 mL) at 0 ºC under N_2. DCC (7 mg, 33 µmol, 1.1 eq.) was added and the solution was stirred for 15 minutes at 0 ºC. NHS (4 mg, 33 µmol, 1.1 eq.) and 12.7 mg of dopamine hydrochloride (DOPA) were dissolved in a mixture solvent containing 20 mL of $CHCl_3$, 10 mL of DMF, was added and the solution stirred for 1 hour at 0 ºC and for 14 hours at RT under N_2. Solvent was removed under reduced pressure, leaving a brown residue, 50 mL aq NaOH were added to remove the Fmoc group. Swirled mixture for 30 min.

Synthesis of 2-amino-*N*-[2-(3,4-dihydroxyphenyl)ethyl]-3-methylpentanamide 3

Fmoc protected isolucine (0.353 mg, 1.0 eq.) was dissolved in $CHCl_3$ (3 mL) at 0 ºC under N_2. DCC (7 mg, 33 µmol, 1.1 eq.) was added and the solution stirred for 15 minutes at 0 ºC. NHS (4 mg, 33 µmol, 1.1 eq.) and 12.7 mg of dopamine hydrochloride (DOPA) were dissolved in a mixture solvent containing 20 mL of $CHCl_3$, 10 mL of DMF, was added and the solution stirred for 1 hour at 0 ºC and for 14 hours at RT under N_2. Solvent was removed under reduced pressure, leaving a pale brown residue. Added 50 mL aq NaOH were added to remove the Fmoc group. Swirled mixture for 30 min.

Synthesis of amino acid fuctionalized Fe_3O_4 nanoparticles (Fe_3O_4-DA-Phe)/ (Fe_3O_4-DA-Val)/ (Fe_3O_4-DA-Ile)

Magnetite nanoparticles (50 mg, 216 µmol) were suspended in a solution of **1** (10.8 mg, 36 µmol) in methanol (3 mL) under nitrogen and sonicated for 6 hours. The dispersed particles were magnetically separated and the supernatant solution decanted and collected. The residue was washed with methanol (3 × 10 mL) to remove any unreacted **1**; each time the particles were re-dispersed by sonication and isolated by external magnet, followed by decantation and collection of the supernatant solution. After this, the particles were resuspended in methanol (10 mL) and the solvent removed under reduced pressure. Drying under high vacuum gave the coated nanoparticles (Fe_3O_4-DA-Phe) as a black powder. Similar procedure was followed for the synthesis of (Fe_3O_4-DA-Val) and (Fe_3O_4-DA-Ile).

General Experimental Procedure for the Synthesis of Coumarins

A mixture of *o*-hydroxy benzaldehyde (2 mmol), 1,3-dicarbonyl compound (2 mmol) and Fe_3O_4-DA-Phe (30mg) was mixed in a 50 mL flask and irradiated under microwave for the time indicated in (Table **6.1**). The reaction progress was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature which then solidified within an hour. The resulting solidified mixture was diluted with ethyl acetate (5 mL) and the catalyst was separated by using external magnet and dried for reuse. The reaction mixture was washed twice with water and solvent was evaporated under reduced pressure which yielded the crude product, which was further purified by recrystallization. The same procedure was used for synthesis of derivatives. All synthesized coumarin derivatives were characterized using analytical techniques such as IR and ^{1}H NMR. The identity of these compounds was established by comparison of IR, ^{1}H NMR spectral data and their melting points with those of reported samples (Table **4**) [23-33]. Spectral data for all compounds are listed.

Ethyl 2-oxo-2*H*-chromene-3-carboxylate (**3a**); IR (KBr) cm^{-1}: 1744, 1656, 1614, 1543, 1431, 1291, 960, 775 cm^{-1} ; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 8.7 (s, 1H, CH), 7.63-7.66 (m, 2H, Ar-H), 7.43-7.48 (m, 2H, Ar-H), 4.4 (q, 2H, CH_2), 1.4 (t, 3H, CH_3).

3-Acetyl-2*H*-chromen-2-one **(3b)**; IR (KBr) cm^{-1}: 1732, 1677, 1613, 1557, 1455, 1233, 1210, 979, 756 cm^{-1} ; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 8.51 (s, 1H, CH), 7.64-7.67 (m, 2H, Ar-H), 7.33-7.39 (m, 2H, Ar-H), .2.73 (s, 3H, CH_3).

Ethyl 7,8-dihydroxy-2-oxo-2H-chromene-3-carboxylate (**3c**); IR (KBr) cm^{-1} : 3476, 3214, 2973, 1738, 1693, 1618, 1588 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 8.90 (b, 2H, OH), 8.75 (s, 1H, CH), 7.27 (d, 1H, Ar-H), 6.87 (d, 1H), 4.19 (q, 2H, CH_2),1.30 (t,3H, CH_3).

Ethyl 8-methoxy-2-oxo-2*H*-chromene-3-carboxylate(**3d**); IR (KBr) cm^{-1}:1732, 1685, 1598, 1548, 1282, 1201, 954, 812, 765 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 8.44 (s, 1H, CH),7.22~7.38 (m, 3H, Ar-H), 4.4 (q, 2H, CH_2), 3.99 (s, 3H, OCH_3), 1.4 (t, 3H, CH_3).

3-acetyl-8-methoxy-2*H*-chromen-2-one (**3e**); IR (KBr) cm^{-1}: 1735, 1686, 1602, 1568, 1282, 1201, 950, 801, 766 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 8.48 (s, 1H, CH), 7.18~7.29 (m, 3H, Ar-H) 3.99 (s, 3H, OCH_3), 2.73 (s, 3H, CH_3).

Ethyl 7-methoxy-2-oxo-2H-chromene-3-carboxylate (**3f**); IR (KBr) cm^{-1}: 3052, 2986, 1619, 1381, 1216 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 8.51 (s, 1H,CH), 7.50 (d,1H, Ar-H), 6.93 (d, 1H, Ar-H), 6.80 (d, 1H,Ar-H), 4.40 (q, 2H,CH_2), 3.90 (s,3H, OCH_3), 1.40 (t, 3H,CH_3)

3-acetyl-7-methoxy-2*H*-chromen-2-one(**3g**); IR (KBr) cm^{-1}: 1736, 1672, 1616, 1504, 1366, 1210, 989, 837, 767 cm^{-1}; ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 8.50 (s, 1H, CH), 7.55 (d, 1H, Ar-H), 6.91 (q, 1H, Ar-H), 6.84 (d, 1H, Ar-H), 3.92 (s, 3H, OCH_3), 2.71 (s, 3H, CH_3).

Ethyl 7-(diethylamino)-2-oxo-2*H*-chromene-3-carboxylate (**3h**); IR (KBr) cm^{-1}: 3465, 3008, 1716, 1676, 1206, 960, 834, 787 cm^{-1}; ^1H NMR (DMSO, 300 MHz) δ (ppm): 8.81 (s, 1H,CH), 7.62-7.66 (d, 1H, Ar-H), 6.77 (d, 1H, Ar-H), 6.54 (s, 1H,Ar-H), 4.25-4.28(q, 2H,CH_2), 3.3-3.5(q, 4H, CH_2), 1.23-1.32(t, 3H,CH_3), 1.14-1.18 (t, 6H,CH_3).

3-acetyl-7-(diethylamino)-2H-chromen-2-one (**3i**); IR (KBr) cm^{-1}:3356., 2966, 1723, 1661, 1560, 1472, 1214, 1186 cm^{-1}; ^1H NMR (DMSO, 300 MHz) δ (ppm): 8.70 (s, 1H, CH),7.46 (d, 1H, Ar-H), 6.60 (d, 1H, Ar-H), 6.53(d, 1H,Ar-H), 3.37 (q, 4H, CH_2), 2.65 (s,3H, CH_3), 1.20 (t, 6H, CH_3);

7-(diethylamino)-2-oxo-2*H*-chromene-3-carbonitrile **(3j)**; IR (KBr) cm^{-1}: 3305, 2998, 2230, 1715, 1645, 1297, 958, 760 cm^{-1}; ^1H NMR (DMSO, 300 MHz) δ (ppm): 8.50 (s, 1H, CH), 7.80 (s, 1H, Ar-H), 7.73-7.76 (d, 1H, Ar-H), 7.03-7.06 (d, 1H,Ar-H), 4.13- 4.20 (m, 4H,CH_2), 1.17(t, 6H, CH_3).

Ethyl 8-hydroxy-2-oxo-2H-chromene-3-carboxylate (**3k**); IR (KBr): 3303, 3045, 2984, 1746, 1696, 1611 cm^{-1}; ^1H NMR (DMSO, 300 MHz) δ (ppm): 10.8 (s, 1H .OH), 8.69 (s, 1H,CH), 7.28 (m, 1H, Ar-H), 7.10- 7.19 (m, 2H, Ar-H), 4.30 (q, 2H, CH_2), 1.32 (t, 3H, CH_3),

Ethyl 7-hydroxy-2-oxo-2*H*-chromene-3-carboxylate(**3l**); IR (KBr): 3550, 3470, 1739, 1617 cm^{-1}; ^1H NMR (DMSO, 300 MHz) δ (ppm): 9.60(s, 1H, OH), 8.67 (s,1H ,CH) 7.75 (d, 1H, Ar-H), 6.84 (d, 1H,Ar-H), 6.73 (s, 1H,Ar-H), 4.20 (q, 2H, CH_2),1.30 (t, 3H, CH_3).

CONCLUSION

In conclusion we have developed the iron oxide nanoparticles functionalized with dopamine conjugated amino acids as alternative in asymmetric organocatalysis and examined their catalytic activity for synthesis of coumarins. We have developed an efficient, facile and environmentally-acceptable synthetic methodology for the synthesis of coumarin derivatives using magnetically supported Aminocatalysis *via* the enamine mechanism under solvent-free condition. The advantages of this environmentally benign and safe protocol include a simple reaction setup, very mild reaction conditions, high product yields, short reaction times, and the possibility for reusing the catalyst, chemoselectivity and solvent-free conditions.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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