Hyperbranched 5-sulfosalicylic acid-TDI-chitosan decorated by Fe$_3$O$_4$ nanoparticles: a highly efficient solid acid organocatalyst for the synthesis of quinazoline derivatives under green conditions

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Abstract

In this research, a new magnetic decorated hyperbranched chitosan by grafting of 5-sulfosalicylic acid using toluene-2,4-diisocyanate linker (CS-TDI-SSA-Fe3O4) was designed and prepared conveniently. The obtained magnetic biopolymeric nanomaterial was properly characterized by using FT-IR, EDX XRD, FESEM, TGA and VSM spectroscopic, microscopic, or analytical methods. The supramolecular CS-TDI-SSA-Fe3O4 nanocomposite was investigated, as a heterogeneous solid acidic organocatalyst, to promote three-component synthesis of 2,3-dihydroquinazoline-4(1H)-one derivatives under green chemistry conditions. The CS-TDI-SSA-Fe3O4 nanocatalyst was demonstraed to act as a highly efficient solid acid for the synthesis of various quinazoline derivatives, as an important pharmaceutical scaffold, through multicomponent strategy. The reaction proceeds very well in the presence of CS-TDI-SSA-Fe3O4 solid acid nanocatalyst in EtOH to afford corresponding 2,3-dihydroquinazoline-4(1H)-one derivatives in high to excellent yields. Key advantages of the present protocol are the use of a renewable and biopolymeric and biodegredable solid acid as well as simple procedure for preparation of the hybrid material. Furthermore, the CS-TDI-SSA-Fe3O4 catalyst can be used at least five times for the synthesis of quinazoline derivatives with a slight decrease in its catalytic activity.

Introduction

Hyperbranched polymers have received significant attention in recent decade[1-3]. The impact of these polymers has been intensified by their integration with nanotechnology, which has showed a dramatically trend in the last decade[4-8]. Indeed, nanotechnology plays an important role in both academic exploration and industrial sectors with the extensive potential of applications in all fields of science including chemistry, biomedicine, mechanics, material science, sensors, safety, pharmaceutical, adsorbents and various aspects of technology[9-18]. One of the more widespread branches of nanotechnology is nanocatalyst[19-22]. Due to their high surface area, high catalytic properties and environmental benign, the nanocatalysts have shown significant impact on green chemistry (GC). Among these, heterogeneous catalytic systems and associated magnetic nanoparticles (MNP) have received great attraction from scientists recently, since they have unique properties including high thermal stability, structural diversity, easy modifications, strong absorption, low toxicity, and a variety of advantages such as ease of separation and reusability[23-39]. Moreover, the designed-procedures for the preparation of nanomaterials including magnetic nanoparticles and their catalytic activities are entirely verified in the field of greener and atom-economic reactions especially multicomponent reactions (MCRs)[12,21,40-47].This impact would be more deepened if the naturally occurring, renewable and biodegradable biopolymers such as chitosan, cellulose, alginate, etc be used in the structure of magnetic nanomaterials[12,23,34,48-50].

(MCRs) are convergent reactions, in which more than two commercially accessible precursors have been mixed together to react and form new important acyclic or heterocyclic products[51-55].MCRs have emerged as an interesting tool that allows the simple synthesis of complex molecules in one-pot synthesis, without

separating and purifying intermediates; therefore, it leads to cost, time and energy reduction[49,56-63]. On the other hand, (MCRs) are widely used for the synthesis of many pharmaceuticals or chemicals[39,64-71].

Based on literature survey, 2,3-dihydroquinazolin-4(1H)-ones (DHQs) are an important class of nitrogen containing heterocyclic scaffolds that have attracted much attention and used as a central core for the synthesis of different pharmaceuticals and biologically active materials[72-78].

Quinazolines and their derivatives are one of the most important compounds that have various applications in a wide range of medicinal activities including analgesic, antioxidant, anti-inflammatory, anti-blood pressure, anti-tuberculosis, antibacterial, antiviral, and anti-cancer activities[76,77,79-82]. For example, DHQ derivatives such as A, B and C are valuable compounds as diuretic, antibacterial and anti-inflammatory, respectively. (**Figure 1**)[83-86].

The synthesis of DHQs and their derivatives were previously carried out in several steps[87]. While, in MCRs the production of these products were accomplished by simply changing the reactant components in only one-step.

Since quinazoline derivatives have a vital impact on chemical and medicinal transformations, a variety of catalytic systems have been utilized for the synthesis of DHQs based on MCR strategy. Several recent instances comprise magnetic EDTA coated copper based nanocomposite[88], hercynite@sulfuric acid[89], Ni−CP[90], PdCl$_2$[91], hydroxyapatite nanoparticles[92], tribromide ion immobilized on magnetic nanoparticles[93], silica sulfuric acid[94,95], sulfamic acid[96], cobalt aluminate (CoAl$_2$O$_4$)[97], HClO$_4$/ZrO$_2$[98], MCM-41-SO$_3$H[99], β-cyclodextrin[100], montmorillonite K-10[101], Al/Al$_2$O$_3$ nanoparticles[102], benzene-1,3,5-tricarboxylic acid-functionalized MCM-41[87], sulfamic acid grafted to cross-linked chitosan by dendritic units[103], Zn-MOF for PHQ[104], and p-aminobenzoic acid grafted on silica-coated magnetic nanoparticles[105]. Some of these methods have disadvantages include long reaction times, low yield, harsh reaction conditions, and the use of expensive or toxic catalysts. Therefore, to avoid these limitations, the discovery of an efficient, easily available catalyst with high catalytic activity and short reaction times for the preparation of quinazoline derivatives is still in demand. Recently, the development of efficient, fast, simple, low-cost, easy-to-use, and environmentally friendly recyclable catalyst and green solvents under mild reaction conditions have performed for the MCR synthesis of DHQs[106].

In continuing our researches for developing new heterogeneous catalysts mainly based on biopolymers[21,34,42,63,80,103,107,108], we wish herein to report designing and preparation of a novel supramolecular nonmagnetic organocatalyst, namely (CS-TDI-SSA-Fe$_3$O$_4$, **1**), through magnetic decoration of a modified chitosan by grafting of toluene-2,4-diisocyanate (**TDI**) and 5-sulfosalicylic acid (**SSA**) on its backbpne. The prepared catalyst **1** promotes the three-component one-pot reaction of isatoic anhydride (**2**) with various amines **3** and aldehydes **4** to prepare biologically active quinazoline derivatives **5** in good to excellent yields and short reaction times (**Figure S1**).

Results and discussion

The structure, morphology and composition of the as-prepared CS-TDI-SSA-Fe$_3$O$_4$ organocatalyst (1) was properly characterized using various suitable spectroscopic, microscopic, or analytical techniques including FTIR, EDX XRD, FESEM, TGA and VSM. The process for the preparation of the organocatalyst (1) is illustrated in **Figure 2**.

The FTIR spectra of Chitosan and CS-TDI-SSA-Fe$_3$O$_4$ catalyst 1 are illustrated in (Figure 3a-b), respectively. According to Fig. 3a, the absorption bands at 3100−3444 cm^{-1} are attributed to the stretching vibration of N−H bonds of amine groups. In addition, the absorption band at 2923 cm^{-1} belongs to the stretching vibration of aliphatic C−H bonds. As shown in Fig. 3b, the absorption bands at 2400−3400 cm^{-1} are assigned to the stretching vibration of O−H bonds. Also, the absorption band at 3400 cm^{-1} belongs to the asymmetric and symmetric stretching vibration of N-H bonds of amine groups. On the other hand, the signal at 1740 cm^{-1} is ascribed to ester functional group. Whereas, the adsorption band at 1666 cm^{-1} is related to the stretching vibration of C=O bond of amide groups. Furthermore, the absorption band at 588 cm^{-1} is attributed to the Fe−O bonds groups.

Figure 4 shows the EDX analysis of the CS-TDI-SSA-Fe$_3$O$_4$ organocatalyst (1), which confirms the presence of C, O, N, S and Fe elements in its structure. In addition, the EDX mapping shows uniform particle distribution of the structure.

FESEM images of CS-TDI-SSA-Fe$_3$O$_4$ nanomaterial (1) have demonstrated changes in the morphology of the chitosan from sheets after grafting of 5-sulfosalicylic acid using toluene-2,4-diisocyanate linker and magnetic decoration, which confirms the formation of the desired nanocomposite. Moreover, the nanoparticles have a uniform dispersion with almost spherical morphology and the average particle size of 20 − 55 nm (Figure 5).

Using thermogravimetric analysis (TGA), the thermal stability of the prepared catalyst (1) was examined in the temperature range of 50−500 °C (Figure 6). As can be seen, there are two stages of weight loss observed between 250 and 400 °C. Since the degradation range of the original chitosan is about 200−220°,[109] this increase in the thermal stability at a higher temperature range, 250−400 °C, demonstrates that the toluene diisocyanate organic units have been linked successfully on the surface of chitosan.

The XRD pattern of CS-TDI-SSA-Fe$_3$O$_4$ (1) is illustrated in (Figure 7). There are symmetrical reflections at 2θ of 20.82°, 25.76°, and 37.14°, which are characteristic of the CS-TDI-SSA-Fe$_3$O$_4$ (1) structure. Matching of the obtained XRD pattern of CS-TDI-SSA-Fe$_3$O$_4$ (1) with the standard patterns of chitosan (JCPDS Card no. 00-039-1894), 5-Sulfosalicylic acid (JCPDS Card no. 00-042-1766), and Fe$_3$O$_4$ (JCPDS Card no. 01-076-0956) confirms the successful preparation of the desired nanomaterial.

The magnetic properties of the CS-TDI-SSA-Fe$_3$O$_4$ nanocatalyst (1) was determined by using VSM analysis at room temperature through applying a magnetic field from −1000 to +1000 oersted (Figure 8).

According to the resulting curve, the phenomenon of hysteresis was not observed, since there is not any residual loop in the curve and this characteristic demonstrates that no accumulation happens in the presence of a magnetic field. Furthermore, the S-shape curve for CS-TDI-SSA-Fe$_3$O$_4$ nanocatalyst (1) exhibits excellent paramagnetic behaviour without any hindrance or reluctance. In fact, the maximum magnetic saturation (Ms) is 41.99 emu/g. Indeed, this magnetic property is enough for the easy separation of the catalyst (1) from the reaction mixture by employing an external magnet.

Optimization of conditions for the synthesis of 2,3-dihydroquinazoline derivatives in the presence of CS-TDI-SSA-Fe3O4 organocatalyst (1).

In this section, the efficacy of CS-TDI-SSA-Fe$_3$O$_4$ nanocomposite (1) was examined in the model reaction for the synthesis of **DHQ** derivatives. Therefore, different parameters including solvent, catalyst loading, temperature, and reaction time were investigated to determine the optimal reaction conditions (**Table 1**). The model reaction was considered in the presence of 4-chlorobenzaldehyde (**4a**, 0.5 mmol), isatoic anhydride (**2**, 0.5 mmol), and ammonium acetate (**3a**, 1 mmol) for the synthesis of **DHQ** derivatives under different conditions. The results are summarized in **Table 1**. The amount of the catalyst **1** has played a vital role in the model reaction. Consequently, after 1440 min under reflux conditions, the model reaction in the absence of the catalyst **1** affords a poor yield of the desired 2-(4-chlorophenyl)-2,3-dihydroquinazoline-4-(1H)-one (**5a**) (**entry 1**, **Table 1**). The highest yield of the desired product **5a** was obtained by using 20 mg of the catalyst **1** in EtOH under reflux conditions (**entry 2**, **Table 1**). Moreover, the effect of other solvents including Solvent-free, H$_2$O, MeOH, MeCN, CH$_2$Cl$_2$, THF and toluene was also studied on the progress of the model reaction under same catalyst loading (**entries 5−11**). Subsequently, among all the screened solvents EtOH was selected as the best solvent in the next experiments. The effect of lower catalyst loadings was further studied (**entries 3−4**). Moderate yields of the desired product **5a** were obtained in all considered cases. The progress of the model reaction in EtOH to afford the desired product **5a** was investigated at various temperatures rather than reflux conditions (**entries 12 and 14**). Based on the obtained results, EtOH under reflux conditions can be considered as the most desirable solvent.

After that, in order to extend the catalytic application of CS-TDI-SSA-Fe$_3$O$_4$ (1), the three-component condensation of aldehyde derivatives (**4a−j**, 0.5 mmol), isatoic anhydride (**2**, 0.5 mmol), and ammonium acetate (**3a**, 1 mmol) was performed under optimal conditions for the synthesis of **DHQ** derivatives (**5a−j**). The results are summarized in **Table 2**.

The possible mechanism for the synthesis of 2,3-dihydroquinazoline derivatives in the presence of CS-TDI-SSA-Fe$_3$O$_4$ (1)

The mechanism of action of the catalyst **1** in the model reaction is proposed in (**Figure 9**). First, the isatoic anhydride (**2**) is activated by CS-TDI-SSA-Fe$_3$O$_4$ supramolecular nanocomposite (**1**) and forms intermediate (**I**)**,** which is undergoes the nucleophilic addition of the amine **3a** to afford intermediates (**II**). After that, the elimination CO$_2$ results in intermediate (**III**). Then, the N-nucleophilic attack of the

anthranilamide (**III**) on the activated carbonyl functional group of aldehydes **4,** produces iminium intermediate (**IV**), which creates the intermediate (**V**) by losing a molecule of H_2O. Subsequently, intramolecular nucleophilic attack of the amide nitrogen to the activated imine moiety produces desired hetero-annulated products **5** and the catalyst **1**.

One of the benefits of the heterogeneous catalysts is their easy separation from the reaction mixture and subsequent reusing in chemical transformations. On the other hand, due to the importance and the price of catalytic systems, the reusability of the catalyst is very important in the industry. In this part of our study, the recyclability of CS-TDI-SSA-Fe_3O_4 nanomaterial (**1**) was explored in the model reaction for several runs. After completion of the indicated reaction, the magnetic nanocatalyst was removed by using an external magnet from the reaction mixture and washed with Ethyl acetate and n-hexane, respectively. Then, it was dried in an oven at 70 °C for 1 h. The recycled catalyst **1** was reused again in the model reaction. To our delight, after five consecutive cycles, the reaction yield did not decrease considerably and a little loss in the catalytic action of the heterogeneous catalyst **1** was observed (**Figure 10**).

In order to compare the efficiency of hybrid CS-TDI-SSA-Fe_3O_4 organocatalyst (**1**) with other catalysts for the synthesis of desired DHQ derivative **5a**, several parameters including the reaction time, temperature, catalyst loading, and the reaction yield, were taken into consideration and the results are shortened in (Table 3). It can be seen that CS-TDI-SSA-Fe_3O_4 heterogeneous catalyst (**1**) showed higher efficiency than previously reported catalysts for the synthesis of DHQ derivatives.

Experimental section

Reagents and Instruments

All the materials and reagents that utilized in this research were purchased from Merck and Aldrich and used in the processes without further purification except benzaldehyde, which should be used as a freshly distilled sample in the processes. Chitosan (CS, MW = 100−300 kDa) was obtained from Acros Organics. FTIR spectra were recorded as KBr pellets on a Shimadzu FTIR-8400S spectrometer. ^{1}H-NMR spectra (500 MHz) was obtained using Bruker DRX-500 Avance spectrometer in $CDCl_3$, as a solvent, at ambient temperature. For monitoring the reactions' progress, analytical thin layer chromatography (TLC) was performed using Merck 60 F-254 Al 0.2 mm silica gel plates. The melting points were determined on an Electrothermal 9100 apparatus. Magnetization measurements were carried out on a BHV-55 vibrating sample magnetometer (VSM). The curve obtained from thermogravimetric analysis (TGA) was recorded utilizing a Bahr company STA 504 instrument. Energy-dispersive X-ray (EDX) analysis and FESEM imaging were accomplished by a FESEM-SIGM (German) instrument. All products were characterized by spectroscopic methods (IR and ^{1}HNMR spectra), and melting points.

General method for the preparation of the CS-TDI-SSA-Fe_3O_4 organocatalyst (1)

Chitosan (0.1 g), toluene-2,4-diisocyanate , as a linker, (0.2 g) and 5.0 ml of toluene were added into a 10 ml round bottom flask and the mixture was stirred and refluxed on a hotplate stirrer under N_2 atmosphere for 24 h. After that, the precipitation (CS-TDI) was filtered off. The CS-TDI deposit was transferred to another flask followed by adding 5-sulfosalicylic acid (0.2 g), as a catalytic agent, and toluene (3.0 ml). Then the mixture was stirred and refluxed under N_2 atmosphere for 24 h for preparing (CS-TDI-SSA) compound. Magnetization was performed under N_2 atmosphere at the final step. After the completion of the reaction, the content of the reaction container was filtered and then washed with ethanol and water, and then dried in the oven at 70°C.

The magnetization process was accomplished as below. The obtained CS-TDI-SSA (0.2 g), distilled water (10.0 ml), and a mixture of $FeCl_3.6H_2O$ (0.3 g) and $FeCl_2.4H_2O$ (0.15 g) were added to a round bottom double-neck flask, and then the mixture was stirred vigorously at 80 °C followed by adding aqueous NH_3 (25%, 10.0 ml) gradually in 0.5 h under N_2 atmosphere. Then the mixture was stirred harshly at 80 °C for 1 h under mentioned conditions.

Black magnetite deposits were separated from the solution using an external magnet, then washed several times with deionized water and EtOH 96% until reaching to the neutral pH, and finally put into an oven to dry at 70 °C.

General Procedure for the Synthesis of 2,3-Dihydroquinazoline-4(1H)-One Derivatives Catalysed by CS-TDI-SSA-Fe_3O_4 (1)

Aldehyde (**4**, 0.5 mmol), ammonium acetate (**3**, 1.5 mmol), isotonic anhydride (**2**, 0.5 mmol), CS-TDI-SSA-Fe_3O_4 magnetic nanocomposite (**1**, 20), and 2.5 ml EtOH were added into a 10 ml double-neck round bottom flask built in a magnet bar and a condenser. The mixture was placed on a hotplate stirrer and mixed under reflux conditions for 20 min. The progress of the reaction was monitored by thin layer chromatography (TLC) (Diluent: ethyl acetate: n-hexane in a ratio of 3:1). After the completion of the reaction, 2.5 mL of EtOH was added to the reaction mixture to dissolve the product, then the CS-TDI SSA-Fe_3O_4 catalyst (**1**) was removed by an external magnet and put aside to wash and dry for use in the next steps. The desired products were crystal out from the filtrate using water-ethanol system. The final pure crystals were collected by vacuum filtration followed by washing with cold EtOH and drying at 70 °C for 1 h.

Green Chemistry Metrics

In order to cover GC principles several metrics including E-factor, atom economy (AE), carbon (CE), process mass intensity (PMI) and reaction mass efficiency (RME) have investigated and the results have been summarized in (**Table 4**).

Selected spectral data:

2-(4-Chlorophenyl)-2,3-dihydroquinazolin-4 (1*H*)-one *(5a):*

White solid, melting point: 196-197 °C. ^{1}H NMR (500MHz, CDCl$_3$): δ(ppm) 7.95 (dt, J = 7.8, 1.4 Hz, 1H), 7.58-750 (m, 3H), 7.43 (dd, J = 8.4, 1.3 Hz, 2H), 7.0-732 (m, 1H), 6.92 (t, J = 7.6 Hz, 1H), 6.68 (d, J = 8.1 Hz, 1H), 5.90 (s, 1H), 5.85 (s, 1H); FTIR (KBr, cm^{-1}) v = 3447, 3306, 3187, 1656, 1509.

2-(4-Methylphenyl)-2,3-dihydroquinazolin-4 (1H)-one (**5c**):

White solid, melting point: 227− 228 °C. ^{1}H NMR (500 MHz, CDCl$_3$):

δ(ppm) 7.95 (d, J = 7.8 Hz, 1H), 7.48 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.27 (s, 3H), 6.91 (t, J = 7.6 Hz, 1H), 6.67 (d, J = 8.1 Hz, 1H), 5.87 (s, 1H), 5.79 (s, 1H), 2.4 (s,3H); FTIR (KBr, cm^{-1}) v = 3450, 3312,3192, 2924, 1658, 1510, 1295.

2-Phenyl-2,3-dihydroquinazolin-4 (1H)-one (**5j**):

White solid, melting point: 215-217 °C. ^{1}H NMR (500MHz, CDCl$_3$): δ(ppm) 8.00 − 7.94 (m, 1H), 7.62 (dd, J = 6.7, 3.0 Hz, 2H), 7.50 − 7.44 (m, 3H), 7.41 − 7.32 (m, 1H), 6.93 (t, J = 7.6 Hz, 1H), 6.70 (d, J = 8.1 Hz, 1H), 5.92 (d, J = 10.0 Hz, 2H), 4.43 (s, 1H). FTIR (KBr, cm^{-1}) v = 3300, 3184, 2928, 1656, 1512.

Conclusions

In summary, we have developed a simple procedure for preparation of a solid acid hybrid material by using biopolymeric chitosan, toluene-2,4-diisocyanate and 5-sulfosalicylic acid and magnetic Fe$_3$O$_4$ (CS-TDI-SSA-Fe$_3$O$_4$). The obtained nanomaterial-was employed, as an effective oranocatalyst, for the synthesis of 2,3-dihydro quinazoline-4(1H)-one derivatives via the one-pot three-component condensation of isotonic anhydride, aromatic aldehyde, and amine. The advantages of this method include easy separation and reusability of the catalyst, high to excellent yield of products, the use of a green solvent and mild reaction conditions. The investigation of GC metrics demonstrates that this catalyzed reaction meet the requirements of GC principles. Moreover, the solid acidic organocatalyst was recovered and reused at least five times without a significant decrease in its activity.

Declarations

Availability of data and materials

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Acknowledgements

Contributions

R.P.S. worked on the topic, as her MSc thesis, and prepared the initial draft of the manuscript. Prof. M.G.D. is the supervisor of Mrs. R.P.S., Dr. E.V., Miss. N.H. and Mr. M.D. as his MSc. and Ph.D students. Also, he edited and revised the manuscript completely. E.V. worked closely with R.P.S. for doing experiments, interpreting of the characterization and preparation of the initial draft of the manuscript. N.H. worked closely with R.P.S. for doing experiments and drawing of graphs of the initial draft of manuscript. M.D worked closely with R.P.S. for interpreting of the characterization data and drawing of graphs during manuscript preparation.

Ethics declarations

The authors declare no competing interests.

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Tables

Tables 1, 2 and 4 are available in the Supplementary Files section.

Table 3 Comparative synthesis of compound 5a using the reported heterogeneous catalysts versus the present method.

Entry	Catalyst	Catalyst Loading	Condition reaction	Time (min)	Yield (%)	Ref.
1	Silica sulfuric acid	20 mol%	Solvent −free	300	80	[94]
2	Sulfamic acid	10 mol%	H_2O	35	89	[96]
3	Cobalt aluminat ($CoAl_2O_4$)	20 mg	EtOH	130	82	[97]
4	CS-TDI-SSA-Fe_3O_4	20 mg	EtOH	20	91	This work

Figures

(a) Fenquizone

(b) Janoxepin

(c) Evodiamine
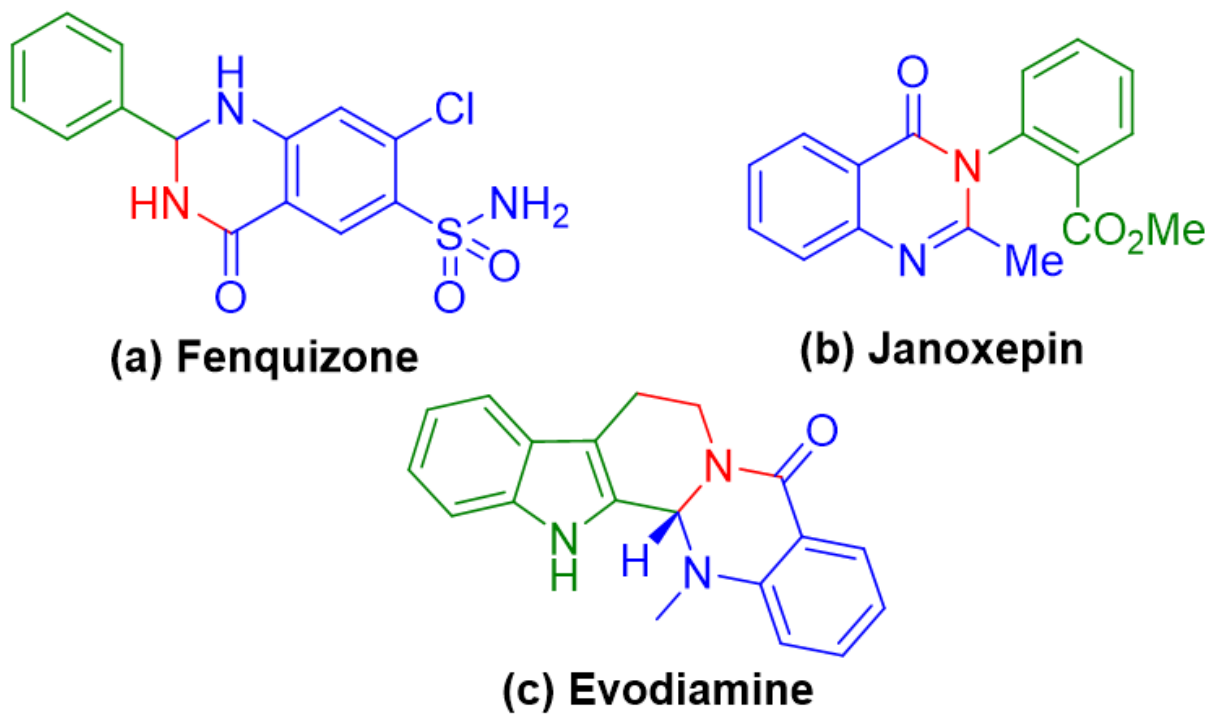
Figure 1

Selected examples illustrating the medicinal importance of quinazolinones.
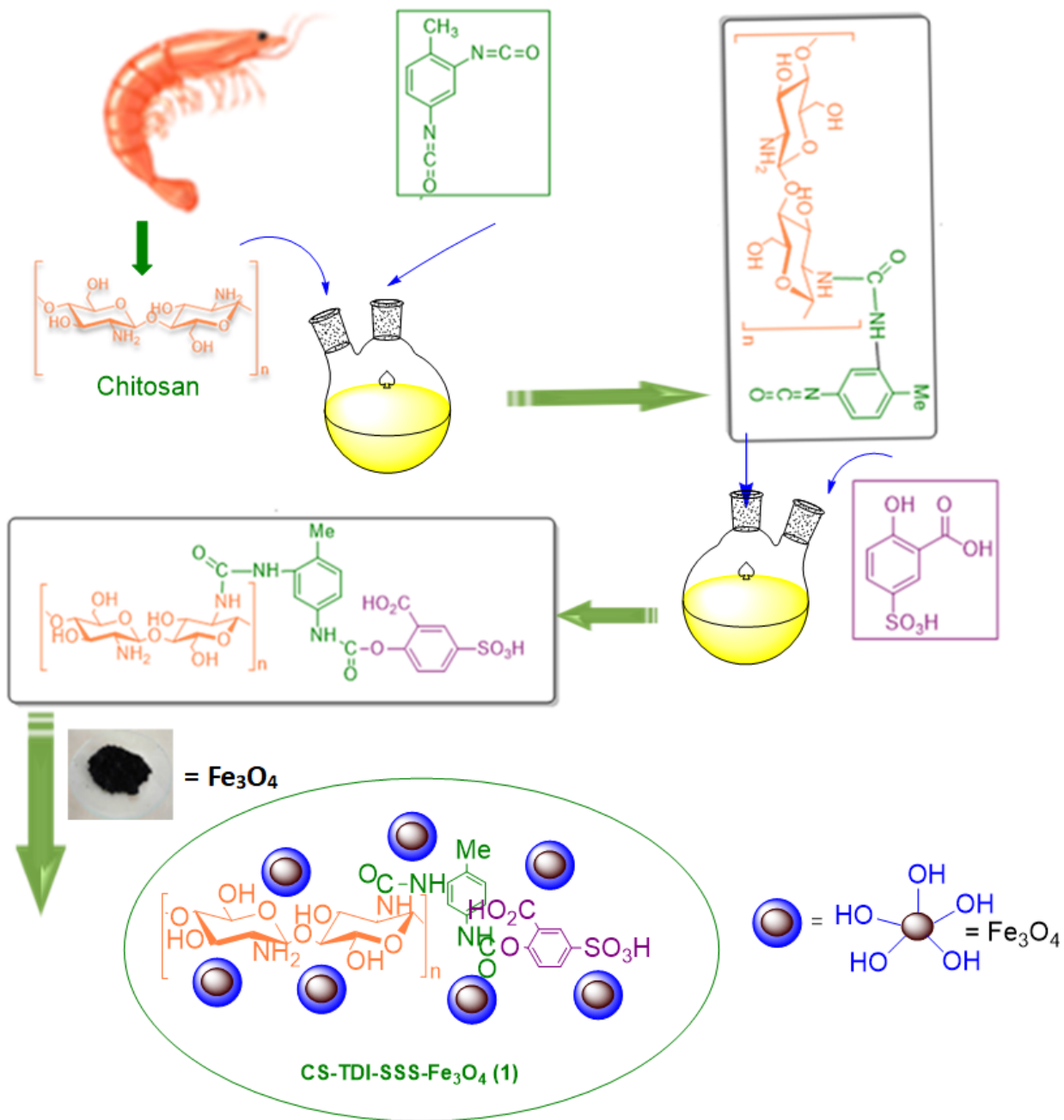
Figure 2

Schematic preparation of the magnetic decorated modified chitosan by grafting of 5-sulfosalicylic acid using toluene-2,4-diisocyanate linker (CS-TDI-SSA-Fe3O4, 1)
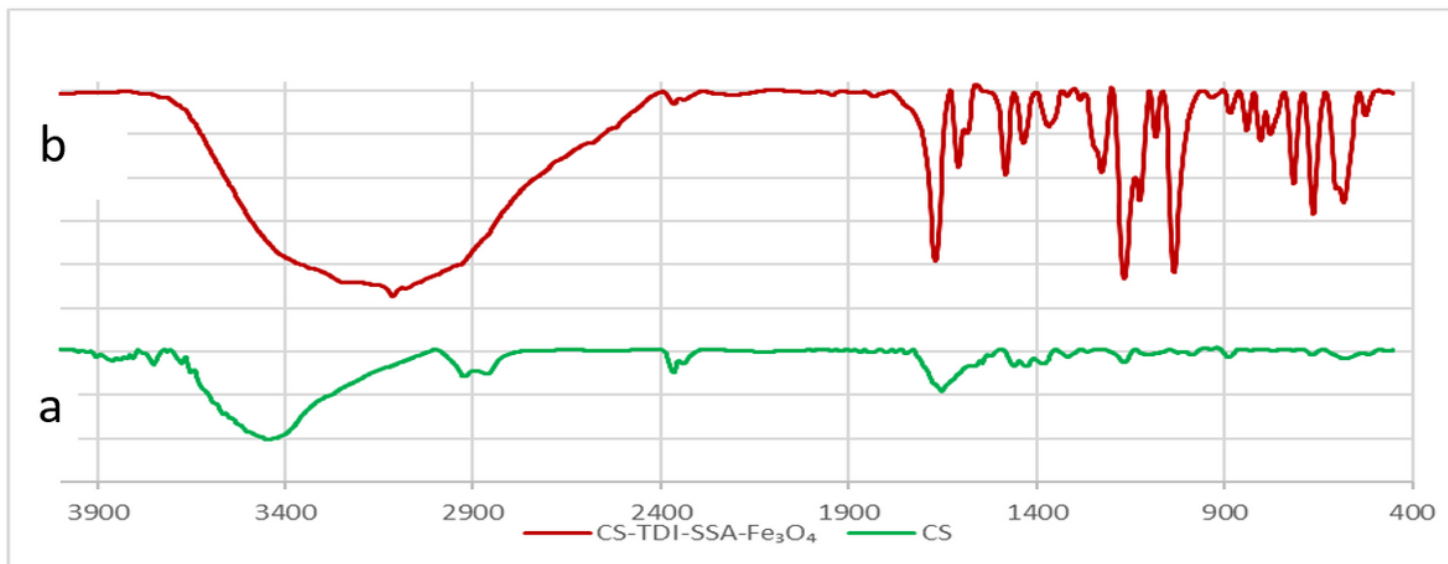
Figure 3

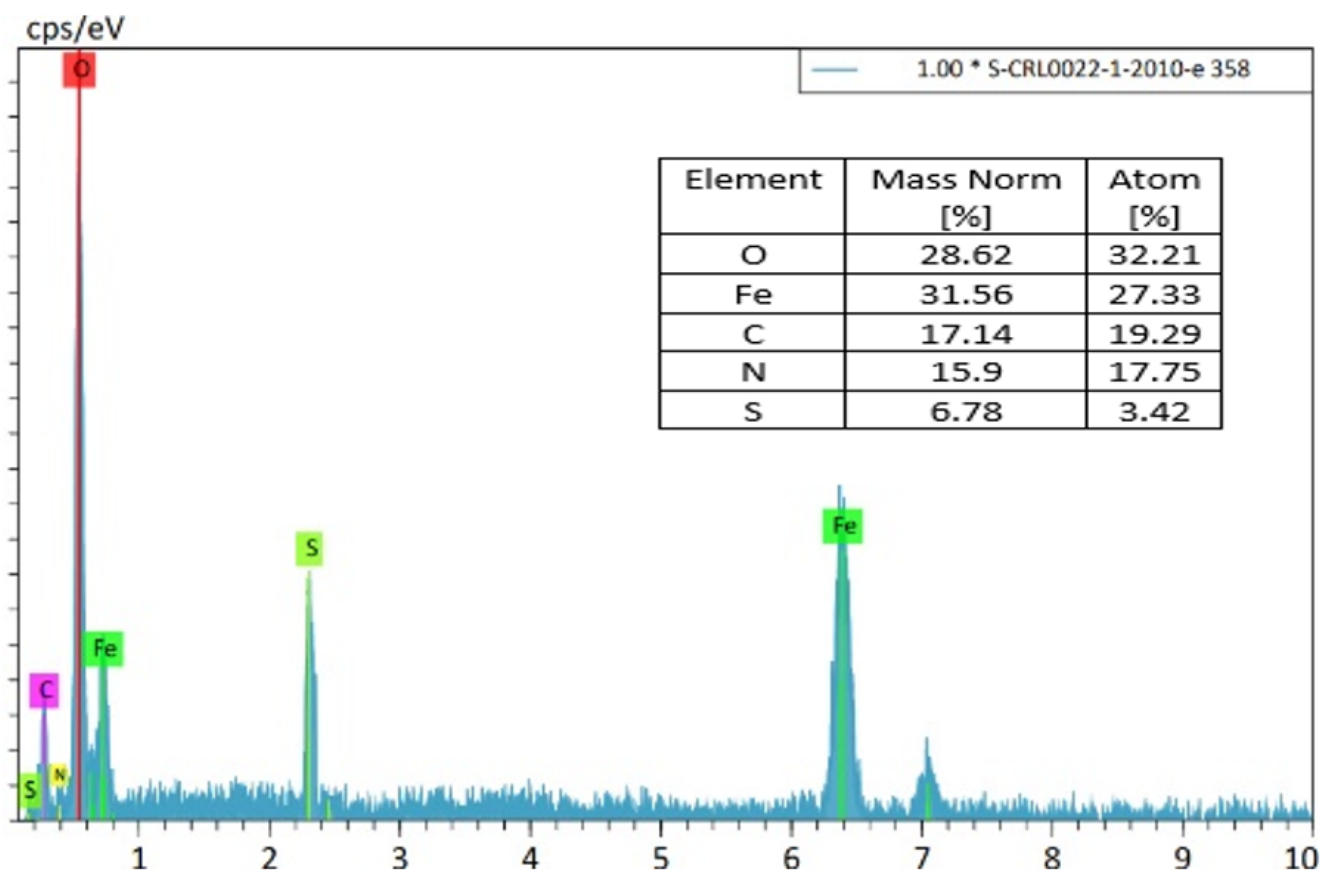FTIR spectra of the commercial Chitosan (**a**), (CS-TDI-SSA-Fe3O4 catalyst **1**, **b**).

Element	Mass Norm [%]	Atom [%]
O	28.62	32.21
Fe	31.56	27.33
C	17.14	19.29
N	15.9	17.75
S	6.78	3.42

1.00 * S-CRL0022-1-2010-e 358

Figure 4

The EDX spectrum of the CS-TDI-SSA-Fe3O4 organocatalyst (**1**).
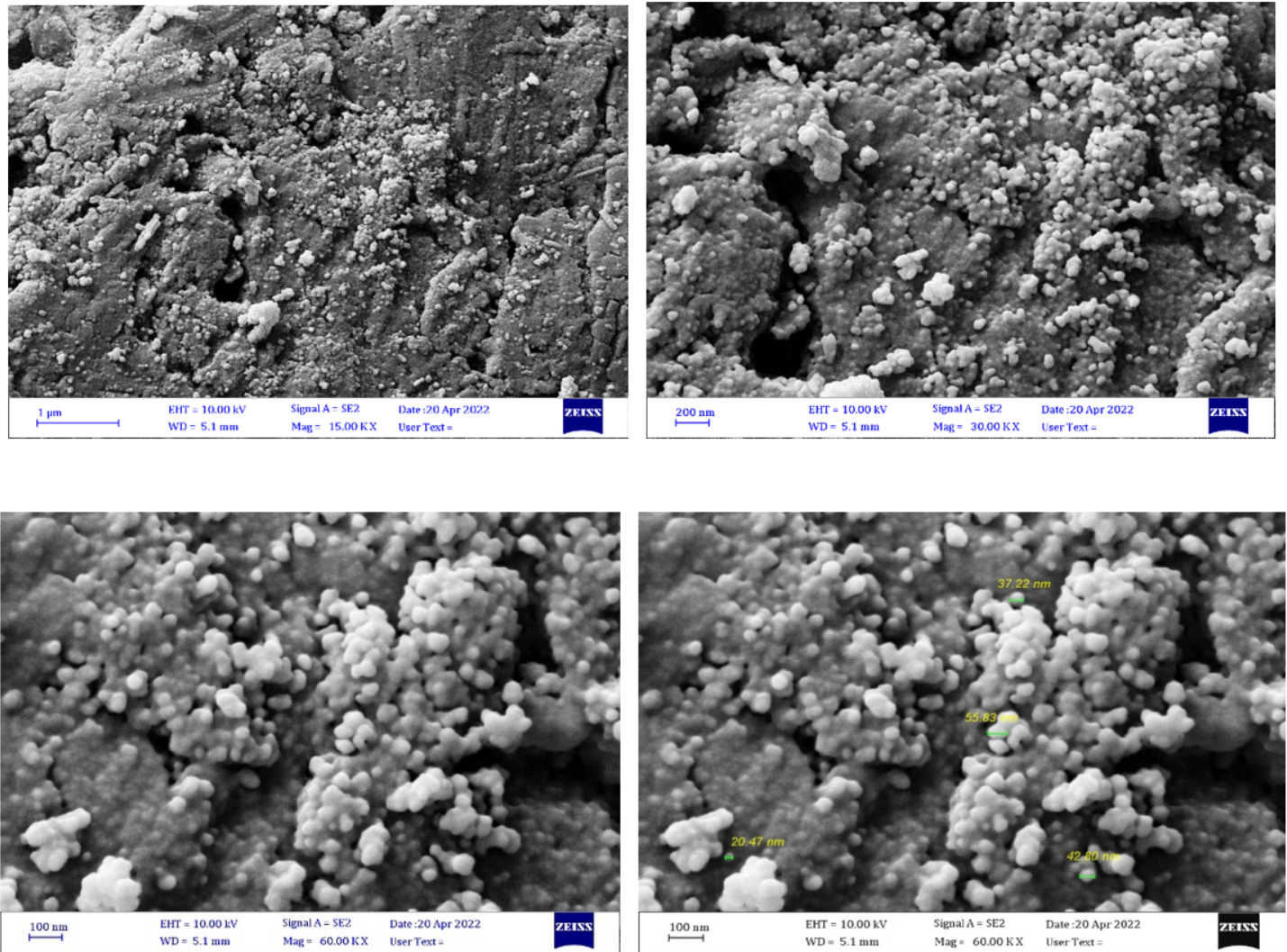
Figure 5

FESEM images of CS-TDI-SSA-Fe$_3$O$_4$ nanomaterial (**1**).

Figure 6

TGA curve of CS-TDI-SSA-Fe$_3$O$_4$ organocatalyst (**1**).
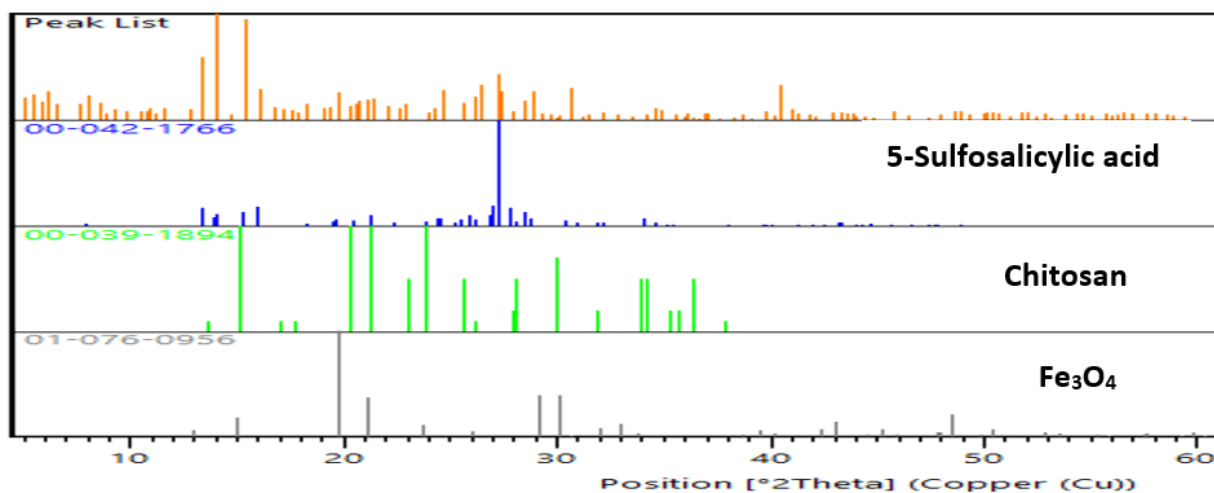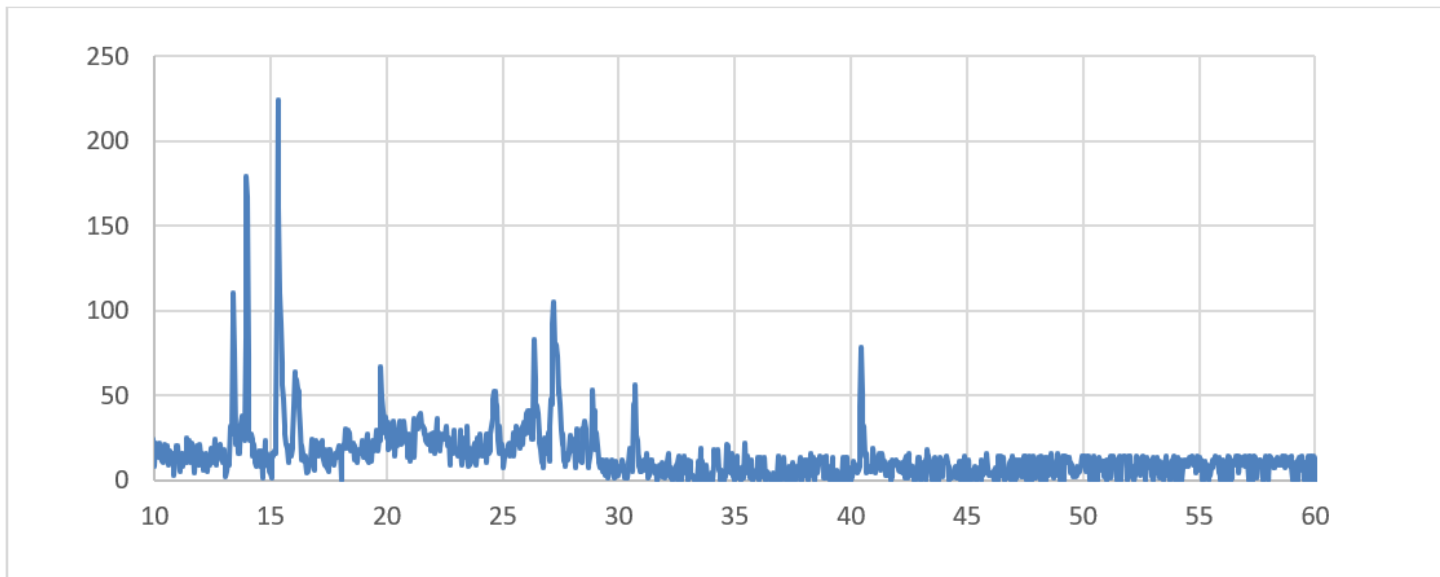
Figure 7

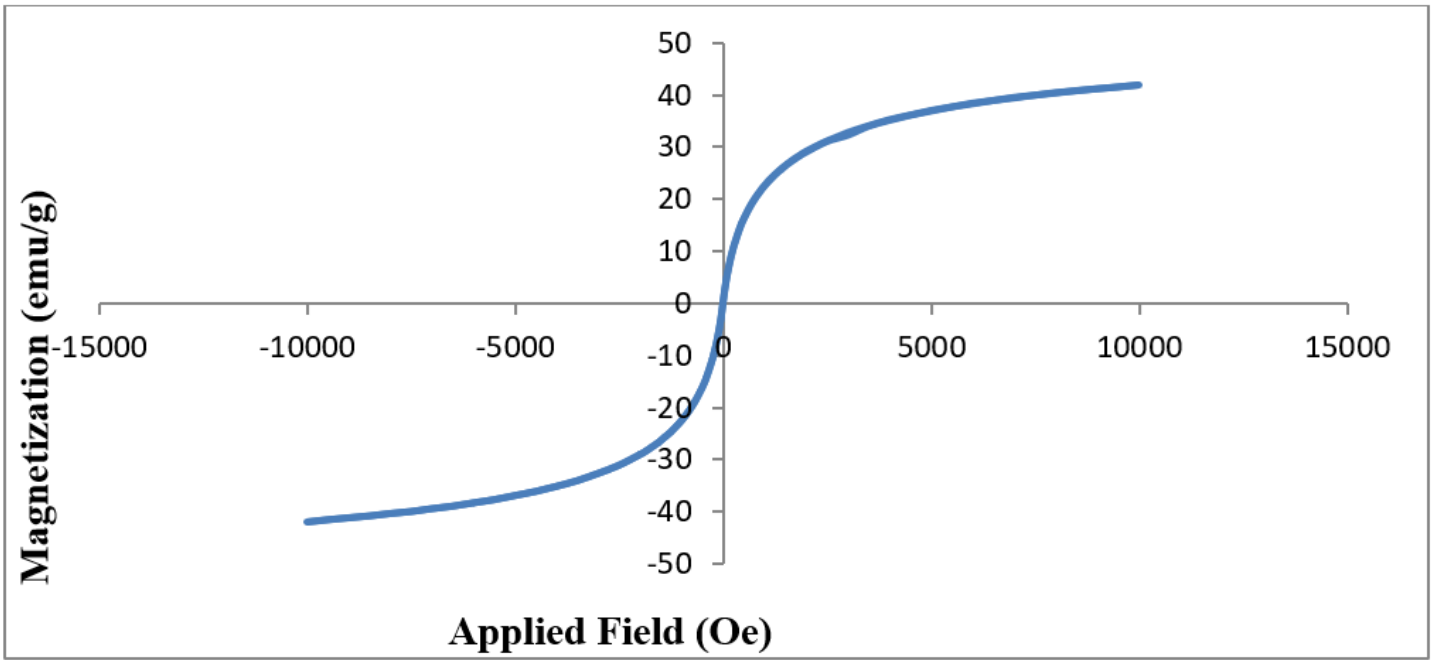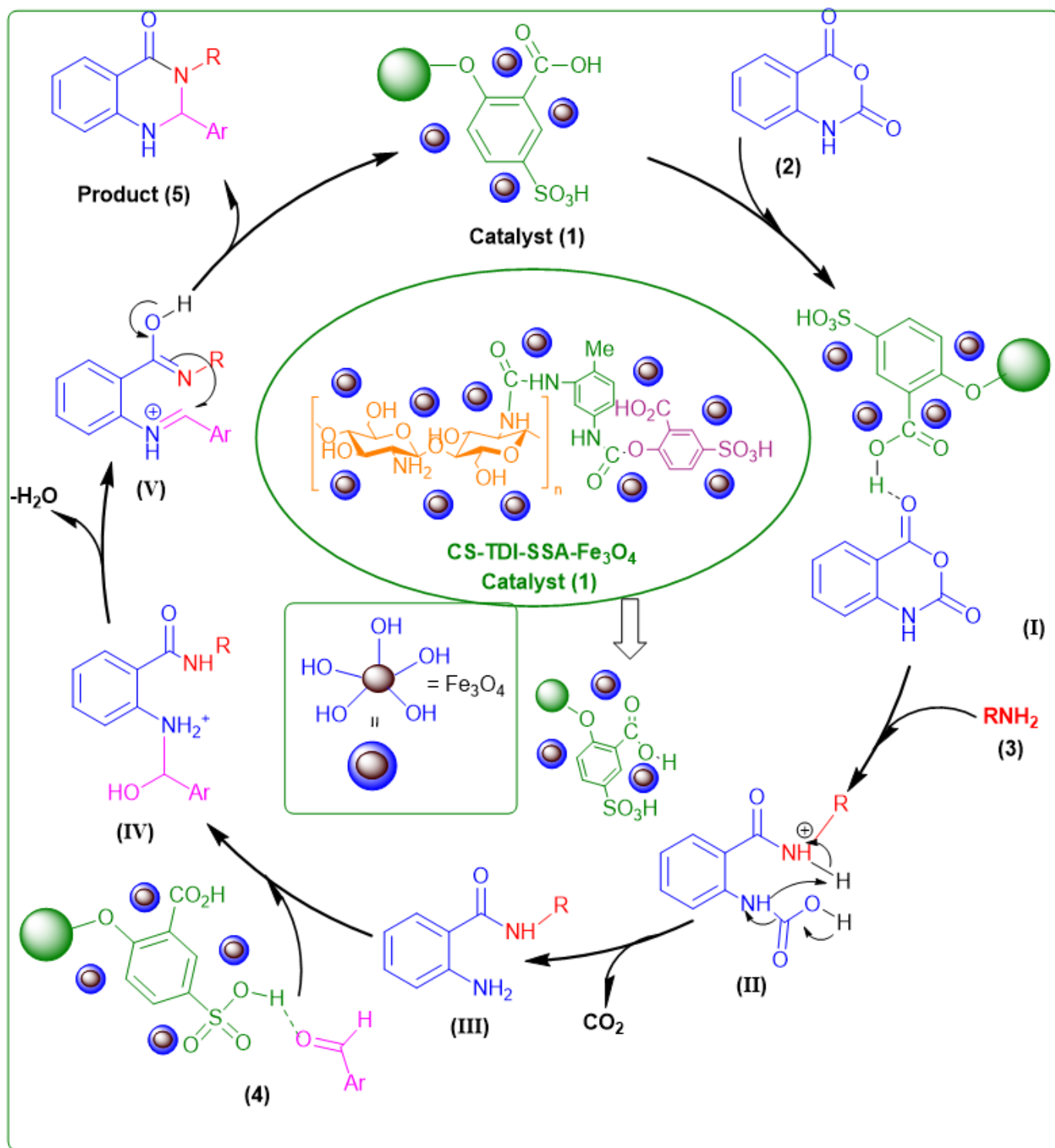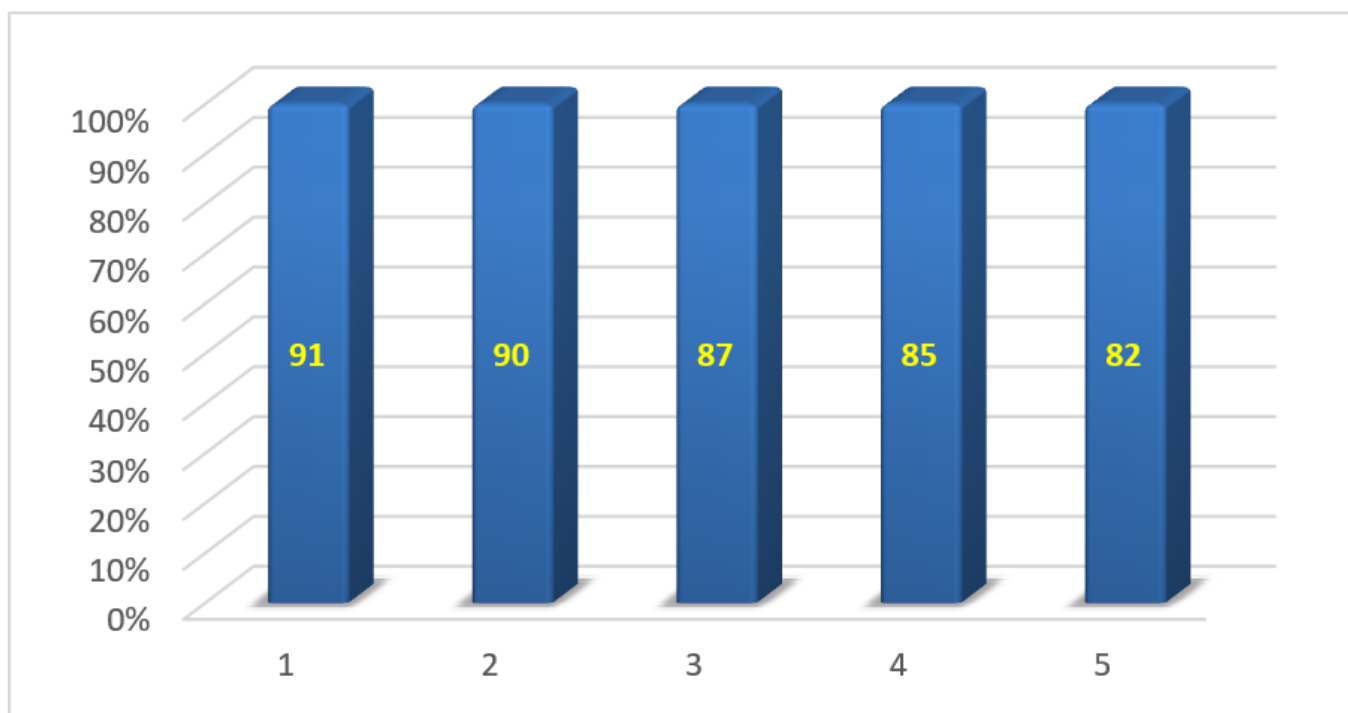Wide-angle XRD pattern of the CS-TDI-SSA-Fe$_3$O$_4$ nanomaterial (1).

Figure 8

VSM pattern of the CS-TDI-SSA-Fe$_3$O$_4$ catalyst (1).

Figure 9

The proposed mechanism for the synthesis of 2,3-dihydroquinazoline derivatives 5 catalyzed by the biobased multifunctional CS-TDI-SSA-Fe$_3$O$_4$ solid acid nanocomposite (1).

Figure 10

Reusability of the CS-TDI-SSA-Fe$_3$O$_4$ organocatalyst (1) in the model reaction to afford 5a.

Supplementary Files

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- Tables.docx
- ElectronicSupporting05052023.docx