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Facile and efficient method for the synthesis of tetrahydrobenzo [*b*] pyrans and spirooxindoles catalysed by nano-Fe_3O_4@dextrin/$Si(CH_2)_3$/DABCO as a natural-based nanocatalyst in green media

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Original Research

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Abstract:

As a natural-based catalyst, nano-Fe_3O_4@dextrin/$Si(CH_2)_3$/DABCO was fabricated and characterized with different analytical methods such as field emission scanning electron microscopy, X-ray diffraction, Fourier-transform infrared spectroscopy, X-ray mapping, energy-dispersive X-ray spectroscopy, thermogravimetric analysis, and vibrating sample magnetometer. The mentioned new natural magnetic nanocatalyst was employed for the three-component synthesis of tetrahydrobenzo[*b*]pyrans and spirooxindoles from aromatic aldehyde or isatin, malononitrile, and 1,3-dicarbonyl compounds in green media for the required time. The major advantages of these protocols include atom economy, short time of reaction, simplicity of operation, lack of toxic solvents, excellent yields of products, easiness of separation, and reusability of the catalyst.

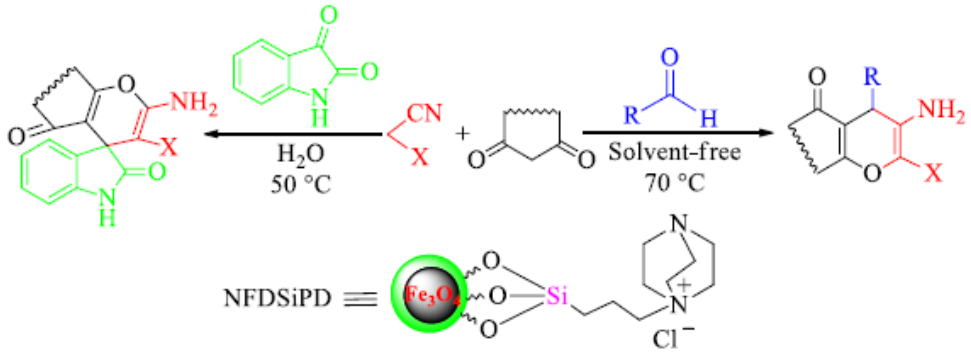
Keywords: Nano-dextrin; DABCO; Natural-based catalyst; Tetrahydrobenzo[*b*]pyran; Spirooxindole

1. Introduction

Natural-based catalysts have a wide range of distinctive features, including the ability to be conducted under mild conditions, different types of stereoselectivity in chemical reactions, high catalytic activities, and removal of undesired side reactions [1]. Biopolymer dextrin has recently demonstrated extensive attention to the development of functional materials with favorable characteristics due to its easy availability, low cost, chemical structure, biodegradable nature, and non-cytotoxicity [2, 3]. Dextrin is widely considered for different applications such as cosmetics, textiles, and foods [2].

1,4-Diazobicyclo [2.2.2] octane (DABCO) is a commercially accessible, affordable, and widespread catalyst that is used in organic reactions [4]. It has been lately applied as the most frequent catalyst in organic synthesis (e.g., in the Baylis-Hillman [5] and [2+2] cycloaddition [6] reactions. Further, DABCO was taken into account as one of the foremost catalysts for the multi-component synthesis of dihydropyrano[*c*]chromene derivatives [7].

The most widespread technique for synthesizing different tetrahydrobenzo[*b*]pyrans is a one-pot multi-component condensation of malononitrile, aryl aldehydes, and 1,3-dicarbonyl compounds using the Michael addition and cyclization. Considering the importance of the functionalized 4*H*-pyrans, different homogeneous and heterogeneous catalysts have been applied for this purpose, including SB-DABCO@eosin[8], Fe_3O_4@G.tea/Cu[9], Glycine[10], Chitosan-ZnO[11], CESA[12], Fe_3O_4@GO-NH_2[13], L-Proline[14], and rGO@Fe_3O_4@$ZrCp_2Cl_2$[15] catalysts. The pyran compositions have several noticeable medicinal



Scheme 1. Synthesis of tetrahydrobenzo[b]pyran and spirooxindole derivatives using NFDSiPD as a natural nanocatalyst.

and biological features[16] such as anticancer[17, 18], anti-inflammatory[19], antibacterial[20], antimicrobial[21], antiinfluenza[22], anti-HIV[23], and antiproliferative[24] activities. It is noteworthy that 4*H*-pyrans can be extensively employed for treating Parkinson's, Huntington's, Alzheimer's, and human inflammatory TNF-mediated diseases [25–27]. Compounds with spirooxindole ring exhibit high biological activity such as anti-malarial [28], antimycobacterial [29], anti-tubercular [30], and antifungal [31]. The spirooxindole system is the core structure of some pharmacological agents and natural products [32–34]. The classical method for the preparation of spirooxindole derivatives involves a two-step reaction [35]. Recently, several methods for the synthesis of these compounds via three-component reactions malononitrile, 1,3-dicarbonyl, and isatin in the presence of different catalysts have been reported in the literature [36–40]. Nonetheless, most of the above-mentioned methods for the synthesis of tetrahydrobenzo[*b*]pyrans and spirooxindoles had several disadvantages, including long reaction times, low yields of products, and toxic solvents. Thus, developing clean, applicable, secure, and high-yielding methods are felt necessary.

Accordingly, we intended to prepare tetrahydrobenzo[*b*]pyrans and spirooxindoles using one-pot three-component condensation in the presence of nano-Fe_3O_4@dextrin/Si$(CH_2)_3$/DABCO (NFDSiPD), which is considered a natural-based recyclable basic nanocatalyst (Scheme 1).

2. Experimental

Materials and methods

All reagents were purchased from Aldrich and Merck and used without further purification. The nano-dextrin was provided from Yazd Pishgam Sarir Chemical Industrial Company (Yazd, I.R.IRAN). The melting points were measured on a Büchi B-540 apparatus. The X-ray powder diffraction of the catalyst was performed on a Philips Xpert MPD diffractometer using a Cu-K$_\alpha$ source (λ = 1.54 Å) in the 2θ range of 10–80 °C. Field emission scanning electron microscopy analyses were conducted using Mira 3-XMU. Moreover, thermogravimetric analysis was recorded on a Stanton red craft STA-504. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker-Avance spectrometer in DMSO-d_6 solutions. The reactions were monitored by TLC and FT-IR spectra were recorded on a Bruker FT-IR spectrophotometer 106 (Bruker Equinox 55). Magnetic measurements were performed using a vibration sample magnetometer (VSM, Meghnatis Daghigh Kavir Co. Kashan Kavir, Iran). Eventually, the energy-dispersive X-ray spectroscopy (EDS) of NFDSiPD was measured by an EDS instrument and Phenom ProX.

Preparation of nano-Fe_3O_4@dextrin

For this purpose, 1.5 g of nano-dextrin was dissolved in 100 mL of 0.05 M acetic acid, followed by adding $FeCl_2.4H_2O$ (1.29 g, 0.0065 mol) and $FeCl_3.6H_2O$ (3.51 g, 0.013 mol) and stirred for 6 h at 80 °C. In addition, 6 mL of 25% NH_4OH was added dropwise into the reaction composition with continuous stirring. The obtained mixture was cooled to room temperature after 30 min; then, nano-dextrin coated over magnetic nanoparticles was separated by an external magnet. Finally, the magnetic precipitate was washed three times with distilled water and then dried at 80 °C for 4 h.

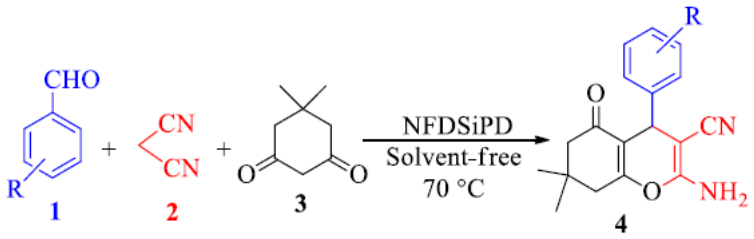
Preparation of NFDSiPD

First, a mixture of nano-Fe_3O_4@dextrin (1 g) and 3-chloropropyltrimethoxysilane (3.4 mL) were stirred in chloroform (10 mL) for 5 h under reflux conditions. After the completion of the reaction, the resulting product was removed by an external magnet, washed with chloroform to remove any unreacted material, and finally dried in an oven at 50 °C overnight. Next, 1 g nano-Fe_3O_4@dextrin@Si$(CH_2)_3$Cl was combined with 0.5 g DABCO, and 10 mL of ethyl acetate was added as a solvent to the reaction mixture under reflux for 8 h. Finally, the catalyst was collected magnetically, washed three times with dichloromethane, and dried at 60 °C.

General procedure for the synthesis of tetrahydrobenzo[*b*]pyran derivatives

NFDSiPD (0.02 g) was added to a mixture of aromatic aldehydes (1.0 mmol), dimedone (1.0 mmol), and malononitrile (1.0 mmol) under solvent-free conditions and stirred at 70 °C for the suitable time. Following reaction completion, as monitored with TLC, the obtained mixture was diluted with hot ethanol (5 mL) so that to easily

Table 1. Synthesis of tetrahydrobenzo[*b*]pyrans using NFDSiPD catalyst.[a]



Entry	R	Product	Time (min)	Yield [b] (%)	M.P. (°C)[Ref.]
1	C_6H_5-	**4a**	10	94	232-234[41]
2	4-Cl-C_6H_4-	**4b**	5	96	211-212[41]
3	4-NO_2-C_6H_4-	**4c**	5	91	179-180[42]
4	4-OH-C_6H_4-	**4d**	25	89	268-270[43]
5	3-NO_2-C_6H_4-	**4e**	15	85	210-212[42]
6	2-NO_2-C_6H_4-	**4f**	20	88	232-234[41]
7	4-Br-C_6H_4-	**4g**	30	88	208-210[44]
8	2-Cl-C_6H_4-	**4h**	35	85	215-217[45]
9	3-OH-C_6H_4-	**4i**	25	80	222-224[46]
10	2,6-Cl_2-C_6H_3-	**4j**	40	79	252-254[47]
11	4-OMe-C_6H_4-	**4k**	30	84	209-211[47]
12	4-F-C_6H_4-	**4l**	10	87	189-191[43]
13	2,4-Cl_2-C_6H_3-	**4m**	25	85	286-188[44]
14	2-Furyl-	**4n**	15	89	218-220[47]
15	4-OH-3-OMe-C_6H_3-	**4o**	40	79	229-231[48]
16	4-$(CH_3)_2$CH-C_6H_4-	**4p**	25	90	200-203[13]
17	4-Me-C_6H_4-	**4q**	30	87	210-212[9]
18	2,4-$(OMe)_2$-C_6H_3-	**4r**	40	83	173-175[49]
19	4-CO_2CH_3-C_6H_4-	**4s**	15	82	254-255[50]
20	3-Br-C_6H_4-	**4t**	25	78	219-221[51]
21	C_6H_5-CH=CH-	**4u**	20	88	206-208[52]

[a] Reaction conditions: aldehyde (1 mmol), malononitrile (1 mmol), dimedone (1 mmol), and NFDSiPD (0.02 g).
[b] Isolated yield.

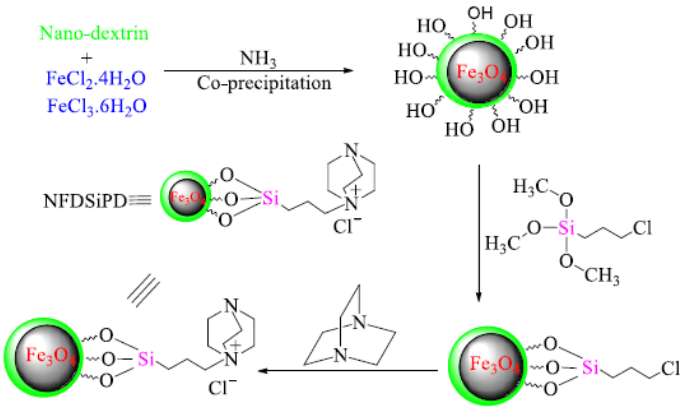
separate the catalyst by an external magnet, followed by adding cold water to the residue and collecting the solid product via filtration. The products were approximately pure in all cases and demonstrated the expected analytical data. Eventually, the recovered catalyst was washed several times with ethanol, dried, and employed for the following runs.

General procedure for the synthesis of spirooxindole derivatives

For the synthesis of spirooxindole, isatin (1.0 mmol), 1,3-diketone (1.0 mmol), malononitrile or ethyl cyanoacetate (1.0 mmol), NFDSiPD (0.04 g), and water (5 ml) was stirred at 50 °C for the suitable time. After the end of the reaction, the catalyst was separated by an external magnet, the reaction mixture was cooled to room temperature. The precipitate was filtered and recrystallized from EtOH to afford pure desired products.

Selected characteristic data for selected products

2-Amino-4-(4-chlorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (Table 1, 4b)
White solid, m.p. 211–212 °C. FT-IR (ATR) (cm^{-1}): 3422 (NH_2), 3336 (NH_2), 2184 (CN), 1659 (C=O), 1637 (C=C), 1209 (C–O). ^{1}H NMR (400 MHz, DMSO-d_6)/δ (ppm): 0.95 (s, 3H), 1.01 (s, 3H), 2.10 (d, *J*=16.0 Hz, 1H), 2.23 (d, *J*=16.0 Hz, 1H), 2.44–2.54 (m, 2H), 4.18 (s, 1H), 7.08 (s, 2H, NH_2), 7.16 (d, *J*=7.6 Hz, 2H), 7.33 (d, *J*=7.6 Hz, 2H).



Scheme 2. Preparation of NFDSiPD.

^{13}C NMR (100 MHz, DMSO-d_6)/δ (ppm): 27.31, 28.80, 32.24, 35.60, 50.40, 58.23, 112.80, 120.07, 128.76, 129.59, 131.61, 144.21, 158.96, 163.08, 196.13.

2-Amino-4-(furan-2-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (Table 1,4n)
Cream powder, m.p. 218–220 °C. FT-IR (ATR) (cm^{-1}): 3390 (NH_2), 3327 (NH_2), 2194 (CN), 1677 (C=O), 1665 (C=C), 1215 (C–O). ^{1}H NMR (400 MHz, DMSO-d_6)/δ (ppm): 0.99 (s, 3H), 1.05 (s, 3H, 2.15 (d, *J*=16.0 Hz, 1H), 2.29 (d, *J*=16.0 Hz, 1H), 2.43–2.68 (m, 2H), 4.33 (s, 1H), 6.09 (d, *J*=4.0 Hz, 1H), 6.31 (m, 1H), 7.12 (s, 2H, NH_2), 7.47 (d, *J* = 4.0 Hz,1H). ^{13}C NMR (100 MHz, DMSO-d_6)/δ (ppm): 26.51, 28.39, 28.93, 31.79, 49.85, 55.31, 105.03, 110.31, 110.42, 119.52, 141.73, 155.67, 159.23, 163.25, 195.42.

(E)-2-amino-7,7-dimethyl-5-oxo-4-styryl-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (Table 1,4u)
Yellow solid, mp 206–208 °C. FT-IR (ATR) (cm^{-1}): 3383 (NH_2), 3292 (NH_2), 2181 (CN), 1680 (C=O), 1649 (C=C), 1215 (C–O). ^{1}H NMR (400MHz, DMSO-d_6)/δ (ppm): 1.01 (s, 3H), 1.04 (s, 3H), 2.21 (d, 1H, *J*=16.0 Hz), 2.29 (d, 1H ,*J*=16.0 Hz), 2.39-2.50 (m, 2H, CH_2), 3.82 (d, 1H , *J*=8.0 Hz), 6.08(dd, 1H, *J*=16.0, 8.0 Hz) ,6.37 (d, 1H ,J=16.0 Hz,(7.08(s, 2H, NH_2), 7.23(t, 1H, *J*=8.0 Hz), 7.31 (t, 2H, *J*=8.0 Hz), 7.39 (d, 2H, *J*=8.0 Hz); ^{13}C NMR (100MHz, DMSO-d_6) /δ (ppm): 26.8, 28.1, 31.8, 32.7, 50.0, 55.1, 111.8, 119.8, 126.1, 127.4, 128.3, 129.2, 131.0, 136.4, 159.1, 162.3, 195.9.

Ethyl 2 amino 7,7 dimethyl **2′***,5 dioxo 5,6,7,8 tetrahydrospiro[chromene 4,***3′** *indoline] 3 carboxylate (6b)*
White solid, m.p. 230–232 °C. FT-IR (ATR) (cm^{-1}): 3366, 3175, 3109, 2960, 1711, 1685, 1613, 1525, 1473, 1397, 1222, 1057, 909, 745, 674. ^{1}H NMR (500 MHz, DMSO-d_6)/δ (ppm): 0.81 (t, 3H, CH_3),0.94 (s, 3H, CH_3), 1.01 (s, 3H, CH_3), 2.03 (d, *J*=16.0 Hz, 1H), 2.16 (d, *J*=16.0 Hz, 1H), 2.50-2.51 (m, 2H, CH_2), 3.67-3.74 (m, 2H, CH_2), 6.68 (d, *J*=7.5 Hz, 1H), 6.77 (t, *J*=7.5 Hz, 1H), 6.84 (d, *J*=7.5 Hz, 1H), 7.05 (t, *J*=7.5 Hz, 1H), 7.85 (s, 2H, NH_2), 10.13 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6)/δ (ppm): 13.18, 27.97, 31.62, 46.66, 51.14, 70.90, 76.35, 106.57, 113.14, 126.69, 136.04, 144.09, 157.35, 159.16, 162.48, 167.71, 177.55, 179.87, 182.66, 194.73.

7′*-Amino-2,***2′***,***4′***-trioxo-***1′***,***2′***,***3′***,***4′***-tetrahydrospiro [indoline-3,***5′***-pyrano [2,3-d]pyrimidine] -***6′***-carbonitrile (6c)*
White solid, m.p. 273–275 °C. FT-IR (ATR) (cm^{-1}): 3467, 3303, 3157, 2202, 1677, 1614, 1528, 1439. ^{1}H NMR (500 MHz, DMSO-d_6)/δ (ppm): 6.79 (s, *J*=6.5 Hz, 1H), 6.92 (t, *J*=7.0 Hz, 1H), 7.12-7.17 (m, 2H), 7.37 (s, 2H, NH_2), 10.48 (s, 1H, NH), 11.13 (s, 1H, NH), 12.30 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6)/δ (ppm): 46.47, 57.79, 86.83, 116.98, 121.84, 123.66, 128.47, 138.53, 149.27, 153.36, 157.70, 158.27, 161.46, 177.68.

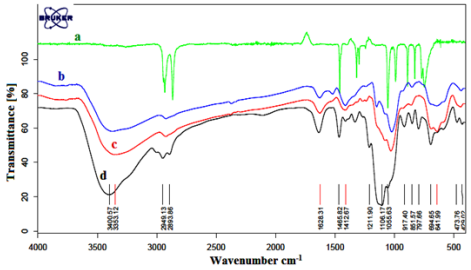


Figure 1. The spectra of FT-IR (a) DABCO, (b) nano-Fe_3O_4@dextrin, (c) nano-Fe_3O_4@dextrin/Si$(CH_2)_3$Cl, and (d) NFDSiPD.

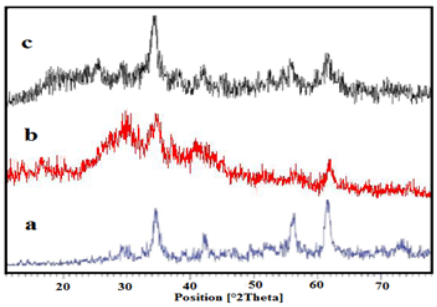


Figure 2. The XRD pattern of (a) Fe_3O_4, (b) nano-Fe_3O_4@dextrin, and (c) NFDSiPD.

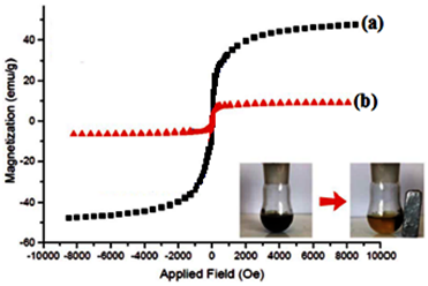


Figure 3. Magnetization curves obtained using VSM for the (a) Fe_3O_4, and (b) NFDSiPD at room temperature.

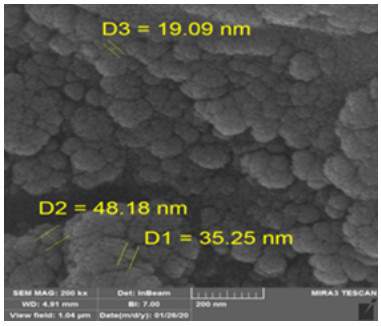


Figure 5. FESEM analysis of NFDSiPD.

3. Results and discussion

NFDSiPD was prepared as an economical and natural-based catalyst on earlier discussions on designing, providing, and applying effective and eco-friendly catalytic systems. The synthetic policy for NFDSiPD had three steps. First, core-shell nanomagnetic dextrin was provided through one-step chemical co-precipitation of ferric and ferrous salts in the presence of nano-dextrin as natural precursors under alkaline conditions. Then, nano-Fe_3O_4@dextrin/$Si(CH_2)_3Cl$ was synthesized by the reaction of nano-Fe_3O_4@dextrin with 3-chloropropyltrimethoxysilane under reflex conditions, and finally, the dried nano-Fe_3O_4@dextrin/$Si(CH_2)_3Cl$ reacted with DABCO in ethyl acetate at reflux temperature. The chlorine atoms were substituted with the *N*-nucleophiles in DABCO (Scheme 3).

The prepared nanocatalyst was fully characterized by Fourier transform infrared (FT-IR), X-ray diffraction (XRD), thermogravimetric (TGA), vibrating sample magnetometer (VSM), field emission scanning electron microscopy (FESEM), and X-ray spectroscopy (EDS) analyses.

The FT-IR spectra of the DABCO, nano-Fe_3O_4@dextrin, nano-Fe_3O_4@dextrin/$Si(CH_2)_3Cl$, and NFDSiPD were investigated and the results were shown in Figure 1. In the FT-IR spectra of the DABCO, the peaks that appeared about 2867 and 1461 cm^{-1} were attributed to CH_2 stretching and bending vibrations, and the peak at 1056 cm^{-1} was attributed to C-N stretching vibration. (Figure 1(a)). In the FT-IR spectra of nano-Fe_3O_4@dextrin, broad bands at around 560–630 and 1000 cm^{-1} indicate the Fe/O and C-O stretching vibrations, respectively. The FT-IR of nano-Fe_3O_4@dextrin/$Si(CH_2)_3Cl$ show characteristic absorption bands for C-O, Si-O, and C-Cl stretching at 1000, 1100 and 600-800 cm^{-1}, respectively (Figure 1(b,c)). The peak at 1628 cm^{-1} is attributed to the bending vibration of H–O–H that shows adsorbed water in a catalyst [53]. All the above FT-IR results produce strong evidence for the synthesis of NFDSiPD.

The X-ray diffraction patterns of magnetic (a) Fe_3O_4, (b) nano-Fe_3O_4@dextrin, and (c) NFDSiPD catalyst were displayed in Figure 2. As has been reported in the literature, the standard patterns of Fe_3O_4 have some intense characteristic diffraction peak at 2θ=30 , 35 , 43 , 53 , 57 , and 62 (JCPD 79-0417) [54]. The same peaks were also observed in the XRD pattern of nano-Fe_3O_4@dextrin and NFDSiPD that are in accordance with the pattern of Fe_3O_4. Also, the additional peak at 2θ=20 shows the existence of Si in the nanocatalyst structure (Figure 2 c).

The magnetic properties of the NFDSiPD catalyst were examined by VSM at room temperature (Figure 3). It is obvious from Figure 3 a that the synthesized Fe_3O_4 nanoparticles (MNPs) showed a saturation magnetization value of 50 emu/g, which decreased to 6 emu/g for NFDSiPD (Figure 3 b). Regardless of the decrease in magnetization value, the obtained nanocatalyst can be separated effortlessly from the solution *via* an external magnet.

TGA-DTA analysis curves of the NFDSiPD catalyst (Figure 4) show that the catalyst is stable up to 200 °C. The weight loss (5%) at 50–110 °C is attributed to the removal of adsorbed water molecules. The significant decrease in weight loss (45%) observed at a temperature between 200 °C and 480 °C is likely to correspond to the

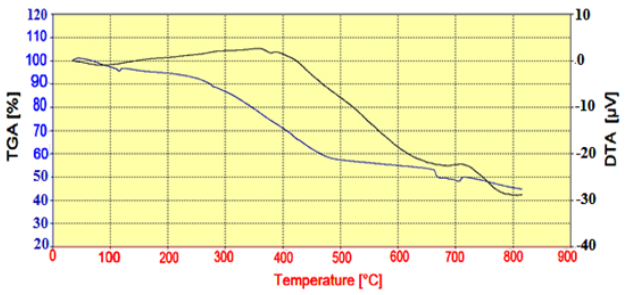


Figure 4. TGA-DTA curves for NFDSiPD.

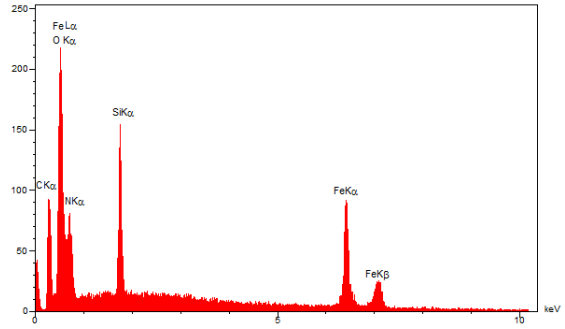
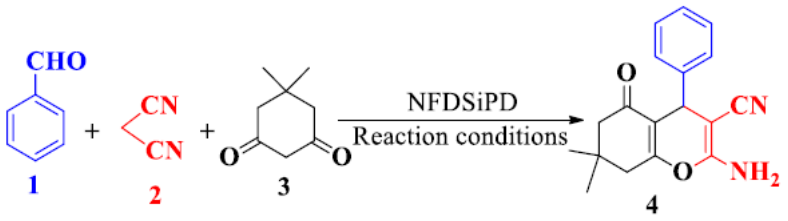


Figure 6. EDS analysis of NFDSiPD.

Table 2. Optimization of reaction conditions for the synthesis of benzo[*b*]pyrans.[a]



Entry	Catalyst (g)	Solvent	Temp. (°C)	Time (min)	Yield [b] (%)
1	0.02	EtOH	60	25	83
2	0.02	H_2O	60	40	65
3	0.02	H_2O:EtOH (1:1)	60	20	85
4	0.02	H_2O:EtOH (2:1)	60	30	72
5	0.02	H_2O:EtOH (1:2)	60	20	77
6	0.02	-	60	15	90
7	0.01	-	60	45	67
8	0.03	-	60	15	89
9	0.02	-	70	10	94
10	0.02	-	50	20	87
11	0.02	-	r.t.	60	55
12	None	-	70	120	28

[a] Reaction conditions: bezaldehyde (1 mmol), dimedone (1 mmol), malononitrile (1 mmol).
[b] Isolated yield.

decomposition of nano-dextrin. The differential thermal analysis (DTA) graph (Figure 4) is in good agreement with the TG curve as the exothermic peak.

The Surface morphology of the NFDSiPD was examined by FESEM (Figure 5). The result demonstrates that the sample consists of homogeneous spherical nanoparticles with diameters in the range of 19.09-48.18 nm.

The EDS demonstrated that elements such as Si, Fe, N, O, and C were present in the catalyst (Figure 6). Also, Figure 7 illustrates the X-ray mapping of the NFDSiPD catalyst. As can be seen, the homogenous presence of DABCO and 3-chloropropyltrimethoxysilane on the surface of Fe_3O_4@dextrin MNPs was confirmed.

Furthermore, the mesoporous structure of synthetic compounds has been demonstrated by BET analysis (Figure 8). Displaying the N_2 adsorption–desorption isotherms and hysteresis loop, along with the BET plot, provided better confirmation of the mesoporous structure. The BET analysis of the nanoparticles shows a surface area of about 2.42 m^2g^{-1}, the pore size of the mesopore compound equal to 1.64 nm, and the $\frac{p}{po}$ of the nanoparticle reported 0.005 cm^3g^{-1}.

To represent the catalytic activity of NFDSiPD nanoparticles, the synthesis of tetrahydrobenzo[*b*]pyrans *via* MCRs was evaluated to study the effectiveness of the provided nanocatalyst. To this end, reaction conditions (e.g., amount of catalyst, temperature, and solvent) were optimized, and the reaction between dimedone, benzaldehyde, and malononitrile was considered a model reaction for identifying the optimum condition. First, the model reaction was

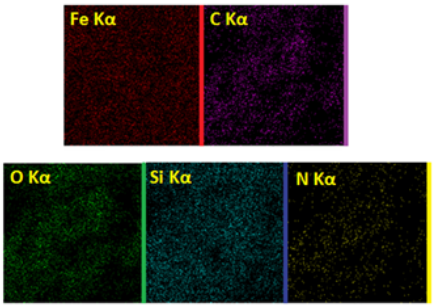


Figure 7. The X-ray mapping of NFDSiPD.

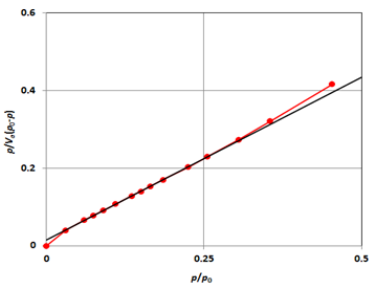
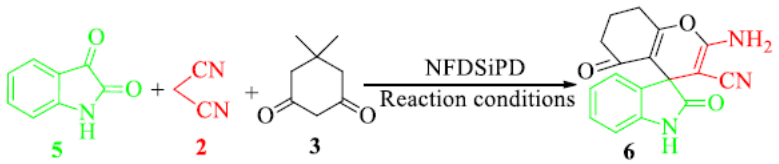


Figure 8. BET curves for NFDSiPD.

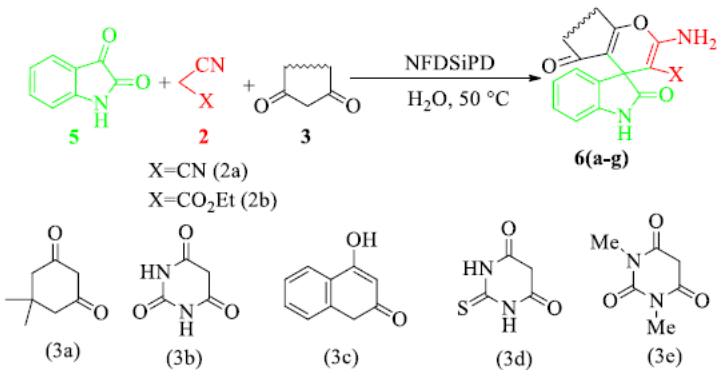
Table 3. Optimization of reaction conditions for the synthesis of spirooxindoles.[a]



Entry	Catalyst (g)	Solvent	Temp. (°C)	Time (min)	Yield [b] (%)
1	0.04	H_2O	60	20	92
2	0.04	EtOH	60	40	65
3	0.04	H_2O:EtOH (1:1)	60	50	45
4	0.04	CH_2Cl_2	60	60	35
5	0.04	MeOH	60	60	40
6	0.04	-	60	40	70
7	**0.04**	**H_2O**	**50**	**15**	**95**
8	0.04	H_2O	40	20	90
9	0.04	H_2O	70	25	88
10	0.03	H_2O	50	15	93
11	0.05	H_2O	50	20	87

[a] Reaction conditions: isatin (1 mmol), dimedone (1 mmol), malononitrile (1 mmol).
[b] Isolated yield.

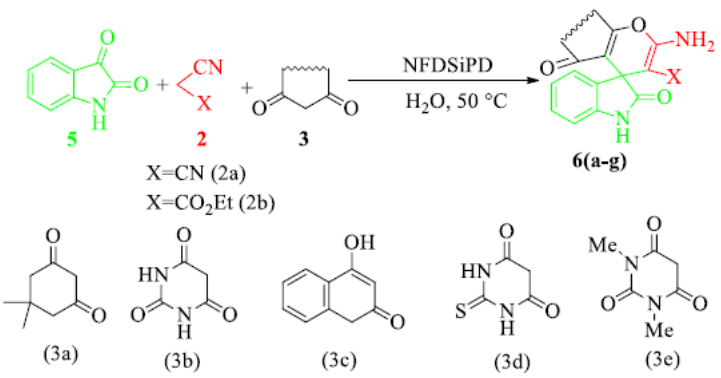
Table 4. Synthesis of spirooxindoles using NFDSiPD catalyst. [a]



Entry	Diketone	X	Product	Time (min)	Yield [b] (%)	M.P. (°C)[Ref.]
1	3a	2a	**6a**	15	95	294-296[37]
2	3a	2b	**6b**	25	90	230-232[37]
3	3b	2a	**6c**	15	92	273-275[38]
4	3c	2a	**6d**	20	92	292-293[38]
5	3c	2b	**6e**	30	90	215-217[38]
6	3d	2a	**6f**	15	93	243-245[38]
7	3e	2a	**6g**	30	88	221-223[55]

[a] Reaction conditions: isatin (1 mmol), malononitrile or ethyl cyanoacetate (1 mmol), 1,3-diketone (1 mmol), and NFDSiPD (0.04 g).
[b] Isolated yield.

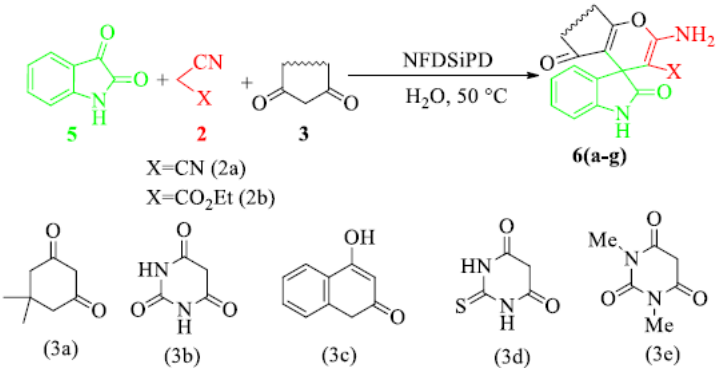
Table 5. Comparison of the efficiency of NFDSiPD catalyst with other reported catalysts for the synthesis of **4a**.



Entry	Catalyst	Conditions	Time (min)	Yield (%)[Ref.]
1	[DABCO-PDO][CH_3COO]	H_2O, 80 °C	15	95[56]
2	[Ch][OH]	H_2O, 80 °C	120	96[57]
3	[EtNH(CH_2)$_2$COH][AcO]	Solvent-free, 60 °C	11	88[58]
4	ChCl/urea/thiourea DES	H_2O, 100 °C	17	90[59]
5	Fe_3O_4@SiO_2/DABCO	H_2O, 80 °C	30	90[60]
6	Fe_3O_4@SiO_2@TiO_2	Solvent-free, 100 °C	20	93[47]
7	NFDSiPD	Solvent-free, 70 °C	10	94[a]

[a] Present work.

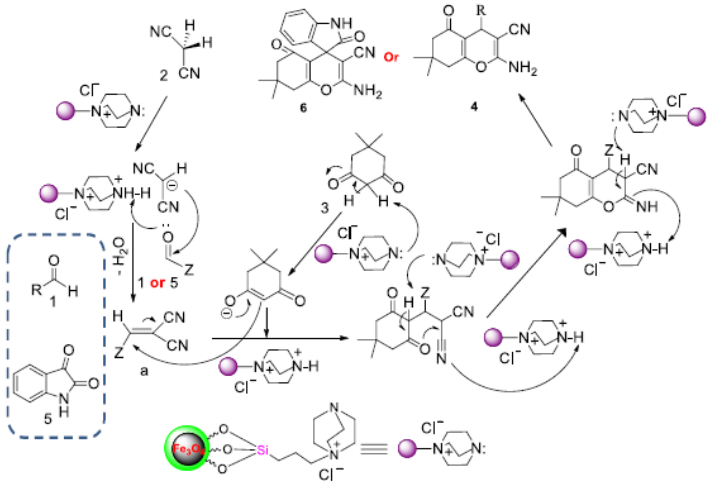
Table 6. Comparison of the efficiency of NFDSiPD catalyst with other reported catalysts for the synthesis of **6a**.



Entry	Catalyst	Conditions	Time (min)	Yield (%)[Ref.]
1	BN@Fe_3O_4	H_2O, 80 °C	30	92[40]
2	HMT	H_2O, 60 °C	20	95[37]
3	TBAB	H_2O, Reflux	30	92[38]
4	TEBA	H_2O, 60 °C	120	94[36]
5	NFDSiPD	H_2O, 50 °C	15	95[a]

[a] Present work.

performed in different solvents and solvent-free conditions in the presence of 0.02 g of NFDSiPD catalyst at 60 °C (Table 2, entry 1-6). In this circumstance, the best result was achieved in the solvent-free condition with 90% yields (Table 2, entry 6). Then, the model reaction was conducted with various amounts of catalyst to find a superior condition for the synthesis of tetrahydrobenzo[*b*]pyrans (Table 2, entry 7-8). Based on data in Table 2, the high catalytic activity of NFDSiPD was obtained in the presence of 0.02 g of this catalyst. Ultimately, the temperature impact was examined (Table 2, entry 9-11), and the most desirable result was achieved in solvent-free conditions in the



Scheme 3. Plausible mechanism for the synthesis of tetrahydrobenzo[b]pyrans and spirooxindoles in the presence of NFDSiPD.

presence of 0.02 g of the NFDSiPD catalyst at 70 °C. The corresponding product was obtained in 94% yields in these conditions (Table 2, entry 9). To influence the presence of the catalyst, the reaction was conducted without a catalyst, resulting in the production of a low-yield product after 2 h (Table 2, entry 12).

Using the optimal reaction conditions,, tetrahydrobenzo[*b*]pyrans were synthesized by different aldehydes. The obtained data (Table 1) revealed that tetrahydrobenzo[*b*]pyrans were appropriately synthesized with a wide range of aldehydes in good-to-excellent yields and a short reaction time, highlighting the high catalytic activity of NFDSiPD nanoparticles. Then, the evaluation of various conditions was studied for the synthesis of spirooxindole derivatives. After some preliminary experiments, the reaction between isatin, dimedone, and malononitrile in the presence of 0.04 g of catalyst at 50 °C in aqueous media could afford 2 Amino 7,7 dimethyl 2′,5 dioxo 5,6,7,8 tetrahydrospiro[chromene 4,3′ indoline] 3 carbonitrile in excellent yield (Table 3, entry 6).

To establish the scope of this reaction, the effect of changing the 1,3-diketones, malononitrile or ethyl cyanoacetate in the isatin was tested under solvent-free conditions. The result is presented in Table 4. According to the proposed mechanisms shown in Scheme **??**, the NFDSiPD nanoparticles in the catalytic cycle for the synthesis of tetrahydrobenzo[*b*]pyrans and spirooxindoles act as a base catalyst. Initially, the NFDSiPD catalyst promotes the reaction between aldehyde or isatin and malononitrile to form intermediate **a**. Then, activated dimedone reacts with the Knoevenagel product **a** *via* Michel addition, followed by cyclization and tautomerization yielding the desired products **4** or **6**.

Tables 5 and 6 present the comparison results of the catalytic activity of NFDSiPD with that of other previously reported catalysts for the synthesis of the tetrahydrobenzo[*b*]pyrans and spirooxindoles. Based on the findings, the presence of NFDSiPD has led to high-yielding products. Furthermore, the presence of NFDSiPD provided a shorter reaction time and a milder reaction condition without the use of any solvents.

Following each reaction run, the nanocatalyst was separated and washed several times with ethanol and applied for the synthesis of tetrahydrobenzo[b]pyran and spirooxindole under optimized conditions. The recycled catalyst could be employed five times with no considerable loss of its catalytic activity, providing the corresponding product in high yields (Figure 9).

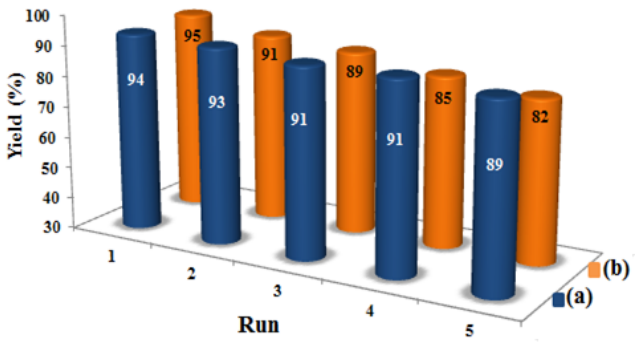


Figure 9. Reusability of nanocatalyst in the synthesis of (a) tetrahydrobenzo[*b*]pyrans (**4a**) (b) spirooxindole (**6a**).

4. Conclusions

In the current study, the NFDSiPD catalyst was presented as a novel, natural-based, and effective heterogeneous catalyst for synthesizing a variety of pharmaceutically interesting substituted tetrahydrobenzo[*b*]pyrans and spirooxindoles using one-pot condensation. The mentioned protocols provided green and easy workup procedures, with mild reaction conditions, short reaction time, and excellent product yields, along with a magnetically removable catalyst. This heterogeneous nanocatalyst includes a favorable potential for synthesizing other associated heterocyclic compositions via MCRs owing to its remarkable features, especially a plethora of reactive functional groups in its structure.

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Ethical Approval
This manuscript does not report on or involve the use of any animal or human data or tissue. So the ethical approval does not applicable.

Availability of Data and Materials
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interests
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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