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Synthesis of some chiral compounds using (MWCNTs)-COOH/Fe_3O_4-CaO magnetic nanostructures

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Abstract: The condensation of dimedone with sugars in the presence of a catalytic amount of (MWCNTs)-COOH/Fe_3O_4-CaO magnetic nanostructure gave some asymmetric furan derivatives in good yields. The products were identified by FT-IR, NMR spectra, and elemental analysis.

Keywords: Asymmetric, Furan derivatives, (MWCNTs)-COOH/Fe_3O_4-CaO, Magnetic nanomaterial, Sugars.

Introduction

The potential advantages of heterogeneous catalysts could potentially allow for the development of environmentally benign processes in both academic and industrial settings [1–3]. In recently years, among the various heterogeneous catalysts, magnetic nanoparticles have attracted much attention for their high surface area [4,5]. The combination of carbon nanotubes (CNTs) and inorganic nanoparticles have formed nanostructures that have superior properties [6]. Magnetic metal oxide NPs immobilized acid functionalized multi-walled carbon nanotubes (MWCNTs)-COOH have shown superior catalytic activities for the synthesis of organic reactions, due to the presence of a very active site on the large surface of (MWCNTs–NPs) hybrid structures [7,8]. On the other hand, CaO was often used as a heterogeneous catalyst because of its low toxicity, regeneration, high basicity, and high catalytic activity [9]. Prompted by these facts and as part of our research program on the development of convenient methods using reusable catalysts for the synthesis of organic compounds [10–12]. We report here the results of our investigation on the application of MWCNT–COOH/Fe_3O_4-CaO magnetic nanocompounds as heterogeneous, cheap, and eco-friendly catalysts in the synthesis of some chiral furan derivatives.

Results and discussion

The present paper reports the results of research aimed to verify the activity of the (MWCNT)-COOH/Fe_3O_4-CaO hybrid as an effective catalyst in the synthesis of furan derivatives.

The catalytic activity of (MWCNTs)-COOH/Fe_3O_4-CaO and heterocyclic compounds characterization

(MWCNTs)-COOH/Fe_3O_4-CaO (7 mol%) was used as an efficient catalyst for the synthesis of furan derivatives. Because of its excellent capacity, the exceedingly simple workup and good yields (MWCNTs)-COOH/Fe_3O_4-CaO was proved to be a good catalyst for these reactions.

Our initial investigation started with the model reaction of d-ribose and dimedone (Scheme 2) was carried out by using various amounts of (MWCNTs)-COOH/Fe_3O_4-CaO in various solvents and solvent-free conditions. As shown in Table 1, the optimum amount of catalyst was 7 mol%. Decreasing the amount of catalyst leads to a decrease in the yield of the reaction while increasing the amount of catalysts, the optimum amount of (MWCNTs)-COOH/Fe_3O_4-CaO was 7 mol% as shown in Table 2. Increasing the amount of the catalyst to more than 7 mol% does not improve the yield of the product any further.

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Table 1. The reaction of d-ribose (1 mmol) and dimedone (1 mmol) under different conditions.

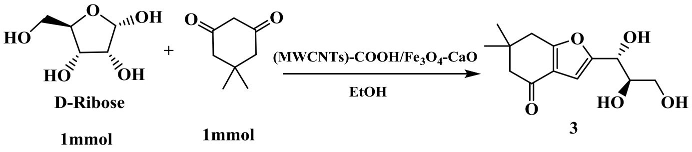
Entry	**Solvent**	**MWCNTs)-COOH/ Fe_3O_4-CaO (mol%)**	**Time (hour)**	**Yield[a] (%)**
1	THF_{dry}	-	4	trace
2	THF_{dry}	3	3	25
3	THF_{dry}	5	3	46
4	THF_{dry}	7	3	61
5	THF_{dry}	10	3	61
6	EtOH	-	4	trace
7	EtOH	3	3	42
8	EtOH	5	3	58
9	EtOH	7	2	95
10	EtOH	10	2	95
11	H_2O	-	4	trace
12	H_2O	3	3	32
13	H_2O	5	3	45
14	H_2O	7	3	61
15	H_2O	10	3	60
16	$CH_2Cl_{2\ dry}$	-	4	trace
17	$CH_2Cl_{2\ dry}$	3	3	28
18	$CH_2Cl_{2\ dry}$	5	3	49
19	$CH_2Cl_{2\ dry}$	7	3	62
20	$CH_2Cl_{2\ dry}$	10	3	63
21	CH_3CN	-	4	trace
22	CH_3CN	3	3	45
23	CH_3CN	5	3	55
24	CH_3CN	7	3	67
25	CH_3CN	10	3	67
26	DMF	-	3	trace
27	DMF	3	4	42
28	DMF	5	3	59
29	DMF	7	3	78
30	DMF	10	3	79
31	Solvent-free	-	3	46
32	Solvent-free	3	3	54
33	Solvent-free	5	3	60
34	Solvent-free	7	3	71
35	Solvent-free	10	3	70

[a] Isolated yield

In the absence of (MWCNTs)-COOH/Fe_3O_4-CaO, the result of the reaction on the TLC plate even after 4h of the reaction wasn't good. The best yield of the product was acquired with 7 mol% of (MWCNTs)-COOH/Fe_3O_4-CaO in EtOH under mild reaction conditions (Table 1, Entry 9). It is important to note that, under the same conditions, (MWCNTs)-COOH or Fe_3O_4-CaO NPs displayed almost no activity. D-arabinose did not react with dimedone and the yield of the reaction did not exceed more than 10% even after 10 h. It is clear that modification of (MWCNTs)-COOH with Fe_3O_4-CaO remarkably increased its catalytic activity.

We extended our study to different organic reactions to evaluate the scope and potential limitations of this methodology (Table 2, entries 1–5). In almost all cases, the reactions proceeded smoothly within 2-3 hours, providing the corresponding products in good isolated yields. The products were isolated, purified, and analysed by NMR and IR. For example, the ^{1}H

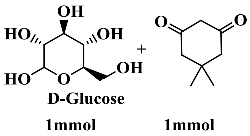
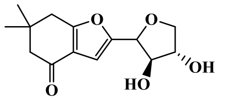
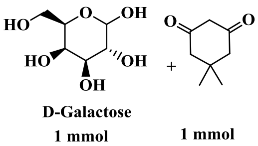
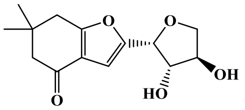
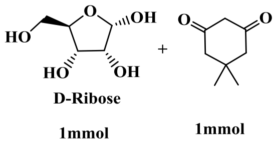
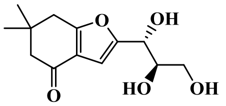
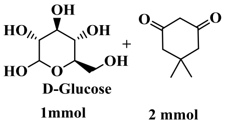
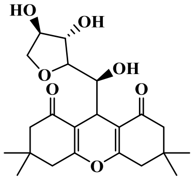
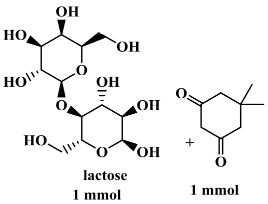
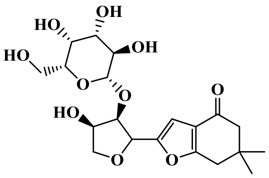
NMR spectrum of 6,6-dimethyl-2-((1R,2R)-1,2,3-trihydroxypropyl)-6,7-dihydrobenzo furan-4(5H)-one ۳ shows doublet at 5.47, 4.72, and triplet at 4.52 ppm for OH protons, 4.39, 3.66, 3.55, and 3.45 ppm for CH protons 2.31, and 2.77pm for CH_2 protons. Two singlet signals attributed to Me protons have appeared at 1.06, and 1.07 ppm, respectively [15].



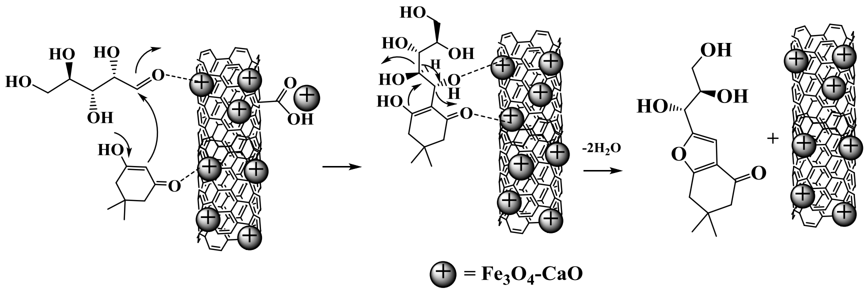
Scheme 2. Synthesis of 6,6-dimethyl-2-((1R,2R)-1,2,3-trihydroxypropyl)-6,7-dihydrobenzofuran-4(5H)-one 3.

Thereafter, we carried out the synthesis of furan derivatives with 7 mol% of (MWCNTs)-COOH/Fe_3O_4-CaO in ethanol (Table 2).

Table 2. Synthesis of some asymmetric compounds using (MWCNTs)-COOH/Fe_3O_4-CaO.

Entry	Raw Materials	Product	Time (h)/	Yield%
1		 1 [15]	2	95
2		 2	2	90
3		 3 [15]	2	95
4		 4	3	93
5		 5	3	92

A plausible mechanism for the reaction of dimedone and sugar is envisaged in (Scheme **3**). It is proposed that CO group of sugar is first activated by (MWCNTs)-COOH/Fe_3O_4-CaO. Nucleophilic addition of dimedone to the activated oxygen followed by the loss of H_2O generates an intermediate, which is further activated by (MWCNTs)-COOH/Fe_3O_4-CaO. Then, an intramolecular cyclodehydration to give compound **3**. To investigate the efficiency of the (MWCNTs)-COOH/Fe_3O_4-CaO, we compared some other metal oxide NPs for the synthesis of compound 3 and the results were summarized in Table **3**. The metal oxide NPs were synthesized according to the previously reported procedures [41-45]. As shown in Table **3**, the best catalyst for the synthesis of compound **3** is (MWCNTs)-COOH/Fe_3O_4-CaO, using this metal oxide as a catalyst offers several advantages such as excellent yields, short reaction times, a simple procedure, and using ethanol as a green solvent in contrast with other metal oxides.



Scheme 3. A plausible mechanism for the synthesis of compound **3** using (MWCNTs)-COOH/Fe_3O_4-CaO.

Table 3. Comparison of the efficiency of different catalysts in the synthesis of compound **3** in ethanol.

Entery	**Catalyst**	**Amount of catalyst (mol%)**	**Time (hours)**	**Yeild %**
1	Fe_3O_4 MNPs	7	4	57
2	Fe_3O_4@SiO_2-SO_3H MNPs	7	4	64
3	CaO NPs	7	4	58
4	ZnO-CaO NPs	7	4	76
5	(MWCNTs)-COOH/Fe_3O_4-CaO	7	2	95

The catalyst was simply separated by an external magnet, washed with ethanol and water, and dried at 100 °C for 2 h. The recovered catalyst was then re-entered to a fresh reaction mixture under the same conditions and recycled 5 times without considerable loss of activity (Table **4**). More recycling of the nano catalyst led to a gradual reduction during the recovering and washing steps.

Table 4. Recycling of the (MWCNTs)-COOH/Fe_3O_4-CaO.

Number of cycles	**Yield^a (%)**
1	95
2	94
3	93
4	90
5	89

^{a} Isolate Yield.

Conclusion

In conclusion, (MWCNTs)-COOH/Fe_3O_4-CaO was used as a reusable efficient catalyst for synthesis of furan derivatives in ethanol. We have described a rapid and very efficient one-pot three component reaction between dimedon and sugars for the synthesis of some chiral compounds. We have demonstrated that eco-friendly, low-cost and high yielding reaction. This strategy will not only give practical synthetic methods but also assures the expansion of the versatility of clean organic reactions in ethanol. (MWCNTs)-COOH/Fe_3O_4-CaO hybrid showed high catalytic activity in organic reactions and increased the rate of the reaction without pollution. In addition, this study provides a new alternative to the poultry waste from the eggshell for its use in the biosynthesis of organic and heterocyclic compounds.

Experimental

Chemicals and Instrumentation

Solvents and chemicals were purchased from Aldrich and Merck. (MWCNTs)-COOH (OD: 20-30 nm) was purchased from US Research Nanomaterials, Inc. (MWCNTs)-COOH/Fe_3O_4-CaO was FT-IR measurements were recorded on a Shimadzu 8400s spectrometer with KBr plates. The NMR spectra were determined on Bruker XL 400 (400 MHz) instruments; Mass-spectrometric measurements were made on an Agilent 6890 N Network GC system. The elemental analysis was performed by the microanalytical service of the Daypetronic Company. Melting points were obtained on an Electrothermal 9100 without further corrections.

Preparation of (MWCNTs)-COOH/Fe_3O_4-CaO:

(MWCNTs)-COOH/Fe_3O_4-CaO hybrid was synthesised according to the literature [13, 14]. Waste quail eggshells were thoroughly cleaned and air-dried after the removal of the inner membrane layer. Cleaned eggshells were crushed into small pieces and dried at 80°C for 24 h in the oven. The functionalize (MWCNTs)-COOH (0.3 g), the dried eggshells (0.1 g), and $FeSO_4$ (0.1 g) were added to 50 ml of acetic acid in a flask. The mixture was kept in an ultrasonic bath for 30 min and then slowly stirred outside the ultrasonic device for another 2 hours, under reflux conditions. The solvent was evaporated and the resulting precipitate was calcined at 250°C for 3 hours to obtain magnetically (MWCNTs)-COOH/Fe_3O_4-CaO.

General procedure for the synthesis of compounds 1-5 in the presents of (MWCNTs)-COOH/Fe_3O_4-CaO

Dimedone (1 mmol, 0.14 g), sugar (1 mmol), and (MWCNTs)-COOH/Fe_3O_4-CaO (7 mol%) were mixed and reacted in ethanol (10 ml) under reflux conditions. The completion of the reaction was determined by TLC using *n*-hexane: ethyl acetate (2:1) and appeared by a UV lamp (254 & 366 nm). In the end, the catalyst was separated by an external magnet, filtered, washed with ethanol and water, dried at 80 °C for 1h, and reused for the same reaction. The residue of the reaction mixture was evaporated, and the crude product was purified by short-column chromatography on silica gel ($CHCl_3$: MeOH / 10:1). This column chromatography operation was repeated to give pure compounds (1-5) as colorless powders. The products were determined by CHN analyses, NMR, and FT-IR spectra.

1-(4-bromophenyl)-2-((3R,4R)-3,4-dihydroxytetrahydrofuran-2-yl)-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydro-1H-indol-5-ylium 1:

Reaction of d-glucose (1 mmol) and dimedone (1 mmol), colorless powder. FT-IR spectrum, ν, cm^{-1}: 3445.7 (OH), 3404.9 (OH), 3060.8 (CH_{aro}), 2959.2 (CH_{aliph}), 2866.5 (CH_{aliph}), 1729.2 (C=O), 1609.5 (C=C), 1571.2 (C=C), 1489.5 (C=C), 1398.1 (C-O), 1280.4 (C-O), 1123.6 (C-O), 1073.2 (C-O), 1041.5 (C-O. ^1H NMR spectrum (400 MHz, DMSO-*d6*), δ ppm (*J*, Hz): 5.33 (1H, s, CH), 3.9-4.18 (6H, m, OH & CH), 1.63 (2H, d, *J* = 7.6 Hz, CH_2), 1.35 (2H, d, *J* = 7.6 Hz, CH_2), 0.89 (3H, s, CH_3), 0.87 (3H, s, CH_3). ^{13}C NMR spectrum (100 MHz, DMSO-*d6*), δ, ppm: 191.08, 167.45, 132.50, 132.16, 132.07, 129.12, 125.01, 67.85, 35.52, 30.24, 28.82, 23.64, 22.36, 14.57, 11.26. Found, %: C, 63.47; H, 6.86. $C_{۱٤}H_{۱۸}O_5$ (266.12). Calculated, %: C, 63.15; H, 6.81.

9-((S)-((2S,3S,4R)-3,4-dihydroxytetrahydrofuran-2-yl)(hydroxy)methyl)-3,3,6,6-tetramethyl-10-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione 2:

Reaction of d-galactose (1 mmol) and dimedone (2 mmol), colorless powder. FT-IR spectrum, ν, cm^{-1}: 3409.9 (OH), 2954.3 (CH_{aliph}), 2872.6 (CH_{aliph}), 1687.7 (C=O), 1616.7 (C=C), 1475.6 (C=C), 1402.8 (C=C), 1262.3 (C-O), 1223.6 (C-O), 1035.6 (C-O). ^1H NMR spectrum (400 MHz, DMSO-*d6*), δ ppm (*J*, Hz): 4.62 (1H, t, *J* = 9.6 Hz, CH), 4.37 (1H, t, *J* = 6.8 Hz, CH), 3.73 (1H, t, *J* = 6.8 Hz, CH), 3.37-3,48 (3H, br, OH), 3.45 (1H, t, *J* = 9.6 Hz, CH_2), 3.38 (4H, m, CH_2), 2.24 (1H, d, *J* = 12.8 Hz, CH_2), 2.14 (1H, d, *J* = 16.2 Hz, CH_2), 1.95 (3H, m, CH_2), 1.86 (2H, s, CH_2), 1.06 (3H, s, CH_3), 1.00 (3H, s, CH_3). ^{13}C NMR spectrum (100 MHz, DMSO-*d*6), δ, ppm: 192.46, 175.42, 115.94, 110.12, 90.27, 71.01, 70.59, 70.10, 51.62, 49.17, 38.02, 35.25, 34.20, 31.87, 29.31, 28.84, 28.36. Found, %: C, 63.35; H, 6.78. $C_{14}H_{18}O_5$ (266.12). Calculated, %: C, 63.15; H, 6.81.

10-(4-bromophenyl)-9-((2S,3S,4R)-3,4-dihydroxytetrahydrofuran-2-yl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione 4:

Reaction of d-glucose (1 mmol) and dimedone (2 mmol), colorless powder. FT-IR spectrum, ν, cm^{-1}: 3428.7 (OH), 2959.2 (CH), 2870.3 (C=O), 1714.1 (C=C), 1613.4 (C=C), 1473.4 (C=C), 1228.8 (C-O), 1148.7 (C-O), 1025.2 (C-O). ^{1}H NMR spectrum (400 MHz, DMSO-*d*6), δ ppm (*J*, Hz): 4.95 (1H, s, CH), 4.67 (1H, s, CH), 4.34 (1H, s, CH), 4.01-4.30 (br, OH), 3.37-3.65 (3H, m, CH), 3.05 (1H, d, *J* = 14.2 Hz, CH), 2.27 (1H, d, *J* = 14.6 Hz, CH), 2.05 (1H, s, CH), 2.01 (2H, s, CH), 1.84 (1H, d, CH), 1.01 (3H, s, CH_3), 0.96 (3H, s, CH_3), 0.92 (6H, s, $2CH_3$). ^{13}C NMR spectrum (100 MHz, DMSO-*d*6), δ, ppm: 192.51, 174.73, 113.83, 100.99, 90.59, 81.34, 73.79, 72.63, 70.31, 63.19, 61.16, 52.38, 51.48, 50.07, 34.25, 32.52, 31.83, 31.44, 31.34, 29.49, 29.19, 28.65, 28.12. Found, %: C, 64.96; H, 7.48; O, 35.62. $C_{22}H_{30}O_7$ (406.20). Calculated, %: C, 65.01; H, 7.44.

2-((3R,4R)-4-hydroxy-3-(((2S,3R,4S,5R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)tetrahydrofuran-2-yl)-6,6-dimethyl-6,7-dihydrobenzofuran-4(5H)-one 5:

Reaction of lactose (1 mmol, 0.34 g) and dimedone (1 mmol, 0.14g) colorless powder. FT-IR spectrum, ν, cm^{-1}: 3411.9 (OH), 2953.9 (CH_{aliph}), 2871.2 (CH_{aliph}), 1665.1 (C=O), 1618.8 (C=C), 1476.9 (C=C), 1404.8 (C=C), 1264.4 (C-O), 1225.1 (C-O), 1147.1 (C-O), 1118.4 (C-O), 1066.1 (C-O). ^{1}H NMR spectrum (400 MHz, DMSO-*d*6), δ ppm (*J*, Hz): 4.70 (1H, t, *J* = 6.4 Hz, CH), 4.29 (1H, d, *J* = 7.2 Hz, CH), 4.03 (1H, d, *J* = 7.2 Hz, CH), 3.63 (1H, br, CH), 3.50 (1H, br, CH), 3.49 (4H, br, CH), 3.45-3.72 (br, OH), 3.42 (2H, d, *J* = 7.2 Hz, OH), 3.28 (1H, t, *J* = 8.8 Hz, CH), 3.21 (1H, s, CH), 2.21 (1H, s, CH_2), 2.05 (2H, s, CH_2), 1.94-1.98 (3H, br, CH_2), 1.00 (3H, s, CH_3), 0.99 (3H, s, CH_3). ^{13}C NMR spectrum (100 MHz, DMSO-*d*6), δ, ppm: 192.45, 179.16, 167.45, 132.16, 129.65, 123.42, 116.20, 100.46, 91.86, 79.62, 73.87, 73.64, 72.94, 70.39, 63.42, 51.72, 38.52, 31.64, 30.24, 29.27, 28.81, 28.57. Found, %: C, 56.33; H, 6.65. $C_{20}H_{28}O_{10}$ (428.17). Calculated, %: C, 56.07; H, 6.59.

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