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## A novel protocol for solvent free synthesis of 4,6-diaryl-3,4-dihydropyrimidine-2(1*H*)ones catalyzed by metal oxide-MWCNTs nanocomposites

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#### Abstract

A Biginelli-type condensation is described using acetophenone as active methylene compounds with aldehydes and urea to furnish pyrimidinone analogues under solvent free conditions. In this paper, besides the preparation of nanocomposites based on MWCNTs, we also focus on investigating the catalytic efficiency of CNT/metal oxide composites. The requisites of a good catalyst are high activity, selectivity, reusability, reasonable cost and long lifetime. The application of solvent free conditions and transition metal oxides decorated-CNTs (MOx-CNTs) nanocomposites as attractive, effective and reusable catalysts, lead to the efficient synthesis of 4,6diaryl-3,4-dihydropyrimidin-2-(1H)-ones. This recyclable heterogeneous catalytic system provides a simple strategy to generate a variety of pyrimidinones under solvent free conditions. Utilization of easy reaction condition, recyclable green catalyst, reduced environmental impacts and simple work-up make this methodology as an interesting option for the eco-friendly synthesis of Biginelli-type compounds.

Keywords: Nanocomposites, TiO2-CNTs, Heterocycle, Heterogeneous catalyst, Pyrimidinone

#### Introduction

Nitrogen heterocyclic compounds have attracted considerable attention to design biologically active molecules, because their structural subunits exist in many natural products as well as pharmaceuticals [1]. Pyrimidine moiety is an important class of heterocycles including nitrogen and is responsible for the properties of many pharmaceutically significant natural products and synthetic compounds [2]. The pyrimidine ring is a key structural moiety of a series of natural compounds (antibiotics, nucleic acids, hormones, alkaloids and vitamin

 $B_1$  [3,4], life-supporting substances (vitamins, coenzymes, and uric acid) [5], synthetic medicines (Veronal, Sulfadiazine, Fluorouracil, Glivec, Rosuvastatin, and barbiturates) [3,5], chemotherapeutic drugs (fluorouracil) [3], herbicides, dyes, and many more compounds [4]. Preparation of these non-planar dihydropyrimidinones (DHPMs) is now recognized as a powerful heterocyclic synthesis with many important applications and has been the subject of several reviews [3,6-8]. With regard to the pharmacological profile and medicinal applications of functionalized dihydropyrimidinones and -thiones, Biginelli reaction to synthesize these compounds has received renewed interest and this cyclocondensation process was enlarged by the variation of CH-acidic carbonyl compound building blocks [9]. Very recently, simple alkyl acetoacetates are employed as the active methylene building blocks for novel synthesis of Biginelli-like scaffold [7], but other types of 3oxoalkanoic esters, benzoylacetic esters or thioesters can also be used successfully [6]. Also, cycloalkanones [10],  $\beta$ -keto carboxylic acid [11], cyclic ketones and substituted  $\alpha$ -keto acids [12] or acyclic and cyclic ketones [13] can be used instead of esters to produce pyrimidinones. Also, primary, secondary and tertiary acetoacetamides [6] and nitroacetone [14] serve as viable substrates and good building blocks. In addition, condensations can be achieved by employing  $\beta$ -diketones, cyclic  $\beta$ -diketones such as cyclohexane-1,3-dione [15],  $\beta$ -ketolactones [16], cyclic  $\beta$ -diesters [17] or  $\beta$ -diamides [17,18], benzocyclic ketones [19], and other cyclic  $\beta$ -dicarbonyl compounds [20]. In addition, the Biginelli-type reaction was recently investigated using acetophenones instead of 1,3-dicarbonyl compounds in a few publications [21,22]. This could be a significant and useful extension of the Biginelli reaction, allowing access to a large number of multifunctionalized pyrimidinone derivatives [6,7,23].

In recent years, special attention has been paid to decorate carbon nanotubes, i.e. filling of the inside of CNTs [24] or supporting of the outside of CNTs [25], owing to further improves of their properties. The unique properties such as the large surface areas and high electric conductivity make carbon nanotubes an ideal and valuable material to support metal oxide nanoparticles in many potential applications [25]. CNTs-inorganic composites, including CNT-supported transition metals and/or metal oxides are an important family of inorganic heterostructures [26]. Studies have shown that metal NPs/CNTs nanocomposites exhibited good catalytic behaviour under various chemical reactions and considerably improved activity, stability, and selectivity in heterogeneous catalysis [27]. The high catalytic efficiency was achieved by the effective charge transferring from metal to CNTs. Chemical and physical properties of metal NPs/CNTs composites naturally depend on the type of the metal. Numerous synthetic methodologies have been developed to prepare CNT-based nanocomposites by linking active inorganic components including noble metals [28], transition metals and their

oxides and sulphides [29,30], on the surface of CNTs. These approaches include impregnation method [31], hydrothermal and solvothermal process [32,33], sol–gel technique [34], electron-beam evaporation [35] and chemical vapour deposition [36]. In general, surface modification of CNTs with strong acid creates functional groups on the surfaces. This increase the surface binding sites, which usually leads to anchoring the precursors of metal nanoparticles, good dispersion of metal NPs and small metal nanoparticles [37].

Developing a simple, efficient and green methodology is needed for the Biginelli-type reactions. Herein, the present investigation deals a novel solid phase and heterogeneous neat strategy towards DHPMs. Our new approach reports to use metal oxides based on multi-walled carbon nanotubes as catalysts for the Biginelli-like condensation reaction under solvent free conditions. For this purpose, the reaction of aromatic aldehydes, acyclic ketones (acetophenone) and urea was investigated over  $MO_x$ -CNTs as an effective acid catalytic system (Scheme 1).



Scheme 1.MOx-CNTs promoted preparation of Biginelli-like compounds under solvent free conditions

#### 2. Results and discussion

We prompted to prepare 3,4-dihydropyrimidin-2(1*H*)-one scaffolds with the solvent free condensation of acetophenone, aromatic aldehydes and urea in the Biginelli-type reaction. The employed synthetic is outlined in Scheme 1 to generate 4,6-diaryl-3,4-dihydropyrimidin-2(1*H*)-ones. The cyclocondensation of acetophenone (1), benzaldehyde (2) and urea (3) yielding the dihydropyrimidone (4) was used as benchmarking reaction. The reactions have developed in the presence of a number of transition metal oxides supported on CNTs (MnO<sub>2</sub>-CNTs, NiO-CNTs, Fe<sub>3</sub>O<sub>4</sub>-CNTs and TiO<sub>2</sub>-CNTs) as green and recyclable catalysts or promoters. The nanocomposites can be easily prepared according to literature procedures. These supported catalysts promote the reactions due to its potential Lewis acidity. Initially, the activities of the catalysts in the solvent free synthesis of various substituted 3,4-dihydropyrimidin-2(1*H*)-ones were found to decrease in the following order: TiO<sub>2</sub>-CNTs > MnO<sub>2</sub>-CNTs > Fe<sub>3</sub>O<sub>4</sub>-CNTs > NiO-CNTs (Table 1). The results show that all of the above nanocomposites could promote the reaction, but TiO<sub>2</sub>-CNTs catalyst is significantly more effective

than other acid catalysts in the Biginelli-type reaction and it provides better results with high yields and short times. The most important advantage of titanium is the more number of unoccupied d-orbitals of the metal nanoparticles resulting stability.

Table 1.	Effect of various promo	ter/catalysts on	the Biginelli-ty
Entry	Catalyst	Time (min)	Yield (%)
1	MWCNTs-COOH	10	20
2	MnO <sub>2</sub> -CNTs	10	87
3	NiO-CNTs	10	69
4	Fe <sub>3</sub> O <sub>4</sub> -CNTs	10	80
5	TiO <sub>2</sub> -CNTs	10	98
6	MnO <sub>2</sub> NPs	10	48
7	NiO NPs	10	40
8	Fe <sub>3</sub> O <sub>4</sub> NPs	10	45
9	TiO <sub>2</sub> NPs	10	55

Table 1. Effect of various promoter/catalysts on the Biginelli-type reaction <sup>a</sup>

<sup>a</sup> 1.5:1:1 mmol urea:acetophenone:benzaldehyde

In order to optimize the reaction conditions, the catalytic efficiency of nanocomposites was studied with various amounts of TiO<sub>2</sub>-CNTs in the model reaction. The results reveal that 0.03 g of nanocatalyst provided the best effects in terms of reaction time, economy of catalyst charge and purity of products. Higher amount of catalyst did not improve the rate considerably. This behaviour was explained by this fact that catalyst active sites exist in a certain concentration more than that is required for the reactant molecules, and hence the additional amount of nanocomposites does not increase the rate of the reaction. The results are presented in Table 2.

Table 2. Optimization of amount of TiO2-CNTs catalyst

Catalyst (g)	0	0.01	0.02	0.03	0.04	
Time (min)	10	10	10	10	10	
Yield (%)	61	76	90	98	98	

After the success of the reaction, we carried out the condensation reaction under solvent free conditions at 100

°C and in various solvents with varying polarity and protic nature such as ethanol, dioxane, propanol, acetonitrile, toluene, THF, cyclohexane, and DCM. As indicated in Table 3, the polar solvents such as ethanol, methanol and acetonitrile were much better than non-polar solvents. The results could be explained with the much better solubility of the reagents and the much better dispersion of the catalyst in the polar solvents. We also carried out the model reaction under solvent free conditions. Thus, in the present system, we selected tion solvent free conditions as optimized reaction medium from points of view of the reaction yields and environmental damage.

Entry	Solvent	Time (min)	Y leid (%)
1	EtOH	10	90
2	Dioxane	10	55
3	MeCN	10	86
4	Toluene	10	35
5	THF	10	44
6	Cyclohexane	10	15
7	MeOH	10	88
8	DCM	10	20
9	Solvent free	10	98
		*	

Table 3. Optimization	of reaction	medium for	r the Biginelli-lil	ke reaction
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Encouraged by the remarkable obtained results, then we investigated the scope and versatility of the process. Aromatic aldehydes substituted with either electron-donating or electron-withdrawing group reacted successfully with urea and acetophenone and gave the products of 4,6-diaryl-3,4-dihydropyrimidin-2(1H)-ones in high yields. The results are listed in Table 4, which clearly indicates the generality of the reaction. Apparently, the nature of the substituents does not affect significantly on the reaction time and yield for the employed reaction conditions.

				M.]	p (°C)	
Entry	R	Product	Time (min)	Yield (%)	Found	Reported
1	Н	<b>4</b> a	10	98	229–231	228–230 [38]
2	2,4-Cl <sub>2</sub>	<b>4</b> b	25	85	272–274	271–274 [39]
3	4-OMe	4c	20	80	259–262	259–261 [39]
4	2-Cl	4d	15	88	261–263	264–265 [39]
5	4-Me	<b>4</b> e	30	77	249–251	248–250 [39]
6	2,6-Cl <sub>2</sub>	<b>4</b> f	20	86	275–277	274–276 [39]
7	3-OMe	4g	15	89	257–259	257–258 [39]
8	3,4-(OMe) <sub>2</sub>	4h	20	86	242–244	243–245 [39]
9	3-Br	<b>4</b> i	10	92	256-258	258–259 [38]
10	4-OH	4j	35	74	255–257	257–258 [38]
11	2-OMe	4k	15	89	265–267	266–267 [39]
12	4-Cl	41	10	90	268–269	267–269 [38]
13	3-ОМе-4- ОН	4m	25	83	267–269	267–268 [39]

Table 4. Solvent free synthesis of 4,6-diaryl-3,4-dihydropyrimidin-2(1H)-ones using TiO<sub>2</sub>-CNTs

One of the most important features of the present protocol is the recyclability and reusability of the catalyst. The reusability of the catalyst was also investigated after the completion of the same model reaction under optimized conditions. For this purpose, hot ethanol was added to the mixture and the solid catalyst was filtered, then was washed in ethyl acetate for several times and was dried in oven for the next reactions. It is interesting to note that the supported catalyst could be recyclable for five consecutive times without any significant loss of activity (Figure 1).



Figure 1. Recyclability of catalyst in one-pot synthesis of dihydropyrimidinones

The physical morphologies of the composites were examined using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Figure 2 shows SEM results about details on the interaction of CNTs and the deposited metal oxide nanoparticles. From the TEM micrograph, the  $TiO_2$  nanoparticles were dispersed completely homogeneous in the MWCNTs. Therefore, it is confirmed that  $TiO_2$ -MWCNT composites were successfully prepared.



**Figure 2**. SEM of the a) TiO<sub>2</sub>–CNT, b) NiO-CNT, c) Fe<sub>3</sub>O<sub>4</sub>-CNT, d) MnO<sub>2</sub>-CNT and e and f) TEM images obtained from TiO<sub>2</sub>–CNT catalysts.

The EDX data revealed the presence of the main elements such as C, O and metal (Ti, Ni, Fe and Mn) and other impure elements (Figure 3). The Au signal originates from the substrate used for coating. The results of EDX elemental microanalysis of the nanocomposites are listed in Table 5.



**Figure 3**. EDX elemental microanalysis of the a) TiO<sub>2</sub>/MWCNTs, b) NiO-CNTs, c) Fe<sub>3</sub>O<sub>4</sub>-CNTs, and d) MnO<sub>2</sub>-CNTs nanocomposites.

	Sample		Element	W%	Element A%		
C		М	0	С	М	0	С
	TiO <sub>2</sub> -CNTs	17.72	17.49	40.86	7.38	21.81	67.84
	NiO-CNTs	24.63	13.63	40.24	8.84	17.95	70.61
	Fe <sub>3</sub> O <sub>4</sub> -CNTs	13.66	17.17	58.78	3.91	17.13	78.12

Table 5. EDX elemental microanalysis of metal-CNTs composites

#### MnO<sub>2</sub>-CNTs 5.70 10.02 66.73 1.63 9.82 87.15

The structures of the prepared  $TiO_2$ -CNT composites were investigated using X-ray diffraction (XRD). XRD patterns of oxidized CNTs and titanium oxide composites are shown in Figure 4. The observed diffractions confirm the presence of both the MWCNT (25.92°, 43.24°) and  $TiO_2$  in the samples.

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Figure 4. XRD spectra of MWCNT-COOH and TiO2/MWCNT nanocomposites

× CC

Figure 5 shows the Raman spectra of acid treated MWCNTs and metal oxide nanoparticles supported on acid treated MWCNTs. In Figure 5a, signals in 1596 and 1307 cm<sup>-1</sup> are corresponding to acid treated MWCNTs. In Figure 5b, signals correlated to TiO<sub>2</sub> can be shown at approximately 164-608 cm<sup>-1</sup>. The signals at 222–603 cm<sup>-1</sup> are corresponding to Fe<sub>3</sub>O<sub>4</sub> in the Figure 5c. Also, the vibration modes correlated to NiO is presented at 220–1139 cm<sup>-1</sup> (Figure 5d). As shown in Figure 5e, signals at 311–609 cm<sup>-1</sup> are related to MnO<sub>2</sub>.



**Figure 5.** Raman spectra of a) MWCNTs-COOH, b) TiO<sub>2</sub>/MWCNTs, c) Fe<sub>3</sub>O<sub>4</sub>-CNTs, d) NiO-CNTs and e) MnO<sub>2</sub>-CNTs nanocomposites

Fig. 6 shows the FT-IR of oxidized MWCNTs-COOH,  $Fe_3O_4$ -CNTs, TiO\_2-CNTs, MnO\_2-CNTs and NiO-CNTs composites. The broad absorptions appearing at around 3436 cm<sup>-1</sup> and 591 cm<sup>-1</sup> are attributed to the O–H stretching and bending vibrations, respectively. Attachment of the carboxylic groups to the surface of CNTs resulting peak at 1720 cm<sup>-1</sup> assigned to C=O stretching vibrations. The bands at 1158 and 1627 cm<sup>-1</sup> originated from the graphitic component and stretching vibration of C=C of MWCNTs, respectively. Compared to the oxidized CNTs, absorption bands at 583, 450 cm<sup>-1</sup> is owing to the stretching vibrations of Fe–O (Fig 6b). From Fig 6c the stretching vibrations of Ti–O appeared at 616 and 1428 cm<sup>-1</sup>. The bands at 428 and 567 are corresponding to the stretching vibrations of Mn–O (Fig 6d). Also, the bands at 404, 517, 574 and 720 are correlated to the stretching vibrations of Ni–O Fig 6e).



Figure 6. FT-IR measurements of a) acid treated MWCNTs, b) Fe<sub>3</sub>O<sub>4</sub>-CNTs, c) TiO<sub>2</sub>-CNTs, d) MnO<sub>2</sub>-CNTs and e) NiO-CNTs composites

The possible mechanism of the reaction is showed in Scheme 2. In this process, the presence of CNTs leads to good dispersion and small size of metal oxide NPs. The nanocomposites act as a Lewis acid, catalyzed condensation between the aldehyde and ketone to generate adduct **I**. The key step of the present reaction is the formation of the chalcone **II** thought cross-aldol condensation of aldehyde and ketone. The Michael addition of urea to chalcone **II** produces ureide **III**, which subsequently eliminates water and cyclizes to form dihydropyrimidinone [40].



Scheme 2. Possible mechanism for the Biginelli-type reaction

Thus the use of  $TiO_2$ -CNTs nanocomposites as a green and heterogeneous catalyst is an environmentally clean technique for the Biginelli-type condensation. These results not only provide a new aspect for solvent free organic synthesis catalyzed by  $TiO_2$ -CNTs, but also extend the utility of ketones with single carbonyl group providing 5-unsubstituted 3,4-dihydropyrimidin-2-(1*H*)-ones in Biginelli reactions. All the products were identified by comparing their physical (mps) and spectral data (<sup>1</sup>H NMR, <sup>13</sup>C NMR and IR) with authentic samples.

#### 3. Experimental

All chemicals were purchased with high purity from Merck and Fluka chemical companies. MWCNTs were purchased from Nanotech Port Co. (Taiwan). These MWCNTs were produced with outer diameter between 10 and 20 nm via the chemical vapor deposition (CVD, or sometimes called catalytic pyrolysis). The progress of the reactions was monitored by TLC on silica-gel plates of 2 mm thickness, which was visualized with UV light (solvent: petroleum ether: ethyl acetate 7:3 v/v). The melting points were determined on an Electrothermal MK3 apparatus were expressed in °C and are uncorrected. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded using a Bruker DRX-400 spectrometer. Chemical shifts ( $\delta$ ) are reported in ppm downfield from TMS, coupling constants (J) values are given in Hz. Spin multiplicities are given as s (singlet), d (doublet), t (triplet) and m (multiplet) as well as b (broad). FT-IR spectra were determined on a Perkin Elmer FT-IR 550 spectrophotometer using KBr pellets and absorbencies are reported in cm<sup>-1</sup>. The nanocomposites materials were studied by scanning electron microscopy (SEM, TESCAN model VEGA II operated at a 15 kV accelerating voltage) and Transmission electron microscopy (TEM, Zeiss EM10C operated at 80 kV accelerating voltage). XRD patterns were obtained on a Holland Philips Xpert X-ray diffraction (XRD) diffractometer (CuK, radiation,  $\lambda$ = 0.154056 nm and 40 kV voltage), at a scanning speed of 2°/min from 10° to 100° (20). The Raman spectra were measured on a Bruker SENTERRA spectrometer with spectral range: 200-3500cm<sup>-1</sup>, CCD detector and Laser wavenumber 785 nm (High spatial & spectral resolution (Spectral Resolution:  $< 3 \text{ cm}^{-1}$ ).

#### 3.1. Preparation of composites

The nanocomposites were prepared according to reported procedures in the literature. In brief, CNTs was functionalized by adding 100 mL acid solution containing 2.5 M HNO<sub>3</sub> and 0.5 M  $H_2SO_4$  at 100 °C for 6 h. Then, the acid-treatment CNTs were obtained by rinsing with deionized water and by drying in the air at 100 °C. MnO<sub>2</sub>-CNTs were prepared in a direct redox reaction with mixing aqueous solution of KMnO<sub>4</sub> and modified

CNTs under ultrasound irradiation. Then, acetic acid was added until pH 2 and was refluxed at 70 °C for 3 h. Then, the mixture was separated by centrifuging and was washed with deionized water and acetone and was dried at 70 °C for 12 h in a vacuum oven [41]. NiO/MWNTs composites were prepared by mixing NiCl<sub>2</sub>·6H<sub>2</sub>O aqueous solution with acid treated MWCNTs. Next, NH<sub>4</sub>OH was dropped into the suspension to pH 8 under sonication for 20 min and the mixture was soaked in the solution for 5 h. Finally, intermediate product (Ni(OH)<sub>2</sub>/MWNTs) was separated by centrifuging and were washed with deionized water and was calcinated at 400 °C for 2 h to be achieved NiO/MWNTs nanocomposites [42]. Fe<sub>3</sub>O<sub>4</sub>/CNT composites were prepared by chemical coprecipitation of aqueous solution (NH<sub>4</sub>)<sub>2</sub>Fe(SO<sub>4</sub>)<sub>2</sub>.6H<sub>2</sub>O (0.4 mmol) and NH<sub>4</sub>Fe(SO<sub>4</sub>)<sub>2</sub>.12H<sub>2</sub>O (0.8 mmol) at 50 °C in purified CNTs under sonication for 10 min. Next, to precipitate the iron oxides, 5 M NH<sub>4</sub>OH aqueous solution was added (pH 11–12) and the reaction was continued at 50 °C for 30 min under mechanical stirring. Then, the samples were separated from the suspension by magnet and were washed with doubly distilled water and were dried in a vacuum oven at 100 °C for 24 h [43]. TiO<sub>2</sub>-CNTs were prepared by adding TiCl<sub>4</sub> solution consist of a little HCl to acid treated MWCNTs under sonication for 2 h. Then, the suspension was stirred at room temperature for 22 h and up to 80 °C for 3 h. At last, the mixture was centrifuged and was calcinated in furnace at 370 °C for 3 h [44].

#### 3.2. General method for the synthesis of Biginelli-like products under solvent free technique

 $TiO_2$ -CNTs (0.03 g) was added as a suitable catalyst to a mixture of benzaldehyde (1 mmol), acetophenone (1 mmol), and urea (1.5 mmol). The substrates were mixed under solvent free conditions for the needed time. After completion (monitored by TCL), the reaction mixture was cooled to room temperature and after adding ethanol, catalyst was separated by simple filtration due to its heterogeneous nature. Then, the filtrate was poured onto crushed ice and was stirred for 5-10 min. The precipitate was filtered through a sintered funnel after stirring, and was dried. For further purification, the product was recrystallized from ethanol.

#### 4. Conclusions

We expanded the synthetic scope of Biginelli condensation to ketones other than active methylene compounds to synthesize interesting Biginelli-type scaffolds. Therefore, a simple and new catalytic method was introduced in the synthesis of 5-unsubstituted 3,4-dihydropyrimidin-2-(1H)-ones in a single operation by cyclocondensation reaction with substituted aromatic aldehydes, acetophenone and urea using several metal oxides-CNTs as catalyst under solvent free conditions. It revealed that application of solvent free conditions in the presence of

 $MO_x$ -CNTs nanocomposites would be ideally suited to synthesize this privileged heterocycles. Moreover, TiO<sub>2</sub>-CNTs as a green heterogeneous catalyst can be used with considerable advantages such as high catalytic efficiency, mild reaction conditions, operational simplicity, green sustainable conditions, and therefore as an alternative is more attractive than above mentioned nanocomposites and many Lewis acids. We believe this methodology is superior to existing methodologies to prepare 3,4-dihydropyrimidin-2(1*H*)-ones.

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Scheme 1.MOx-CNTs promoted preparation of Biginelli-like compounds under solvent free conditions

Figure 1. Recyclability of catalyst for one-pot synthesis of dihydropyrimidinones

Figure 2. SEM of the a) TiO<sub>2</sub>-CNT, b) NiO-CNT, c) Fe<sub>3</sub>O<sub>4</sub>-CNT, d) MnO<sub>2</sub>-CNT and e and f) TEM images

obtained from TiO2-CNT catalysts.

Figure 3. EDX elemental microanalysis of the a) TiO<sub>2</sub>/MWCNTs, c) NiO-CNTs, d) Fe<sub>3</sub>O<sub>4</sub>-CNTs, and e) MnO<sub>2</sub>-

CNTs nanocomposites.

Figure 4. XRD spectra of MWCNT-COOH and TiO<sub>2</sub>/MWCNT nanocomposites

Figure 5. Raman spectra for a) MWCNTs-COOH, b) TiO2/MWCNTs, c) Fe3O4-CNTs, d) NiO-CNTs and e)

MnO<sub>2</sub>-CNTs nanocomposites

Figure 6. FT-IR measurements of a) acid treated MWCNTs, b) Fe<sub>3</sub>O<sub>4</sub>-CNTs, c) TiO<sub>2</sub>-CNTs, d) MnO<sub>2</sub>-CNTs and e) NiO-

CNTs composites

Scheme 2. Possible mechanism for the Biginelli-type reaction

#### Highlights

- easy reaction condition, recyclable green catalyst, reduced environmental impacts
- The catalyst is high activity, selectivity, reusability, reasonable cost, and long lifetime.
- . Bit • TiO<sub>2</sub>-CNTs catalyst is significantly more effective than other acid catalysts in the Biginelli-type