Microwave Assisted Fast Synthesis of CuO Nanoflakes: Catalytic Application in the Synthesis of 1,4-Dihydropyridine

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CuO nanoflakes were successfully synthesized by microwave irradiation, using copper(II) sulphate and sodium hydroxide (NaOH) as the starting materials and ethanol as the solvent. The CuO nanoflakes were characterized by using techniques such as X-ray powder diffraction, field emission scanning electron microscopy, and UV–visible absorption spectroscopy, Fourier transform infra-red spectroscopy. The synthesized CuO nanoflakes were found to have morphology like nanoflakes with narrow size distribution and high purity. Moreover, the synthesized CuO nanoflakes were used as an efficient catalyst for synthesis of a series of dihydropyridine derivatives. Optimization studies with different catalysts and solvents reveal that CuO nanoparticle in the water/ethanol mixture is efficient catalyst/solvent system for the synthesis of dihydropyridine derivative.

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1. Introduction

In recent years, application of nanoparticles as a catalyst in organic synthesis gained considerable attention because they are reusable and removable from the reaction medium by simple filtration. Moreover, nanocatalysts reported to have high efficiency owing to their large surface to volume ratio, which increases their catalytic activity. Likewise, the supported magnetic nanocatalysts are of considerable interest in organic synthesis because they are feasible alternatives to conventional catalysts, readily obtainable, easily separable by an external magnet and high degree of chemical stability in most of the organic and inorganic solvents [1–10]. The dihydropyridine derivatives are one of the important heterocyclic ring systems because of their extensive pharmacological properties and they are also analogues of NADH coenzymes. Moreover, the dihydropyridyl compounds possesses a wide range of biological activity and medicinal properties e.g. smooth muscle selective, antihistamines, cardioselective. The dihydropyridines is a topic of interest for study because they have fascinating heterocyclic nucleus with multiple reaction centers [11, 12].

Furthermore, cytotoxic activity of 4-substituted phenyl dihydropyridines against human oral squamous carcinoma is an important aspect. The well known dihydropyridine compounds such as nifedipine, nitrendipine and nimodipine [13, 14] were reported as commercially useful molecules which are calcium channel blockers. Consequently, a variety of potential drugs are commercially available for the treatment of congestive heart failure [15, 16] and neuroprotective agent [17] which possesses dihydropyridine nucleus. In addition, various medicinal applications viz. antihypertensive, hepatoprotective, bronchodilators, geroprotective, antiatherosclerotic, antitumour, antiplatelet, antimutagenic, antiadipotic, and aggregation inhibitory activity were shown by some of the dihydropyridine derivatives [18–21]. These compounds were also found as potential calcium channel blockers in medicinal and bioorganic chemistry [22] and NADH models [23], respectively. Moreover, the 1,4-dihydropyridines also acts as a flexible intermediate in the synthesis of natural products owing to their higher reactivity [24].

Consequently, various synthetic methods were developed owing to a wide range of biological medicinal and pharmacological importance of dihydropyridine derivatives. Some of the synthetic methods are use of microwave irradiation technique [25, 26], refluxing at high temperature [27–31], use of ionic liquid [32], use of catalysts like SiO\textsubscript{2}/HClO\textsubscript{4} [33], SiO\textsubscript{2}/NaHSO\textsubscript{4} [34], I [35], bakers’ yeast [36], metal triflates [37], tetrabutylammonium hydrogen sulfate [38], organocatalysts [39], PTSA [40], iron trifluoroacetate [41], TMSCl [42] and Ni nanoparticles [43].

Literature survey reveals that various synthetic methodology for synthesis of 1,4-dihydropyridine derivatives possess some disadvantages such as costly reagents, lengthy work-up procedures, moisture sensitivity, toxic and harsh reaction conditions. Therefore, development of fast and efficient methodology with an efficient, green solvent/catalyst system for the synthesis of 1,4-dihydropyridine is an important challenge for organic chemists.

Therefore, it is a topic of interest to synthesize nanoparticles with high surface area and to focus their catalytic application in organic synthesis [44–48]. Therefore, we reported herein CuO nanoflakes as a efficient

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catalyst for the synthesis of 1,4-dihydropyridine derivatives through one-pot four-component Hantzsch condensation reaction using aromatic aldehyde, ethyl acetoacetate/methyl acetoacetate and ammonium acetate in ethanol as solvent, in excellent yield utilizing microwave assisted technology. The novelty of this proposed method lies in the use of ethanol as a green, less toxic solvent, low-cost catalyst (synthesized in laboratory with readily available starting materials) and simple synthetic methodology, mild reaction conditions, high yields, simple work-up, easy filtration and reusability of catalyst.

2. Experimental

2.1. General

All solvents, chemicals and reagents procured from Merck and Sigma Aldrich. Melting points were determined on Digital Melting Point apparatus and are uncorrected. The field emission scanning electron microscopy (FESEM) images were obtained on a Seron AIS 2100. The Fourier transform infrared (FT–IR) spectra were recorded on a Bruker alpha FTIR spectrometer and UV-vis spectroscoopy was studied on Shimadzu 1800 setup at J.B. Science College, Wardha. The $^1$H NMR spectra were recorded on Bruker DRX– 300 Avance spectrometer at 300.13 MHz at SAIF, Chandigarh, Punjab University, and Punjab. The elemental analyses were done with an Elemental Analyser system at SAIF, Chandigarh, Punjab University, and Punjab. All the reagents used in this synthesis are of analytical grade and used without further purification. The X-ray diffraction (XRD), FESEM analyses were carried out at SAIF, IIT Bombay. BET surface area analysis was studied at Material Science Center, IIT Kharagpur.

2.2. CuO nanomaterial preparation

25 ml ethanolic solution of 0.5 M CuSO$_4$·5H$_2$O (copper(II) sulfate 5-hydrate, 99.95%) stirred for 5 min on magnetic stirrer and 25 ml ethanolic solution of 0.5 M NaOH added dropwise to the ethanolic solution of copper sulphate with vigorous stirring for about 15 min. The resulting mixture placed in the scientific microwave oven with the specification of 650 W for about 10 min. During the reflux the change in color of the solution varies from sky blue to colorless and then slowly turns to brick red. This indicates the formation of CuO nanomaterial. The solution were cooled to room temperature and the obtained precipitate was centrifuged, washed first with distilled water and then with absolute ethanol and with acetone in sequence and dried in oven at 100°C for 3 h. The final product was collected and used for characterization.

2.3. Synthesis of diethyl 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate

A mixture of an aromatic aldehyde (1 mmol), ethyl acetoacetate (2 mmol), and ammonium acetate (1.3 mmol) and copper oxide nanoflakes (CuO), vigorously agitated in water (2 mL) at 70°C for the stipulated period of time, till the completion of the reaction (checked by TLC). After completion of the reaction, few drops of ethanol were added to the reaction mixture (to assist granulation of the products). The catalyst, being insoluble in ethanol/water, was separated by centrifugation. The catalyst was removed by filtration and the filtrate was added to crushed ice. A solid product was obtained, which was filtered, washed with water, and crystallized from aqueous ethanol, if needed (Fig. 1).

Fig. 1. Scheme of one pot four component synthesis of 1,4-dihydropyridine.

2.4. Recycling of catalyst

To examine the reusability, the catalyst was recovered by filtration from the reaction mixture after dilution with ethanol, washed with methanol, and reused as such for subsequent experiments (up to three cycles) under similar reaction conditions. The observed fact that yields of the product remained comparable in these experiments established (Table I) the recyclability and reusability of the catalyst without any significant loss of activity.

<table>
<thead>
<tr>
<th>Number of cycle</th>
<th>% Yield</th>
</tr>
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<tbody>
<tr>
<td>1st</td>
<td>93</td>
</tr>
<tr>
<td>2nd</td>
<td>90</td>
</tr>
<tr>
<td>3rd</td>
<td>89</td>
</tr>
</tbody>
</table>

2.5. Optimization studies of synthesis of 1,4-dihydropyridine

In the present work, the reaction conditions optimized with respect to the catalyst, solvent and reactants for carbon–carbon (C–C) and carbon–heteroatom (C–N) bond formation. The physical characterization is given in Table II.

In continuation of this research, the reaction conditions were optimized on the basis of the catalyst, solvent and reactants for carbon–carbon and carbon–heteroatom bond formation. To test the efficiency of the catalytic activity, we chose to focus our initial studies on the cyclization reaction of aldehydes, ammonium acetate and ethylacetoacetate in the presence of different catalysts such as Al$_2$O$_3$, TiO$_2$SiO$_2$, CuO and also in the presence of regular CuO (purchased from Sigma Aldrich).
Physical characterization of the synthesized compounds.

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>la</td>
<td>C₁₉H₂₂N₂O₆</td>
<td>374.38</td>
<td>120</td>
<td>169 ÷ 171</td>
<td>93</td>
<td>0.54</td>
</tr>
<tr>
<td>2</td>
<td>lb</td>
<td>C₁₇H₂₁NO₃</td>
<td>319.35</td>
<td>115</td>
<td>165 ÷ 168</td>
<td>90</td>
<td>0.57</td>
</tr>
<tr>
<td>3</td>
<td>lc</td>
<td>C₂₀H₂₅NO₅</td>
<td>359.41</td>
<td>100</td>
<td>160 ÷ 162</td>
<td>85</td>
<td>0.65</td>
</tr>
<tr>
<td>4</td>
<td>ld</td>
<td>C₂₁H₂₅NO₄</td>
<td>355.43</td>
<td>105</td>
<td>223 ÷ 225</td>
<td>85</td>
<td>0.70</td>
</tr>
<tr>
<td>5</td>
<td>le</td>
<td>C₁₉H₂₂N₂O₆</td>
<td>374.38</td>
<td>105</td>
<td>172 ÷ 174</td>
<td>75</td>
<td>0.65</td>
</tr>
<tr>
<td>6</td>
<td>lf</td>
<td>C₁₉H₂₂BrN₄O₄</td>
<td>408.29</td>
<td>95</td>
<td>210 ÷ 213</td>
<td>65</td>
<td>0.65</td>
</tr>
<tr>
<td>7</td>
<td>lg</td>
<td>C₁₉H₂₃NO₅</td>
<td>345.39</td>
<td>80</td>
<td>241 ÷ 242</td>
<td>93</td>
<td>0.60</td>
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<tr>
<td>8</td>
<td>lh</td>
<td>C₁₉H₂₂BrN₄O₄</td>
<td>408.29</td>
<td>95</td>
<td>210 ÷ 213</td>
<td>65</td>
<td>0.65</td>
</tr>
<tr>
<td>9</td>
<td>li</td>
<td>C₁₈H₂₂N₂O₄</td>
<td>330.38</td>
<td>60</td>
<td>211 ÷ 212</td>
<td>90</td>
<td>0.60</td>
</tr>
<tr>
<td>10</td>
<td>lj</td>
<td>C₁₉H₂₂N₂O₆</td>
<td>374.39</td>
<td>102</td>
<td>223 ÷ 225</td>
<td>88</td>
<td>0.70</td>
</tr>
<tr>
<td>11</td>
<td>lk</td>
<td>C₁₇H₂₁NO₃</td>
<td>319.35</td>
<td>115</td>
<td>165 ÷ 168</td>
<td>90</td>
<td>0.57</td>
</tr>
</tbody>
</table>

The significant results of Table III corresponds to the reactivity of catalytic nanoparticles determined by the energy of surface atoms on surface of nanoparticle.

For the optimization of the reaction conditions, we proceed the model reaction using CuO nanoparticles in various solvents.

One-pot synthesis of diethyl 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate in various catalysts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time [min]</th>
<th>Yields [%]</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>SiO₂</td>
<td>100</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>Al₂O₃</td>
<td>120</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>TiO₂</td>
<td>140</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>CuO</td>
<td>160</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>CuONps</td>
<td>120</td>
<td>85–90</td>
</tr>
</tbody>
</table>

*isolated yields

One-pot synthesis of diethyl 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate in various solvents*.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time [min]</th>
<th>Yields [%]*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>toluene</td>
<td>240</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>acetonitrile</td>
<td>180</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>ethanol</td>
<td>120</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>ethanol/water mixture (30:70)</td>
<td>140</td>
<td>80–90</td>
</tr>
</tbody>
</table>

*reflux conditions, *isolated yields.

The results in Table IV show that a mixture of water/ethanol is the most efficient solvent for this multicomponent reaction. This is not surprising, insight of the fact that the hydrogen bonding between water/ethanol and the substrate can promote the nucleophilic attack of the reactants.

3. Results and discussion

The CuO nanocatalyst was synthesized by a modified precipitation method in which the reaction was carried out under scientific microwave oven using an ethanol/water mixture (30:70) as a green medium. Then, it was characterized by powder X-ray diffraction (PXRD), scanning electron microscopy (SEM), and FTIR spectral analysis. The SEM analysis was done to study particle size and the CuO nanoparticle morphology was identified based on the analysis of SEM images.

3.1. Characterization of CuO nanoparticles

3.1.1. XRD

The structural property of as-synthesized CuO nanomaterial is analyzed by the powder XRD. Figure 2 illustrates the XRD patterns of as-synthesized CuO nanostructures. The XRD pattern is the replica of the JCPDS pattern with reference code 00-044-0706. No characteristic peaks of impure phases, such as Cu(OH)₂ or Cu₂O were detected. This indicates the formation of single phase pure monoclinic CuO nanomaterial.

3.1.2. FESEM

Figure 3 shows the morphology and size of the synthesized nanomaterial investigated by FESEM. FESEM images of as synthesized CuO reveal the growth of nanoparticles from the nucleating center whose maximum diameter is around 400 nm (Fig. 3). Morphology and size of the
3.1.3. FTIR

The synthesized nanostructure subjected to FTIR investigation (Fig. 4). The spectrum exhibited several strong bands below 700 cm$^{-1}$ i.e. at 633, 607, 598, 587, 570, 557 cm$^{-1}$ (Cu–O link stretch and O–Cu–O asymmetric vibrations) which confirmed the formation of monoclinic CuO phase. The characteristic band at 607 cm$^{-1}$ is due to Cu–O stretching.

3.1.4. UV-vis spectroscopy

Figure 5 depicts the UV-vis spectra of as synthesized CuO nanomaterial which shows the wide absorption in visible region which is in well agreement with the CuO nanostructures.

3.1.5. BET surface area

The effective Brunauer–Emmett–Teller (BET) surface area of the as-synthesized samples was measured using a Quantachrome ChemBET TPR/TPD analyzer. Figure 6 shows the isotherm of N$_2$ adsorption of the nanoparticles. The effective BET specific surface area of as synthesized nanoparticles is found to be 17.00 m$^2$/g.

3.2. Spectroscopic data of synthesized compounds

IR, $^1$H NMR, $^{13}$C NMR and mass spectral data of compounds 1a-1f are given below. The spectral data are in good correlation to the suggested structure of the compounds.

1. Diethyl 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (1a):

% Yield: 85; m.p. 169–171°C.

IR, $\nu_{\text{max}}$/cm$^{-1}$: 3342 (NH), 1703 (CO), 1643 (CO), 1523 (C–H and ring C=C), 1485(C=C), 1369 (sym. CH$_3$ in O–CH$_2$–CH$_3$), 1345 (CN), 1299–1258 (C–O–C).

$^1$H NMR (500.1 MHz, CDCl$_3$), $\delta$: 1.23 (3 H, Me), 2.40 (3 H, CH$_3$), 4.09 (2 H, CH$_2$), 5.09 (1 H, CH), 5.80 (1 H, NH), 7.27–8.13 (4 H, Ar–H). $^{13}$C NMR (125.8 MHz, CDCl$_3$), $\delta$: 14.88 (CH$_3$), 18.66 (CH$_3$), 59.35 (CH$_2$),
2. Diethyl 4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1b):

% Yield: 90; m.p. 165–168°C.
IR (νmax/cm⁻¹): 3334 (NH), 2978 (C–H), 1686 (C=O), 1639 (C–O), 1529 (=C–H and C=C), 1487 (C=C in furan), 1371 (CH₃ in O–CH₂–CH₃), 1326 (C–N in C₄N–N), 1296 (C–O–C). ¹H NMR (500.1 MHz, CDCl₃), δ: 1.26 (3 H, CH₃), 2.33 (2 H, CH₂), 4.14 (3 H, CH₃), 5.20 (1 H, CH), 5.81 (1 H, NH), 5.94–7.27 (3 H, Ar–H).

3. Diethyl 4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1c):

% Yield: 85; m.p. 160–162°C.
IR (νmax/cm⁻¹): 3324 (N–H), 2974 (C–H), 1696 (C=O), 1649 (C–O), 1529 (=C–H and ring C=C), 1487 (C=C), 1371 (CH₃ in O–CH₂–CH₃), 1326 (C–N in C₄N–N), 1295 (C–O–C). ¹H NMR (500.1 MHz, CDCl₃), δ: 0.88 (3 H, CH₃), 1.23 (2 H, CH₂), 2.33 (3 H, CH₃), 3.90 (1 H, CH), 4.07 (1 H, NH), 6.74–7.26 (4 H, Ar–H).

4. Diethyl-2,6-dimethyl-4-(2-phenylethylene)-1,4-dihydropyridine-3,5-dicarboxylate (1d):

% Yield: 85; m.p. 223–225°C.
IR (νmax/cm⁻¹): 3334 (N–H), 2978 (C–H), 1686 (C=O), 1639 (C–O), 1487 (C=C), 1214 (C–O–C). LCMS (m/z): calculated (M⁺+Na): 378, found 378.38.

5. Diethyl 2,6-dimethyl-4-(2-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (1e):

% Yield: 75; m.p. 172–174°C.
IR (νmax/cm⁻¹): 3343 (N–H), 2888 (C–H), 1702 (C=O), 1642 (C–O), 1523 (=C–H and ring C=C), 1485–1433 (C=C), 1369 (CH₃ in O–CH₂–CH₃), 1346 (C–N in –N), 1298–1248 (C–O–C). ¹H NMR (500.1 MHz; CDCl₃), δ: 1.93 (3 H, CH₃), 2.466 (3 H, CH₃), 2.42 (2 H, CH₂), 5.09 (1 H, CH), 5.84–7.27 (4 H, Ar–H). 6.46 (1 H, NH).

6. Diethyl 4-(2-bromophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1f):

% Yield: 65; m.p. 210–213°C.
¹H NMR (500.1 MHz; CDCl₃), δ: 1.05 (3 H, CH₃), 2.12 (3 H, CH₃), 2.30 (2 H, CH₂), 5.00 (1 H, CH), 6.77–7.58 (4 H, Ar–H), 5.82 (1 H, NH).

7. Diethyl 4-(4-hydroxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1g):

Rf: 0.60; % Yield: 93; m.p. 241°C.
IR spectrum (νmax/cm⁻¹): 3344 (N–H), 2986 (C–H), 1792 (C=O), 1716 (C=O), 1540 (=C–H and ring C=C), 1218 (C–O–C).
Mass (m/z): calculated (M⁺+Na): 368, found 368.28.
UV (absorption): 400 nm.

8. Diethyl-4-(4-bromobenzyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1h):

Rf: 0.70; % Yield: 60; m.p. 211°C.
¹H NMR: (500.1 MHz; CDCl₃; Me₄Si): 1.41 (t, 3 H, CH₃), 2.32 (s, 3 H, CH₃), 2.41 (q, 2 H, CH₂), 5.19 (s, 1 H, CH), 5.93–6.20 (m, 4 H, Ar–H), 4.41 (s, 1 H, NH).

9. Diethyl 2',6'-dimethyl-1',4'-dihydro-2',4'-bipyridine-3',5'-dicarboxylate (1i):

IR (νmax/cm⁻¹): 3100 (N–H), 2927 (C–H), 1685 (C=O), 1632 (C=O), 1504 (=C–H and ring C=C), 1428 (C–C), 1377 (CH₃ in O–CH₂–CH₃), 1300 (C–N in C₄Ar–N), 1266 (C–O–C). ¹H NMR (500.1 MHz, CDCl₃; Me₄Si), 1.12 (3 H, CH₃), 2.32 (2 H, CH₂), 2.48 (3 H, CH₃), 4.15 (1 H, CH), 4.721 (1 H, NH), 5.60–8.71 (4 H, Ar–H). MS (m/z): calculated (M⁺+K): 369, found 368.28.

10. Diethyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (1j):

IR (νmax/cm⁻¹): 3343 (N–H), 2888 (C–H), 1702 (C=O), 1642 (C–O), 1523 (=C–H and ring C=C), 1485–1433 (C=C), 1369 (CH₃ in O–CH₂–CH₃), 1346 (C–N in –N), 1298–1248 (C–O–C). ¹H NMR (500.1 MHz, CDCl₃, Me₄Si): 1.193 (3 H, CH₃), 2.466 (3 H, CH₃), 2.42 (2 H, CH₂), 5.09 (1 H, CH), 5.84–7.27 (4 H, Ar–H), 6.46 (1 H, NH).

11. Diethyl 4-(furan-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1k):

IR (νmax/cm⁻¹): 3344 (N–H), 2960 (C–H), 1697 (C=O), 1644 (C=O), 1539 (=C–H and ring C=C), 1475 (C=C), 1369 (CH₃ in O–CH₂–CH₃), 1320 (C–N in C₄Ar–N), 1296 (C–O–C). ¹H NMR (500.1 MHz, CDCl₃, Me₄Si): 1.23 (3 H, CH₃), 2.32 (3 H, CH₃), 2.18 (2 H, CH₂), 5.19 (1 H, CH), 5.94–6.20 (3 H, Ar–H), 4.30 (1 H, NH).

3.3. Spectral representation for representative compound — diethyl 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (1a)

Diethyl 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (1a) was characterized by ¹H NMR (Fig. 7), LC–MS (Fig. 8), FTIR (Fig. 9), and ¹³C DEPT NMR (Fig. 10) spectral analysis.

Fig. 7. ¹H NMR spectrum of 1a.

Diethyl 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (1a) was additionally characterized by ¹³C distortionless enhancement by polarization transfer (DEPT).
The DEPT spectral analysis is a useful spectroscopic method for determination of different types of primary, secondary and tertiary carbon atoms. The DEPT spectroscopic method gives different signals for CH, CH$_2$ and CH$_3$ groups by variation of the selection angle parameter. The DEPT spectrum of 1a (Fig. 8) shows the signals for CH and CH$_3$ in an upward direction while the signal of CH$_2$ in the opposite direction. So the structure is confirmed by $^{13}$C DEPT spectra.

The spectral data confirm the structure of synthesized compounds. The optimization study reveals that the CuO nanoparticle as an effective catalyst for synthesis of 1,4-dihydropyridine derivative, i.e. 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (1a). Moreover, the proposed protocol is microwave assisted, environmental benign, proficient, and fast method for synthesis of bio-inspired dihydropyridine derivative.

4. Conclusion

A competent, simplistic and economical method for the synthesis of functionalized dihydropyridine derivatives was reported here, using CuO nanoflakes as a catalyst in an ethanol/water mixture green media. The products were obtained in remarkable yields and the reaction times were considerably low. The present protocol represents an easy and a remarkable method for the three-component reactions to synthesize some dihydropyridine derivatives using unique nanoscale materials. Moreover, the reusability of this CuO nanocatalyst is one of its important character and also this potency inspired us to use it for commercial and industrial organic synthesis applications.

References


