Evaluation of Nano-Fe₃O₄ as a Green Catalyst for the Synthesis of Mono, bis and tris Diindolyl Methanes

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Abstract: Fast and clean synthesis of mono, bis and tris diindolylmethanes from various aldehydes and indoles in the presence of an efficient reusable catalyst, nano-Fe₃O₄, in high yield and short reaction time is reported.

Keywords: Diindolylmethanes, reusable, nano-Fe₃O₄.

Introduction

It is well known that diindolylmethanes (DIMs) and related compounds exhibit a wide range of biological activities such as antibacterial and antitumor properties. Diindolylmethanes are the most active cruciferous substances for promoting beneficial estrogen metabolism in women and men. DIMs increase the body’s natural metabolism of hormones and promote good estrogen (2-hydroxyestrogen). This indole antioxidant is patented for alleviating symptoms of fibromyalgia. Thus indol and its derivatives have been a topic of research interest. Several synthetic methods for the preparation of DIMs have been reported by using catalysts such as lanthanide triflate, FeCl₃, HOAc, molecular iodine, montmorillonite clay K-10, indium trichloride and triflate, trifluoroacetic acid, aluminium chloride, ion exchange resin, lithium perchlorate, copper (II) bromide, molibdatophosphoric acid, scandium (III) trifluormethanesulfonate, zirconium (IV) chloride, bentonite, lewis acids in ionic liquids, ceric ammonium nitrate, silica supported sodium hydrogen sulphate and amberlyst, diphosphateoctadecatungstic acid and Zr⁴⁺-dodecyl sulfates. Most of these methods suffer from various disadvantages such as long reaction time, use of expensive lewis acids, toxic metal ions, and harsh reaction condition, excess of toxic or organic solvents, low yield and cumbersome product isolation procedure. Due to these problems, development of an efficient and versatile method for the preparation of DIMs is an important aspect and there is a scope for the further improvement towards milder reaction conditions, improved yields and green procedure.
In continuation of our ongoing studies to synthesize heterocyclic and pharmaceutical compounds at mild and practical protocols [25-27], Herein, we wish to report our preliminary results on the preparation of nano-Fe$_3$O$_4$ (Figure 1) and their application as a green catalyst for the synthesis of mono, bis and tris diindolylmethanes, as shown in (Scheme 1).

**Experimental**

Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were determined on a Shimadzu IR-470 spectrometer. $^1$H NMR and $^{13}$C NMR spectra were recorded on a 500 MHz and 125MHz Bruker DRX-500 in CDCl$_3$ as solvent and TMS as internal standard. Chemicals were purchased from Merck and Fluka. Elemental analyses were done on a Carlo-Erba EA1110CNNO-S analyzer and agreed with the calculated values. All solvents used were dried and distilled according to standard procedures.

**General procedure for the synthesis of 3a-w in the presence of nano-Fe$_3$O$_4$**

A mixture of aldehyde 1 (1mmol) (scheme 2, entries 3m-u, 0.5 mmol and scheme 3, entry 3v-w, 0.3mmol), indole derivatives 2 (2 mmol) and catalytic amount of nano-Fe$_3$O$_4$ in H$_2$O (10 mL) were stirred for the required reaction times (5-10min) at room temperature. The progress of the reaction was monitored by TLC (EtOAc: petroleum ether 1:4). After completion of the reaction, the mixture was filtered in the presence of an efficient magnetic bar. The crude product was recrystallized from ethanol to produce diindolylmethanes derivatives 3a-w as pure crystalline products in 90-98% yields.

**1,4-bis((2-(di(1H-indol-3-yl)methyl)phenoxy)methyl)benzene (3m):**

IR (KBr) $\nu = 3413, 3053, 2923, 1593, 1555, 1485, 1238$ cm$^{-1}$; $^1$H NMR (500 MHz, DMSO): $\delta = 7.69$ (s, 2H), 7.4 (d, $J = 7.8$ Hz, 2H), 7.2 (d, $J = 8.1$ Hz, 2H), 7.16-7.18 (m, 2H), 7.0 (t, $J = 7.9$ Hz, 3H), 6.92 (s, 2H), 6.89 (t, 1H), 6.57 (d, $J = 1.6$Hz, 2H), 6.39 (s, 1H), 5.0 (s, 2H) ppm; $^{13}$C NMR (125 MHz, DMSO): $\delta = 147.6, 138.5, 136.9, 133.2, 133.1, 128.8, 127.7, 126.7, 124.4, 124.2, 123.0, 121.2, 119.3, 118.5, 116.5, 111.6, 70.0, 37.9$ ppm; Anal.calcd for C$_{54}$H$_{42}$N$_{4}$O$_{2}$: C, 83.26; H, 5.43; N, 7.19. Found: C, 83.56; H, 5.51; N, 7.09.

**1,4-bis((2-(2-(2-methyl-1H-indol-3-yl)methyl)phenoxy)methyl)benzene (3n):**

IR (KBr) $\nu = 3400, 3051, 3024, 2914, 1589, 1520, 1483, 1217$ cm$^{-1}$; $^1$H NMR (500 MHz, DMSO): $\delta = 10.68$ (s, 2H), 7.20-7.21 (m, 3H), 7.01-7.06 (m, 2H), 6.88 (t, $J = 7.4$ Hz, 2H), 6.81-6.84 (m, 5H), 6.66 (t, $J = 7.5$ Hz, 2H), 6.13 (s, 1H), 4.91 (s, 2H), 1.99 (s, 6H) ppm; Anal.calcd for C$_{58}$H$_{50}$N$_{4}$O$_{2}$: C, 83.42; H, 6.04; N, 6.71. Found: C, 83.51; H, 6m bt.34; N, 6.57.
1,4-bis(4-(di(1H-indol-3-yl)methyl)phenoxy)methyl)benzene (3o):
IR (KBr) v = 3413, 3053, 2923, 1608, 1541, 1506, 1456, 1234 cm⁻¹; ¹H NMR (500 MHz, DMSO): δ = 10.70 (s, 2H), 7.43 (s, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.25-7.28 (m, 3H), 7.03 (t, J = 7.7Hz, 2H), 6.91 (d, J = 8.6Hz, 2H), 6.85 (t, J = 7.6Hz, 2H), 6.80 (d, J = 2 Hz, 3H), 5.77 (s, 1H), 5.0 (s, 2H) ppm; Anal.calcd for C₅₃H₄₂N₄O₂: C, 83.26; H, 5.43; N, 7.19. Found: C, 83.41; H, 5.68; N, 7.09.

1,4-bis((4-(bis(2-methyl-1H-indol-3-yl)methyl)phenoxy)methyl)benzene (3p):
IR (KBr) v = 3409, 3055, 2916, 1602, 1540, 1460, 1298 cm⁻¹; ¹H NMR (500 MHz, DMSO): δ = 10.71 (s, 2H), 7.45 (s, 2H), 7.2 (d, J = 7.9 Hz, 2H), 7.0 (d, J = 8.5Hz, 2H), 6.87-6.91 (m,4H), 6.82 (d, J = 7.9Hz, 2H), 6.68 (t, J = 7.6Hz, 2H), 5.86 (s, 1H), 5.07 (s, 2H), 2.06 (s, 6H) ppm. Anal.calcd for C₃₈H₅₈N₄O₂: C, 83.42; H, 6.04; N, 6.71. Found: C, 83.51; H, 6.34; N, 6.57.

1,4-bis((4-(bis(1-methyl-1H-indol-3-yl)methyl)phenoxy)methyl)benzene (3q):
IR (KBr) v = 3053, 2925, 1595, 1550, 1481, 1458, 1240 cm⁻¹; ¹H NMR (500 MHz, DMSO): δ = 7.42 (d, J = 7.9 Hz, 2H), 7.30 (t, J = 8.1 Hz, 2H), 7.19-7.26 (m, 4H), 6.99-7.04 (m, 4H), 6.89 (d, J = 7.9 Hz, 2H), 6.58 (s, 2H), 5.17 (s, 1H), 5.06 (s, 2H), 3.67 (s, 6H) ppm; ¹³C NMR (125 MHz, DMSO): δ = 156.31, 137.80, 136.36, 133.89, 133.86, 128.8, 128.7, 127.5, 120.5, 118.3, 113.4, 112.6, 109.4, 70.1, 66.3, 33.6 ppm; Anal.calcd for C₃₈H₅₈N₄O₂: C, 83.42; H, 6.04; N, 6.71. Found: C, 83.61; H, 6.57; N, 6.09.

1,5-bis(2-(1H-indol-3-yl)methyl)phenoxy)pentane (3r):
IR (KBr) v = 3460, 3406, 2927, 1631, 1452, 1245 cm⁻¹; ¹H NMR (500 MHz, DMSO): δ = 10.7 (s, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 7.9 Hz, 2H), 7.14 (t, J = 7.62 Hz, 2H), 7.02 (t, J = 8.0 Hz, 2H), 6.89 (d, J = 8.1 Hz, 1H), 6.85 (t, J = 7.3Hz, 2H), 6.80 (t, J = 7.4Hz, 3H), 6.20 (s, 1H), 3.77 (t, J = 6.0Hz, 2H), 1.54 (m, 2H), 1.24 (m, 1H) ppm; ¹³C NMR (125 MHz, DMSO): δ = 156.56 , 137.43 , 133.98, 129.83, 127.74, 127.68, 124.48, 121.64, 120.75, 119.70,118.95, 118.80, 112.67, 112.26, 68.36, 32.43, 29.29, 22.95 ppm; Anal.calcd for C₅₃H₄₂N₄O₂: C, 82.23; H, 5.95; N, 7.52.; Found: C, 82.01; H, 5.68; N, 7.83.

1,5-bis(2-(bis(1H-indol-3-yl)methyl)phenoxy)pentane (3s):
IR (KBr) v = 3469, 3413, 2925, 1625, 1460, 1232 cm⁻¹; ¹H NMR (500 MHz, DMSO): δ = 10.65 (s, 2H), 7.16 (d, J = 7.5 Hz, 2H), 7.00 (d, J = 7.0 Hz, 2H), 6.80-6.82 (m, 3H), 6.75-6.78 (m, 3H), 6.61 (t, J = 7.1 Hz, 2H), 6.02 (s, 1H), 3.48 (br, 2H), 2.01 (br, 2H), 1.96 (s, 6H), 1.11 (m, 1H) ppm; Anal.calcd for C₅₅H₅₂N₄O₂: C, 82.47; H, 6.54; N, 6.99. Found: C, 82.64; H, 6.33; N, 6.73.

1,6-bis(2-(1H-indol-3-yl)methoxy)hexane (3t):
IR (KBr) v = 3409, 3055, 2916, 1602, 1540, 1460, 1298 cm⁻¹; ¹H NMR (500 MHz, DMSO): δ = 10.7 (s, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 7.9 Hz, 2H), 7.10-7.14 (m, 2H), 6.99 (t, J = 7.76 Hz, 2H), 6.92 (d, J = 8.01 Hz, 1H), 6.83 (t, J = 7.6Hz, 2H), 6.79 (t, J = 7.5Hz, 1H), 6.76 (d, J = 1.67Hz, 2H), 6.01 (s, 1H), 3.86 (t, J = 6.0Hz, 2H), 1.47 (br, 2H), 1.19 (br, 2H) ppm; ¹³C NMR (125 MHz, DMSO): δ = 156.56, 137.41, 134.03, 129.88, 127.74, 127.73, 127.65, 121.62, 120.75, 119.64, 118.92, 118.82, 112.67, 112.23, 68.44, 32.28, 29.62, 26.13 ppm; Anal.calcd for C₅₃H₆₄N₄O₂: C, 82.29; H, 6.11; N, 7.38. Found: C, 82.27; H, 6.33; N, 7.81.

1,4-bis(4-(bis(2-methyl-1H-indol-3-yl)methyl)-2-methoxyphenoxy)butane (3u):
IR (KBr) v = 3420, 3085, 2934, 1602, 1560, 1467, 1460, 1298 cm⁻¹; ¹H NMR (500 MHz, DMSO): δ = 10.7 (s, 2H), 7.21 (d, J = 8.0 Hz, 2H), 6.88 (m, 5H), 6.82 (td, J = 8.3 Hz, 1H),
6.69 (t, J = 7.2 Hz, 2H), 6.62 (dd, J = 8.3 Hz, J = 1.3 Hz, 2H), 5.86 (s, 1 H), 3.86 (t, J = 6.0 Hz, 2H), 3.98 (br, 2H), 3.56 (s, 3H), 2.07 (s, 6H), 1.85 (br, 2H) ppm; \(^{13}\)C NMR (125 MHz, DMSO): \(\delta = 149.59, 147.21, 137.60, 132.75, 129.18, 121.44, 120.35, 119.35, 118.35, 118.73, 114.25, 113.57, 113.40, 111.35, 68.85, 56.38, 26.52, 12.82 \) ppm; Anal. calc. for C\(_{36}\)H\(_{54}\)N\(_4\)O\(_4\): C, 79.40; H, 6.43; N, 6.61. Found: C, 79.22; H, 6.27; N, 6.91.

1,3,5-tris((4-(di(1H-indol-3-yl)methyl)phenoxy)methyl)benzene (3v):

Light red solid, IR (KBr) \(\nu = 3431, 3100, 2980, 1635, 1506, 1480, 1387, 1206, 1173 \) cm\(^{-1}\); \(^1\)H NMR (500 MHz, DMSO-\(d_6\)): \(\delta = 10.71 \) (s, 6H), 6.74 - 7.50 (m, 45H), 5.72 (s, 3H), 5.01 (s, 6H) ppm; \(^{13}\)C NMR (250 MHz, DMSO-\(d_6\)): \(\delta = 40.08, 69.48, 111.85, 114.67, 115.24, 118.54, 118.82, 119.58, 121.25, 123.87, 127.05, 129.66, 137.03, 137.73, 138.15, 156.91 \) ppm; Anal. Calc. for C\(_{78}\)H\(_{60}\)N\(_6\)O\(_3\): C, 82.95; H, 5.35; N, 7.44. Found: C, 82.62; H, 5.26; N, 7.91.

2,4,6-tris(4-(di(1H-indol-3-yl)methyl)phenoxy)-1,3,5-triazine (3w):

IR (KBr) \(\nu = 3421, 3050, 2921, 1600, 1575, 1500, 1470, 1365, 1240, 1150 \) cm\(^{-1}\); \(^1\)H NMR (500 MHz, DMSO-\(d_6\)): \(\delta = 10.8 \) (s, 6H), 7.85 (m, 6H), 7.35 (m, 12H), 7.32 (d, \(J = 7.8 \) Hz, 6H), 7.00 (d, \(J = 8.4 \) Hz, 6H), 6.83-6.89 (m, 12H), \(5.84 \) (s, 3H) ppm; \(^{13}\)CNMR (250 MHz, DMSO-\(d_6\)): \(\delta = 173.58, 149.91, 143.45, 137.00, 129.44, 127.52, 124.09, 121.67, 121.45, 119.76, 119.00, 118.27, 111.90, 30.11 \) ppm; Anal. Calc. for C\(_{72}\)H\(_{51}\)N\(_9\)O\(_3\): C, 79.32; H, 4.72; N, 11.56. Found: C, 79.32; H, 4.72; N, 11.51.

Results and discussion

Initially, the condensation reaction of 4-nitrobenzaldehyde and indole in the presence of Fe\(_3\)O\(_4\) and nano-Fe\(_3\)O\(_4\) was done and the results were listed in Table 1.

As depicted, nano-Fe\(_3\)O\(_4\) proved to be better catalyst than Fe\(_3\)O\(_4\) for the synthesis of diindolylmethanes. With the best catalyst in hand, we moved to study the effects of catalyst amount on the model reaction and the results were listed in (Table 1). 50mg of nano-Fe\(_3\)O\(_4\) is sufficient to push the reaction forward completion and 10mg and 30mg of catalyst was not enough. Higher amount of catalyst did not lead to significant change in the reaction yields.

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>Catalyst amount(%)</th>
<th>Time(min)</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>-</td>
<td>720</td>
<td>No reaction</td>
</tr>
<tr>
<td>2</td>
<td>Fe(_3)O(_4)</td>
<td>50mg</td>
<td>80</td>
<td>65</td>
</tr>
<tr>
<td>3</td>
<td>Nano-Fe(_3)O(_4)</td>
<td>50mg</td>
<td>5</td>
<td>98</td>
</tr>
<tr>
<td>4</td>
<td>Nano-Fe(_3)O(_4)</td>
<td>10mg</td>
<td>30</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>Nano-Fe(_3)O(_4)</td>
<td>30mg</td>
<td>15</td>
<td>96</td>
</tr>
<tr>
<td>6</td>
<td>Nano-Fe(_3)O(_4)</td>
<td>100mg</td>
<td>5</td>
<td>98</td>
</tr>
</tbody>
</table>

a. isolated yield.
With the best quantity of nano-Fe₃O₄ in hand, we were interested to synthesis several diindolylmethanes at room temperature with this catalyst. The results are summarized in Table 2.

**Table 2. Synthesis of diindolylmethanes in the presence of nano-Fe₃O₄.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>aldehydes</th>
<th>Time(min)</th>
<th>Yield(%)</th>
<th>M.P( °C)</th>
<th>Found</th>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>4- NO₂ C₆H₄CHO</td>
<td>5(80)²</td>
<td>98(65)ᵃ</td>
<td>235-236</td>
<td>222-228 [23]</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>3- NO₂ C₆H₄CHO</td>
<td>5</td>
<td>94</td>
<td>261-263</td>
<td>265–266 [23]</td>
<td></td>
</tr>
<tr>
<td>3c</td>
<td>C₆H₅CHO</td>
<td>7</td>
<td>85</td>
<td>112-113</td>
<td>125–127 [23]</td>
<td></td>
</tr>
<tr>
<td>3d</td>
<td>2-Cl C₆H₄CHO</td>
<td>10</td>
<td>83</td>
<td>76-77</td>
<td>72-74[7]</td>
<td></td>
</tr>
<tr>
<td>3e</td>
<td>4-Cl C₆H₄CHO</td>
<td>5</td>
<td>96</td>
<td>80-82</td>
<td>77–81 [23]</td>
<td></td>
</tr>
<tr>
<td>3f</td>
<td>2-OCH₃ C₆H₄CHO</td>
<td>7</td>
<td>84</td>
<td>129-130</td>
<td>134–136 [23]</td>
<td></td>
</tr>
<tr>
<td>3g</td>
<td>4- OCH₃ C₆H₄CHO</td>
<td>10</td>
<td>82</td>
<td>187-188</td>
<td>191–193 [23]</td>
<td></td>
</tr>
<tr>
<td>3h</td>
<td>4- CH₃ C₆H₄CHO</td>
<td>10</td>
<td>84</td>
<td>92-94</td>
<td>95–97 [23]</td>
<td></td>
</tr>
<tr>
<td>3i</td>
<td>4- OH C₆H₄CHO</td>
<td>10</td>
<td>87</td>
<td>122-124</td>
<td>122–124 [23]</td>
<td></td>
</tr>
<tr>
<td>3j</td>
<td>Thiophen-2-carbaldehyde</td>
<td>7</td>
<td>86</td>
<td>149-150</td>
<td>151-153[7]</td>
<td></td>
</tr>
<tr>
<td>3k</td>
<td>Furan-2-carbaldehyde</td>
<td>7</td>
<td>89</td>
<td>310-312</td>
<td>322-323[7]</td>
<td></td>
</tr>
<tr>
<td>3l</td>
<td>Indole-3-carbaldehyde</td>
<td>5</td>
<td>92</td>
<td>165-166</td>
<td>160[24]</td>
<td></td>
</tr>
</tbody>
</table>

ᵃ. A mixture of aldehyde 1a (1mmol) and indole derivatives 2 (2 mmol) and 0.05g Fe₃O₄ in 10 ml H₂O were stirred for the required reaction times. ᵇ. Isolated yield. ᶜ. The products were characterized by comparison of their spectroscopic and physical data with those of samples synthesized by reported procedures.

Interestingly, this reaction due to their reduced pollution, low cost, simplicity in process and handling using nano-Fe₃O₄ as catalyst, also afforded an efficient protocol for the synthesis of bis diindolylmethanes (Figure 1, Entry 3m-u) and tris diindolylmethanes (Figure 2, Entry 3v-u) as novel arylmethanes in high yields and short reaction time. The results are summarized in Table 3.
Table 3. Synthesis of bis and tris diindolylmethanes in the presence of nano-Fe₃O₄.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield(%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>m.p. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3m</td>
<td>9</td>
<td>83</td>
<td>212-214</td>
</tr>
<tr>
<td>2</td>
<td>3n</td>
<td>7</td>
<td>81</td>
<td>193-194</td>
</tr>
<tr>
<td>3</td>
<td>3o</td>
<td>7</td>
<td>92</td>
<td>151-152</td>
</tr>
<tr>
<td>4</td>
<td>3p</td>
<td>7</td>
<td>89</td>
<td>206-208</td>
</tr>
<tr>
<td>5</td>
<td>3q</td>
<td>8</td>
<td>88</td>
<td>281-283</td>
</tr>
<tr>
<td>6</td>
<td>3r</td>
<td>7</td>
<td>96</td>
<td>191-195</td>
</tr>
<tr>
<td>7</td>
<td>3s</td>
<td>9</td>
<td>93</td>
<td>184-185</td>
</tr>
<tr>
<td>8</td>
<td>3t</td>
<td>8</td>
<td>91</td>
<td>291-292</td>
</tr>
<tr>
<td>9</td>
<td>3u</td>
<td>7</td>
<td>93</td>
<td>284-285</td>
</tr>
<tr>
<td>10</td>
<td>3v</td>
<td>8</td>
<td>91</td>
<td>202-204</td>
</tr>
<tr>
<td>11</td>
<td>3w</td>
<td>9</td>
<td>94</td>
<td>234-235</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yield.

Figure 2

Figure 3
Apart from the mild condition of the process and its excellent results, the simplicity of product isolation, replacement of carcinogenic solvent with H$_2$O and the possibility to recycle nano-Fe$_3$O$_4$ offer a significant advantage. After the reaction was completed, the catalyst could be easily attracted by an efficient magnetic bar. After further treatments including washing with CHCl$_3$ and activation at 80°C, the recycled catalyst has been examined in next run. Studies on the synthesis of 3a as model substrate showed that the recovered catalyst could be successively recycled in subsequent reactions without any decrease of yields (Figure 4).

![Figure 4. Reusability of nano-Fe$_3$O$_4$ in the synthesis of 3a.](image)

We propose a possible mechanism for the nano-Fe$_3$O$_4$ catalyzed synthesis of diindolylmethanes (3) (Scheme 2). We suggest that, nano-Fe$_3$O$_4$ catalyze the formation of iminium ion (4) in a reversible reaction with the aldehyde. The higher reactivity of the iminium ion compared to the carbonyl species could facilitate nucleophilic attack of indole to aldehyde (1), via intermediate (5) and after the treatment of second molecules of indole and the elimination of nano-Fe$_3$O$_4$, (3) might be produced.

![Scheme 2](image)

The selectivity of the present methods is also demonstrated by competitive reactions of indol with arylaldehydes with electron donating and electron withdrawing substitutents. For example, when a 1:1 mixture of 4-methoxybenzaldehyde and 4-nitrobenzaldehyde was allowed to react with two equivalents of indole in the presence of nano-Fe$_3$O$_4$ under modified conditions, it was found that the arylaldehydes bearing withdrawing substituents
was chemo selectively converted to the corresponding bis(indolyl)methane but the aryl aldehydes with donating group was converted slightly (Scheme 3).

All of compounds summarized in (Table 2 and Figure 1 and 2) were characterized by spectroscopic methods (IR, $^1$HNMR and $^{13}$CNMR) and elemental analysis.

**Conclusion**

Finally, we develop an efficient and convenient procedure for the synthesis of diindolylmethanes through electrophilic reaction of indoles and aldehydes over nano-Fe$_3$O$_4$ catalyst. This procedure offer advantages such as reduced reaction time, mild reaction condition, productivity and higher yield, ease of execution and economic viability of the catalyst. This simple process combined with easy of recovery and reuse of catalyst make this procedure economic, begin and a waste free chemical process for the synthesis of diindolylmethanes.

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**References**

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