

## **A novel, efficient, and recyclable biocatalyst for Michael additions and its iron (III) complex as promoter for alkyl oxidation reactions**

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### **Supporting Data**

#### *Apparatus and Instrumentation*

Melting points were recorded on Gallenkamp apparatus and are reported uncorrected. The Fourier Transform Infrared (FTIR) spectra were recorded in KBr pellets on a JASCO *FT-IR-6300*, system at a resolution of 4 cm<sup>-1</sup> ranging 400-4000 cm<sup>-1</sup>. NMR measurements were made using a Bruker DPX spectrometer, at 600 MHz for <sup>1</sup>H-NMR and 125 MHz for <sup>13</sup>C-NMR, in DMSO-d<sub>6</sub> as solvent using TMS as internal standard. Solid state NMR spectra were recorded at 600 MHz Bruker Avance II spectrometer, 150 MHz for <sup>13</sup>C NMR. Mass spectra were measured on a GCMS DFS-Therm spectrometer, with EI 70 eV. Elemental analyses were made by means of ELEMENTAR-VARIO MICROCUBE Elemental Analyzer.

#### ***1. Application of Cs-g-PCPA, graft copolymer, against unmodified chitosan beads, as a heterogeneous basic catalyst for Michael addition reactions***

##### ***1.1 Reaction of 3 with dimedone 4***

Mixtures of benzylidene-malononitrile **3** (1.54 g, 10.0 mmol) with dimedone **4** (10.0 mmol) in the presence of 50 mL absolute ethanol were stirred at reflux for 3 h. The solution contained 10%wt. of the catalyst (Method A using chitosan beads and Method B using **Cs-g-PCPA** (G% = 64%) beads). The solid product formed in this process was separated by filtration and recrystallized from ethanol.

##### ***2-amino-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile 5***

The compound was obtained as colorless crystals; m.p. 230-231°C; Lit.<sup>1</sup> 233-234°C. IR (KBr):  $\nu = 1691$  (C=O), 2220 (CN), 3341, 3420 (NH<sub>2</sub>) cm<sup>-1</sup>, <sup>1</sup>H NMR (DMSO-d<sub>6</sub>):  $\delta = 0.96$  (s, , 3H, CH<sub>3</sub>), 1.05 (s, , 3H, CH<sub>3</sub>), 2.09 – 2.24 (s, , 2H, CH<sub>2</sub>), 2.48 (s, , 2H, CH<sub>2</sub>), 4.14 (s, 1H, CH, C-4 pyran), 7.08 (s, 2H, NH<sub>2</sub>), 7.16 – 7.29 (m, 5H, phenyl-H); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>):  $\delta = 26.9$  (CH<sub>3</sub>), 28.5 (CH<sub>3</sub>), 31.9 (C(CH<sub>3</sub>)<sub>2</sub>), 35.7 (C-4, pyran), 40.1, 50.1 (CH<sub>2</sub>), 59.6 (CH<sub>2</sub>), 112.9, 118.7 (CN), 126.0, 126.7, 127.8, 143.8, 158.1, 162.7 (aromatic carbons), 195.0 (C=O); MS, m/z (%), 294.1 (M<sup>+</sup>, 29), 217.1 (66), 55.1 (100). Anal. Calcd. for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.36; H, 6.10; N, 9.43. % Yields: Method A (Cs beads; %Yield = 75), Method B (Cs-g-PCPA beads; %Yield = 95).

### *1.2 Reaction of 3 with Barbituric and thiobarbituric acids*

Mixtures of benzylidene-malononitrile **3** (10.0 mmol) and barbituric **6a** and thiobarbituric acid **6b** (10.0 mmol) in the presence of 50 mL absolute ethanol were stirred at reflux for 3 h. The solutions contained 10%wt of the catalyst (Method A using chitosan beads and Method B using Cs-g-PCPA (G% = 64%) beads). The solid products formed in these processes were separated by filtration and recrystallized from ethanol.

#### ***7-amino-2,4-dioxo-5-phenyl-2,3,4,5-tetrahydro-1H-pyrano[2,3-d]pyrimidine-6-carbonitrile 7a***

This compound was obtained as Pale yellow crystals; m.p. 207°C,<sup>2,3</sup> IR(KBr):  $\nu = 1686$ , 1715 (C=O), 2190 (CN), 3305, 3390 (NH<sub>2</sub>) cm<sup>-1</sup>, <sup>1</sup>H NMR (DMSO-d<sub>6</sub>):  $\delta = 4.24$  (s, 1H, H-4), 7.08 (s, 2H, NH<sub>2</sub>), 7.13 – 7.34 (m, 5H, Phenyl), 11.51 (s, 1H, NH), 12.07 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>):  $\delta = 33.7$ , 58.0, 82.4, 117.6 (CN), 126.8 (p-C, Phenyl), 127.1 (o-C, Phenyl), 128.4 (m-C, Phenyl), 144.8 (i-C, Phenyl), 124.1, 128.7, 129.0, 144.1, 152.2, 158.6 (C-2, C-6), 161.7, 184.3 (C=O); MS, m/z (%), 282.1 (M<sup>+</sup>, 70), 77.1 (100). Anal. Calcd. for C<sub>14</sub>H<sub>10</sub>N<sub>4</sub>O<sub>3</sub>: C, 59.57; H, 3.57; N, 19.85. Found: C, 59.49; H, 3.47; N, 19.68. % Yields: Method A (Cs beads; %Yield = 65), Method B (Cs-g-PCPA; %Yield = 80).

#### ***7-amino-4-oxo-5-phenyl-2-thioxo-2,3,4,5-tetrahydro-1H-pyrano[2,3-d]pyrimidine-6-carbonitrile 7b***

This compound was obtained as pale yellow crystals; m.p. 190°C; IR(KBr):  $\nu = 1690$  (C=O), 2192 (CN), 3280, 3310 (NH<sub>2</sub>) cm<sup>-1</sup>, <sup>1</sup>H NMR (DMSO-d<sub>6</sub>):  $\delta = 4.22$  (s, 1H, H-5),

7.09 (s, 2H, NH<sub>2</sub>), 7.11-7.27 (m, 5H, phenyl), 10.86 (s, 1H, NH), 12.03 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>): δ = 36.1, 59.7, 87.7, 118.4, 118.7, 128.9, 130.6, 142.2, 149.0, 151.9, 158.0, 163.1; MS, m/z (%), 298.1 (M<sup>+</sup>, 37), 77.1 (100). Anal. Calcd. for C<sub>14</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S: C, 56.37; H, 3.38; N, 18.78; S, 10.75. Found: C, 56.11; H, 3.16; N, 18.60; S, 10.67. % Yields: Method A (Cs beads; %Yield = 60), Method B (Cs-g-PCPA; %Yield = 76).

### 1.3 *Gewald's reaction of 3-oxoalkanenitriles*

To mixtures of 3-oxoalkanenitriles **9a,b** (4.0 mmol) in dry 1,4-dioxane (15.0 mL) were added sulfur (4.8 mmol, 154 mg), methyl cyanoacetate **10** (4.0 mmol, 396 mg, 350 mL). The solutions also contained 10%wt of the catalyst (Method A using chitosan beads and Method B using **Cs-g-PCPA** (G% = 64%) beads). The mixtures were then stirred at reflux for 8 h, filtered to remove the solid catalyst and extracted with chloroform (2 x 10 mL). The combined organic layers were washed with brine, dried with anhydrous MgSO<sub>4</sub> and evaporated giving the solid products, which were recrystallized from ethanol.

#### ***Methyl-2-amino-5-cyano-4-phenylthiophene-3-carboxylate 11a***

This compound was obtained as yellow solid; M.p. 110°C (Lit.<sup>2,3</sup> m.p. 109-111°C). IR(KBr): ν = 1668 (C=O), 2230 (CN), 3310 (br, NH<sub>2</sub> groups) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>): δ = 3.64 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 5.22 (br s, 2H, NH<sub>2</sub>), 7.29 – 7.87 (m, 5H, Phenyl); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>): δ = 26.7 (CO<sub>2</sub>CH<sub>3</sub>), 127.8, 130.1, 139.6, 141.3, 151.9, 159.0, 169.0; MS, m/z (%), 259.1 (M<sup>+</sup>, 12), 195.1 (100). Anal. Calcd. for C<sub>13</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>S: C, 60.45; H, 3.90; N, 10.85; S, 12.41. Found: C, 60.31; H, 3.72; N, 10.57; S, 12.14. % Yields: Method A (Cs beads; %Yield = 50), Method B (Cs-g-PCPA; %Yield = 75).

#### ***Methyl-2-amino-5-cyano-4-(1-methyl-1H-pyrrol-2-yl)thiophene-3-carboxylate 11b***

This compound was obtained as Orange solid; M.p. 139°C (Lit.<sup>2,3</sup> m.p. 138-142°C). IR(KBr): ν = 1658 (C=O), 2236 (CN), 3325 (NH<sub>2</sub> groups) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>): δ = 1.34 (s, 3H, CH<sub>3</sub>, ester), 3.14 (s, 3H, N-CH<sub>3</sub>), 3.81 (s, 2H, CH<sub>2</sub>, ester), 4.42 (br s, 2H, NH<sub>2</sub>), 6.19 (m, 1H, H-4'), 7.05 (d, 1H, J = 2.5 Hz, H-5'), 7.24 (d, 1H, J = 2.5, H-3'); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>): δ = 23.2 (CO<sub>2</sub>CH<sub>3</sub>), 29.7 (N-CH<sub>3</sub>), 105.8, 113.1, 115.8, 116.9, 118.5, 131.0, 145.1, 158.0, 160.3, 169.8; MS, m/z (%), 262.1 (M<sup>+</sup>, 18), 195.1 (100). Anal. Calcd. for C<sub>12</sub>H<sub>11</sub>N<sub>3</sub>O<sub>2</sub>S: C, 55.16; H, 4.24; N, 16.08; S, 12.27. Found: C, 55.04; H, 3.97; N, 15.87; S, 12.05. %Yields: Method A (Cs beads; %Yield = 60%), Method B (Cs-g-PCPA; %Yield = 80).

#### *1.4 Reaction of enamionitriles 12a,b with dimedone 4*

Mixtures of the 3-(piperidinyl-1-yl)acrylonitrile **12a**, 3-morpholino-acrylonitrile **12b**, (10.0 mmol) and dimedone **4** (10 mmol) in 30 mL absolute ethanol containing the catalyst (10%wt.) (Method A using chitosan beads and Method B using **Cs-g-PCPA** (G% = 64%) beads). The mixtures were stirred at reflux for 5 h and filtered to give solids, which were recrystallized from ethanol.

#### *7,7-Dimethyl-2-(piperidine-1-yl)-7,8-dihydroquinolin-5(6H)-one 13a*

The compound was obtained as colorless crystals. m.p.: 145°C. Anal. Calcd. for C<sub>16</sub>H<sub>22</sub>N<sub>2</sub>O: C, 74.38; H, 8.58; N, 10.84. Found: C, 74.48; H, 8.52; N, 10.73. % Yields: Method A (Cs beads; %Yield = 80), Method B (Cs-g-PCPA; %Yield = 90). The crystal structure data has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number **CCDC 824677**.

#### *7,7-Dimethyl-2-morpholino-7,8-dihydroquinolin-5(6H)-one 13b*

The compound was obtained as colorless crystals. m.p.: 129°C. Anal. Calcd. for C<sub>15</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>: C, 69.20; H, 7.74; N, 10.76. Found: C, 69.23; H, 7.68; N, 10.64. %Yields: Method A (Cs beads; %Yield = 65), Method B (Cs-g-PCPA; %Yield = 85). The crystal structure data has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number **CCDC 824678**.

## *2. Application of the Cs-g-PCPA/Fe(III) chelate as an oxidizing catalyst*

### *(Oxidation of methyl pyridazinone)*

Hydrogen peroxide (30%, 5 mmol) was added carefully to a pre-heated solutions of methyl pyridazinones **14a,b** (1 mmol) in glacial acetic acid (5 mL) containing 10%wt of the **Cs-g-PCPA(G=64%)/Fe(III)** chelate. The mixtures were then stirred at reflux until thin layer chromatography indicated that the reactions were complete. The crude product mixtures were poured into 20 mL ice/water mixture and an stirred for 30 min. Extraction with CH<sub>2</sub>Cl<sub>2</sub> gave organic layers that were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure to yield analytically pure products **15a,b**.

#### *7-amino-2-phenylfuro[3,4-d]pyridazin-1(2H)-one 15a*

The compound was obtained as yellow powder. (%Yield: 72%; m.p. 198°C). IR (KBr,  $\text{cm}^{-1}$ ):  $\nu = 3350$  and  $3330$  ( $\text{NH}_2$ ),  $1660$  ( $\text{CO}$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-d}_6$ ,  $\delta = 6.07$  (s, 2H,  $\text{NH}_2$ ),  $7.46$  (s, 1H, pyridazinone),  $7.51$  (m, 5H, phenyl),  $8.14$  (s, 1H, furan).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-d}_6$ ,  $\delta = 114.1, 121.6, 126.8, 130.7, 131.2, 139.9, 140.8, 144.0, 147.2$  (aromatic carbons),  $168.2$  ( $\text{C=O}$ ). MS ( $m/z$  (%)):  $227.1$  ( $\text{M}^+$ , 12),  $77.1$  (100). Anal. Calcd. for  $\text{C}_{12}\text{H}_9\text{N}_3\text{O}_2$ : C, 63.43; H, 3.99; N, 18.49. Found: C, 63.28; H, 3.78; N, 18.29.

***7-amino-2-(4-chlorophenyl)furo[3,4-d]pyridazin-1(2H)-one 15b***

The compound was obtained as pale yellow powder. (%Yield: 66%; m.p. 215°C). IR (KBr,  $\text{cm}^{-1}$ ):  $\nu = 3360$  and  $3330$  ( $\text{NH}_2$ ),  $1668$  ( $\text{CO}$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-d}_6$ ,  $\delta = 6.29$  (s, 2H,  $\text{NH}_2$ ),  $7.25$  (d, 2H, o-H,  $J = 8.00$  Hz, aryl),  $7.69$  (d, 2H, m-H,  $J = 8.00$  Hz, aryl),  $8.26$  (s, 1H, furan).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-d}_6$ ),  $\delta = 113.1, 124.4, 126.9, 128.6, 129.0, 133.1, 139.1, 151.7, 155.9$  (aromatic carbons),  $171.9$  ( $\text{C=O}$ ). MS ( $m/z$  (%)):  $261.1$  ( $\text{M}^+$ , 4),  $111.1$  (100). Accurate Mass;  $261.0298$  ( $\text{C}_{12}\text{H}_8\text{O}_2\text{N}_3\text{Cl}_1$ ).

References:

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