

Ag/KF/CP@MWCNTs promoted green synthesis of amide derivatives using primary amines: Reduction of Organic pollutant

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Abstract: The reaction between dimethyl acetylenedicarboxylate and various NH-acids in the presence of catalytic amounts of Ag/KF/CP@MWCNTs leads to amide derivatives in excellent yields. The Ag/KF/CP@MWCNT is generated by water extract of rhizome *Petasites hybridus* as an environmentally media and moderate base. Also, Ag/KF/CP@MWCNT leads to increasing of yield of products and has notable reusability. Besides, reducing organic pollutants of the 4-nitrophenol (4-NP) was carried out by generating Ag/KF/CP@MWCNTs in water at room temperature. The results displayed the Ag/KF/CP@MWCNT reduced pollutants of organic compounds in a short time. The synthesized pyrrolo [1,2,4]triazoloquinazoline have high antioxidant power. The present protocol offers the advantages of clean reaction, short reaction time, high yield, easy purification and affordability of the catalyst.

Keywords: Amide derivatives, 8-aminoquinoline, Dialkyl acetylenedicarboxylates, various NH-acids.

Introduction

In medicinal chemistry, the heterocyclic compounds have a well-known subject due to having wide area of biological activities of these compounds [1]. Therefore these compounds are very important and for the synthesis of these compounds existed many procedures. MCRs open diverse avenues to create novel concatenations in one pot fashion leading to diverse biologically potent heterocyclic scaffolds. Having a cascade of reactions occurring in one pot is highly beneficial in the context of modern trends for organic synthesis, where sustainability is as relevant as efficiency and selectivity. Multicomponent reactions being atom economic, efficient and extremely convergent in nature offer a number of advantages over stepwise sequential approaches [2-11].

A major challenge in modern chemistry is the design of highly efficient chemical reactions with the minimum number of synthetic steps and short reaction times. Butyrolactones are an important structure unit in natural products and intermediates in organic synthesis [12, 13]. There has been considerable work on the synthesis of these compounds due to the discovery of many naturally occurring cytotoxic or antitumor agents. Although this ring system has been the objective of synthetic projects in a number of laboratories, the number of basically different approaches is not large [14-17]. MWCNTs have been widely investigated, due to large surface area and high adsorption ability. Dyes and pigments are two important components that are used in generating processes of food, drug, textile and printing. Producing dyes and pigments comes to about $\sim 7 \times 10^5$ tons in one year, which is hazardous for aquatic system organisms. ^[37] For this reason, discovering the green

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and eco-friendly procedures for removing of dyes and pigments pollutants from environment is very important. Most of the procedures that have been reported in the literature have used much energy and generated adverse by-products. Therefore, high efficiency methods or active synthesized compounds are required for eliminating or decreasing these problems.

Results and discussion

We now report a synthesis of amid derivatives **3** in high yields through the reaction of dimethyl acetylenedicarboxylate (DMAD) with various NH-acids in the presence of catalytic amounts of Ag/KF/CP@MWCNT. Our results are summarized in Table 1. The reaction of aniline (**1a**) with DMAD in the presence at room temperature leads to the amide derivative **3a** in 93% yield (Table 1). No other compound was obtained from the residue by column chromatography. The structure of the product was deduced from its elemental analyses and its IR, ¹H NMR, ¹³C NMR, and mass spectral data. The ¹H NMR spectrum of **3a** exhibited two singlets identified as methoxy ($\delta = 3.72$ ppm) and olefinic ($\delta = 7.01$ ppm) protons along with multiplets ($\delta = 6.65, 7.23, 7.31$, and

7.48 ppm) for the aromatic protons. The ¹³C NMR spectrum of **3a** showed eleven distinct resonances in agreement with the proposed structure. Also, the ¹H NMR spectrum of **3d** exhibited two singlets identified as methoxy ($\delta = 3.88$ ppm) and olefinic ($\delta = 6.67$ ppm) protons along with multiplets ($\delta = 7.27-8.46$ ppm) for the aromatic protons. The NH proton resonance appears at $\delta = 9.34$ ppm. The ¹³C NMR spectrum of **3d** showed 15 distinct resonances in agreement with the proposed structure.

A possible mechanism for the formation of **3a** is proposed in Scheme 1. It is reasonable to assume that **3a** results from initial addition of Ag/KF/CP@MWCNT as green solvent to the acetylenic ester and subsequent protonation of the 1,3-dipolar intermediate **4** by **1a**. Then, the positively charged ion **4** might be attacked by the conjugated base of the NH-acid to produce the nitrogen ylide **6**, which undergoes proton-transfer reaction to produce **7**. The 1,3-dipolar ion **7** is converted to **8**. The product **3a** is formed by intramolecular lactonization of **9**. Similar mechanism can be proposed for the formation of **3b-3e**.

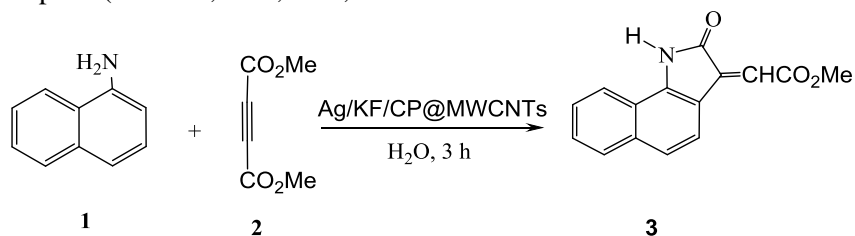
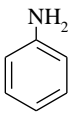
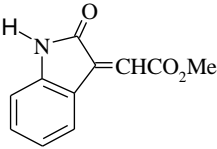
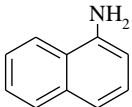
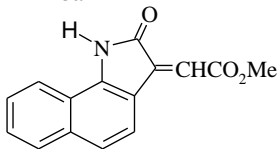
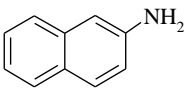
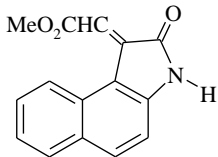
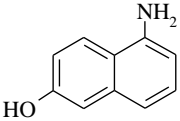
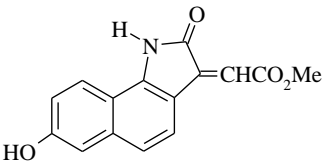
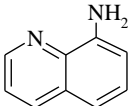
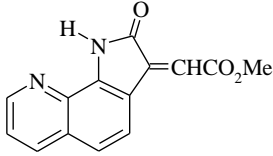
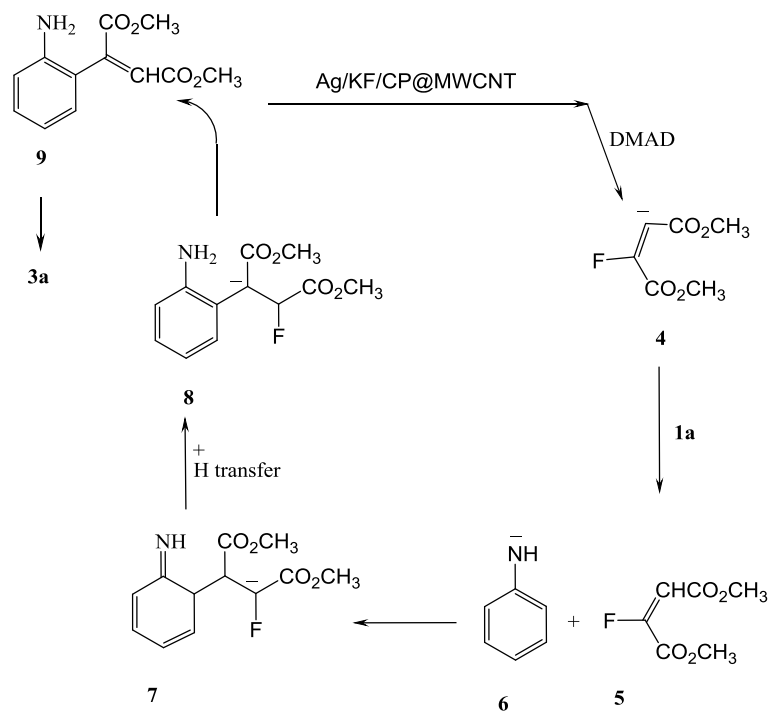


Table 1: Reaction of DMAD with primary amines in the presence of *N*-formylmorpholine.

Entry	Starting materials	Product	Yield (%)
1	 <p>1a</p>	 <p>3a</p>	93
2	 <p>1b</p>	 <p>3b</p>	94
3	 <p>1c</p>	 <p>3c</p>	90
4	 <p>1d</p>	 <p>3d</p>	85
5	 <p>1e</p>	 <p>3e</p>	86



Scheme 1: Proposed mechanism for formation of **3**

New synthesized organometallic catalyst promoted reduction of organic pollutant

Another subject addressed by the current research was to examine organometallic nanocatalyst effect on elimination of organic pollutant such as 4-nitrophenol. The effect of prepared Ag/KF/CP@MWCNT on reduction of 4-NP as high performance organometallic catalyst was studied in water at room temperature. The UV-Vis spectrum from the mixture of reaction at ambient temperature was relied on to confirm the dye reduction processes. The reduction of 4-NP did not occur in the absence of catalyst and NaBH₄ and did not display significant consideration. Therefore, the Ag/KF/CP@MWCNT needed for reduction of 4-NP to 4-aminophenol. The variation of reaction conditions was monitored by UV-Vis analysis exhibited in Figure 1. In UV-Vis spectrum, the peak at 317 nm was attributed to the absorption of 4-nitrophenol in water but when 4-nitrophenol was converted to 4-nitrophenolate ion, the peak at 317 nm shifted to 400 nm as a red shift. After adding the new prepared aqueous solution of NaBH₄, the color was altered from yellow to colorless. If Ag/KF/CP@MWCNT was not added in the solution, the peak seen at 400 nm was not altered even after 15 h confirming that reduction of 4-NP did not take place in the absence of catalyst

Ag/KF/CP@MWCNT with NaBH₄ and just opposite when the Ag/KF/CP@MWCNT was in 4-nitrophenol solution without NaBH₄, no considerable change in the color was seen. To eliminate organic pollutant, the prepared organometallic nanocatalyst and NaBH₄ were needed and in the presence of catalyst and reducing agent, the peak of absorbance at 400 nm reduced to about zero quickly within 5 min. A new peak was generated after reducing at 300 nm attributed to the formation of 4-aminophenol and was regularly enhanced by lightening the yellow colour of the reaction solution.

Furthermore, for reusability of synthesized catalyst, the external magnet was used and magnetic catalyst was completely separated from mixture of reaction without any variation in catalytic activity. This method for reduction of organic pollutant is advantageous and employing the organometallic bio-catalyst Ag/KF/CP@MWCNT is effective and ecologically positive and it is also an inexpensive process for the removal and photo decreasing of 4-NP.

Conclusion

In summary, the reaction between DMAD and anilines and Ag/KF/CP@MWCNT leads to amide derivatives in excellent yields. The presented one-pot

reaction carries the advantage that not only is the reaction performed under neutral conditions, but the substances can be mixed without any activation or modification.

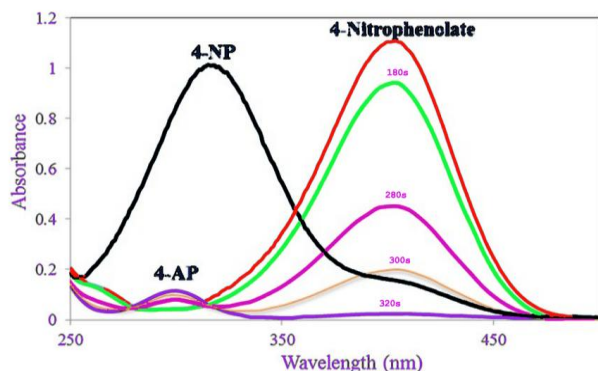


Figure 1. Reduction of the 4-NP to 4-AP by UV-Vis analysis

Experimental section

Typical procedure for the synthesis of 3a:

To a stirred solution of **1a** (0.19 g, 2 mmol) and DMAD (0.28 g, 2 mmol) in 10 mL water was added Ag/KF/CP@MWCNT (0.2 g) as catalyst at room temperature. The reaction mixture was then stirred for 3 h. The solvent was removed under reduced pressure and the residue was separated by silica gel column chromatography (Merck 230-400 mesh) using *n*-hexane-EtOAc (4:1) as eluent to give **3a**.

Compound 3a:

Yellow oil; yield 0.38 g, 93%. IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1735 and 1650 (C=O). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ = 3.72 (3 H, s, OMe), 6.65 (1 H, d, $^3J_{\text{HH}} = 7.9$ Hz, CH), 7.01 (1 H, s, CH), 7.23 (1 H, dd, $^3J_{\text{HH}} = 7.9$ Hz, $^3J_{\text{HH}} = 7.5$ Hz, CH), 7.31 (1 H, dd, $^3J_{\text{HH}} = 7.8$ Hz, $^3J_{\text{HH}} = 7.5$ Hz, CH), 7.48 (1 H, d, $^3J_{\text{HH}} = 7.8$ Hz, CH) ppm. $^{13}\text{C NMR}$ (125.7 MHz, CDCl_3): δ = 52.6 (OCH₃), 111.2 (CH), 122.1 (CH), 123.1 (CH), 123.5 (C), 124.3 (CH), 130.6 (CH), 138.2 (C), 153.5 (C), 165.3 (C=O), 166.5 (C=O) ppm. MS (EI, 70 eV): m/z (%) = 204 (M^+ , 12), 189 (17), 160 (47), 145 (73), 144 (36), 132 (100), 91 (14), 76 (68), 59 (42). Anal. Calcd for $\text{C}_{11}\text{H}_8\text{O}_4$ (204.2): C, 64.71; H, 3.95%. Found: C, 65.18; H, 3.99%.

Compound 3b:

Brown crystals, mp 176-178 °C, yield 0.48 g, 94%. IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1715 and 1616 (C=O). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ = 4.02 (3 H, s, OMe), 6.94 (1 H, s, CH), 7.59 (1 H, dd, $^3J_{\text{HH}} = 7.6$ Hz, $^3J_{\text{HH}} = 6.9$ Hz,

CH), 7.62 (1 H, dd, $^3J_{\text{HH}} = 7.6$ Hz, $^3J_{\text{HH}} = 5.1$ Hz, CH), 7.63 (1 H, d, $^3J_{\text{HH}} = 5.1$ Hz, CH), 7.81 (1 H, d, $^3J_{\text{HH}} = 6.3$ Hz, CH), 8.10 (1 H, d, $^3J_{\text{HH}} = 6.9$ Hz, CH), 8.46 (1 H, d, $^3J_{\text{HH}} = 6.3$ Hz, CH) ppm. $^{13}\text{C NMR}$ (125.7 MHz, CDCl_3): δ = 53.2 (OCH₃), 111.4 (CH), 118.2 (C), 121.7 (CH), 122.5 (CH), 122.9 (C), 124.5 (CH), 127.2 (CH), 127.6 (CH), 129.2 (CH), 134.8 (C), 143.2 (C), 151.7 (C-O), 159.9 (C=O), 164.5 (C=O) ppm. MS (EI, 70 eV): m/z (%) = 254 (M^+ , 5), 251 (22), 223 (100), 195 (38), 135 (56), 113 (84), 109 (54), 55 (78). Anal. Calcd for $\text{C}_{15}\text{H}_{10}\text{O}_4$ (254.2): C, 70.86; H, 3.96%. Found: C, 70.40; H, 3.81%.

Compound 3c:

Green powder, mp 113-115 °C, yield 0.46 g, 90%. IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1724 and 1620 (C=O). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ = 4.06 (3 H, s, OMe), 6.59 (1 H, s, CH), 7.46 (1 H, d, $^3J_{\text{HH}} = 8.1$ Hz, CH), 7.55 (1H, dd, $^3J_{\text{HH}} = 7.2$ Hz, $^3J_{\text{HH}} = 6.1$ Hz, CH), 7.64 (1 H, dd, $^3J_{\text{HH}} = 7.2$ Hz, $^3J_{\text{HH}} = 8.1$ Hz, CH), 7.77 (1 H, d, $^3J_{\text{HH}} = 8.4$ Hz, CH), 7.92 (1 H, d, $^3J_{\text{HH}} = 6.1$ Hz, CH), 8.02 (1 H, d, $^3J_{\text{HH}} = 8.4$ Hz, CH) ppm. $^{13}\text{C NMR}$ (125.7 MHz, CDCl_3): δ = 53.5 (OCH₃), 110.1 (CH), 115.5 (CH), 117.3 (CH), 123.3 (C), 126.1 (CH), 127.9 (CH), 128.1 (CH), 129.4 (C), 130.9 (C), 134.6 (CH), 145.9 (C), 154.9 (C), 159.5 (C=O), 167.8 (C=O) ppm. MS (EI, 70 eV): m/z (%) = 254 (M^+ , 10), 251 (45), 223 (100), 135 (50), 113 (84), 109 (65), 55 (75). Anal. Calcd for $\text{C}_{15}\text{H}_{10}\text{O}_4$ (254.2): C, 70.86; H, 3.96%. Found: C, 70.39; H, 3.82%.

Compound 3d:

Orange powder, mp 187-189 °C, yield 0.46 g, 85%. IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3435 (OH), 1712 and 1617 (C=O). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ = 3.89 (3 H, s, OMe), 6.67 (1 H, s, CH), 7.27 (1 H, d, $^4J_{\text{HH}} = 3.2$ Hz, CH), 7.29 (1 H, dd, $^3J_{\text{HH}} = 8.7$ Hz, $^4J_{\text{HH}} = 3.2$ Hz, CH), 7.50 (1 H, d, $^3J_{\text{HH}} = 8.5$ Hz, CH), 7.96 (1 H, d, $^3J_{\text{HH}} = 8.7$ Hz, CH), 8.45 (1 H, d, $^3J_{\text{HH}} = 8.5$ Hz, CH), 9.34 (1 H, s, OH). $^{13}\text{C NMR}$ (125.7 MHz, CDCl_3): δ = 52.6 (OCH₃), 111.3 (CH), 114.2 (C), 114.4 (CH), 120.5 (CH), 121.9 (C), 123.0 (CH), 124.7 (CH), 124.9 (CH), 124.9 (C), 134.9 (C), 139.7 (C), 151.7 (C), 159.9 (C=O), 164.4 (C=O). MS (EI, 70 eV): m/z (%) = 270 (M^+ , 20), 242 (100), 239 (26), 211 (78), 155 (100), 126 (42), 77 (26). Anal. Calcd for $\text{C}_{15}\text{H}_{10}\text{O}_5$ (270.2): C, 66.67; H, 3.73%. Found: C, 66.91; H, 3.65%.

Compound 3e:

Pale yellow crystals, mp 155-157 °C, yield 0.44 g, 86%. IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1714 and 1619 (C=O). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ = 3.91 (3 H, s, OMe), 7.2

(1 H, s, CH), 7.35 (1 H, d, $^3J_{\text{HH}} = 8.5$ Hz, CH), 7.45 (1 H, dd, $^3J_{\text{HH}} = 8.5$ Hz, $^3J_{\text{HH}} = 6.7$ Hz, CH), 7.50 (1 H, d, $^3J_{\text{HH}} = 7.2$ Hz, CH), 8.15 (1 H, d, $^3J_{\text{HH}} = 6.7$ Hz, CH), 8.78 (1 H, d, $^3J_{\text{HH}} = 7.2$ Hz, CH). ^{13}C NMR (125.7 MHz, CDCl_3): $\delta = 52.8$ (OCH₃), 112.7 (CH), 116.9 (C), 117.6 (CH), 122.1 (CH), 127.9 (C), 129.4 (C), 136.1 (CH), 137.95 (C), 148.2 (CH), 148.2 (CH), 150.4 (C), 159.5 (C=O), 164.4 (C=O) ppm. MS (EI, 70 eV): m/z (%) = 255 (M⁺, 5), 224 (100), 195 (45), 128 (65), 109 (54), 77 (24), 59 (78), 31 (52). Anal. Calcd for C₁₄H₉NO₄ (255.2): C, 65.88; H, 3.55%. Found: C, 65.50; H, 3.46%.

The Ag/KF/CP@MWCNT application in reduction of 4-NP :

For this purpose, the mixture of Ag/KF/CP@MWCNT (0.005 g) and 4-nitrophenol solution (25 mL, 2.5 mM) was stirred for 2 min at room temperature in the beaker and the newly produced NaBH₄ (25 mL, 0.25 M) was added to previous mixture as reducing agent, which could remove pollutants in the presence of catalyst. After adding the aqueous NaBH₄ to the first mixture, the solution color of varied from pale yellow to lemon-colored. The stirring of the mixture was continued until the mixture color became colorless. Next, for measuring the UV-Vis absorption, 1 mL of the solution was diluted to 25 mL at sure times. The concentration of 4-Nitrophenol varied between 200-700 nm at room temperature and it was checked by the UV-Vis absorption spectra. The main point in the catalyst is its reusability in the same reactions. To confirm this point, the catalyst was removed from the mixture of reaction and washed with ethanol and finally dried to be reused in the same reaction.

References

- [1] Domling, A. *Chem Rev* **2006**, *106*, 17.
- [2] Tietze, L. F.; Rackelmann, N. N. *Pure. Appl. Chem.* **2004**, *11*, 1967.
- [3] Domling, A.; Ugi, I. *Angew. Chem. Int. Ed.* **2000**, *39*, 3168.
- [4] Kolb, J.; Beck, B.; Almstetter, M.; Heck, S.; Herdtweck, E.; Domling, A. *Mol. Divers.* **2003**, *6*, 297.
- [5] Domling, A.; Ugi, I.; Werner, B. *Molecules* **2003**, *8*, 53.
- [6] Bon, R. S.; Vliet, B. V.; Sprenkels, N. E.; Schmitz, R. F.; Kanter, F. J. J.; Stevens, C. V.; Swart, M.; Bickelhaupt, F. M.; Groen, M. B.; Orru, R. V. *J. Org. Chem.* **2005**, *70*, 3542.
- [7] Banfi, L.; Basso, A.; Guanti, G.; Kielland, N.; Repeto, C.; Riva, R. *Ugi J. Org. Chem.* **2007**, *72*, 2151.
- [8] Galliford, C. V.; Scheidt, K. A. *J. Org. Chem.* **2007**, *72*, 1811.
- [9] Li, C. J.; Chan, T. H. *Comprehensive Organic Reactions in Aqueous Media*; John Wiley & Sons, **2007**.
- [10] Chanda, A.; Fokin, V. V. *Chem. Rev.* **2009**, *109*, 725.
- [11] Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159.
- [12] Grieco, P. A. *Synthesis* **1975**, 67.
- [13] Gammill, R. B.; Wilson, C. A.; Bryson, T. A. *Synthetic Commun.* **1975**, *5*, 245.
- [14] Newaz, S. S. *Aldrichemica Acta* **1977**, *10*, 64.
- [15] Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94.
- [16] Petraghani, N.; Ferraz, H. M. C.; Silva, G. V. J. *Synthesis* **1986**, 157.
- [17] Sarma, J.; Sharma, R. P. *Heterocycles* **1986**, *24*, 441.