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## Ultrasmall Monodisperse NiO Nanocrystals as a Heterogeneous Catalyst for the A<sup>3</sup>-Coupling Reaction Toward Propargylamines

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#### **Abstract**

Ultrasmall monodisperse NiO nanoparticles (7–9 nm) were synthesized through thermal decomposition of Ni-oley-lamine complexes. Various measurement techniques involving Fourier-transform infrared spectroscopy (FT-IR), diffuse reflectance UV-Vis spectroscopy (DRS), X-ray diffractometer (XRD), energy dispersive X-ray analysis (EDX), scanning electron microscopy (SEM), dynamic light scattering technique (DLS), and vibrating sample magnetometer (VSM) were employed to characterize the synthesized catalyst. Propargylamine derivatives were synthesized with aldehydes, terminal alkynes and primary amines through a one-pot A<sup>3</sup>-coupling reaction by using a 3 mol% amount of the NiO nanocrystals at 80 °C under solvent-free conditions with good to excellent yields. The structures of the products were confirmed by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy. The catalyst presents many advantages including being environmentally friendly, easy to recover, reusable, stable, and applicable to a wide variety of substrates, as well as having cost-effective preparation.

Keywords: Monodisperse, NiO nanocrystals, heterogeneous catalyst, A<sup>3</sup>-cupling, propargylamine

#### 1. Introduction

The expanding of environmentally benign, practical, economical and efficient synthetic procedures has been a major concern of many chemical researches. 1,2 Inasmuch as, one of the initial principles in green chemistry is to minimize the number of steps in chemical synthesis, being followed by some other rules, such as atom economy, elimination of hysteresis, eschewing the use of toxic or hazardous reagents and solvents.<sup>3,4</sup> Multicomponent reactions (MCRs) have been captivating academia and industry due to possessing a number of eminent conceptual and synthetic merits including sustainability, operational simplicity, cost-effectiveness, and high convergence which are all in accordance with green chemistry values.5 Among all known MCRs, acetylene-Mannich reaction is an intriguing approach to synthesize propargylamines whose structural motifs have been found in different natural products and have been utilized as precursors of various biologically active components comprising  $\beta$ -lactams, isosteres, peptides, allylamines and oxazoles.<sup>6,7</sup> Classical method of propargylamines synthesis involves the nucleophilic addition of a metal acetylide to C=N electrophiles by exploiting highly active organometallic compounds combining organolitium, organozinc or Grignard reagents.<sup>8-11</sup> Hence, this method is less appealing owning to harsh reaction conditions, high moisture sensitivity of functional groups, and operational complexity. 12 Thus the efforts have been devoted to synthesize these nitrogen-containing compounds through three component reaction condition with various modified catalysts. Transition metals as heterogeneous catalysts have garnered a lot of attention since the first type of these catalysts was applied by Li et al in 2002 when they had performed lots of work with copper and ruthenium. 13 Afterwards, miscellaneous transition metal catalysts including different metals such as Cu, Ag, Au, Fe, Ni, Ir, In, and Zn were developed for synthesis of propargylamines; however the main disadvantage of these catalyst being their aggregation. 14-21

Nanomaterials in the size range of 10–100 nm have attracted a lot of attention in the last few decades because

they show special physical and chemical properties compared to bulk materials. Accordingly, nanoparticles with a size of 3-10 nm also have unique properties and behavior different from nanoparticles with a larger size, which makes them to have a special function. The use of these ultrasmall (US) nanomaterials as catalysts in organic reactions is a new and effective approach in this field. 22,23 The nanoparticles properties capture them to become a connector between homogenous and heterogeneous catalytic systems.<sup>24,25</sup> Among all nanomaterials which have been investigated most of them involve copper, gold, silver, iron, and so on, while nickel nanoparticles studies are limited only to a few research papers, albeit this metal is cheaper than the others and requires mild reaction conditions for obtaining high yields. <sup>26-31</sup> All of the reported works using nickel as a catalyst have been limited to Ni(II) ion complexes such as NiCl<sub>2</sub>,<sup>32</sup> MNPs@BimNiCl<sub>2</sub>,<sup>33</sup> Ni-MOF,<sup>34</sup> and Ni<sup>II</sup>-IL/SiO<sub>2</sub>. 35 Also, nickel alongside copper as the metallic form has been used in such cases as Cu-Ni bimetallic<sup>36</sup> and Ni-Cu-Fe trimetallic nanoparticles.<sup>37</sup> In this study, propargylamines will be synthesized for the first time by utilizing ultrasmall monodisperse NiO nanocrystals as a heterogeneous catalyst. The monodisperse nanoparticles of NiO with particle size about 6 nm were synthesized using reported procedure by Hyeon and coworkers published in 2004.38 Different aldehydes and amines will be applied to generalize the research. Herein, the questions posed with this research are that whether the catalyst is appropriate to synthesize different propoargylamine compounds or does the catalyst possesse high efficiency, stability, reusability and fulfils the other criteria which are important for a truly efficient catalyst.

### 2. Experimental Section

#### 2. 1. Materials and Instrumentations

Nickel di(acetylacetonate) [Ni(acac)<sub>2</sub>], oleylamine, triphenylphosphine (TPP), diphenyl ether (DE), and all other commercially available chemicals were purchased from Merck Chemical Company and were of high purity. The applied solvents were purified by standard procedures. Melting points were measured by a Yanagimoto Micro Melting Point apparatus in open capillary tubes. Fourier transform infrared (FT-IR) spectra were obtained (in KBr) by Nicolet FT-IR spectrophotometer. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Bruker DRX-400 spectrometer with CDCl<sub>3</sub> as the solvent at 25 °C and chemical shifts are given in ppm relative to Me<sub>4</sub>Si. The mass spectra were recorded on a Shimadzu QP 1100-Ex mass spectrometer by direct inlet at 70 eV, and signals are given as m/z with relative intensity (%) in brackets. The XRD patterns were obtained by an X'PertPro (Philips) instrument with 1.54 Å wavelength of the X-ray beam and Cu anode material. Microscopic morphology of the nanoparticles was visualized by SEM (MIRA 3 TESCAN). Energy-dispersive X-ray

spectroscopy (EDX) of the nanoparticles was imaged by a Sigma ZEISS, Oxford Instruments Field Emission. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silicagel polygram SILG/UV 254 plates (from Merck Company).

#### 2. 2. Synthesis of NiO Nanoparticles

The synthesis protocol for preparation of ultrasmall NiO nanoparticles is a modified method which was developed by Taeghwan and co-workers and employs the thermal decomposition of metal-surfactant complexes.<sup>24,39</sup> Initially, Ni(acac)<sub>2</sub> (0.32 g) and oleylamine (1.5 mL) were mixed under N2 atmosphere at 100 °C. Afterwards, the freshly prepared Ni-oleylamine complex was added to a round-bottom flask containing a solution of TPP (1.8 g) in DE (2.5 mL) at 200 °C. After elapsing a short time the solution color changed from dark green to black due to the formation of colloidal Ni nanoparticles. The resultant solution was kept in 280 °C for 1 h and then the temperature was decreased to the ambient temperature. Thereafter, pure ethanol (200 mL) was added to the reaction chamber which caused Ni nanoparticles precipitation. In the following, the precipitate was centrifuged and washed with ethanol (3×50 mL) and then exposed to dry air for 24 h to form NiO nanoparticles and the resultant product was kept at 60 °C.

# 2. 3. Synthesis of Propargylamine Derivatives by NiO Nanoparticles Catalyst

All of the reactions were carried out at 80 °C in a 25 mL one-capped round-bottom flask equipped with a magnetic stirring bar in a paraffin bath. Generally, a mixture of the selected aldehyde (1.0 mmol), secondary amine (1.1 mmol) and alkyne (1.2 mmol) was added in the flask along with the catalytic amount of the NiO nanocrystals (3 mol %, 2.3 mg) as the catalyst. The reaction progress was examined by TLC, and after the completion of the reaction absolute ethanol (10 mL) was added and the resulting mixture was centrifuged. The catalyst was separated from the reaction mixture by centrifugation and washed with CH<sub>2</sub>Cl<sub>2</sub> (3×5 mL) and methanol (3×5 mL) for recycling to be reused in the next run. The product was purified over silica gel by column chromatography (10% EtOAc in hexane) to give the desired propargylamines. All of the products are known compounds and have been reported already.

**4-(1,3-Diphenylprop-2-yn-1-yl)morpholine (4a).** Yield: 0.258 g (93%); light red oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.67–2.68 (m, 4H, 10-CH<sub>2</sub>, 14-CH<sub>2</sub>), 3.77–3.80 (m, 4H, 11-CH<sub>2</sub>, 13-CH<sub>2</sub>), 4.84 (s, 1H, 7-CH), 7.33–7.44 (m, 6H,

ArH), 7.56–7.58 (m, 2H, ArH), 7.68–7.70 (m, 2H, ArH);  $^{13}$ C NMR (CDCl<sub>3</sub>): δ 50.35 (C7), 57.21 (C10, C14), 68.54 (C11, C13), 84.08 (C8), 88.49 (C15), 115.17 (C16), 116.31 (C19), 121.96 (C21, C17), 123.67 (C2), 124.82 (C18, C20), 126.16 (C1, C3), 130.43 (C4), 131.87 (C6), 136.54 (C5); FT-IR (KBr disk): v cm<sup>-1</sup> 3059, 3014, 2984, 2957, 2950, 1598, 1489, 1449, 1318, 1280. MS m/z (%) 277 (M<sup>+</sup>, 32), 246 (11), 191 (100), 189 (45), 165 (16), 86 (25), 77 (31), 56 (27).

**4-(3-Phenyl-1-(para-tolyl) prop-2-yn-1-yl)morpholine** (**4b).** Yield: 0.268 g (92%); light orange oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.39 (s, 3H, Me), 2.65–2.67 (m, 4H, 10-CH<sub>2</sub>, 14-CH<sub>2</sub>), 3.75–3.76 (m, 4H, 11-CH<sub>2</sub>, 13-CH<sub>2</sub>), 4.78

(s, 1H, 7-CH), 7.20–7.22 (m, 2H, ArH), 7.34–7.36 (m, 3H, ArH), 7.53–7.55 (m, 4H, ArH);  $^{13}$ C NMR (CDCl<sub>3</sub>):  $\delta$  22.08 (C22), 49.14 (C7), 58.36 (C10, C14), 67.15 (C11, C13), 83.65 (C8), 87.91 (C15), 114.25 (C16), 117.55 (C19), 120.74 (C21, C17), 120.95 (C2), 122.33 (C18, C20), 123.85 (C1, C3), 126.80 (C4), 128.03 (C6), 132.17 (C5); FT-IR (KBr disk): v cm<sup>-1</sup> 3024, 2946, 2925, 2862, 2820, 2230, 1486, 1446, 1314, 1109. MS m/z (%) 291 (M<sup>+</sup>, 37), 260 (22), 205 (100), 77 (42), 56 (28).

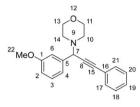
**4-(1-(4-Nitrophenyl)-3-phenylprop-2-yn-1-yl)morpholine (4c).** Yield: 0.306 g (95%); yellowish oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.63–2.66 (m, 4H, 10-CH<sub>2</sub>, 14-CH<sub>2</sub>), 3.75–3.76 (m, 4H, 11-CH<sub>2</sub>, 13-CH<sub>2</sub>), 4.89 (s, 1H,

7-CH), 7.38–7.39 (m, 3H, ArH), 7.53–7.55 (m, 2H, ArH), 7.87 (d, J = 8.1 Hz, 2H, ArH), 8.24 (d, J = 8.1 Hz, 2H, ArH);  $^{13}$ C NMR (CDCl<sub>3</sub>):  $\delta$  49.90 (C7), 61.45 (C10, C14), 67.04 (C11, C13), 83.16 (C8), 89.78 (C15), 122.31 (C16), 123.48 (C19), 128.45 (C21, C17), 128.72 (C2), 129.33 (C18, C20), 131.85 (C4, C6), 135.48 (C3, C1), 145.45 (C5), 149.23 (C2); FT-IR (KBr disk):  $\nu$  cm<sup>-1</sup> 3067, 2958, 2854, 2216, 1690, 1522, 1450, 1347, 1275, 1113, 1006. MS m/z (%) 322 (M<sup>+</sup>, 10), 236 (41), 200 (57), 190 (37), 86 (18), 77 (30), 56 (100).

*N*,*N*-Dimethyl-4-(1-morpholino-3-phenylprop-2-yn-1-yl) aniline (4d). Yield: 0.282 g (88%); yellowish oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.62–2.66 (m, 4H, 19 10-CH<sub>2</sub>, 14-CH<sub>2</sub>), 2.97 (s, 6H, NMe<sub>2</sub>), 3.73–3.74 (m, 4H, 11-

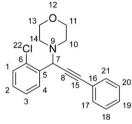
CH<sub>2</sub>, 13-CH<sub>2</sub>), 4.70 (s, 1H, 7-CH), 6.73 (d, J = 8.0 Hz, 2H, ArH), 7.32–7.33 (m, 3H, ArH), 7.45–7.51 (m, 4H, ArH); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  44.11 (C23), 49.25 (C24), 61.70 (C10, C14), 67.03 (C11, C13), 84.15 (C8), 87.54 (C15), 113.85

(C1, C3), 118.80 (C16), 120.41 (C19), 123.74 (C21, C17), 130.40 (C18, C20), 131.21 (C4), 134.38 (C6), 148.01 (C2), 149.21 (C5); FT-IR (KBr disk): v cm<sup>-1</sup> 3084, 2955, 2892, 2854, 1965, 1611, 1521, 1150. MS *m/z* (%) 320 (M<sup>+</sup>, 40), 215 (100), 276 (62), 234 (12), 219 (27), 101 (17), 86 (20), 56 (65).



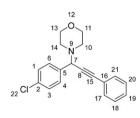
**4-(1-(3-Methoxyphenyl)-3-phenylprop-2-yn-1-yl)mor-pholine (4e).** Yield: 0.280 g (91%); yellowish oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.66–2.67 (m, 4H, 10-CH<sub>2</sub>, 14-CH<sub>2</sub>), 3.77–3.79 (m, 4H, 11-CH<sub>2</sub>, 13-CH<sub>2</sub>), 3.86 (s,

3H, OCH<sub>3</sub>), 4.79 (s, 1H, 7-CH), 6.86 (s, 1H, 6-CH), 7.25–7.36 (m, 6H, ArH), 7.53–7.54 (m, 2H, ArH); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 49.99 (C7), 55.24 (C22), 62.01 (C10, C14), 67.20 (C11, C13), 85.15 (C8), 88.54 (C15), 113.10 (C2), 114.39 (C6), 120.99 (C4), 123.03 (C16), 128.36 (C21), 128.42 (C17), 129.28 (C18, C20), 131.88 (C19), 132.17 (C3), 139.57 (C5), 159.71 (C1); FT-IR (KBr disk): ν cm<sup>-1</sup> 3057, 2995, 2851, 1965, 1599, 1486, 1449, 1317, 1150, 1048. MS *m/z* (%) 307 (M<sup>+</sup>, 14), 221 (38), 178 (20), 135 (32), 87 (100), 77 (55), 43 (85).



4-(1-(2-Chlorophenyl)-3-phenylprop-2-yn-1-yl)morpholine (4f). Yield: 0.290 g (93%); yellow oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.67–2.70 (m, 4H, 10-CH<sub>2</sub>, 14-CH<sub>2</sub>), <sup>20</sup> 3.67–3.77 (m, 4H, 11-CH<sub>2</sub>, 13-CH<sub>2</sub>), 5.14 (s, 1H, 7-CH), 7.25–7.29 (m, 2H, 2-CH, 4-CH), 7.33–7.35 (m, 3H, 18-CH, 19-CH,

20-CH), 7.41–7.43 (m, 1H, 3-CH), 7.50–7.52 (m, 2H, 17-CH, 21-CH), 7.75–7.77 (m, 1H, 1-CH);  $^{13}$ C NMR (CDCl<sub>3</sub>):  $\delta$  49.87 (C7), 58.96 (C10, C14), 67.14 (C11, C13), 84.70 (C8), 88.40 (C15), 122.82 (C16), 125.58 (C3), 126.39 (C18, C20), 128.38 (C21), 128.41 (C17), 129.18 (C19), 130.58 (C2), 130.93 (C1), 131.85 (C4), 134.69 (C6), 135.56 (C5); FT-IR (KBr disk): v cm<sup>-1</sup> 3047, 2997, 2897, 2750, 1562, 1472, 1452, 1324, 1274, 1117, 1055. MS m/z (%) 313 (M+2+, 8), 311 (M+, 23), 280 (14), 225 (100), 189 (57), 86 (84), 56 (61).



**4-(1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-yl)morpholine** (**4g**). Yield: 0.293 g (94%); yellow oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.61–2.62 (m, 4H, 10-CH<sub>2</sub>, 14-CH<sub>2</sub>), 3.73–3.75 (m, 4H, 11-CH<sub>2</sub>, 13-CH<sub>2</sub>), 4.77 (s, 1H, 7-CH), 7.36–7.37 (m, 5H, ArH), 7.51–7.52

(m, 2H, ArH), 7.58–7.60 (m, 2H, ArH); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 49.85 (C7), 61.40 (C10, C14), 67.15 (C11, C13), 84.43 (C8), 88.98 (C15), 122.77 (C16), 128.43 (C1, C3), 128.48

(C18, C20), 129.70 (C19), 129.94 (C17, C21), 131.88 (C4, C6), 133.61 (C2), 136.53 (C5); FT-IR (KBr disk): v cm<sup>-1</sup> 3070, 3029, 2957, 2857, 1494, 1454, 1428, 1113, 1075, 1034. MS m/z (%) 313 (M+2+, 11), 311 (M+, 35), 280 (8), 225 (100), 189 (19), 135 (40), 86 (22), 77 (24), 56 (47).

**4-(1-(3-Nitrophenyl)-3-phenylprop-2-yn-1-yl)morpholine (4h).** Yield: 0.293 g (91%); light yellow oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.63–2.69 (m, 4H, 10-CH<sub>2</sub>, 14-CH<sub>2</sub>), 3.76–3.78 (m, 4H, 11-CH<sub>2</sub>, 13-CH<sub>2</sub>), 4.90

(s, 1H, 7-CH), 7.34–7.38 (m, 3H, ArH), 7.54–7.62 (m, 3H, ArH), 8.02 (d, J = 7.6 Hz, 1H, 2-CH), 8.18 (d, J = 7.7 Hz, 1H, 4-CH), 8.56 (s, 1H, 6-CH);  $^{13}$ C NMR (CDCl<sub>3</sub>):  $\delta$  49.78 (C7), 61.24 (C10, C14), 66.95 (C11, C13), 83.17 (C8), 89.76 (C15), 122.36 (C16), 122.85 (C21, C17), 123.41 (C18, C20), 128.39 (C19), 128.71 (C6), 129.15 (C2), 131.83 (C3), 134.48 (C4), 140.36 (C5), 148.39 (C1); FT-IR (KBr disk):  $\nu$  cm<sup>-1</sup> 3085, 3028, 3002, 2986, 2882, 1506, 1473, 1419, 1263, 1208, 1168, 1121, 1045, 1014. MS m/z (%) 322 (M<sup>+</sup>, 16), 236 (30), 200 (41), 190 (24), 86 (100), 56 (67).

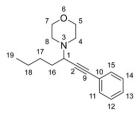
**4-(1-(Furan-2-yl)-3-phenyl-prop-2-yn-1-yl) morpholine (4i).** Yield: 0.235 g (88%); yellowish white oil;  $^{1}$ H NMR (CDCl<sub>3</sub>):  $\delta$  2.63–2.72 (m, 4H, 5-CH<sub>2</sub>, 9-CH<sub>2</sub>), 3.74–3.83 (m, 4H, 6-CH<sub>2</sub>, 8-CH<sub>2</sub>), 4.89 (s, 1H, 2-CH), 6.37 (t, J = 3 Hz, 1H, 18-CH), 6.52 (d, J = 2.8 Hz, 1H, 17-

CH), 7.31–7.35 (m, 3H, ArH), 7.45–7.52 (m, 3H, ArH);  $^{13}$ C NMR (CDCl<sub>3</sub>):  $\delta$  49.61 (C2), 56.12 (C5, C9), 66.95 (C6, C8), 82.85 (C3), 87.02 (C10), 109.76 (C17), 110.13 (C18), 122.57 (C11), 128.35 (C13, C15), 128.50 (C12, C16), 131.87 (C14), 142.87 (C19), 150.76 (C1); FT-IR (KBr disk): v cm<sup>-1</sup> 3063, 3028, 2932, 1604, 1495, 1453, 1261, 1152, 1028. MS m/z (%) 267 (M<sup>+</sup>, 11), 239 (18), 221 (17), 181 (100), 152 (34), 115 (9), 86 (25), 77 (47), 56 (28).

**4-(3-Phenyl-1-(thiophen-2-yl) prop-2-yn-1-yl)morpholine (4j).** Yield: 0.244 g (86%); white oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.66–2.74 (m, 4H, 5-CH<sub>2</sub>, 9-CH<sub>2</sub>), 3.73–3.82 (m, 4H, 6-CH<sub>2</sub>, 8-CH<sub>2</sub>), 5.01 (s, 1H, 2-CH), 6.97–6.99 (m, 1H, 18-CH), 7.25–

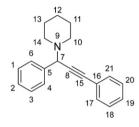
7.27 (m, 1H, 17-CH), 7.30–7.31 (m, 1H, 19-CH), 7.34–7.36 (m, 3H, ArH), 7.51–7.54 (m, 2H, ArH);  $^{13}$ C NMR (CDCl<sub>3</sub>):  $\delta$  49.69 (C2), 57.83 (C5, C9), 67.15 (C6, C8), 84.29 (C3), 87.63 (C10), 122.69 (C11), 125.57 (C18), 125.87 (C17), 126.36 (C16), 126.44 (C12), 128.39 (C13), 128.48 (C15), 128.84 (C14), 131.89 (C19), 142.80 (C1);

FT-IR (KBr disk): v cm<sup>-1</sup> 3062, 3028, 2955, 2934, 2248, 1607, 1490, 1454, 1125, 1109, 1065, 1016. MS *m/z* (%) 283 (M<sup>+</sup>, 9), 197 (100), 86 (62), 83 (20), 77 (35), 56 (27).



**4-(1-Phenylhept-1-yn-3-yl) morpholine** (**4k**). Yield: 0.221 g (86%); white oil;  $^{1}$ H NMR (CDCl<sub>3</sub>): δ 1.02 (t, J = 7.0 Hz, 3H, 19-CH<sub>3</sub>), 1.38–1.39 (m, 4H, 17-CH<sub>2</sub>, 18-CH<sub>2</sub>), 1.60–1.62 (m, 2H, 16-CH<sub>2</sub>), 2.95–2.96 (m, 4H, 4-CH<sub>2</sub>, 8-CH<sub>2</sub>), 3.63–3.68

(m, 4H, 5-CH<sub>2</sub>, 7-CH<sub>2</sub>), 3.81–3.82 (m, 1H, 1-CH), 7.45–7.48 (m, 3H, ArH), 7.69–7.72 (m, 2H, ArH);  $^{13}$ C NMR (CDCl<sub>3</sub>):  $\delta$  14.21 (C19), 21.70 (C18), 25.24 (C17), 34.47 (C16), 54.14 (C1), 57.30 (C4, C8), 67.79 (C5, C7), 87.45 (C2), 88.21 (C9), 123.64 (C10), 126.87 (C15, C11), 128.45 (C13), 129.70 (C12, C14); FT-IR (KBr disk): v cm<sup>-1</sup> 3035, 3020, 2964, 2874, 2234, 1568, 1479, 1439, 1328, 1263, 1184, 1120, 1064. MS m/z (%) 257 (M<sup>+</sup>, 19), 242 (8), 200 (100), 184 (22), 128 (35), 115 (18), 77 (42), 56 (26).



1-(1,3-Diphenylprop-2-yn-1-yl)piperidine (4l). Yield: 0.255 g (93%); red oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.45–1.58 (m, 6H, 11-CH<sub>2</sub>, 12-CH<sub>2</sub>, 13-CH<sub>2</sub>), 2.38–2.41 (m, 4H, 10-CH<sub>2</sub>, 14-CH<sub>2</sub>), 4.94 (s, 1H, 7-CH), 7.33–7.94 (m, 10H, ArH); <sup>13</sup>C NMR

(CDCl<sub>3</sub>):  $\delta$  24.15 (C12), 26.07 (C11, C13), 52.47 (C7), 56.11 (C10, C14), 82.18 (C15), 87.19 (C8), 121.10 (C16), 126.01 (C19), 126.86 (C21, C17), 127.24 (C2), 127.60 (C18, C20), 128.74 (C1, C3), 129.03 (C4), 129.17 (C6), 138.41 (C5); FT-IR (KBr disk): v cm<sup>-1</sup> 3084, 3020, 2994, 2967, 1452, 1408, 1349, 1319, 1300. MS m/z (%) 275 (M<sup>+</sup>, 15), 232 (7), 192 (14), 191 (100), 189 (50), 165 (18), 115 (24), 84 (37), 77 (30).

#### 3. Results and Discussion

# 3.1. Characterization of the NiO Nanoparticles Catalyst

The properties, structure, size and size distribution of the synthesized NiO nanoparticles were measured by various techniques including FT-IR spectroscopy, TEM, SEM, DLS, DRS, XRD, EDX and VSM analysis. As shown in Figure 1 the FT-IR spectra of the catalyst delineates an absorption band at 443 cm<sup>-1</sup> which is related to the vibration band of Ni–O stretching bond. As can be seen, no other peaks are observable in the spectra which confirms that the catalyst is without any impurity or any organic residues which would likely arise from organic components that consumed during the preparation process of nanoparticle.

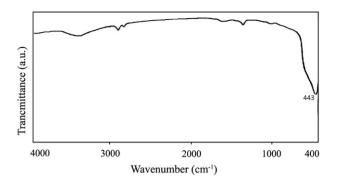


Figure 1. The FT-IR spectrum of the NiO nanoparticles

To observe the purity phase and local geometry of the crystalline scaffold of the synthesized NiO nanoparticles, X-ray diffraction analysis was carried out. As can be observed, the whole Ni nanoparticles are oxidized to the NiO nanoparticles without showing any impurities and all the peaks are in good agreement with the cubic structure of the catalyst according to the library patterns (JCPDS No. 71-1179). The estimated size of nanoparticles by Debye–Scherrer equation was measured to be around 8.4 nm (Figure 2).

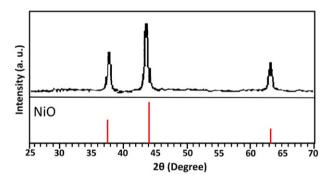


Figure 2. The XRD pattern of the NiO nanoparticles

To determine the size, size distribution, and morphology employing various measurement techniques is required due to basic differences in each represented method [39]. The SEM analysis of the synthesized catalyst exhibits that the size of the NiO nanocrystal is around 7–9 nm which confirms the XRD results (Figure 3a). The SEM image of the NiO ultrasmall nanoparticles was also determined. As can be seen, the NiO nanoparticles are spherical and possess high uniformity (Figure 3).

In accordance with the SEM image of the NiO nanoparticles, the particle size distribution histogram was provided by DLS technique and is shown in Figure 4, the dispersion nanoparticles size are not scattered and the mean value and standard deviation could be estimated to be  $7.9 \pm 1$  nm according to the provided size distribution histogram.

The single point BET analysis was used to determine the specific surface area of the NiO nanoparticles. The sur-

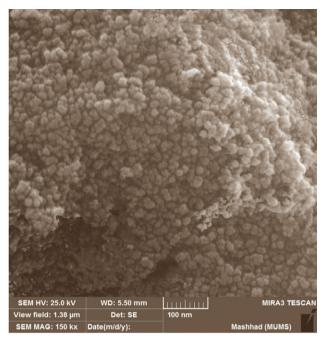
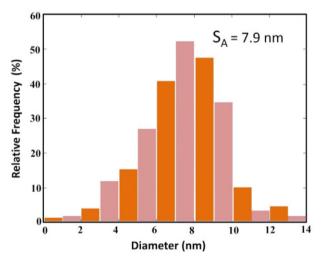


Figure 3. The SEM image of the NiO nanocrystals



**Figure 4.** Histogram showing the particle size and size distribution of US-NiO nanocrystals

face area of nanoparticles was found to be 33.7 m²/g and a mean particle size of 8.7 nm was calculated from the  $d_{\rm BET}$  = 6000/ $\tilde{n}S$  equation (S is specific surface area in m²/g, d is the diameter in nanometer, and  $\tilde{n}$  is the theoretical density in g/cm³). This value is close to that obtained by SEM and XRD image and indicates that the powder consists of mono-dispersed solid crystals; also agglomeration and heaping of nanoparticles does not happen.

The EDX micrograph was also provided to prove the existence of nickel elements in the prepared nanoparticles (Figure 5). According to the graph, no other peaks in the spectrum from elements except Ni were observed thus confirming that the NiO nanoparticles are pure.

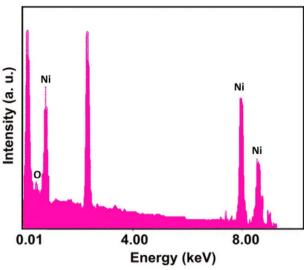


Figure 5. The energy dispersive X-ray analyzer of the NiO nanoparticles

The UV-Vis diffuse reflectance spectroscopy (DRS) measurement which is dispersed in ethanol was performed to achieve the optical property and consequently crystallinity of the nanoparticles (Figure 6). A strong absorption band has been observed in UV gamut (360 nm) which is attributed to the nanoparticles absorption in ratio of their crack bonds' absorption.

#### 3.2. Reaction Optimization

The prepared ultrasmall nanocrystals of NiO were used as a catalyst in the A<sup>3</sup>-coupling reaction of aromatic and aliphatic aldehydes, secondary amines, and phenylacetylene as the terminal alkyne (Scheme 1).

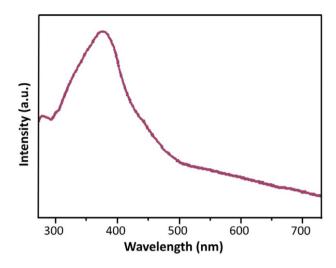
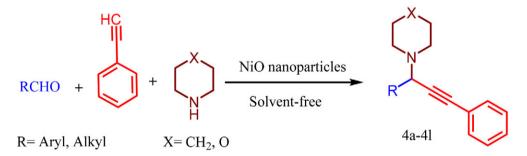


Figure 6. UV-Vis DRS of the US-NiO nanoparticles

ic and aprotic solvents including toluene, DMF, DMSO, THF, CH<sub>2</sub>Cl<sub>2</sub>, MeCN, H<sub>2</sub>O, and MeOH under different temperatures, also reflux condition were investigated. It is obvious that the application of aprotic solvents with various conditions gave favorable results. Hence, utilizing protic solvents was not encouraged. According to the outputs, when dicholoromethane was employed (entry 10) propitious yield was obtained while using MeOH as a protic solvent represented good yield (entry 8). The highest yield was achieved under solvent-free conditions at 80 °C (bath of paraffin) with the shortest reaction time (entry 12).

According to Table 1, entries 11–14, temperature optimization for the solvent-free conditions was in demand. The best result for solvent-free temperature optimization



**Scheme 1.** General procedure of the  $A^3$ -coupling reaction

In continuation of our research, our first efforts were devoted to optimize reaction conditions. Therefore, the optimization was examined for solvent, temperature and catalyst. To put the purpose in action, the reaction among benzaldehyde (1 mmol), morpholine (1.1 mmol) and phenylacetylene (1.2 mmol) was selected as the model reaction carried out in the presence of the synthesized NiO nanoparticles as a reusable and heterogeneous catalyst. As depicted in Table 1, for solvent optimization, various prot-

was obtained at 80 °C (entries 11–14) which is evidence that further increase or decreases in the temperature did not lead to any distinguishable alteration.

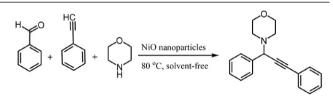
The amount of catalyst is a crucial player factor in the yield of the reaction. A glance at Table 2 reveals that in the absence of the catalyst (entry 1) merely a negligible amount of product was obtained, this result demonstrating that using the catalyst is an obligatory factor for the progression of the reaction. Additionally, the best result was achieved

**Table 1.** The effects of various solvents and temperature on model reaction using NiO nanoparticles catalyst<sup>a</sup>

Entry	Solvent	Temperature [°C]	Time [h]	Yield <sup>b</sup> [%]
1	MeCN	Reflux	10	54
2	DMF	100	10	52
3	DMSO	100	10	65
4	Toluene	Reflux	10	69
5	$H_2O$	Reflux	10	18
6	$H_2O$	90	10	12
7	MeOH	Reflux	10	28
8	MeOH	40	10	20
9	THF	Reflux	10	38
10	$CH_2Cl_2$	38	6	44
11	Solvent-free	r.t.	10	54
12	Solvent-free	80	3	96
13	Solvent-free	60	5	80
14	Solvent-free	100	3	95

 $<sup>^{\</sup>rm a}$  Reaction conditions: benzaldehyde (1.0 mmol), phenylacetylene (1.2 mmol), morpholine (1.1 mmol), NiO nanoparticles (0.03 mmol, 2.3 mg).  $^{\rm b}$  Based on isolated yields.  $^{\rm c}$  The bold entry 12 represents the best conditions.

**Table 2.** Optimization of the catalyst amount of NiO nanoparticles on model reaction<sup>a</sup>



Entry	mass [mg] NiO	Time [h]	Yield <sup>b</sup> [%]
1	0 (0 mol %)	24	trace
2	0.7 (1 mol %)	8	48
3 <sup>c</sup>	2.3 (3 mol %)	3	96
4	3.7 (5 mol %)	3	96
5	7.5 (10 mol %)	3	96

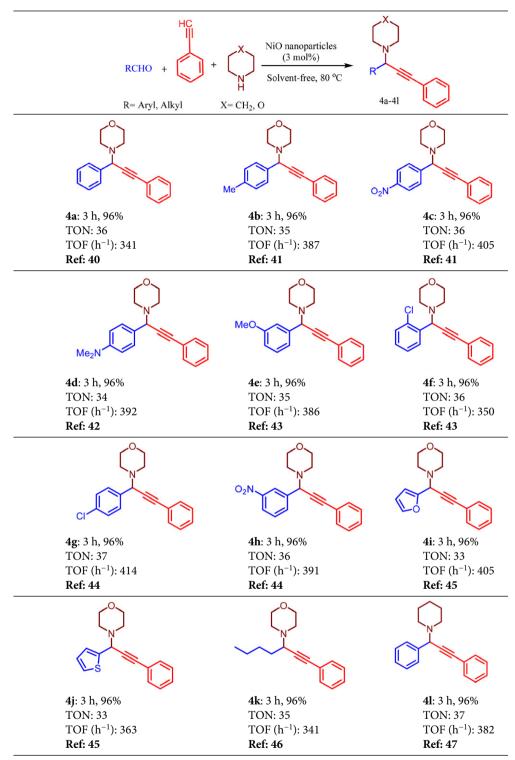
 $<sup>^{\</sup>rm a}$  Reaction condition: benzaldehyde (1.0 mmol), phenylacetylene (1.2 mmol), morpholine (1.1 mmol).  $^{\rm b}$  Based on isolated yields.  $^{\rm c}$  The bold entry 3 represents the best conditions.

when 2.3 mg of the catalyst were loaded into the reaction vessel (entry 3). It was observed that further increase of the catalyst amount did not affect the reaction yield.

After optimization of the reaction conditions, the next step of our study was based on determining the scope and limitation of the current protocol with the ultrasmall NiO nanoparticles as heterogeneous catalyst. Therefore, a number of different propargylamines were synthesized with applying various initial moieties including disparate aldehydes possessing electron withdrawing and electron

donating functional groups, along with morpholine and pyridine as the secondary amines, also phenylacetylene as a fixed part of the reaction. The information regarding synthesized propargylamines is summarized in Table 3. Apparently, the reactions were accomplished successfully with good to high yields and in a short reaction time for all the prepared products. Furthermore, it is highly important to point out that the desired products involving benzaldehyde derivatives with an electron-withdrawing group were obtained in excellent yields (4c, 4g and 4h), whereas ben-

Table 3. NiO nanoparticles catalyzed three-component synthesis of propargylamines<sup>a</sup>



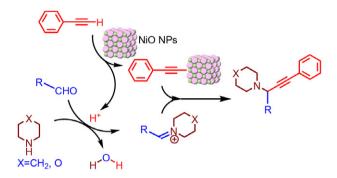
<sup>&</sup>lt;sup>a</sup> Reaction conditions: aldehyde (1.0 mmol), phenylacetylene (1.20 mmol), secondary amine (1.1 mmol), NiO nanoparticles as catalyst (2.3 mg) under solvent-free conditions at 80 °C. <sup>b</sup> Based on isolated yields.

zaldehyde having an electron-donating group gave the products in lower yields (4b and 4d).

The proposed reaction mechanism for the catalytic reaction in the presence of US-NiO nanoparticles is shown

in Scheme 2. The first step is the C–H activation of the alkyne moiety *via* adsorption on the surface of the catalyst and producing alkynyl–[NiO] complex. Then, the aromatic or aliphatic aldehydes are activated by the catalyst

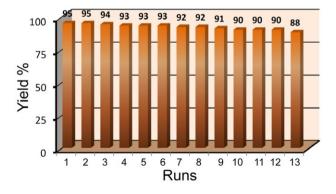
through van der Waals interactions between ion pair of the oxygen atom from the carbonyl and the Ni atom of the catalyst. Nucleophilic attack of the alkynyl–[NiO] complex upon iminium ion formed from the reaction of aldehyde and amine produces the desired propargylamine and releases the NiO catalyst for the next catalytic cycle.



**Scheme 2.** Proposed reaction mechanism for the catalytic reaction

We also investigated the catalyst leaching study in this method. After the reaction was run, in half of the time of the reaction completion, the NiO catalyst was separated by centrifuge from the reaction media and the solution phase was subjected without any fresh catalyst added under the same reaction conditions. The reaction was monitored after 8 h and thus it was shown that there was no further conversion of substrates to desired propargylamine. This means that any solid nanoparticles or active metal leached from solid nanocatalyst remain in the filtrate.

In green chemistry, an essential matter to express environmentally friendly methods is recovery and reusability of the catalyst. Hence, after reaction completion, the NiO nanocatalyst was separated by centrifuge method. The recovered catalyst was thoroughly washed with  $\rm CH_2Cl_2$  (3×5 mL) and dried at 80 °C for 10 h, and then it was used for consecutive reaction without adding any fresh catalyst. As can be seen in Figure 7, the results show that NiO nano-



 $\label{eq:Figure 7.} \textbf{Figure 7.} \ \textbf{Reusability of ultrasmall NiO nanoparticles in the synthesis of compound \textbf{4a}.$ 

particles can be used at least for 12 sequential runs without important changes in their catalytic activity.

#### 4. Conclusion

To recapitulate, in this paper NiO nanoparticles were used for the first time as a green and efficient heterogeneous catalyst for successful preparation of propargylamines through A<sup>3</sup>-coupling reaction under solvent-free conditions at 80 °C. Ease of preparation, reusability, facile workup, high activity, stability, applicability to a wide variety of substrates, and being cheap are the advantages of this catalyst. The catalyst can be applied for seven successful runs of propargylamines preparation with high yields. Thereafter the aforementioned questions which were addressed by this papers were answered properly.

#### Acknowledgments

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#### **Conflict of Interest**

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

#### 5. References

- 1. C. Wei, Z. Li, C.-J. Li, *Org. Lett.* **2003**, *5*, 4473–4475. **DOI**:10.1021/ol035781y
- W.-W. Chen, R. V. Nguyen, C.-J. Li, *Tetrahedron Lett.* 2009, 50, 2895–2898. DOI:10.1016/j.tetlet.2009.03.182
- 3. M. K. Patil, M. Keller, B.M. Reddy, P. Pale, J. Sommer, *Eur. J. Org. Chem.* **2008**, 4440–4445. **DOI:**10.1002/ejoc.200800359
- M. J. Aliaga, D. J. Ramon, M. Yus, Org. Biomol. Chem. 2010, 8, 43–46. DOI:10.1039/B917923B
- J.-N. Mo, J. Su, J. Zhao, Molecules 2019, 24, 1216–1225.
   DOI:10.3390/molecules24071216
- Z. Xu, H. Wu, H. Li, Z. Du, Y. Fu, ChemistrySelect 2018, 3, 13629–13631. DOI:10.1002/slct.201803313
- E. Ramu, R. Varala, N. Sreelatha, S.R. Adapa, *Tetrahedron Lett.* 2007, 48, 7184–7190. DOI:10.1016/j.tetlet.2007.07.196
- 8. H.-B. Chen, Y. Zhaoa, Y. Liao, RSC Adv. 2015, 5, 37737–37741. DOI:10.1039/C5RA04729C
- J. Clayden, (Ed.) Tetrahedron Organic Chemistry Series, Organolithiums: Selectivity for Synthesis, *Elsevier, Ltd.*, 2002.
   383 p.
- B. J. Wakefield, Organomagnesium Methods in Organic Synthesis, *Academic Press*, London, 1988, 249 p.
- E. Erdik, Organozinc reagents in organic chemistry, CRC Press, London, 1996, 432 p.
- V. A. Peshkov, O. P. Pereshivko, E. V. Van der Eycken, *Chem. Soc. Rev.* 2012, 41, 3790–3807. DOI:10.1039/c2cs15356d

- 13. C. J. Li, C. M. Wei, Chem. Commun. 2002, 268-269.
- J. R. Cammarata, R. Rivera, F. Fuentes, Y. Otero, E. O-Mavárez,
   A. Arce, J. M. Garcia, *Tetrahedron Lett.* **2017**, *58*, 4078–4081.
   **DOI**:10.1016/j.tetlet.2017.09.031
- 15. P. Torabi, M. Moradian, J. Nanostruct. 2019, 3, 478-488.
- J.-L. Huang, D. G. Gray, C.-J. Li, Beilstein J. Org. Chem. 2013, 9, 1388–1396. DOI:10.3762/bjoc.9.155
- H. Alinezhad, K. Pakzad, M. Nasrollahzadeh, *Appl. Organom-et. Chem.* 2020, 34, e5473. DOI:10.1002/aoc.5473
- S. Sakaguchi, T. Mizuta, M. Furuwan, T. Kubo, J. Org. Chem. 2004, 35, 1638–1639. DOI:10.1039/b404430d
- Y. Zhang, P. Li, M. Wang, L. Wang, J. Org. Chem. 2009, 74, 4364–4367. DOI:10.1021/jo900507v
- M. L. Kantam, V. Balasubrahmanyam, K. B. S. Kumar, G. T. Venkanna, *Tetrahedron Lett.* 2007, 48, 7332–7334.
   DOI:10.1016/j.tetlet.2007.08.020
- S. Chandra, A. Kumar, P. K. Tomar, J. Saudi Chem. Soc. 2014, 18, 149–153. DOI:10.1016/j.jscs.2011.06.009
- S. Navalón H. García, Nanomaterials 2016, 6, 123–125.
   DOI:10.3390/nano6070123
- 23. B. H. Kim, M. J. Hackett, J. Park, T. Hyeon, *Chem. Mater.* **2014**, *26*, 59–71. **DOI**:10.1021/cm402225z
- N. Narayan, A. Meiyazhagan, R. Vajtai, *Materials* 2019, 12, 3602–3609. DOI:10.3390/ma12213602
- M. Kidwai, V. Bansal, N. K. Mishra, A. Kumar, S. Mozumdar, Synlett 2007, 10, 1581–1584. DOI:10.1055/s-2007-980365
- 26. M. Mirabedini, E. Motamedi, M. Z. Kassaee, *Chin. Chem. Lett.* **2015**, *26*, 1085–1090. **DOI:**10.1016/j.cclet.2015.05.021
- H. Veisi, M. Farokhi, M. Hamelian, S. Hemmati, RSC Adv.
   2018, 8, 38186–38195. DOI:10.1039/C8RA06819D
- Y. Uozumi, K. Kim, Synfacts 2019, 15, 0408–0408.
   DOI:10.1055/s-0037-1612395
- 29. X. Y. Dong, Z. W. Gao, K. F. Yang, W. Q. Zhang, L. W. Xu, *Catal. Sci. Technol.* **2013**, *1*, 1–3.
- W. Yan, R. Wang, Z. Xu, J. Xu, L, Lin, Z. Shen, Y. Zhou, J. Mol. Catal. Chem. 2006, 255, 81–85.
  - DOI:10.1016/j.molcata.2006.03.055
- 31. B. Sreedhar, A. S. Kumar, P. S. Reddy, *Tetrahedron Lett.* **2010**, *51*, 1891–1895. **DOI:**10.1016/j.tetlet.2010.02.016

- 32. S. Samai, G. C. Nandi, M. S. Singh, *Tetrahedron Lett.* **2010**, *51*, 5555–5558. **DOI**:10.1016/j.tetlet.2010.08.043
- M. Tajbakhsh, M. Farhang, S. M. Baghbanian, R. Hosseinzadeh, M. Tajbakhsh, *New J. Chem.*, **2015**, *39*, 1827–1839.
   **DOI:**10.1039/C4NJ01866D
- 34. G. H. Dang, D. T. Nguyen, D. T. Le, T. Truong, N. T.S. Phan, J. Mol. Catal. A: Chem., 2014, 395, 300–306.
  DOI:10.1016/j.molcata.2014.08.034
- J. Safaei-Ghomi, S. H. Nazemzadeh, Catal. Lett. 2017, 147, 1696–1703. DOI:10.1007/s10562-017-2079-4
- 36. S. V. Katkar, R. V. Jayaram, *RSC Adv.* **2014**, *4*, 47958. **DOI:**10.1039/C4RA06275B
- M. Daryanavard, A. Ataei, P. G. Sheykhabadi, E. Rafiee, M. Joshaghani, *ChemistrySelect*, 2020, 5, 18–27.
   DOI:10.1002/slct.201902617
- 38. J. Park, K. An, Y. Hwang, J. G. Park, H. J. Noh, J. Y. Kim, J. H. Park, N. M. Hwang, T. Hyeon, *Nature Mater.* 2004, 3, 891–895. DOI:10.1038/nmat1251
- J. Park, E. Kang, S. U. Son, H. M. Park, J. Kim, K. W. Kim, H. J. Noh, J. H. Park, C. J. Bae, J. G. Park, T. Hyeon, *Adv. Mater.* 2005, 17, 429–434. DOI:10.1002/adma.200400611
- 40. H. Eshghi, G. H. Zohuri, S. Damavandi, *Eur. J. Chem.* **2011**, *2*, 100–103. **DOI:**10.5155/eurjchem.2.1.100-103.175
- K. M. Reddy, N. S. Babu, I. Suryanarayana, P. S. S. Prasad, N. Lingaiah, *Tetrahedron Lett.* 2006, 47, 7563–7566.
   DOI:10.1016/j.tetlet.2006.08.094
- 42. P. Li, L. Wang, *Tetrahedron* **2007**, *63*, 5455–5459. **DOI:**10.1016/j.tet.2007.04.032
- 43. K. Namitharan, K. Pitchumani, *Eur. J. Org. Chem.* **2010**, *2010*, 411–415. **DOI:**10.1002/ejoc.200901084
- 44. M. L. Kantam, S. Laha, J. Yadav, S. Bhargava, *Tetrahedron Lett.* **2008**, *49*, 3083–3086. **DOI:**10.1016/j.tetlet.2008.03.053
- 45. M. Rahman, A. K. Bagdi, A. Majee, A. Hajra, *Tetrahedron Lett.* **2011**, *52*, 4437–4439. **DOI:**10.1016/j.tetlet.2011.06.067
- 46. A. Weissberg, B. Halak, M. Portnoy, *J. Org. Chem.* **2005**, *70*, 4556–4559. **DOI**:10.1021/jo050237j
- 47. B. Huang, X. Yao, C-J. Li, Adv. Synth. Catal. 2006, 348, 1528–1532. DOI:10.1002/adsc.200606118

#### Povzetek

S pomočjo termičnega razpada Ni-oleilaminskih kompleksov smo pripravili ultramajhne monodispergirane NiO nanodelce (7–9 nm). Za karakterizacijo tako dobljenega katalizatorskega materiala smo uporabili različne metode, vključno z infrardečo spektroskopijo s Fourierjevo transformacijo (FT-IR), difuzno-odbojno UV-Vis spektroskopijo (DRS), rentgensko difraktometrijo (XRD), rentgensko analizo z energijskim razklonom (EDX), vrstično elektronsko mikroskopijo (SEM), dinamično tehniko svetlobnega sipanja (DLS) in magnetometer na vibracije vzorca (VSM). Propargilaminske derivate smo z dobrimi do odličnimi izkoristki sintetizirali iz aldehidov, terminalnih alkinov in primarnih aminov z enolončnim A³-pripajanjem, ob dodatku 3 mol% NiO nanokristalov pri 80 °C pod pogoji brez uporabe topil. Strukture produktov smo potrdili z ¹H in ¹³C NMR spektroskopijo. Uporabljeni katalizator prinaša mnoge prednosti, saj je okolju prijazen, njegova ponovna uporaba je enostavna in učinkovita, je stabilen ter primeren za širok nabor substratov, poleg tega pa je njegova priprava tudi cenovno ugodna.



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