available at www.sciencedirect.com

journal homepage: www.elsevier.com/locate/chnjc

Article

Environmentally friendly, microwave-assisted synthesis of 5-substituted 1*H*-tetrazoles by recyclable CuO nanoparticles via (3+2) cycloaddition of nitriles and NaN₃

R. D. Padmaja ^a, Sourav Rej ^b, Kaushik Chanda ^{a,*}^a Department of Chemistry, School of Advanced Sciences, VIT University, Vellore-632014, India^b Institute of Bioengineering and Nanotechnology, A*STAR, 31 Biopolis Way, Singapore-138669

ARTICLE INFO

Article history:

Received 7 August 2017

Accepted 16 September 2017

Published 5 November 2017

Keywords:

Tetrazoles

CuO nanoparticles

(3+2) cycloaddition

Green chemistry

Microwave irradiation

ABSTRACT

Recyclable CuO nanoparticles were successfully employed to catalyze the microwave-assisted (3+2) cycloaddition reaction between nitriles and NaN₃ to efficiently synthesize 5-substituted 1*H*-tetrazoles. The salient features associated with this protocol are its cost effectiveness, rapid synthesis, stability, reusability, mild reaction conditions without any additives, high tolerance to various functional groups, and excellent yields under microwave irradiation. This environmentally friendly, microwave-assisted, nanoparticle-catalyzed synthetic methodology is seen as an alternative to conventional procedures that involve Lewis acid catalysts and a simple operation to the privileged scaffold.

© 2017, Dalian Institute of Chemical Physics, Chinese Academy of Sciences.

Published by Elsevier B.V. All rights reserved.

1. Introduction

Inorganic nanoparticles possess a high surface-to-volume ratio and, owing to their exposed surface features, they have increasingly been recognized as an important tool in efficient, highly selective catalysis [1–4]. Recently, metal and metal oxide nanocrystals, which preserve essential features of heterogeneous catalysts, have been examined for their organocatalytic, electrical conductivity, and photocatalytic properties [5–9]. Nanocatalysis offers considerable potential for developing processes that align with ‘green chemistry’ principles by seeking to decrease energy requirements and optimizing the use of the available resources. Nanoparticles increase the exposed surface area of a catalyst’s active component, thereby enhancing the contact between reactants and catalyst, while mimicking homogeneous catalysts. Recently, we showed the im-

portance of Cu₂O rhombic dodecahedra nanocrystals for the regioselective synthesis of 1,2,3-triazoles and 3,5-disubstituted isoxazoles in green media [10,11]. In 2014, we demonstrated the first 1,3-dipolar cycloaddition to 1,2,3-triazoles in water using Au nanocrystals [12].

Highly substituted tetrazoles are important therapeutic scaffolds that are present in natural products and pharmaceutical molecules [13–16]. Moreover, they are regarded as a bioisosteric substituent of carboxylic acid during the synthesis of bioactive compounds [17]. Because of their excellent metabolic stability, hydrogen bonding properties, and lipophilicity, these scaffold moieties can facilitate interactions between ligands and receptors to accelerate transport across cell membranes [18–20]. Figure 1 demonstrates the presence of tetrazole moieties in natural products (A); an antihypertensive drug, Losartan (B); and Tomelukast (C), where it is used for its an-

* Corresponding author. E-mail: chandakaushik1@gmail.com

The article is dedicated to my mentor Prof. Michael H Huang for his contribution in metal nanoparticle catalyzed organic reaction.

DOI: 10.1016/S1872-2067(17)62920-6 | http://www.sciencedirect.com/science/journal/18722067 | Chin. J. Catal., Vol. 38, No. 11, November 2017

Fig. 1. Bio-active tetrazole derivatives.

ti-leukotriene and anti-asthmatic properties [21,22]. Furthermore, the tetrazole compound dimethyl thiazolyl diphenyl tetrazolium bromide (MTT) is used in cell-proliferation assays [23].

Many synthetic methods have been employed for the synthesis of tetrazoles, but the most common is the reaction of NaN_3 with organic nitriles. In 2001, for the first time, Sharpless and coworkers [24,25] synthesized 5-substituted 1*H*-tetrazoles by reacting NaN_3 with organic nitriles using ZnCl_2 as the catalyst. Since then, a plethora of homogeneous and heterogeneous catalysts have been used in the synthesis of tetrazole derivatives, including AlCl_3 [26], TBAF [27], ZnO [28], Zn/Al hydrotalcite [29], $\text{Yb}(\text{OTf})_3$ [30], Zn hydroxyapatite [31], $\text{Zn}(\text{OTf})_2$ [32], $\text{Cu}_2(\text{OTf})_2$ [33], Cu_2O [34], ZnBr_2 under microwave irradiation [35], $\text{FeCl}_3\text{-SiO}_2$ [36], $\text{Fe}(\text{OAc})_2$ [37], CdCl_2 [38], $\text{In}(\text{OTf})_3$ [39], I_2 - or silica-supported NaHSO_4 [40], nano- CuFe_2O_4 [41], CoY zeolite [42], Zn-Cu alloy [43], $\text{Cu}(\text{OAc})_2$ [44], $\text{CuSO}_4\cdot 5\text{H}_2\text{O}$ [45], $\text{Et}_3\text{N}\cdot\text{HCl}$ [46], mesoporous ZnS [47], chitosan-derived magnetic ionic liquid [48], AgNO_3 [49], AgNPs [50], WAPO-5 microspheres [51], CAN-HY zeolite [52], $\text{B}(\text{C}_6\text{F}_5)_3$ [53], 4-(*N,N*-dimethylamino)pyridinium acetate [54], cuttlebone [55], CAES [56], diphenyl phosphorazidate [57], $\text{Fe}_3\text{O}_4\text{@chitin}$ [58], activated fuller earth [59], and an ONO pincer-type $\text{Pd}(\text{II})$ complex [60]. In other work, Volter and coworkers [61] recently demonstrated a one-pot conversion of aromatic aldehydes to tetrazole derivatives.

Most of these synthetic methodologies suffer one or more drawbacks. As well as being expensive, some methods require high catalyst loading, long reaction times, and harsh reaction conditions that use the explosive hydrazoic acid. Meanwhile, other routes give low product yields. To overcome these drawbacks, it remains essential to develop an atom-efficient, economic, green, one-pot synthetic methodology that is applicable to a wide range of substrates. In comparison to conventional heating, the application of microwave irradiation accelerates the chemical processes and transformation and results in higher product yields, lower energy usage, different reaction selectivities, and a milder reaction profile. Recent work has focused on organic reactions using CuO nanoparticles because of their nontoxic, nonhazardous, and recyclable nature [62,63]. To develop this area further, we therefore considered combining microwave irradiation and CuO nanoparticles to create a green synthetic methodology with an efficient reusable catalyst to synthesize 5-substituted 1*H*-tetrazoles. Specifically, as part of our wider program oriented towards the synthesis of bioactive heterocycles [64–67], we envisaged a concise route to 5-substituted 1*H*-tetrazole derivatives that involves the mi-

crowave-assisted (3+2) dipolar cycloaddition of readily available nitriles with NaN_3 using recyclable CuO nanoparticles.

2. Experimental

2.1. General

Unless otherwise indicated all common reagents and solvents were used as-obtained from commercial suppliers without further purification. CuO nanopowder (<50 nm particle size TEM) was purchased from Sigma-Aldrich. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on a Bruker DRX400 spectrometer. Chemical shifts were recorded in ppm relative to the internal solvent peak. The coupling constant, J , is given in Hz. Multiplicities of peaks are given as: s (singlet), d (doublet), t (triplet), and m (multiplet). Mass spectra were recorded on a Perkin Elmer Calrus600 GC-MS spectrometer. IR spectra were recorded by a Bomen DA8 3FTS spectrometer. Powder X-Ray diffraction (PXRD) was conducted with $\text{Cu-K}\alpha$ radiation ($\lambda = 0.154178$ nm) on an X-ray diffractometer. Transmission electron microscopy (TEM) was carried out with an accelerating voltage of 200 kV. Microwave-assisted reactions were performed in a Catalyst Scientific Microwave oven system (CATA R; Catalyst System, Pune, India) operating at 2450 MHz and equipped with a glass vial extension by a condenser. An external system was used to monitor and control the reaction temperature.

2.2. Chemistry

2.2.1. General procedure for the synthesis of 5-phenyl-1*H*-tetrazoles (**2a**)

In a round-bottomed flask, we added a mixture of benzonitrile **1** (0.052 g, 0.50 mmol, 1.0 equivalent) and NaN_3 (0.048 g, 0.75 mmol, 1.5 equivalent) to 5 mL of DMF containing 5 mol% of CuO nanoparticles under a N_2 atmosphere. The reaction mixture was irradiated by microwaves at 420 W for 15 min at 75 °C. The progress of the reaction was monitored by TLC. After the reaction had finished, the mixture was filtered to remove the catalyst. The filtrate was acidified with 5 N HCl (20 mL) to neutralize the product, and extracted with ethyl acetate (2×10 mL). The combined organic layer was dried over anhydrous MgSO_4 before the combined filtrate was subjected to evaporation to obtain the crude compound, which was purified over a silica gel column (60–120 mesh) using 50% ethyl acetate in hexane as the eluent to obtain the corresponding 5-phenyl-1*H*-tetrazole (**2a**) as the product.

5-Phenyl-1*H*-tetrazole (**2a**). Pale-white solid. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 8.04–8.03 (m, 2H), 7.59 (m, 3H), 4.06 (brs, NH); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 131.2, 129.4, 126.9, 124.2; IR (KBr, cm^{-1}): 3431, 2980, 2835, 2684, 2600, 2337, 1739, 1606; MS (EI) m/z : 146 (M^+); HRMS (EI, m/z) calculated for $\text{C}_7\text{H}_6\text{N}_4$: 146.0592; found 146.0583 (M^+).

5-(*p*-Tolyl)-1*H*-tetrazole (**2b**). White solid. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 7.92 (d, $J = 8.0$ Hz, 2H), 7.40 (d, $J = 8.0$ Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 155.2, 141.1, 129.9, 126.9, 121.4, 21.0; IR (KBr, cm^{-1}): 3431, 2916, 2845,

2690, 2447, 1878, 1732; MS (EI) m/z : 160 (M⁺).

5-(4-Methoxyphenyl)-1H-tetrazole (**2c**). Pale-white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.99 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 3.85 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 161.4, 154.8, 128.6, 116.3, 114.8, 55.4; IR (KBr, cm⁻¹): 3075, 2931, 2742, 1610, 1502; MS (EI) m/z : 176 (M⁺); HRMS (EI, m/z) calculated for C₈H₈N₄O: 176.0698; found 176.0666 (M⁺).

5-(3-Nitrophenyl)-1H-tetrazole (**2d**). White solid. ¹H NMR (400 MHz, CDCl₃) δ 8.55 (s, 1H), 8.06 (d, J = 7.6 Hz, 1H), 8.37–8.35 (m, 1H), 8.17 (s, 1H), 7.74 (d, J = 7.6 Hz, 1H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 162.3, 148.3, 133.1, 131.2, 126.1, 125.6, 121.5; IR (KBr, cm⁻¹): 3094, 2970, 1643, 1525; MS (EI) m/z : 191 (M⁺); HRMS (EI, m/z) calculated for C₇H₅N₅O₂: 191.0443; found 191.0554 (M⁺).

5-(3-Chlorophenyl)-1H-tetrazole (**2e**). Yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.84 (s, 1H), 7.78 (d, J = 6.8 Hz, 1H), 7.42 (d, J = 6.8 Hz, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 162.3, 133.9, 131.4, 130.9, 126.5, 126.4, 125.6; IR (KBr, cm⁻¹): 3431, 3331, 2972, 2827, 2465, 1654, 1556; MS (EI) m/z : 180 (M⁺); HRMS (EI, m/z) calculated for C₇H₅ClN₄: 180.0203; found 180.0200 (M⁺).

5-(*m*-Tolyl)-1H-tetrazole (**2f**). White solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.84 (d, J = 7.6 Hz, 1H), 7.78 (d, J = 6.8 Hz, 1H), 7.72 (m, 1H), 7.44–7.39 (m, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 138.8, 131.9, 129.3, 127.4, 124.1, 123.9, 20.9; IR (KBr, cm⁻¹): 3061, 2918, 2696, 2605, 1562; MS (EI) m/z : 160 (M⁺).

5-(4-Bromophenyl)-1H-tetrazole (**2g**). Yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.99 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 155.0, 132.5, 128.9, 124.7, 123.6; IR (KBr, cm⁻¹): 2995, 2899, 2723, 2617, 1734, 1600; MS (EI) m/z : 223 (M⁺); HRMS (EI, m/z) calculated for C₇H₅BrN₄: m/z 223.9698; found 223.9790 (M⁺).

5-(4-Chlorophenyl)-1H-tetrazole (**2h**). Yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.04 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 154.9, 135.9, 129.5, 128.7, 123.2; IR (KBr, cm⁻¹): 2997, 2762, 2632, 1691, 1606; MS (EI) m/z : 180 (M⁺); HRMS (EI, m/z) calculated for C₇H₅ClN₄: 180.0203; found 180.0273 (M⁺).

3-(1H-tetrazol-5-yl)aniline (**2i**). Brown solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.18 (t, J = 8.4 Hz, 1H) δ 6.86 (d, J = 6.8 Hz, 3H), 5.59 (s, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 149.9, 130.5, 119.9, 119.2, 118.9, 116.2, 111.9; IR (KBr, cm⁻¹): 3433, 3352, 3223, 2225, 1625; MS (EI) m/z : 161 (M⁺).

5-Benzyl-1H-tetrazole (**2j**). Pale-white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.36–7.32 (m, 2H) 7.28–7.26 (m, 3H), 4.29 (s, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 136.4, 129.2, 129.1, 127.5, 29.3; IR (KBr, cm⁻¹): 3101, 2949, 2854, 1529; MS (EI) m/z : 160 (M⁺); HRMS (EI, m/z) calculated for C₈H₈N₄: 160.0749; found 160.0649 (M⁺).

5-(*o*-Tolyl)-1H-tetrazole (**2k**). White solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.69–7.51 (m, 1H), 7.49–7.38 (m, 3H), 2.48 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 137.6, 131.8, 131.2, 129.9, 126.8, 124.3, 20.9; IR (KBr, cm⁻¹): 2966, 2713, 1737; MS (EI) m/z : 160 (M⁺).

5-(*o*-Bromophenyl)-1H-tetrazole (**2l**). Yellow solid. ¹H NMR (400 MHz, CDCl₃) δ 7.71–7.65 (m, 2H), 7.48–7.44 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 143.4, 134.35, 133.2, 127.7, 125.3,

125.0, 118.8; IR (KBr, cm⁻¹): 3088, 2916, 2223, 1732, 1538; MS (EI) m/z : 223 (M⁺).

4-(1H-tetrazol-5-yl)benzaldehyde (**2m**). White solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.09 (s, 1H), 8.26 (d, J = 8.0 Hz, 2H), 8.12 (d, J = 8.0 Hz, 2H), 3.38 (brs, NH); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 192.7, 165.1, 137.5, 130.4, 127.6; IR (KBr, cm⁻¹): 3406, 2864, 1666, 1575; MS (EI) m/z : 174 (M⁺); HRMS (EI, m/z) calculated for C₈H₆N₄O: 174.0542; found 174.0513 (M⁺).

Methyl 4-(1H-tetrazol-5-yl)benzoate (**2n**). White solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.19–8.14 (m, 4H), 3.89 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 166.0, 155.9, 132.1, 130.6, 129.2, 127.7, 52.9; IR (KBr, cm⁻¹): 3097, 3010, 2954, 1710; MS (EI) m/z : 204 (M⁺); HRMS (EI, m/z) calculated for C₉H₈N₄O₂: 204.0647; found 204.0623 (M⁺).

3. Results and discussion

To determine the catalytic suitability of CuO nanoparticles, we first carried out optimization studies using CuO with benzonitrile (**1a**) and NaN₃ as model substrates. The results from these experiments are summarized in Table 1. An initial attempt to use 2.5 mol% of CuO nanoparticles as the catalyst under solvent-free conditions at 100 °C for 6 h did not yield any **2a** product (Table 1, entry 1). Similarly, no **2a** was produced when the reaction was carried out using acetonitrile or THF as the solvent at refluxing temperatures (Table 1, entries 2 and 3). Subsequent analysis of the reaction mixtures indicated the presence of starting material only. We then focused on reactions with polar protic solvents such as EtOH at refluxing temperature for 10 h, and obtained a yield of **2a** of 50% (Table 1, entry 4). Meanwhile, using H₂O-IPA as the solvent for a reaction at 100 °C did not yield any **2a** (Table 1, entry 5). This suggested that careful choice of solvent is required to obtain high yields of tetrazole derivatives.

Table 1

Optimization of the reaction conditions for the synthesis of 5-phenyl-1H-tetrazole.^a

Entry	Cu(II) catalyst (mol%)	Solvent	Temperature (°C)	Time (h)	Yield ^b (%)
1	2.5	No solvent	100	6	0
2	2.5	CH ₃ CN	Reflux	6	0
3	2.5	THF	Reflux	6	0
4	2.5	EtOH	Reflux	10	50
5	2.5	H ₂ O-IPA	Reflux	10	0
6	2.5	DMSO	130	10	10
7	2.5	Dioxane	Reflux	10	0
8	2.5	EtOAc	Reflux	10	0
9	2.5	DMF	130	10	80
10	5.0	DMF	130	10	85
11	5.0	DMF	MW ^c , 75	0.25	99
12	0	DMF	130	10	0

^a Reaction was performed using **1a** (1 mmol) and NaN₃ (1.5 mmol).

^b Yield of the isolated product.

^c Microwave reactions were carried out in Microwave Model No. CATA R (Catalyst systems, Pune).

Changing the solvent polarity from polar protic to polar aprotic by using a solvent such as DMSO was shown to be ineffective at boosting the yield for this reaction with multiple spots (Table 1, entry 6). The use of dioxane and ethyl acetate as aprotic solvents also failed to produce **2a** (Table 1, entries 7 and 8). However, when the reaction was carried out in DMF for 10 h at 130 °C, an 80% yield of **2a** was achieved (Table 1, entry 9). Increasing the catalyst loading to 5 mol% did not markedly increase the yield after 10 h (Table 1, entry 10). However, performing the same reaction (with 5 mol% catalyst loading) under 15 min of microwave irradiation with DMF as the solvent produced a 99% yield of **2a** (Table 1, entry 11). The final result was derived from an experiment conducted without the CuO nanoparticles; this did not yield any **2a** product (Table 1, entry 12).

Scheme 1 illustrates the nano-CuO catalyzed synthesis of 5-substituted 1*H*-tetrazole derivatives that involve the (3+2) cycloaddition reaction using DMF as the solvent with microwave irradiation. Once the reaction had finished, an acidic treatment produced excellent yields of the substituted 1*H*-tetrazole derivatives.

Encouraged by the synthetic efficiency of the reaction protocol described above, we further investigated the scope of this reaction with a diverse range of nitriles to produce the results that are summarized in Table 2.

The time required to complete the reaction was typically 15–18 min. Following the simple work-up described in Section 2, the corresponding 5-substituted 1*H*-tetrazole derivatives were obtained with excellent yields. To verify whether the observed catalysis was truly heterogeneous or not, additional control experiments were performed. Here, CuO nanoparticles were stirred in DMF at 130 °C for 5 h. After cooling at room temperature, the solution was centrifuged and the precipitated nanocrystals were carefully collected. Freshly measured quantities of **1a** and NaN₃ were added to the solution to investigate whether any of the cyclized product **2a** was obtained. However, after 20 min of microwave irradiation at 75 °C, no tetrazole product was observed. These results ruled out any possible contribution from homogeneous catalysis by leached Cu(II) species in this (3+2) cycloaddition reaction, indicating that the observed catalytic activity was entirely heterogeneous in nature. Finally, the crude products were purified by column chromatography before undergoing spectroscopic characterization using ¹H NMR, ¹³C NMR, and mass spectroscopy (MS).

Aromatic nitriles containing either unsubstituted or electron-withdrawing groups reacted efficiently to obtain the corresponding 1*H*-tetrazole derivatives, producing excellent yields after 15 min. Meanwhile, substrates with electron-donating substituents produced slightly lower yields after reactions of

Scheme 1. Nano-CuO-catalyzed synthesis of substituted 1*H*-tetrazoles in DMF.

Table 2

Nano-CuO-catalyzed microwave-assisted synthesis of substituted 1*H*-tetrazoles.^a

Entry	Aromatic nitrile	Tetrazole product	Isolated yield ^b (%)	Ref.
1			99	[40]
2			90	[46]
3			92	[45]
4			99	[46]
5			95	[39]
6			92	[43]
7			96	[40]
8			98	[40]
9			89	[39]
10			95	[40]
11			90	[46]
12			95	[38]
13			96	[45]
14			95	[42]

^a Reaction conditions: **1** (1 mmol), NaN₃ (1.5 mmol), Cu(II) catalyst (5 mol%)

^b Yield of the isolated product **2**.

18 min owing to the electrophilic nature of the nitrile moiety attached to the aromatic rings. The benzylic nitriles also reacted comprehensively with NaN₃ to obtain high yields of corresponding 1*H*-tetrazoles, whereas aliphatic nitriles appeared unreactive under the present reaction conditions. To diversify the synthetic methodology, we attempted to react organic azides, but no corresponding tetrazoles were obtained.

The optimized synthesis was next tested at a larger scale: employing 2 g of **1a** and 15 min of microwave irradiation obtained a 99% yield of **2a**.

We then examined the recyclability of the CuO nanocrystals. Following the microwave irradiation during the reaction, the reaction mixture was treated with ethyl acetate and water. The CuO nanoparticles were collected by centrifuging the mixture and washed successively with water and acetone before being dried under a vacuum. Another cycle of the reaction was then

Fig. 2. Yield and conversion from (3+2) cycloaddition reaction of benzonitrile with NaN_3 in the presence of reused CuO nanoparticles.

carried out using the same nanocrystals, with this process repeated for five runs. As shown in Fig. 2, even in the fifth run the catalyst facilitated the reaction to the extent that a 90% yield of **2a** was obtained alongside a 95% conversion and with >95% catalyst being recovered.

The TEM images and PXRD peaks of the fresh CuO nanoparticles and those recovered after completing five cycles of the (3+2) cycloaddition reaction shown in Fig. 3 exhibit no noticeable morphological differences, supporting the conclusion that they may be used as recyclable catalysts.

Fig. 3. TEM and PXRD patterns of CuO nanoparticles before (a) and after five reaction cycles (b).

4. Conclusions

We have developed an efficient, environmentally friendly, microwave-assisted approach for the synthesis of biologically useful 5-substituted 1*H*-tetrazole derivatives. Reactions required 15–18 min to produce yields that reached 99% using CuO nanoparticles. Moreover, the CuO nanoparticles were recycled five times without marked loss of catalytic activity. Work is ongoing in our laboratory to further develop CuO-nanoparticle-catalyzed synthesis of bioactive heterocycles for potential biological applications.

Acknowledgments

The authors thank the Chancellor and Vice Chancellor of VIT University for providing opportunity to carry out this study. Further the authors wish to thank the management of this university for providing seed money as research grant. Kaushik Chanda thanks CSIR-Govt of India for funding through Grant No. 01(2913)/17/EMR-II. The authors are thankful to anonymous reviewers for providing constructive comments for the overall improvement of the manuscript.

References

- [1] I. Lee, F. Delbecq, R. Morales, M. A. Albiter, F. Zaera, *Nat. Mater.*, **2009**, 8, 132–138.
- [2] X. Q. Huang, Y. J. Li, Y. J. Li, H. L. Zhou, X. F. Duan, Y. Huang, *Nano Lett.*, **2012**, 12, 4265–4270.
- [3] C. L. Lu, K. Prasad, H. L. Wu, J.-a. A. Ho, M. H. Huang, *J. Am. Chem. Soc.*, **2010**, 132, 14546–14553.
- [4] Y. E. Wu, S. F. Cai, D. S. Wang, W. He, Y. D. Li, *J. Am. Chem. Soc.*, **2012**, 134, 8975–8951.
- [5] K. M. Bratlie, H. Lee, K. Komvopoulos, P. Yang, G. A. Somorjai, *Nano Lett.*, **2007**, 7, 3097–3101.
- [6] J. F. Wang, J. X. Gong, Y. S. Xiong, J. D. Yang, Y. Gao, Y. L. Liu, X. Q. Lu, Z. Y. Tang, *Chem. Commun.*, **2011**, 47, 6894–6896.
- [7] P. Christopher, S. Linic, *ChemCatChem*, **2010**, 2, 78–83.
- [8] C. H. Kuo, Y. C. Yang, S. Gwo, M. H. Huang, *J. Am. Chem. Soc.*, **2011**, 133, 1052–1057.
- [9] M. H. Huang, S. Rej, S. C. Hsu, *Chem. Commun.*, **2014**, 50, 1634–1644.
- [10] K. Chanda, S. Rej, M. H. Huang, *Chem. Eur. J.*, **2013**, 19, 16036–16043.
- [11] K. Chanda, S. Rej, M. H. Huang, *Nanoscale*, **2013**, 5, 12494–12501.
- [12] S. Rej, K. Chanda, C. Y. Chiu, M. H. Huang, *Chem. Eur. J.*, **2014**, 20, 15991–15997.
- [13] M. B. Hossain, D. van der Helm, R. Sanduja, M. Alam, *Acta Crystallogr. C*, **1985**, 41, 1199–1202.
- [14] S. Berghmans, J. Hunt, A. Roach, P. Goldsmith, *Epilepsy Res.*, **2007**, 75, 18–28.
- [15] J. H. Toney, P. M. Fitzgerald, N. Grover-Sharma, S. H. Olson, W. J. May, J. G. Sundelof, D. E. Vanderwall, K. A. Cleary, S. K. Grant, J. K. Wu, J. W. Kozarich, D. L. Pompliano, G. G. Hammond, *Chem. Biol.*, **1998**, 5, 185–196.
- [16] Y. Tamura, F. Watanabe, T. Nakatani, K. Yasui, M. Fujii, T. Komurasaki, H. Tsuzuki, R. Maekawa, T. Yoshioka, K. Kawada, K. Sugita, M. Ohtani, *J. Med. Chem.*, **1998**, 41, 640–649.
- [17] R. J. Herr, *Bioorg. Med. Chem.*, **2002**, 10, 3379–3393.
- [18] R. G. Franz, *AAPS PharmSci.*, **2001**, 3, 1–13.

Graphical Abstract

Chin. J. Catal., 2017, 38: 1918–1924 doi: 10.1016/S1872-2067(17)62920-6

Environmentally friendly, microwave-assisted synthesis of 5-substituted 1*H*-tetrazoles by recyclable CuO nanoparticles via (3+2) cycloaddition of nitriles and NaN₃

R. D. Padmaja, Sourav Rej, Kaushik Chanda *

VIT University, India; Institute of Bioengineering and Nanotechnology, Singapore

We demonstrate that practical, simple, efficient and recyclable CuO nanoparticles can catalyze the (3+2) cycloaddition of nitriles and NaN₃ to synthesize 5-substituted-1*H*-tetrazoles using microwave irradiation.

- [19] F. H. Allen, C. R. Groom, J. W. Liebeschuetz, D. A. Bardwell, T. S. G. Olsson, P. A. Wood, *J. Chem. Inf. Model.*, **2012**, 52, 857–866.
- [20] P. W. Kenny, *J. Chem. Inf. Mod.*, **2009**, 49, 1234–1244.
- [21] D. J. Carini, J. V. Duncia, P. E. Aldrich, A. T. Chiu, A. L. Johnson, M. E. Pierce, W. A. Price, J. B. Santella, G. J. Wells, *J. Med. Chem.*, **1991**, 34, 2525–2547.
- [22] W. S. Marshall, T. Goodson, G. J. Cullinan, D. Swanson, K. D. Haisch, L. E. Rinkema, J. H. Fleisch, *J. Med. Chem.*, **1987**, 30, 682–689.
- [23] M. V. Berridge, P. M. Herst, A. S. Tan, *Biotechnol. Annu. Rev.*, **2005**, 11, 127–152.
- [24] Z. P. Demko, K. B. Sharpless, *J. Org. Chem.*, **2001**, 66, 7945–7950.
- [25] Z. P. Demko, K. B. Sharpless, *Org. Lett.*, **2002**, 4, 2525–2527.
- [26] D. P. Matthews, J. E. Green, A. J. Shuker, *J. Comb. Chem.*, **2000**, 2, 19–23.
- [27] D. Amantini, R. Beleggia, F. Fringuelli, F. Pizzo, L. Vaccaro, *J. Org. Chem.*, **2004**, 69, 2896–2898.
- [28] M. L. Kantam, K. B. S. Kumar, C. Sridhar, *Adv. Syn. Catal.*, **2005**, 347, 1212–1214.
- [29] M. L. Kantam, K. B. S. Kumar, K. J. Phani Raja, *J. Mol. Catal. A*, **2006**, 247, 186–188.
- [30] W. K. Su, Z. Hong, W. G. Shan, X. X. Zhang, *Eur. J. Org. Chem.*, **2006**, 2723–2726.
- [31] M. L. Kantam, V. Balasubrahmanyam, K. B. S. Kumar, *Synth. Commun.*, **2006**, 36, 1809–1814.
- [32] S. Hajra, D. Sinha, M. Bhowmick, *J. Org. Chem.*, **2007**, 72, 1852–1855.
- [33] L. Bosch, J. Vilarrosa, *Angew. Chem. Int. Ed.*, **2007**, 46, 3926–3930.
- [34] T. Jin, F. Kitahara, S. Kamijo, Y. Yamamoto, *Tetrahedron Lett.*, **2008**, 49, 2824–2827.
- [35] J. J. Shie, J. M. Fang, *J. Org. Chem.*, **2007**, 72, 3141–3144.
- [36] M. Nasrollahzadeh, Y. Bayat, D. Habibi, S. Moshaei, *Tetrahedron Lett.*, **2009**, 50, 4435–4438.
- [37] J. Bonnamour, C. Bolm, *Chem. Eur. J.*, **2009**, 15, 4543–4545.
- [38] G. Venkateshwarlu, A. Premalatha, K. C. Rajanna, P. K. Saiprakash, *Synth. Commun.*, **2009**, 39, 4479–4485.
- [39] D. Kundu, A. Majee, A. Hajra, *Tetrahedron Lett.*, **2009**, 50, 2668–2670.
- [40] B. Das, C. R. Reddy, D. N. Kumar, M. Krishnaiah, R. Narender, *Synlett*, **2010**, 391–394.
- [41] B. Sreedhar, A. S. Kumar, D. Yadav, *Tetrahedron Lett.*, **2011**, 52, 3565–3569.
- [42] V. Rama, K. Kanagaraj, K. Pitchumani, *J. Org. Chem.*, **2011**, 76, 9090–9095.
- [43] G. Aridoss, K. K. Laali, *Eur. J. Org. Chem.*, **2011**, 6343–6355.
- [44] M. M. Heravi, A. Fazeli, H. A. Oskooie, Y. S. Beheshtiha, H. Valizadeh, *Synlett*, **2012**, 23, 2927–2930.
- [45] B. Akhlaghini, S. Rezazadeh, *J. Braz. Chem. Soc.*, **2012**, 23, 2197–2203.
- [46] H. Yoneyama, Y. Usami, S. Komeda, S. Harusawa, *Synthesis*, **2013**, 45, 1051–1059.
- [47] L. M. Lang, H. Zhou, M. W. Xue, X. F. Wang, Z. Xu, *Mater. Lett.*, **2013**, 106, 443–446.
- [48] A. Khalafi-Nezhad, S. Mohammadi, *RSC Adv.*, **2013**, 3, 4362–4371.
- [49] P. Mani, A. K. Singh, S. K. Awasthi, *Tetrahedron Lett.*, **2014**, 55, 1879–1882.
- [50] P. Mani, C. Sharma, S. Kumar, S. K. Awasthi, *J. Mol. Catal. A*, **2014**, 392, 150–156.
- [51] D. Kong, Y. Y. Liu, J. Zhang, H. B. Li, X. Y. Wang, G. Y. Liu, B. J. Li, Z. Xu, *New J. Chem.*, **2014**, 38, 3078–3083.
- [52] P. Sivaguru, K. Bhuvaneswari, R. Ramkumar, A. Lalitha, *Tetrahedron Lett.*, **2014**, 55, 5683–5686.
- [53] S. K. Prajapati, A. Nagarsenkar, B. N. Babu, *Tetrahedron Lett.*, **2014**, 55, 3507–3510.
- [54] N. Nowrouzi, S. Farahi, M. Irajzadeh, *Tetrahedron Lett.*, **2015**, 56, 739–742.
- [55] S. S. E. Ghodsinia, B. Akhlaghinia, *RSC Adv.*, **2015**, 5, 49849–49860.
- [56] N. Razavi, B. Akhlaghinia, *RSC Adv.*, **2015**, 5, 12372–12381.
- [57] K. Ishihara, M. Kawashima, T. Shioiri, M. Matsugi, *Synlett*, **2016**, 27, 2225–2228.
- [58] M. Zarghania, B. Akhlaghinia, *RSC Adv.*, **2016**, 6, 31850–31860.
- [59] D. S. Rekunge, K. S. Indalkar, G. U. Chaturbhuj, *Tetrahedron Lett.*

- 2016, 57, 5815–5819.
- [60] A. Vignesh, N. S. P. Bhuvanesh, N. Dharmaraj, *J. Org. Chem.*, **2017**, 82, 887–892.
- [61] K. M. Khan, I. Fatima, S. M. Saad, M. Talha, W. Volter, *Tetrahedron Lett.*, **2016**, 57, 523–524.
- [62] W. Zhang, F. Guo, F. Wang, N. Zhao, L. Liu, J. Li, Z. H. Wang, *Org. Biomol. Chem.*, **2014**, 12, 5752–5756.
- [63] A. Modi, W. Ali, R. R. Mohanta, N. Khatun, B. K. Patel, *ACS Sustainable Chem. Eng.*, **2015**, 3, 2582–2590.
- [64] B. Maiti, K. Chanda, *RSC Adv.*, **2016**, 6, 50384–50413.
- [65] D. R. Meena, B. Maiti, K. Chanda, *Tetrahedron Lett.*, **2016**, 57, 5514–5517.
- [66] S. Rajasekhar, B. Maiti, K. Chanda, *Synlett*, **2017**, 28, 521–541.
- [67] R. N. Rao, B. Maiti, K. Chanda, *ACS Comb. Sci.*, **2017**, 19, 199–228.

可重复使用CuO纳米粒子催化微波辅助的腈和NaN₃环加成反应 合成5-取代1*H*-四唑类

R. D. Padmaja^a, Sourav Rej^b, Kaushik Chanda^{a,*}

^a韦洛尔大学高等科学学院化学系, 韦洛尔632014, 印度

^b生物工程与纳米技术研究所, 138669, 新加坡

摘要: 将可重复使用的CuO纳米粒子成功用于催化微波辅助的腈和NaN₃ [3+2]环加成反应高效合成5-取代1*H*-四唑类化合物. 该法突出特点为成本低、合成快、稳定性高、可重复使用、反应条件温和、无需任何添加物、官能团兼容性好和产率高. 这种环境友好的微波辅助纳米粒子催化合成策略可望替代现有的涉及常规路易斯酸催化剂方法, 以及作为一种简易的合成特殊化合物的方法.

关键词: 四唑类; 氧化铜纳米粒子; (3+2)环加成; 绿色化学; 微波辐射

收稿日期: 2017-08-07. 接受日期: 2017-09-16. 出版日期: 2017-11-05.

*通讯联系人. 电子信箱: chandakaushik1@gmail.com

本文的电子版全文由Elsevier出版社在ScienceDirect上出版(<http://www.sciencedirect.com/science/journal/18722067>).