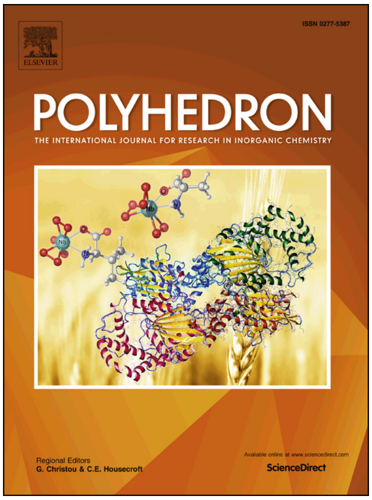

[Cu_3 (BTC) $_2$]: A metal–organic framework as an environment-friendly and economically catalyst for the synthesis of tacrine analogues by Friedländer reaction under conventional and ultrasound irradiation

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[Cu_3 (BTC) $_2$]: A metal–organic framework as an environment-friendly and economically catalyst for the synthesis of tacrine analogues by Friedländer reaction under conventional and ultrasound irradiation

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Keywords: Metal-organic framework, Ultrasonic irradiation, tacrine analogues, [Cu_3 (BTC) $_2$], 5-amino-4-cyano-2-phenyl-1,3-oxazole, Friedländer annulations.

Abastract

Using a green and simple route with ultrasound illumination, atmospheric pressure and room temperature, for synthesizing tacrine analogues in the presence of [Cu_3 (BTC) $_2$] as an environment-friendly and economically catalyst was considered. [Cu_3 (BTC) $_2$] is one of the heterogeneous catalysts on hand capable of being employed, in the Friedländer reaction, whenever 5-amino-4-cyano-2-phenyl-1,3-oxazole and appropriately substituted carbonyl derivatives under conventional and ultrasonic irradiation. The results of this study indicate that the active sites in the [$Cu_3(BTC)_2$] for synthesis of cyclohepta[b] oxazolo[4,5-e]pyridine are mainly copper atoms and the role of Brønsted acid organic ligand in the MOF is negligible. These procedures were properly arranged in order to provide the utmost yields in a short while. The crystal stability in the process of catalysis was investigated by various techniques such as XRD, BET and ICP that demonstrate excellent stability in reaction conditions.

1. Introduction

Tacrine (9-amino-1,2,3,4-tetrahydroacridine or THA, Figure 1) is a reversible inhibitor of acetylcholinesterase (AChE), appears as an important reference with interesting pharmacological properties, and was launched in 1993 as the first drug for the symptomatic treatment of Alzheimer's disease (AD) [1- 3]. However, the use of THA in AD has been limited by severe adverse effects such as hepatotoxicity, which often forces patients to discontinue treatment [4-5]. Additional actions of tacrine has also been discovered later: block of monoamine oxidase activity [6], inhibition of neuronal monoamine uptake processes [7], blockage of certain potassium ion channels [8], interaction with muscarine acetylcholine receptors [9].

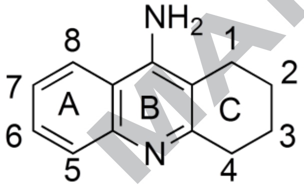
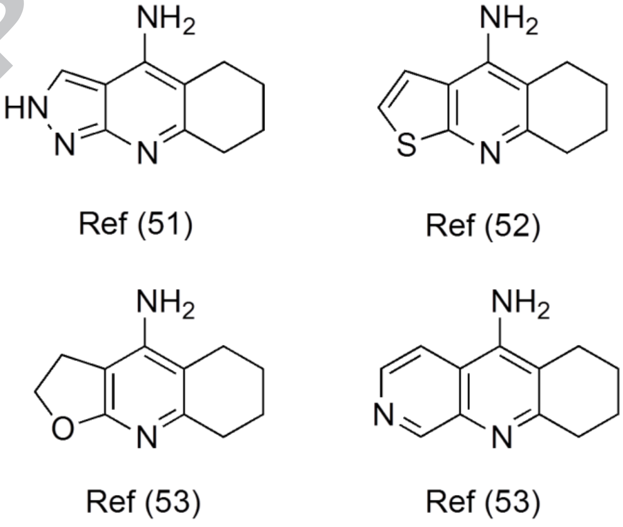


Figure 1. The structure of tacrine.



Ref (51)
Ref (52)
Ref (53)
Ref (53)

Figure 2. Analogues of tacrine, modified Ring A (figure 1).

A Lewis acid, including $ZnCl_2$ [10-11], $SnCl_4$, $SnCl_2$. $2H_2O$ [8], CuCl, $CuCl_2$ [12], $TiCl_4$, P_2O_5, $InCl_3$ [13], $AlCl_3$ [14-15], $BF_3.Et_2O$, $BiCl_3$ [16], $FeCl_3$, $SbCl_3$ [14] or a protic acid such as *p*-toluenesulfonic acid (PTSA) promoted Friedländer condensation reactions between various α-aminonitriles and ketones for the synthesis of tacrine and its analogues [15-16]. However, these homogeneous systems have numerous drawbacks such as low yield, long reaction time, difficult recovery of catalyst, environmental pollution and are limited in terms of substrate applicability [17-18]. Heterogeneous catalyst systems have a number of significant advantages over homogeneous catalysts, like easy recovery, simple catalyst separation and minimize unwanted waste. Also, the Friedländer annulations is traditionally done by heating under reflux conditions, which is a very time consuming process involving high energy consumption [19-20]. Therefore, it is necessary and valuable to find green catalysts and an environmentally friendly process for annulation of a 5-amino-4-cyano-2-phenyl-1, 3-oxazole with an appropriately substituted carbonyl derivative.

Metal-organic frameworks (MOFs), called also as porous coordination networks (PCNs) or porous coordination polymers (PCPs), are crystalline porous substances constructed from metal nodes and organic linkers which have recently been introduced as heterogeneous catalysts [17-18, 21-23]. MOFs have caught widespread interest thanks to being considered as optoelectronic gadgets and interesting catalyst materials lately [24-25]. MOFs can also be used in medical imaging, drug delivery and gas storage [26-28].

$[Cu_3(BTC)_2(H_2O)_3]$ which is also a porous-framework material known as HKUST-1 [29] or MOF-199 [30], incorporates large and numerous cavities with windows measured ~ 6 Aº in diameter [31]. In $[Cu_3(BTC)_2(H_2O)_3]$, when the coordinated water molecules the result would be the opening of Cu (II) sites get open. Alaerts et al. took the initiative to explore the manner in which the anhydrous version of HKUST-1 behaves as an example of a catalyst material for acidity [32]. While being aware of the viable function of a proper catalyst at defect sites, namely exposed carboxlic acides, Alaerts et al. scrutinized three distinct reaction viz. Cyclization of citronellal, isomerization of α-pinene oxide, and rearrangement of α-bromoacetals. The selectivity patterns of these three reactions sound quite different for Brønsted vs. Lewis acid catalyzed pathways. It can be concluded that [$Cu_3(BTC)_2$] demonstrates its primary function as a Lewis acid catalyst [33-34].

Recently published comprehensive articles have revealed that ultrasound chemical applications are a new trend in organic chemistry for a wide variety of syntheses [35-40]. Because of the interaction between the ultrasound and the material, the oscillation of the cavity bubbles is formed, and the bursting of the cavity bubbles causes shock waves. At the same time, high pressure and high temperature occur in places of the reaction environment locally. The ultrasound cavity process may cause free radicals to change the structure of the substance [41-43]. In addition, the use of ultrasonics accelerates the molecular movement of the components involved in the reaction, and thus helps to quickly react between the substrate and the reactant, by increasing the number of successful collisions based on the collision theory.

O-amino-substituted carbonyl compounds namely, *o*-aminobenzaldehydes, *o*-aminoacetophenones, and *o*-aminobenzophenones are utilized in Friedländer reaction. This reaction is produced whether via refluxing or at room temperature in an aqueous, alcoholic and dry 1,2-dichloroethane solution of reactants in high reaction time (around 14 days) [44]. In order to extend this condensation reaction, 2-aminobenzophenones have been employed so as to have the synthesis of the quinolines through the use of [$Cu_3(BTC)_2$] in short reaction times [31].

With regard to these experiences, it proved astonishing to find out that [$Cu_3(BTC)_2$] has seldom been studied as a catalyst agent for acidity in Friedländer reaction between 5-amino-4-cyano-2-phenyl-1,3-oxazole and appropriately substituted carbonyl derivatives under conventional and ultrasonic irradiation. In some reactions, ultrasonic irradiation allows the process to be carried out with ease and produce a high yield product over a very short time [45]. In this work, [$Cu_3(BTC)_2$] is commercially available as Basolite C300 (Sigma–Aldrich). This MOF had a particle size distribution of 15.96 µm (D50), a BET surface area of 1500–2100 m^2 g^{-1}, and a bulk density 0.35 g cm^{-3} [31].

2 Experimental

2.1. Chemicals and apparatus

All reactions were followed up and examined by TLC (Merck, 5539) using EtOAc/n-hexane (1:2 v/v) as a mobile phase. The spots were visualized using by UV (254 nm) followed by dipping in a 1% aqueous potassium permanganate solution and air drying. The removal of solvents was done under vacuum with a rotary evaporator. All melting points are uncorrected and were detected in a capillary tube on a Buchi 510. The IR spectra were recorded on a Bruker Alpha-P FTIR Diamond ATR spectrophotometer. ^1H and ^{13}C NMR spectra were obtained with a Bruker 400 spectrometer. ^1H Chemical shift (δ) were determined in DMSO-d_6 with tetramethylsilane as internal standard. Values with (*) can be interchanged. Elemental analyses were obtained on a Carlo Erba EA 1108 apparatus. High-resolution mass spectra were obtained by a Thermo scientific exactive high resolution MS (ESI probe). The powder X-ray diffraction patterns (XRD) were measured by using a Philips X′pert diffractometer with monochromated Cu-k_α radiation (k = 1.54056 Å). Measurements were obtained between 2θ values of 2.5 and 60° with a step of 300 s (1 step: 1.5°). An Optima 8000 ICP-OES spectrometer was used for determination of Cu species in the reaction mixture. Thermogravimetric analyses (TGA) of the materials were carried out using a thermal analyzer (TGA-50 Shimadzu thermo-balance). Nitrogen adsorption isotherms that were collected with a Micromeritics ASAP 2000 over P/P0 = 0.0–1.0 applied to surface area investigation material used. All reagents, solvents and the [$Cu_3(BTC)_2$], which is commercially available as Basolite C300, were purchased from Sigma-Aldrich. Ultrasound waves generated by an ultrasound bath (Sonic 6mx, 37 kHz with a maximum power output of 240 W, Polsonic, Warsaw, Poland).

2.2 Typical procedure for synthesis of compound 1.

According to our investigation of synthesis oxazole derivatives [46], to a stirred solution of aminomalononitriletosylate (AMNT), (2.71 g, 8.60 mmol) in 1-methyl-2-pyrrolidinone (20 mL), were added 1.0–1.1 equiv of the benzoyl chloride in one portion. The reaction mixture was stirred at room temperature until the reaction was complete. Then, the mixture was diluted with a mixture of EtOAc and Et_2O (1:1), and washed with water, 10 % aqueous $NaHCO_3$, and water. The organic layer was dried, the solvent was evaporated *in vacuo*, and the crude product was purified by flash silica gel chromatography (3:2, CH_2Cl_2: EtOAc).

2.2.1 5-Amino-4-cyano-2-phenyl-1,3-oxazole 1.

Yield (67%) as a yellow solid: mp 150-153℃; IR ν_{max} 3273, 3314, 2207, 1650, 793, 685 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.95 (br s, NH_2, 2 H), 7.76(m, H2′, H6′, 2 H), 7.48 (m, H3′, H4,′ H5′, 3 H);^{13}C NMR (DMSO-d_6, 100 MHz) δ 162.42 (C5), 149.50 (C2), 115.49 (CN), 84.34 (C4), 125.05 (1C, C4′), 130.11 (C1′), 129.24 (2C, C2′, C6′), 126.08 (2C, C3′, C5′); HR MS: *m/z* calcd. for $C_{10}H_7N_3O$ (M-H$^+$) 185.0589, found 184.0509.

2.3 General procedure for the preparation of oxazolo[5,4-b]quinolin 3a and cyclohepta[b] oxazolo[4,5-e]pyridine 3b.

Conventional heating. A mixture of cyclohexanone 2 a (b) 5.37 mmol, and 5-amino-4-cyano-2-phenyl-1,3-oxazole 1 (2.16 mmol, 399.7 mg), activated $[Cu_3(BTC)_2]$ (0.083 mmol, 50 mg) was added and the reaction mixture was heated at 353 K for 2 h. The progress of the reaction was monitored by TLC (1:2 v/v EtOAc/n-hexane as eluent). After completion, the reaction mixture was allowed to cool to room temperature. The reaction mixture was treated with EtOH (96 %) and the catalyst was removed by centrifugation at 4000 rpm during 10 min. Finally, solvent was removed under reduced pressure and the crude product was purified by flash silica gel chromatography (1:2 v/v EtOAc/n-hexane as eluent). To activate the catalyst, $[Cu_3(BTC)_2]$ was dried at 373 K overnight (experimental conditions: 373 K, 5 K min^{-1}, 900 min).

Ultrasound. above All contents were put in an ultrasonic bath, where the surface of reactants is slightly lower than the level of the water, and irradiated at room temperature (20–25 °C) for the periods of time as indicated in Table I, and worked up as described.

2.3.1 2-phenyl-5,6,7,8-tetrahydrooxazolo[5,4-b]quinolin-9-amine 3a.

Melting point 274-276 °C; IR ν_{max} 3400, 3340, 3220, 2930, 2860, 1645, 1630, 1610, 1445, 1335, 1060, 1020 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.21(m, H2′, H6′, 2 H), 7.67 (m, H3′, H4,′ H5′, 3 H), 6.33 (br s, NH$_2$, 2 H), 2.86 (m, H8, 2H), 2.60 (m, H5, 2H), 1.89 (m, H6, H7, 4H);^{13}C NMR (DMSO-d_6, 100 MHz) δ 158.1 (C9a)*, 157.2 (C2)*, 152.4 (C8a), 145.3 (C4), 131.1 (C4′), 129.1 (2C, C3′, C5′), 127.1 (C1′), 126.5 (2C, C2′, C6′), 117.6 (C3a), 111.8 (C4a), 32.9 (C8), 23.1 (C5), 22.5 (C7)**, 22.2 (C6)**; MS (EI) *m/z* (%): 265 [M]$^+$ (100), 264 (60), 250 (19), 238 (12), 237 [M-CO]$^+$ (50), 133 (12), 105 (24), 104 (12), 78 (8), 77 [Ph]$^+$ (23).

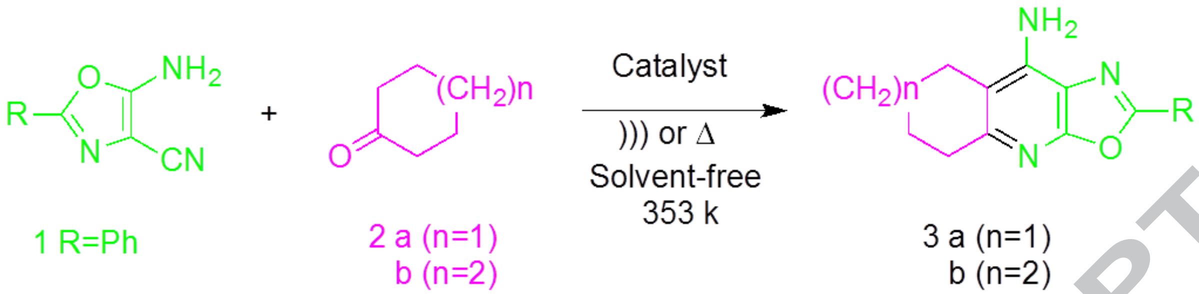
2.3.2 2-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]oxazolo[4,5-e]pyridin-10-amine 3b.

As a white crystals; mp 282-284 °C; IR ν$_{max}$ 3395, 3333, 3198, 2962, 2918, 2850, 1656, 1628, 1487, 1452, 1338, 1286, 1251, 1060 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.05 (m, H2′, H6′, 2 H), 7.54 (m, H3′, H4,′ H5′, 3 H), 6.14 (br s, NH$_2$, 2 H), 2.87 (m, H9, 2H), 2.70 (m, H5, 2H), 1.76 (m, H7, 2H), 1.53 (m, H6, H8, 4H);^{13}C NMR (DMSO-d_6, 100 MHz) δ 158.1 (C9a)*, 157.2 (C2)*, 152.4 (C8a), 145.3 (C4), 131.1 (C4′), 129.1 (2C, C3′, C5′), 127.1 (C1′), 126.5 (2C, C2′, C6′), 117.6 (C3a), 111.8 (C4a), 32.9 (C8), 23.1 (C5), 22.5 (C7)**, 22.2 (C6)**; MS (EI) *m/z* (%): 265 [M]$^+$ (100), 264 (60), 250 (19), 238 (12), 237 [M-CO]$^+$ (50), 133 (12), 105 (24), 104 (12), 78 (8), 77 [Ph]$^+$ (23).

2 Results and discussion

Heterocyclic analogues of anthranilonitrile such as various α-aminonitriles have been studied to react with cyclic ketones [14]. These compounds have paved the way to appearance of multiple fashions for having them synthesized. In conclusion, several Rings A [14] modified structures have been presented (Figure 2).

Following the investigation to synthesize 1,3-oxazoles derivatives [46‹47], the 1,3-oxazole precursor was produced which indicated reliable analytical spectroscopic data. Furthermore, heteronuclear multiple bond correlation (HMBC) and heteronuclear single quantum coherence (HSQC) experiments are used in order to evaluate the reliability of ^{13}C NMR data and the result corresponds with the data demonstrated for 1,3-oxazoles [48]. Three synthesis routes to analogues of tacrine are described [49]: reaction of anthranilonitriles with cyclohexanone and other ketones, reaction of various anilines with α-cyanoketones, and reaction involving anilines and cyclic β-ketoesters.



Scheme 1. Friedländer reaction between 5-amino-4-cyano-1,3-oxazole 1 and the corresponding cycloalkanones 2 (a and b).

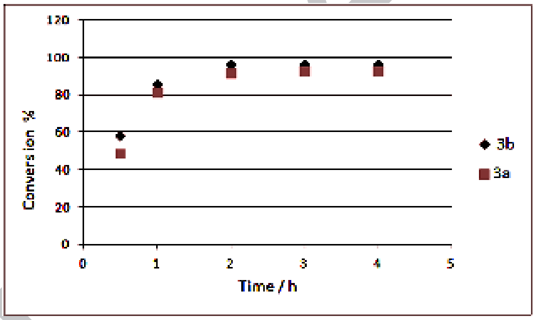


Figure 3. Kinetic profiles for the Friedländer reaction of 1 with 2a (■) and 2b (♦) at 353 K.

We developed the first route with the application of the precursor of 5-amino-4-cyano-2-phenyl-1, 3-oxazole and its reaction with the corresponding cycloalkanones in solvent-free conditions, both under conventional and ultrasonic irradiation. The effects of ultrasound on organic reactions, the energy generated by the destruction of many bubbles generated in the reaction medium by sound waves is likely to provide the energy necessary to form bonds and break them down. Carreiras et al. reported the traditional synthesis of tacrine analogues using an aluminum chloride catalyst in dry 1, 2-dichloroethane solvent under reflux conditions for three days. This synthesis is a very time consuming and energy-consuming process [44]. As part of our interest in the development of synthetically useful methods, we report herein that [$Cu_3(BTC)_2$] is an efficient, reusable, rapidly, economically, safely technique and environmental-friendly catalyst for the Friedländer reactions between 5-amino-4-cyano-2-phenyl-1,3-oxazole 1 and the corresponding cycloalkanones 2 (a and b) to afford the relating oxazolo[5,4-b]quinolin 3a and cyclohepta[b] oxazolo[4,5-e]pyridine 3b (Scheme 1 and Figure 3), employing [$Cu_3(BTC)_2$] for these cyclodehydration reactions not reported in the literature.

Pérez-Mayoral et al. determined the surface area (1499 m^2g^{-1}) of [Cu_3 (BTC) $_2$] by measurement of adsorption isotherms of nitrogen at 77 K by applying the BET method. They also calculated the pore volume (0.642 m^3 g^{-1}) and diameter (1.0 nm) of the catalyst under study by using BJH method. It has also been reported that X-ray powder diffraction has shown that significant structural changes in the catalyst structure have not occurred after the reaction [31]. The use of the catalyst [Cu_3 (BTC) $_2$] reduced the time of the synthesis of oxazolo[5,4-b]quinolines from 72 h under classical conditions to 2 h. Application of ultrasound irradiation in the presence of the [$Cu_3(BTC)_2$] reduced the reaction time to 20 min (Table I). In addition, the yield of products were improved by 10-15% in comparison with those obtained by reflux in dry 1,2-dichloroethane [44]. Because [$Cu_3(BTC)_2$] is prepared from two starting materials $Cu(NO_3)_2.3H_2O$ and benzene-1,3,5-tricarboxylic acid (H_3BTC), Thus, the carboxylic acid group in H_3BTC can play an important role of Brǿnsted acid, and copper can also play the role of lewis acid. In order to find the role of acid active sites in structure [$Cu_3(BTC)_2$], we performed a condensation reaction of 1 with 2b in the presence of $Cu(NO_3)_2.3H_2O$ and H_3BTC (50 mg for each reaction), during 2 hours, the tacrine analogue was purified with a yield of 92% and 25%, respectively (Figure 4).

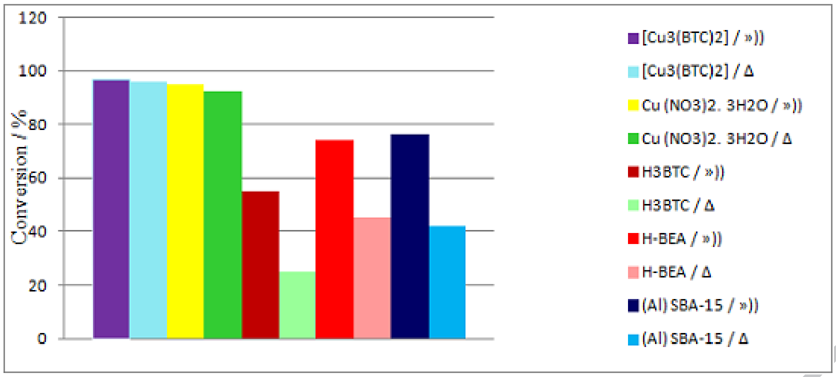


Figure 4. Conversion for Friedländer annulations between 1 and 2b under conventional (Δ, after 2h) and ultrasonic illumination (»)), after 25 min), catalyzed by $[Cu_3(BTC)_2]$, Cu $(NO_3)_2$. $3H_2O$, H_3BTC, H-BEA and (Al) SBA-15.

Table I. Preparation of tacrine analogues 3a (b) under conventional and ultrasound conditions.

				Ultrasound irradiation		Conventional condition	
Entry	Compound	Condition[a]	Catalyst	Time (min)	Yield (%)	Time (h)	Yield (%)
1	3b	EDC[b]/(Reflux)	—[c]	25	—[d]	2	—[d]
2	3a	EDC[b]/(Reflux)	$AlCl_3$	—	—	72	84[e]
3	3b	EDC/(Reflux)	$AlCl_3$	—	—	72	90[e]
4	3a	—[f]/353k	$[Cu_3(BTC)_2]$	20	93	1	82
5	3a	—[f]/353k	$[Cu_3(BTC)_2]$	—	—	2	92
6	3b	—[f]/353k	$[Cu_3(BTC)_2]$	20	97	1	86
7	3b	—[f]/353k	$[Cu_3(BTC)_2]$	—	—	2	96
8	3b	—[f]/353k	$Cu(NO_3)_2.3H_2O$	25	95	2	92
9	3b	—[f]/353k	H_3BTC	25	55	2	25
10	3b	—[f]/353k	H-BEA	25	74	2	45
11	3b	—[f]/353k	(Al) SBA-15	25	76	2	42

[a] Only used for the Conventional condition; [b] Ethylene dichloride; [c] In the absence of catalyst.

[d] Products was not found; [e] Isolated yields from Ref. [44]; [f] Solvent-free.

These results indicate that the active sites in the [$Cu_3(BTC)_2$] for synthesis of 3b are mainly copper atoms and the role of Brønsted acid is negligible. Thus, it can be concluded that the organic ligand in the MOF is in the form of carboxylate. Although the performance of catalyst [$Cu_3(BTC)_2$] and Cu $(NO_3)_2.3H_2O$ is approximately equal to this condensation reaction, the benefits of the heterogeneous [$Cu_3(BTC)_2$] catalyst should not be overlooked. We examined various amounts of [$Cu_3(BTC)_2$] in the range 1-6 mol %, at 4 mol% the optimum conditions for loading the catalyst were obtained. The loading of a catalyst above 4 mol% did not increase the yield. Also, the use of lower catalyst resulted in lower conversion.

In order to compare the catalytic activity of [$Cu_3(BTC)_2$] with other heterogeneous catalysts, H-BEA and (Al)SBA-15 (two different molecular sieves), which mainly show Lewis acidic behavior [50], were used under the same experimental conditions in the Friedländer reaction. Using catalysts H-BEA and (Al)SBA-15 yielded compound 3b, after 2 h of the reaction, in 45% and 42% respectively, in contrast to 96% conversion over [$Cu_3(BTC)_2$]. The results are presented in Table I. This procedure is economical in terms of energy and time and in a milder and cleaner environment. While the preparation of these compounds in the classical manner required 72 h, in the new method, the synthesis of compounds was carried out in a short time (25 min). Because catalyst reuse is critical in industrial application, recovery and reuse of the catalyst, [$Cu_3(BTC)_2$], for Friedländer annulations between 1 and 2b under ultrasonic illumination have been investigated. The catalyst was recycled after use, washed five times with ethanol (96%), Centrifuged and for 5 h at 333 K, it was dried to be used for further experiments. This process was repeated six times while the catalyst maintained its catalytic activity in all cycles. The result is shown in **Figure 5.** It should be noted that in each cycle of reactions, all have been observed under a given condition and for a fixed period of time. The time-conversion plot of each catalyst cycle for product formation 3b (**Figure 6**) shows the durability and stability of the catalyst have been considerably preserved.

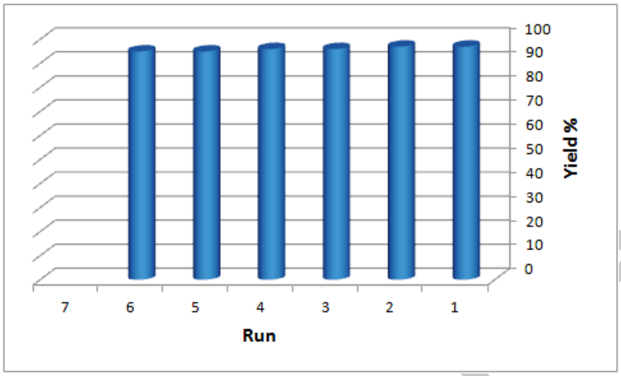


Figure 5. Investigation of the catalyst reusability, [$Cu_3(BTC)_2$], for Friedländer annulations between 1 and 2b under ultrasonic illumination.

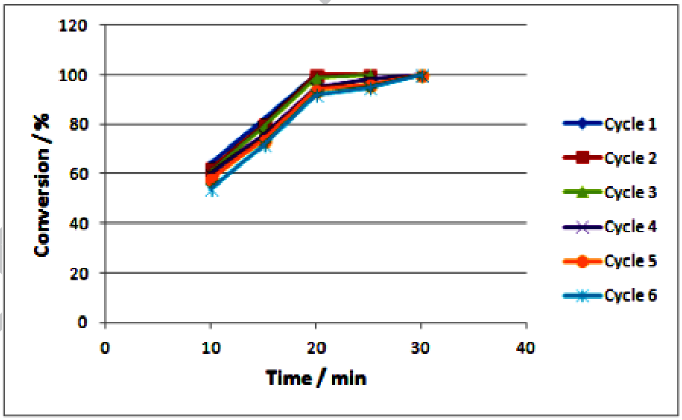


Figure 6. The time-conversion plot of each catalyst cycle for product formation 3b.

Due to the catalyst was heterogeneous and reused; the crystal stability was investigated by various techniques such as XRD, BET and ICP in the catalytic process that demonstrate excellent stability in reaction conditions. X-ray diffraction patterns of different [$Cu_3(BTC)_2$]

samples are shown in Figure 7; These data are in full compliance with literature [34]. However, a comparison of the diffraction patterns corresponding to the [$Cu_3(BTC)_2$] structure before and after several reaction runs did not reveal significant differences. The thermal stability of [$Cu_3(BTC)_2$] was studied in a thermogravimetric analysis (TGA) experiment in inert environment (nitrogen) and reported in Figure 8. The TGA profile shows two major weight loss values between 300 and 650 K. The first major weight loss is attributed to the removal of water that is physically absorbed by the catalytic structure. The exact height of this step depends on the initial degree of hydration of the catalyst. The second stage of the main weight loss indicates the decomposition of the metal-organic structure at 550 K, confirming the indications coming from the previous characterizations [34]. After three reactions runs of 20 minutes each with 1 and 2b, the [$Cu_3(BTC)_2$] samples were activated for 20 h at 130 °C under vacuum and analyzed by measurement of adsorption isotherms of nitrogen at 77 K by applying the BET method. The adsorption and desorption curve of catalyst is shown in Figure 9. With nitrogen physisorption measurements specific surfaces 1236 m^2 g^{-1} and pore volumes 0.60 cm^3 g^{-1} were measured for samples. All sorption curves are type I isotherms typically associated to microporous materials. Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES Analysis) was carried out at the end of the reaction after the reaction using [$Cu_3(BTC)_2$]. The obtained result showed that Cu species in reaction mixture were below the detection limit (ca. 10 ppm), indicating that the catalyst has heterogeneous nature. As a proof of the heterogeneity of the Friedländer reaction of 1 with 2b, a hot filtration test was performed, as shown in Figure 10. After removing the catalyst of the reaction mixture, ceased the reaction. It is obvious that no leaching occurred in the reaction; no conversion was observed without catalyst. We notice that catalytic activity results from the presence of the solid catalyst and does not occur through molecular species that are likely to be present in the reaction mixture. Therefore, the reaction is carried out through heterogeneous mechanism.

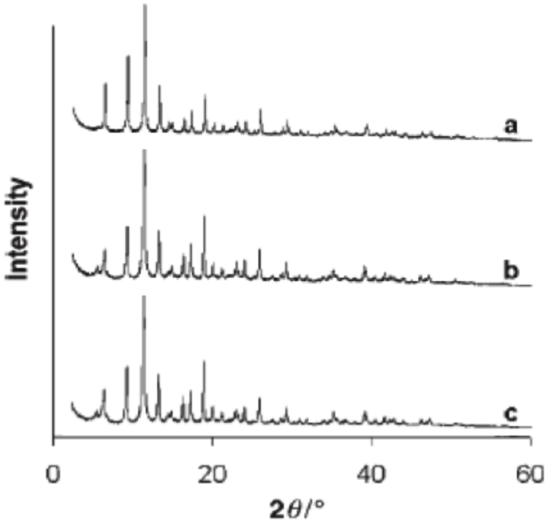


Figure 7. X-ray diffractograms of [$Cu_3(BTC)_2$] after several reaction runs: fresh catalyst, as a reference (c), after six reactions runs of 20 minutes each with 2b and 1 (b), and after three reactions runs of 20 minutes each with 2b and 1 (a).

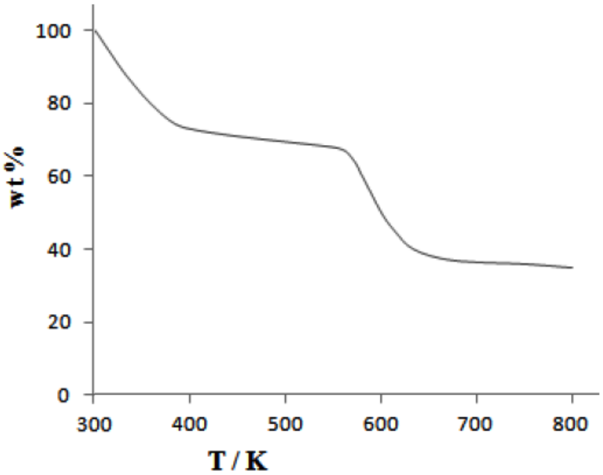


Figure 8. Weight loss in function of temperature for [$Cu_3(BTC)_2$] upon heating (5 $Kmin^{-1}$) in N_2.

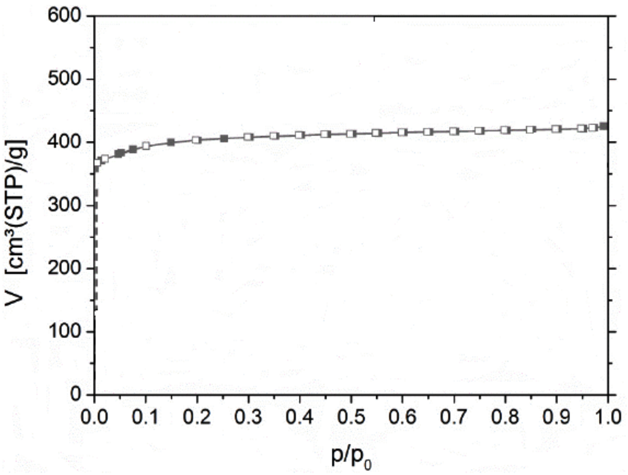


Figure 9. Nitrogen adsorption isotherm of [$Cu_3(BTC)_2$]. Desorption and adsorption curves coincide.

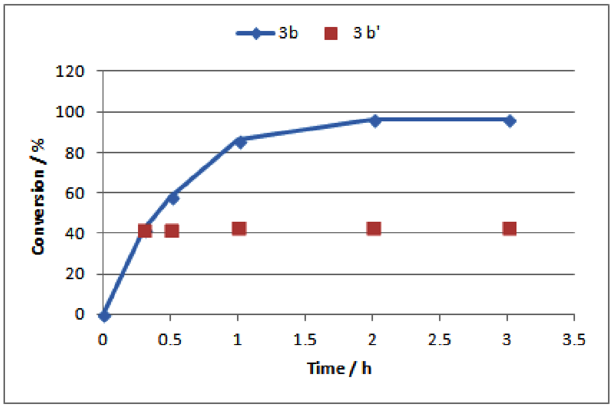


Figure 10. Filtration experiment for the Friedländer reaction between 1 and 2b. After 0.3 h of the reaction time, the catalyst was filtrated. The reaction mixture was further kept at reaction conditions without solid catalyst.

3 Conclusion

Application of ultrasound with the [$Cu_3(BTC)_2$] in the synthesis of organic compounds has led to a reduction in the energy requirements for the environmental and economic impacts of this method. Due to the great importance of green chemistry for the synthesis of organic compounds, an optimized method for the preparation of oxazolo[5,4-b]quinoline derivatives has been developed. The advantages of using ultrasonic illumination in chemical reactions, such as shorter reaction times, higher yield and mild conditions could be of used in industrial applications in the pharmaceutical industry or the standard chemical industry. The critical issues of the MOF stability were studied by various techniques such as XRD, BET and ICP that shows the durability and stability of the catalyst have been considerably preserved in reaction conditions.

Acknowledgement

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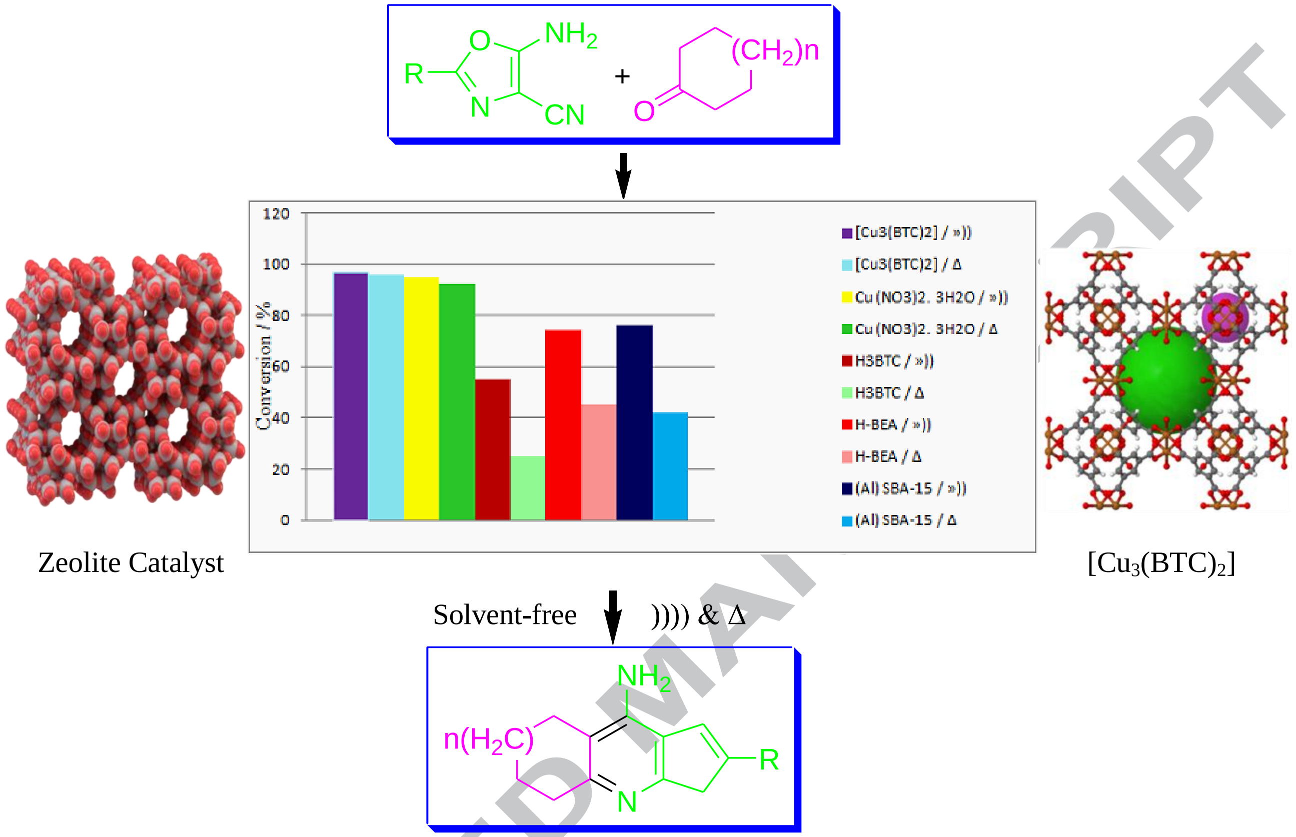
Graphical abstract



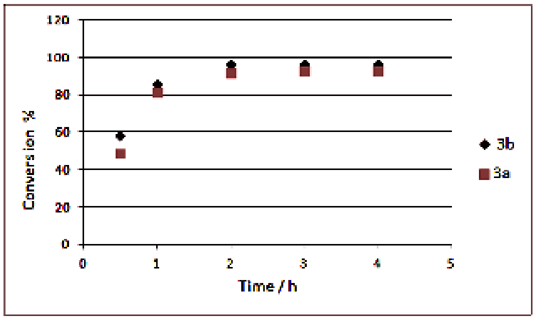


Figure 3. Kinetic profiles for the Friedländer reaction of 1 with 2a (■) and 2b (♦) at 353 K.

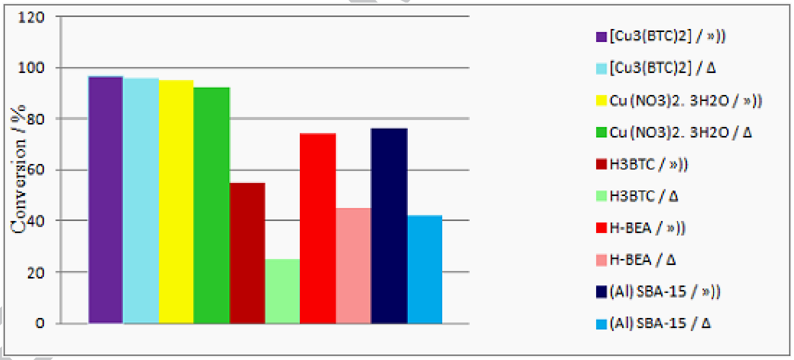


Figure 4. Conversion for Friedländer annulations between 1 and 2b under conventional (Δ, after 2h) and ultrasonic illumination (»)), after 25 min), catalyzed by [$Cu_3(BTC)_2$], Cu $(NO_3)_2$. $3H_2O$, H_3BTC, H-BEA and (Al) SBA-15.

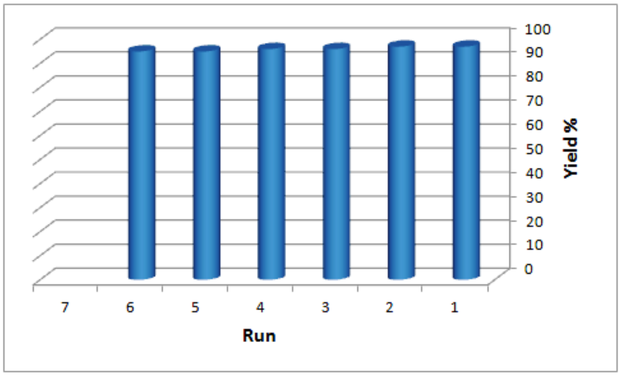


Figure 5. Investigation of the catalyst reusability, [$Cu_3(BTC)_2$], for Friedländer annulations between 1 and 2b under ultrasonic illumination.

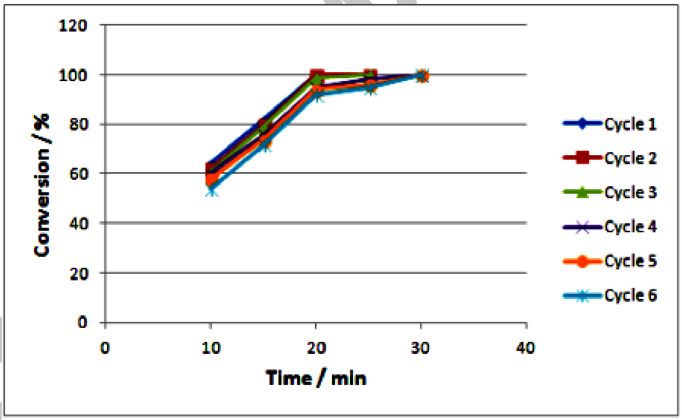


Figure 6. The time-conversion plot of each catalyst cycle for product formation 3b.

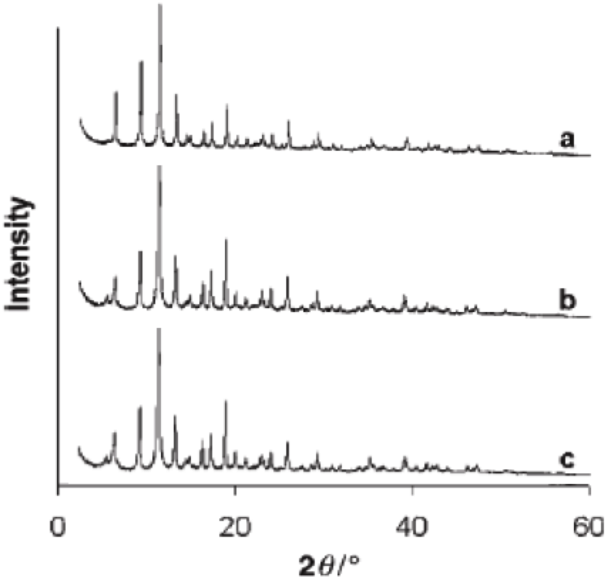


Figure 7. X-ray diffractograms of [$Cu_3(BTC)_2$] after several reaction runs: fresh catalyst, as a reference (c), after six reactions runs of 20 minutes each with 2b and 1 (b), and after three reactions runs of 20 minutes each with 2b and 1 (a).

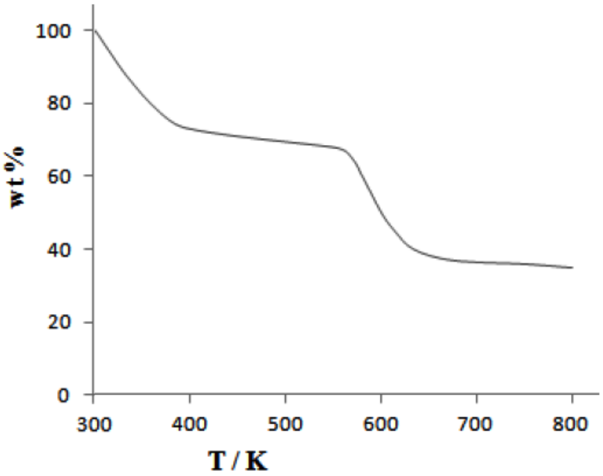


Figure 8. Weight loss in function of temperature for [$Cu_3(BTC)_2$] upon heating (5 $Kmin^{-1}$) in N_2.

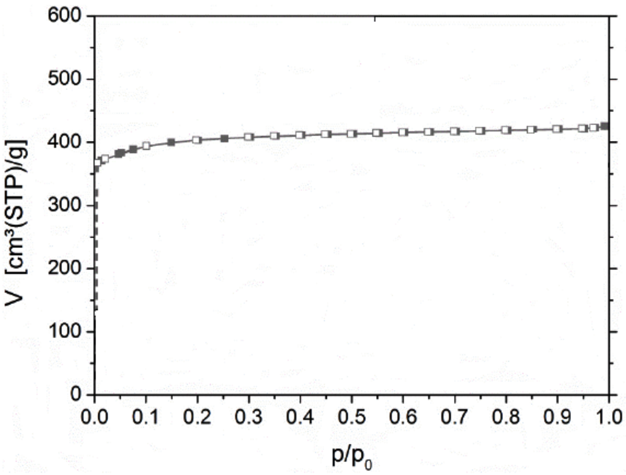


Figure 9. Nitrogen adsorption isotherm of [$Cu_3(BTC)_2$]. Desorption and adsorption curves coincide.

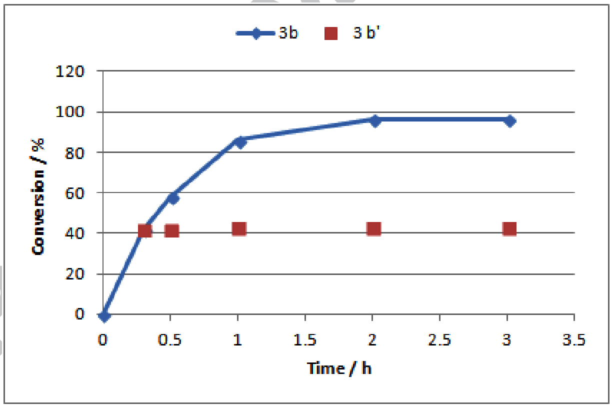


Figure 10: Filtration experiment for the Friedländer reaction between 1 and 2b. After 0.3 h of the reaction time, the catalyst was filtrated. The reaction mixture was further kept at reaction conditions without solid catalyst.

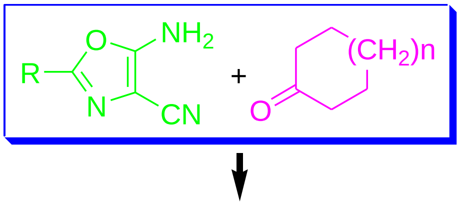
Table I. Preparation of tacrine analogues 3a (b) under conventional and ultrasound conditions.

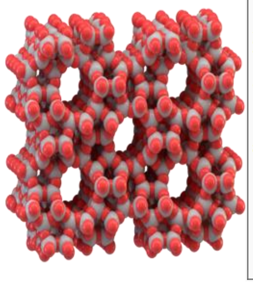
				Ultrasound irradiation		Conventional condition	
Entry	Compound	Condition[a]	Catalyst	Time (min)	Yield (%)	Time (h)	Yield (%)
1	3b	EDC[b]/(Reflux)	–[c]	25	–[d]	2	–[d]
2	3a	EDC[b]/(Reflux)	$AlCl_3$	–	–	72	84[e]
3	3b	EDC/(Reflux)	$AlCl_3$	–	–	72	90[e]
4	3a	–[f]/353k	$[Cu_3(BTC)_2]$	20	93	1	82
5	3a	–[f]/353k	$[Cu_3(BTC)_2]$	–	–	2	92
6	3b	–[f]/353k	$[Cu_3(BTC)_2]$	20	97	1	86
7	3b	–[f]/353k	$[Cu_3(BTC)_2]$	–	–	2	96
8	3b	–[f]/353k	$Cu(NO_3)_2.3H_2O$	25	95	2	92
9	3b	–[f]/353k	H_3BTC	25	55	2	25
10	3b	–[f]/353k	H-BEA	25	74	2	45
11	3b	–[f]/353k	(Al) SBA-15	25	76	2	42

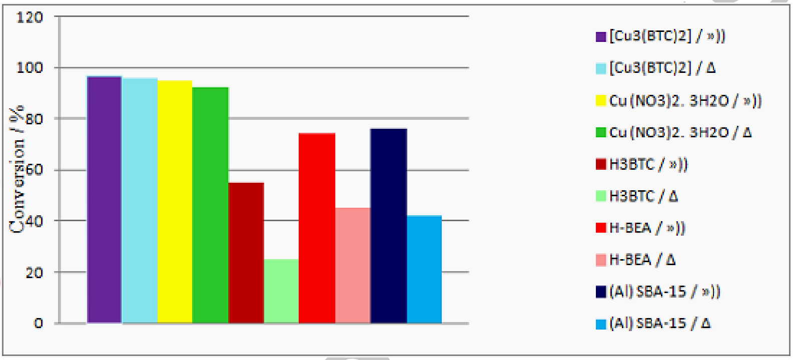
[a] Only used for the Conventional condition; [b] Ethylene dichloride; [c] In the absence of catalyst.

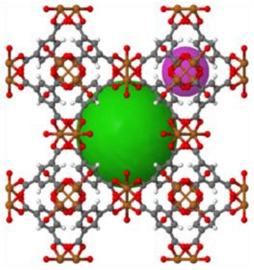
[d] Products was not found; [e] Isolated yields from Ref. [44]; [f] Solvent-free.

Graphical Abstract-synopsis



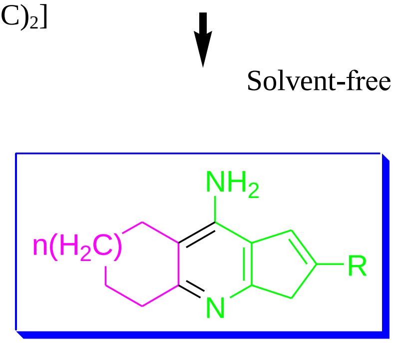






Zeolite Catalyst [$Cu_3(BTC)_2$]

Solvent-free))) & Δ



Using a green and simple route with ultrasound illumination, for synthesizing tacrine analogues was considered. Use of [Cu_3 (BTC) $_2$] as an environment-friendly for improved synthesis of oxazolo[5,4-b]quinoline derivatives was described under mild and clean conditions, and was compared with catalysis activity of H-BEA, (Al)SBA-15, Cu $(NO_3)_2.3H_2O$ and H_3BTC. The results of this study indicate that the active sites in the [Cu3(BTC)2] for synthesis of cyclohepta[b] oxazolo[4,5-e]pyridine are mainly copper atoms and the role of Brønsted acid organic ligand in the MOF is negligible.