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Synthesis and Catalytic Applications of Ruthenium(0) Nanoparticles in Click Chemistry

Avvaru Praveen Kumar, Min-Wook Baek, Chirumarry Sridhar, Begari Prem Kumar, and Yong-Ill Lee*

*Department of Chemistry, Changwon National University, Changwon 641-773, Korea. *E-mail: yilee@changwon.ac.kr*
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Here we report a facile synthesis of ruthenium (Ru) Nanoparticles (NPs) by chemical co-precipitation method. The calcination of ruthenium hydroxide samples at 500 ºC under hydrogen atmosphere lead to the formation of Ru^0 NPs. The size and aggregation of Ru NPs depends on the pH of the medium, and type of surfactant and its concentration. The X-ray diffraction (XRD), scanning electron microscope (SEM) and transmission electron microscope image (TEM) analyses of particles indicated the formation of Ru^0 NPs, and have 10 to 20 nm sizes. As-synthesized Ru^0 NPs are characterized and investigated their catalytic ability in click chemistry (azide-alkyne cycloaddition reactions), showing good results in terms of reactivity. Interestingly, small structural differences in triazines influence the catalytic activity of Ru^0 nanocatalysts. Click chemistry has recently emerged to become one of the most powerful tools in drug discovery, chemical biology, proteomics, medical sciences and nanotechnology/nanomedicine. In addition, preliminary tests of recycling showed good results with neither loss of activity or significant precipitation.

Key Words : Ru^0 Nanoparticles, Chemical co-precipitation, Catalytic activity, Click chemistry

Introduction

The physical and chemical properties of metal nanoparticles (NPs) have directed towards an important matter in current nanoscience research due to interesting applications such as catalysis, optoelectronics, bio-detectors, telecommunications, photonics and sensors.[1,2] Metal NPs possess a high specific surface area to volume ratio and renewable energy which are creditworthy to their catalytic activity in various organic reactions to synthesize new molecules. The transition metal NPs raised a significant care on structural arrangement and elucidation of various applications especially in catalysis of interest[3-5] because they mimic metal surface activation and catalysis at nanoscale indicating higher selectivity and efficiency.[4] Role of catalysis in the development of clean chemical production with limited hazardous and toxic by-products is now well-established as an essential element of sustainable processing.[6]

Ruthenium (Ru) is a rare transition metal belonging to the platinum group and shows very unique and interesting catalytic activities for different reactions. For example, ruthenium is indispensable as a homogeneous catalyst in a variety of organic reactions.[7] It can easily adopt various formal oxidation states from −II to +VIII in chemical bonds,[8] thus giving rise to many compounds with interesting and often unique properties.[9] Despite of many synthesis methods for ruthenium dioxide (RuO_2) NPs[10,11] and stabilized Ru NPs[12,13] there were very few reports on synthesis of Ru NPs having zero oxidation state (Ru^0) which include solvothermal[14] and hydrothermal synthesis.[15]

There were many reports on supported Ru catalysts.[16-18] However, the catalytic activity alters with particle size, electronic state, oxidation state, metal-support *etc.* Intrinsically, the nature of active sites for catalytic reactions can be assessed, which may in turn allow for the rational design of catalysts for desirable reactions. Apart from supported Ru catalysts, free Ru NPs have an advantage like high percentage of Ru which leads to increased homogeneity of resulting NPs which lead to relatively high reactivity. The present work reports a facile, less cost effective and efficient synthesis of Ru^0 NPs by chemical co-precipitation method. In the literature no methods are available to synthesize Ru^0 NPs by chemical co-precipitation method. The co-precipitation is one of the successful techniques for synthesizing NPs having narrow particle size distribution. As-synthesized Ru^0 NPs have applied as nanocatalysts for azide-alkyne cycloaddition reactions (click reactions) using different substrates and results are discussed. Click chemistry is a modular approach that uses only the most practical and reliable chemical transformations. Its applications are increasingly found in all aspects of drug discovery, ranging from lead finding through combinatorial chemistry and target-templated *in situ* chemistry, to proteomics and DNA research, using bioconjugation reactions.[19-21]

Experimental

Preparation of Ru^0 Catalyst. All chemicals and solvents were of analytical grade and used as received without further purification. The typical synthesis of Ru^0 NPs as follows: $RuCl_3.H_2O$ (Aldrich-40.1% Ru) and surfactant (sodium dodecylsulfate (SDS)/cetyltrimethylammonium bromide (CTAB)/polyethylene glycol (PEG) (Sigma-Aldrich) were mixed at different molar ratios. Subsequently, the mixture was adjusted to desired pH using aqueous NH_4OH and the resultant solution was stirred for 2 h. The resultant suspen-

sion was precipitated with 2-propanol and then centrifuged at 5000 rpm under room temperature. The obtained precipitate was washed with water and acetone several times, respectively, and then dried at 60 ºC in an oven. Finally, the dried precipitate was ground and calcined at 500 ºC under hydrogen gas atmosphere for 2 h to produce Ru^0 NPs.

Instrumentation. Thermogravimetric and thermal differential analyses (TG-DTA) of Ru^0 NP samples were performed by a simultaneous *SDT Q200 (USA)* analyzer at a heating rate of 10 ºC min^{-1} under nitrogen gas flow. The XRD patterns of the calcined Ru^0 NPs were recorded using X-ray diffraction (Philips X'pert MPD 3040) with Cu Kα radiation over a 2θ range from 20º to 80º at 2.5º/min. Transmission electron microscopy (JEM 2100F) was performed at an accelerating voltage of 200 kV on a copper grid. Scanning electron microscopy (SEM) images and energy dispersive spectrometry (EDS) of the products were obtained on a field-emission scanning electron micro analyzer (FE-SEM-MIRA II, LMH). ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker Avance-400 spectrometer.

Procedure for Click Reactions. The chemicals for all click reactions were obtained from commercial suppliers and used without purification. All reactions were performed under a nitrogen atmosphere. *Click reactions **1**, **2** & **3**:* To a solution of azide (1.09 mmol, 1 eq) and alkyne (1.31 mmol, 1.2 eq) in THF (10 mL) was added Ru^0 NPs (5 mg). The reaction was flushed with nitrogen, capped and heated to 70 ºC for 4 h. After monitoring the reaction mixture by TLC, the Ru^0 catalyst was collected through filtration wash twice with ethyl acetate (10 × 2) and reused for next reaction. Filtrate was concentrated in vacuum rotary vapor to remove organic solvents to obtained a cured compound which upon purified by column chromatography (ethyl acetate/hexane 1/6) to get corresponding products.

Click Reaction Product 1: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 4.76 (d, *J* = 7.07 Hz, 2H), 4.28-4.45 (m, 2H), 3.88-4.04 (brs, 1H), 1.8-2.00 (m, 2H), 1.17-1.46 (m, 14H), 0.87 (t, *J* = 7.07 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 136.01, 121.29, 59.87, 49.63, 31.34, 28.92, 28.88, 28.75, 28.58, 28.49, 25.95, 22.14, 13.59.

Click Reaction Product 2: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.33-7.39 (m, 3H), 7.26-7.30 (m, 2H), 5.53 (s, 2H), 4.77 (s, 2H), 3.75 (brs, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 134.04, 129.06, 128.80, 128.22, 127.79, 122.31, 55.80, 54.38.

Click Reaction Product 3: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.28-7.35 (m, 3H), 7.19-7.27 (m, 2H), 5.47 (s, 2H), 3.86 (s, 2H), 3.63 (bs, 1H), 2.91(t, *J* = 6.06 Hz, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 134.41, 128.90, 128.54, 127.95, 127.66, 122.29, 61.14, 54.05, 28.75.

Click Reactions 4 & 5: To a solution of azide (2.88 mmol, 3.5 eq) and (alkyne) 2,4,6-tris(prop-2-ynyloxy)-1,3,5-triazine (0.823 mmol, 1 eq) in THF (10 mL) was added Ru^o NPs (10 mg). The reaction was flushed with nitrogen, capped and heated to 70 ºC for 4 hours. After monitoring the reaction mixture by TLC, the Ru^0 catalyst was collected through filtration wash twice with ethyl acetate (10 × 2) and reused for next reaction. Filtrate was concentrated in vacuum rotary vapor to remove organic solvents to obtained a cured compound which upon purified by column chromatography.

Click Reaction Product 4: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 3H), 5.69 (s, 6H), 4.35-4.46 (m, 6H), 1.8-2.07 (m, 6H), 1.15-1.43 (m, 48H), 0.9 (t, *J* = 7.07 Hz, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.55, 137.93, 123.59, 63.02, 50.62, 31.98, 29.79, 29.40, 29.31, 29.19, 28.90, 26.28, 20.96, 14.12.

Click Reaction Product 5: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32-7.42 (m, 18H), 5.61 (s, 6H), 4.36 (s, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.59, 135.31, 129.21, 128.80, 128.27, 128.17, 123.01, 76.85, 54.76.

Results and Discussion

Initially, the experiments were performed to prepare Ru^0 NPs at different pHs ranging from 8 to 11 without adding surfactant. The chemical reactions involved during the formation of Ru^0 NPs can be represented in the following equations:

$$RuCl_3 + NH_4OH \xrightarrow{\text{pH 8, 9, 10 or 11}} Ru(OH)_3\downarrow + 3\,NH_4Cl$$

$$2\,Ru(OH)_3 \xrightarrow[600\ ^oC]{H_2} 2\,RuO_2 + 2\,H_2O + H_2$$

$$2\,RuO_2 \xrightarrow[600\ ^oC]{H_2} 2\,Ru + 4\,H_2O$$

It has been observed the aggregation of Ru^0 NPs in all pHs, and their sizes were 30 ± 2 nm and 25 ± 2 nm for pHs 8 and 9, respectively, there after increased NP size to 40 nm, and also their aggregation. It is recognizable that pH influences Ru^0 NPs size and so pH 9 was preferred for further synthesis. The reason could be as the pH of the ruthenium reaction system changes from acidic to basic, $Ru(OH)_3$ generates by hydrolysis of Ru^{3+}. Subsequently, as pH of the reaction system increased, nucleation of Ru^{3+} nucleus is easier and also growth of Ru^{3+} nucleus is easier to happen to increase Ru NPs size and their aggregation.

In order to reduce size, aggregation and better dispersion of Ru^0 NPs, three different types of surfactants including anionic (SDS), cationic (CTAB) and non-ionic (PEG) were tested. The anionic surfactant, SDS was found to be less aggregation and better dispersion of particles, and then PEG and CTAB, respectively. This could be associated with different mechanisms of different kinds of surfactants. The NPs surface possesses either positive or negative charge in aqueous medium by ionization or dissociation of surface groups and they can absorb ionic surfactants. This consequence in the formation of an electrical double layer to prevent aggregation.[22] Accordingly, Ru^0 NPs acquires positive charges in aqueous solution at basic pHs and therefore, anionic SDS surfactant can easily be absorbed on the surface of the nanoparticle precipitates and form a molecular layer on the surface of the particles to stop their aggregation. Further, the concentration effect of SDS was performed at 5

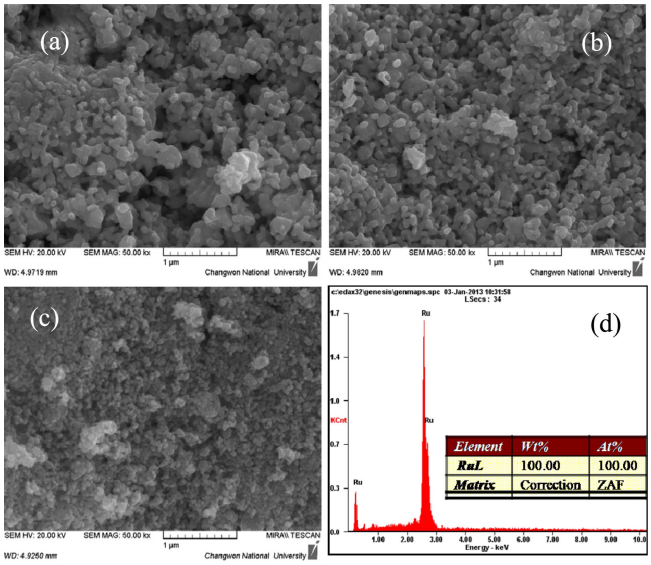


Figure 1. FE-SEM images of Ru^0 NP samples at pH 9.0: Molar ratios of [Ru]:[SDS], (a) 1:25, (b) 1.50, (c) 1:100, and (d) EDAX analysis.

different molar ratios of [Ru]:[SDS] from 1:25 to 1:200, so as to get better dispersion and lower particle sizes. As shown in the Figure 1, a molar ratio of 1:100 (Fig. 1(c)) was found to be low aggregation of Ru^0 NPs and further increase of this molar ratio resulting an increased aggregation, indicated saturated concentration of surfactant. The increased surfactant concentration gives higher viscosity which led to reduced rate of surfactant migration and decreased rate of electrostatic repulsion, thereby promoting the particle aggregation.[23] The EDAX analysis of Ru^0 NPs was presented in Figure 1(d) and shows the existence of only Ru content, indicates the complete reduction of $Ru(OH)_3$ to RuO_2 and then to Ru(0).

The TEM images of Ru^0 NP samples were presented in Figure 2(a) and (b), and confirm the surfactant role to reduce the aggregation and better dispersion Ru^0 NPs. TEM indicates the Ru^0 NPs were formed between 10 to 20 nm sizes. Figure 2(c) shows the selected area electron diffraction pattern (SAED) of Ru^0 NPs. The Ru^0 NPs sample ([Ru]:[SDS] ratio = 1:100) displays six diffused diffraction rings, assigned to the (100), (002), (101), (102), (110), and (103) reflections, respectively, corresponding to hexagonal close-packed (hcp). The effect of Ru content was also carried out by keeping the surfactant concentration constant and varying the concentration of Ru (three different concentrations including 0.25, 0.5, 1 and 2.5 mM). It was observed that the increased concentration of Ru makes to increase the particle size as well as increased aggregation. So, a 0.5 mM concentration of Ru was found to be optimum (Fig. 2(b)).

Figure 3(a) shows the TGA curve of the Ru^0 NPs sample before clacination. From TGA curve it has been observed that the weight loss was up to 500 ºC and after that there was no significant weight loss. This weight loss is due to dehydration process wherein a significant amount of water is released from the $Ru(OH)_3$ sample. Figure 3(b) presents the

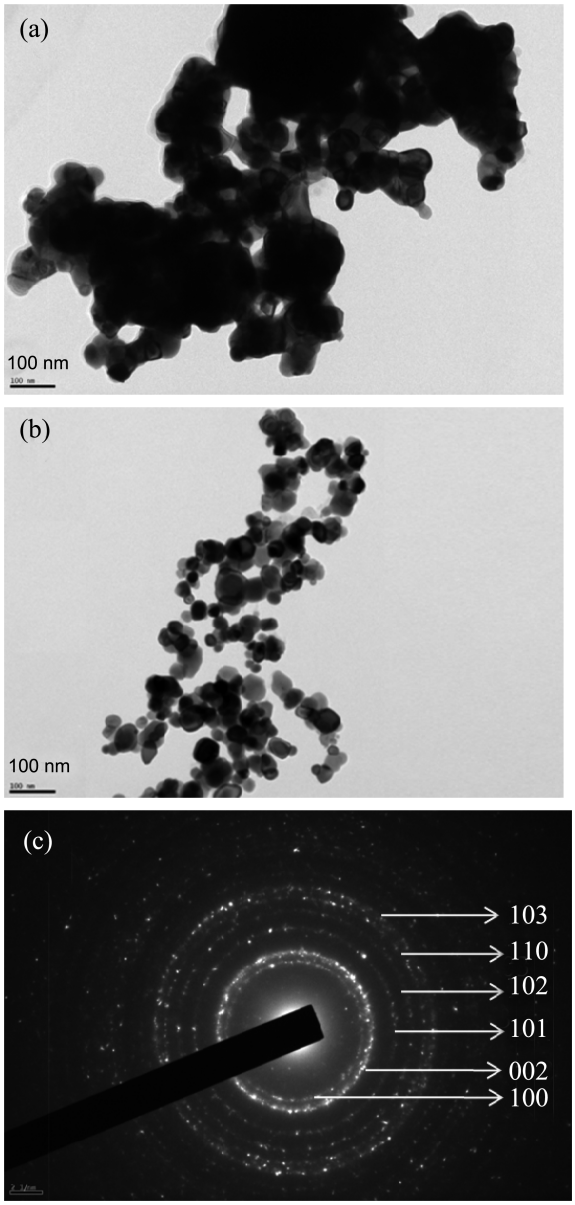


Figure 2. TEM images of Ru^0 NP samples at pH 9.0: (a) No surfactant ([Ru] = 0.5 mM), (b) molar ratios of [Ru]:[SDS] = 1:100, and (c) electron diffraction pattern.

XRD pattern of the Ru^0 NPs calcined at 500 ºC which were prepared using SDS surfactant. The sharp peaks at 38.4, 42.2, 44.0, 58.2, 69.6, and 78.4 degree 2θ are due to the diffractions of the (100), (002), (101), (102), (110), and (103) planes of the hexagonal close-packed (hcp) Ru metal, respectively (ICDD-JCPDS card No. 06-0663). This indicates the reduction of RuO_2 to Ru(0) during calcination in hydrogen gas atmosphere and confirms the formation of Ru^0 NPs.

Click chemistry directs mainly on high degree of efficient reactions that would achieve quantitative conversion under modest conditions and necessitate only facile separations. Click reactions are ideal candidates for broad implementation and development in chemical, biological, pharmaceutical, drug development, medical and biomedical appli-

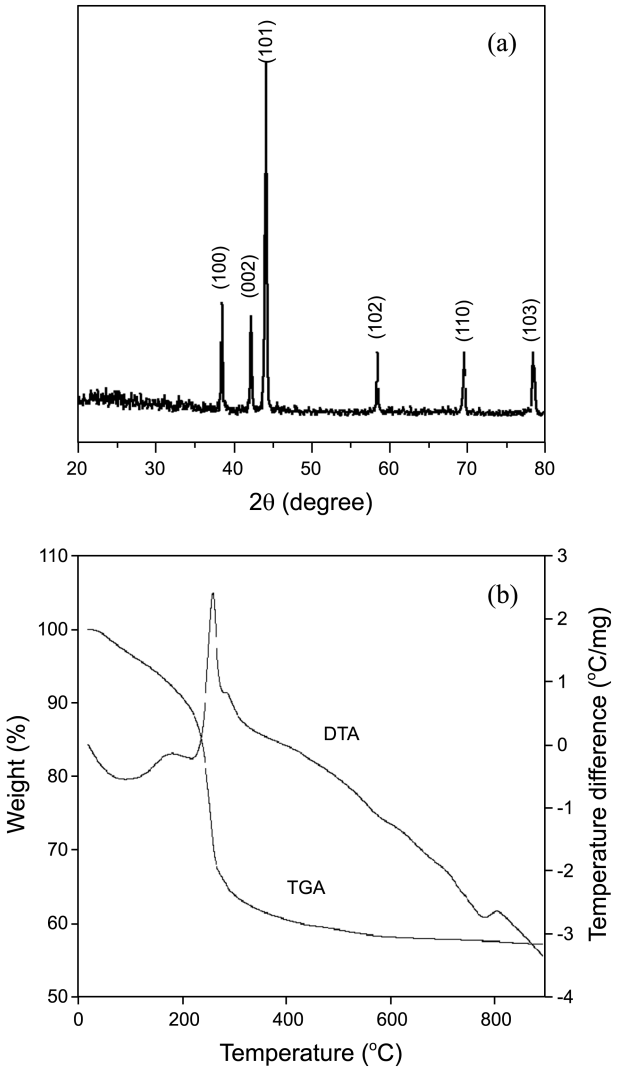
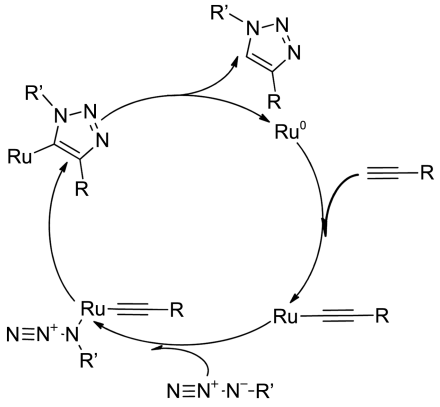


Figure 3. (a) XRD pattern and (b) TG-DTA curves of Ru^0 NP samples at pH 9.0.

cations.[19-21,24,25] The Cu(I)-catalyzed azide-alkyne cycloaddition reactions (click reactions)[26,27] have enabled discovery of novel bioactive compounds and ligands for transition metals, new materials, and bioconjugates, emphasizing its wide range and fidelity.[28,29] Apart from Cu(I), Ru-catalyzed azide-alkyne cycloaddition reactions have received considerable attention during recent years.[30,31,32] Keeping in mind the broad scope of transformations of alkynes catalyzed by ruthenium species, the catalytic activity of as-synthesized Ru^0 NPs in azide-alkyne cycloadditions has been evaluated for the synthesis of 1,2,3-triazoles.

In this work, we synthesized mono-triazoles and tri-triazoles in one molecule. Mono-triazoles were synthesized by considering propyne-1-ol and butyne-1-ol as alkynes and 1-azidodecane and benzyl azide as azides (Table 1). The obtained products were characterized by ^{1}H-NMR and ^{13}C-NMR to confirm the structures **1**, **2** and **3**. ^{1}H-NMR of compound **1** peaks at δ 7.59 (s, 1H) indicates the presence of olefinic proton of triazole ring, δ 4.76 (d, J = 7.07 Hz, 2H) indicates the presence of -CH_2-OH, and the peak at 4.28-



Scheme 1. Proposed mechanism for Ru^0 catalyzed click reactions.

4.45 (m, 2H) presence of -CH_2-N-. ^{13}C-NMR of compounds **1**, **2** and **3** peaks at δ 121.29, δ 122.31 and δ 122.29 clearly indicates 1,4-disubstituted-1*H*-1,2,3-triazole, which is uncommon reaction product using regular Ru catalysts.[33] The proposed mechanism of the Ru^0 NPs catalyzed click reactions was shown in Scheme 1.

Tri-triazole compounds were synthesized by choosing 2,4,6-tris(prop-2-ynyloxy)-1,3,5-triazine (alkyne) and 1-azidodecane and benzyl azide (azides) which are catalyzed by Ru^0 NPs. The compound **4** shows the characteristic peak at δ 7.81 (s, 3H) indicates the presence of three triazole rings, and in ^{13}C-NMR triazine ring carbons were detected at δ 171.57 and triazole ring carbons at δ 137.93 and 123.59. The transformations may be particularly applicable for drug discovery, not just because of its reliability as a linking reaction, but also because of the favorable physicochemical properties of triazoles. Indeed, as-synthesized Ru^0 NPs have

Table 1. Ru^0 NPs catalyzed cycloadditions of azides and alkynes

S. No	Reactants (Azide)	Reactants (Alkyne)	Product	Yield (%)
1	$C_{10}H_{21}-N_3$	OH	$C_{10}H_{21}$ N-N N OH	76%
2	N_3	OH	N-N N OH	73%
3	N_3	OH	N-N N OH	71%
4	$C_{10}H_{21}-N_3$		$C_{10}H_{21}$	60%
5	N_3			64%

to be efficient and selective catalysts for azide-alkyne reactions.

The recyclability of the catalyst was performed for **1** and **2** azide-alkyne reactions. It has been obtained 97% of the reaction products after three cycles of the reactions and did not show significant change in the morphology of the Ru^0 catalyst nanoparticles, which suggests the repetitive catalytic performance. The synthesized Ru^0 nanocatalysts also show the reaction selectivity of azide-alkyne reactions which can be tuned in favor of target products depending on the reaction conditions. Finally, synthesis and catalytic application of Ru^0 nanocatalysts are promising, and also obtained good recovery and recycling results.

Conclusions

Metal nanoparticles are of practical interest due to their unique physical properties, chemical reactivity, and potential applications in catalysis. The present chemical co-precipitation method was simple and easy way to synthesize Ru^0 NPs (ranges from 10-20 nm) which can vary by changing the operational parameters (*i.e.*, pH of the medium and type and concentration of the surfactant). As-synthesized Ru^0 nanocatalyts are used for the azide-alkyne cycloaddition reactions and the reactions proceeded smoothly to form the corresponding products with good yields. The preliminary results of recycling are good for the recovery of these Ru^0 nanocatalysts.

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