Original Research Article

Silica-Imidazole Solid Catalyst for N-Glycine Derivatives Synthesis

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ARTICLE INFORMATION

ABSTRACT

Schiff base was reacted with α-chloroacetic acid to produce N-(α-chlorobenzyl)-N-phenylglycine derivatives (N-Gly) over solid heterogeneous catalyst. Different N-Gly derivatives were synthesized over the catalyst with approximately 90% yield. Both calculated and theoretical elemental analyses of N-Gly derivatives were in agreement with each other. The functional groups of N-Gly derivatives were proved by the FT-IR spectroscopy. The melting points N-Gly derivatives were matched with those in the literature. The catalyst was produced by immobilizing sodium silicate from rice husk with 3–(chloropropyl)triethoxysilane followed by refluxed the product with p-xylyl-di-imidazolium chloride. The results showed that the optimum catalyst conditions were 5 h as reaction time, 0.25 g mass of catalyst, 90 °C as reaction temperature, and toluene as the best solvent.

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Graphical Abstract

R$_1$=H, R$_2$=H   compound 1
R$_1$=NMe$_2$, R$_2$=H compound 2
R$_3$=NMe$_2$, R$_2$=Cl compound 3

Introduction

Heterogeneous catalysis is of high significance in modern society. Since the heterogeneous catalytic reactions happen on surface and effected via several layer atoms of catalysts. Therefore, its importance makes the specific surface of the catalyst as large as possible due to the interaction with the reactant to enhance the efficiency [1]. Heterogeneous catalysis includes systems that the reaction occurs in different phases [2]. The word "phase" here means solid, liquid, gas, or any immiscible liquids such as water and oil. In general, common heterogeneous catalysts are in the solid phase, and the reactants are liquids or gases; for example, heterogeneous catalysts in solid phase metals, metal salts, metal oxides, or some organic materials such as organic hydro peroxides, ion exchangers, and enzymes.

Schiff bases are organic compounds that contain imine groups (–C=N–). It was initially synthesized by Hugo Schiff [3, 4]. These are formed via the condensation of primary amines with carbonyl compounds. Schiff bases were considered as an important widely used organic compound. Furthermore, it has many applications in different fields such as biological, analytical, and inorganic chemistry. Schiff bases have another importance in pharmaceutical and medicinal fields because of a broad spectrum of biological activities like analgesic [5, 6], anti-inflammatory [7, 8], antimicrobial [9, 10], antitubercular [11], anticonvulsant [12], and anticancer [13, 14]. Glycine ($^+$H$_3$NCH$_3$COO$^-$) is the simplest structure among the twenty natural amino acids; it acts as one-third of the collagen composition. The oxygen and nitrogen centers in the structure of amino acids enable them to act as potential sites for the binding metal ion [15]. Although glycine can be isolated from hydrolyzed protein but is not used for industrial production, as it can be manufactured more conveniently by chemical synthesis. The two main processes for glycine synthesis are the amination of chloroacetic acid with ammonia, giving glycine, and ammonium chloride [16]. About 15 thousand tons of glycine is produced annually in this way [17]. Glycine can be further prepared via the hydrolysis of

methyleneaminoacetonitrile by the successive treatments with barium hydroxide and sulfuric acid [18].

Experimental

Materials and methods

Nitric acid (Systerm 65%), Sodium hydroxide (Systerm 99%), CPTES (Sigma Aldrich 95%), Toluene (J.T.Baker 99.8%), α-chloroacetic acid (Systerm 99.5%), Nitro benzene and α,α′-Dichloro-p-xylene (Aldrich 98%), Imidazole (GCC 99%), N,N-dimethyl benzaldehyde (BDH 98%), Potassium carbonate (SDFCL, 98%), Aniline (BDH, 98%), Benzene (Merck, 98%), Absolute ethanol (HmbG Chemical, 99.74%), Glacial acetic acid (Systerm, 99.99%), p-chloroaniline (BDH, 98%), Dioxane (BDH, 98%), and Butanol (Sigma Aldrich, 99.5%) were used in this study. The RH was collected from a rice mill in Al-Muthanna Governorate. All other used chemicals were AR grade or of high purity and were used directly without further purifications Catalyst preparation RHAPrIM.

The catalyst was prepared according to our methods [19]. In general, this method included three steps. Firstly, rice husk was converted into rice husk ash (RHA), and. then immobilized with CPTES to produce silica with an organic functional group (-CH$_2$Cl) and, the product was labeled as RHACCl. The details of this method were mentioned by our team [20]. Secondly, imidazole (1.25 g, 0.018 mol) was refluxed with (1.22 g, 0.007 mol) *p*-xylylene dichloride in 30 mL ethanol overnight. The products were washed with diethyl ether and then about 6% (30 mL) of K$_2$CO$_3$ solution was used to dissolve the product. A white solid precipitated separated after 3 days and the products was labeled as bis-imi (Scheme 1a). Thirdly, 2.0 g, (0.015 mol) bis-imi was mixed with 2.0 g of RHACCl in 30 mL of dry toluene and refluxed for 24 h to produce the catalyst. The catalyst was labeled RHAPrIM (Scheme 1b).

Schiff base synthesis

A mixture of 0.01 mole (0.93 mL) of aniline, 0.01 mole (1.1 mL) of benzaldehyde in 10 mL of ethanol, and one drop of glacial acetic acid were heated in the water bath at 70-80 °C for 30 min. Then, it was left to cool in an ice-water bath, whereby yellowish-white crystals separated. The crystals were filtered, washed with 2% HCl, and then with water, and recrystallized from ethanol [18].
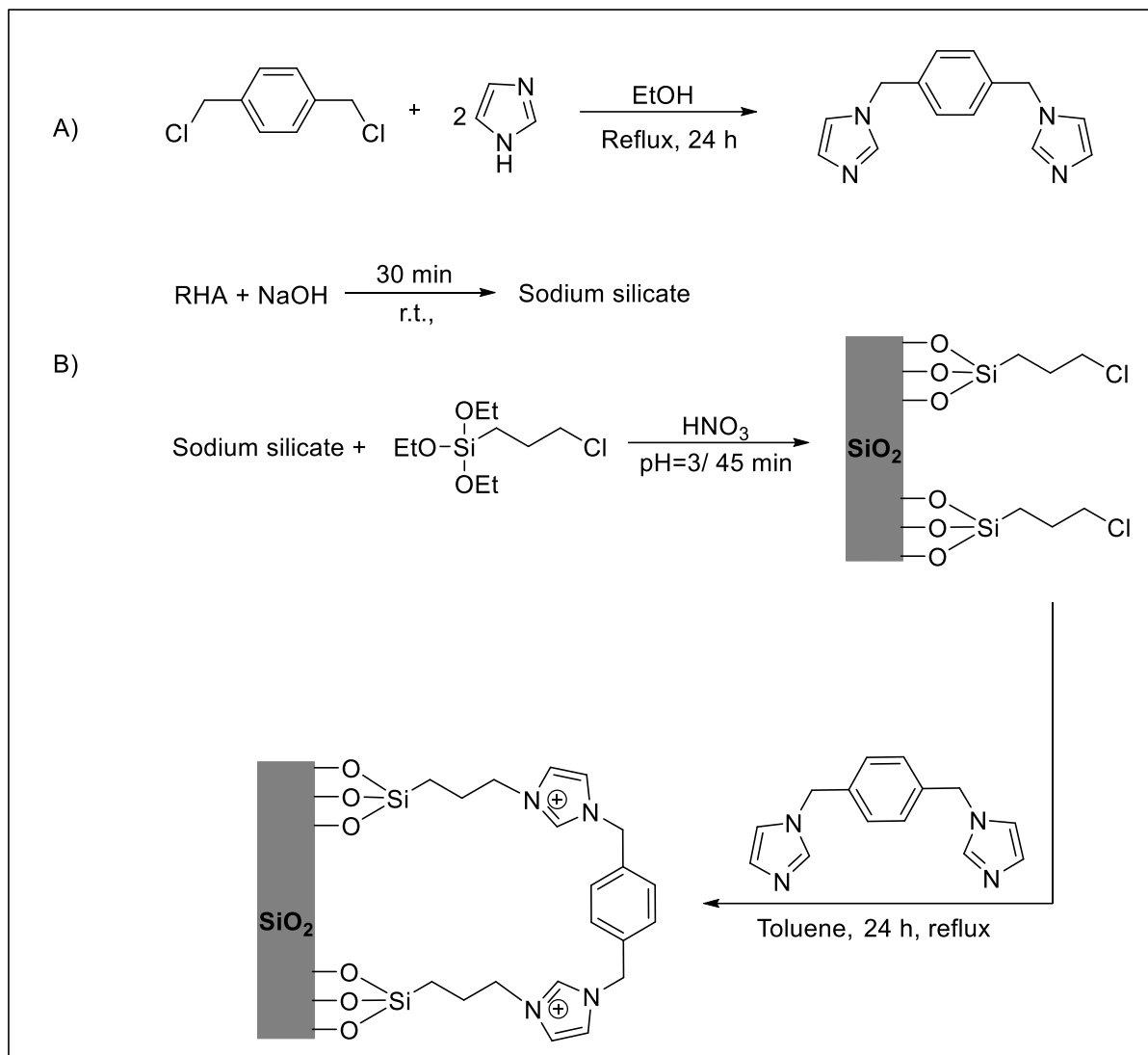
Synthesis of N-(α-chlorobenzyl)-N-phenylglycine (N-Gly) derivatives over the RHAPrIM

The addition reaction of Schiff base was carried out by mixing equal mole (0.01 mol) from each Schiff base and α-chloroacetic acid with 0.2 g of RHAPrIM in a 15 mL of toluene as a solvent under reflux condition (Scheme 2). The reaction was studied in different parameters to reach the optimum conditions of catalyst which may enhance the yield percentage.

Results and Discussion

Catalyst characterization

The RHAPrIM catalyst was characterized by various spectroscopic methods such as TGA/DTA, elemental analysis, FT-IR, TEM, SEM, ^{29}Si, and ^{13}C-MAS NMR spectra. The analyses of these techniques were discussed in detail in our previous publication [19]. Therefore, these will be not repeated in the discussion of these data again. Scheme 1 depicts the general diagram of the preparation catalysts which suggested according to the analysis previously mentions.

Scheme 1. The reaction sequence and the possible structures for (a) bis-imi and (b) for RHAPrIM as suggested by different techniques
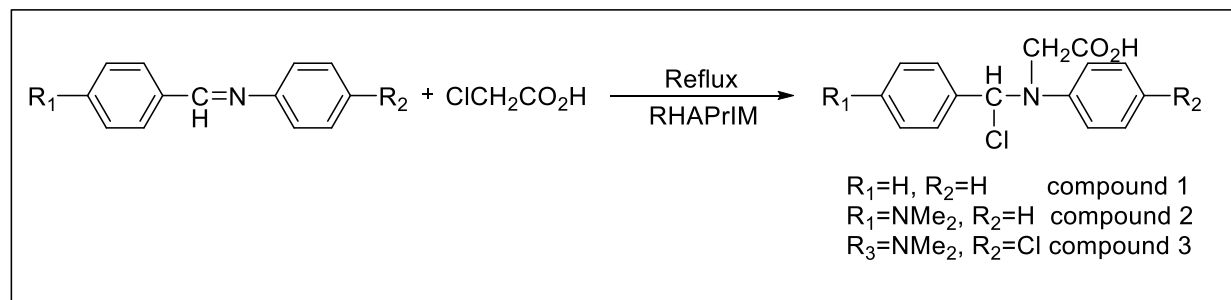
The characterization of N-Gly derivatives over the RHAPrIM

In general, Scheme 2 demonstrated the general reaction of Schiff base derivatives with α-chloro acetic acid over RHAPrIM under refluxed conditions. The FT-IR spectrum of the product (not shown) was following by disappearance of imine groups. Table 1 lists the most functional groups presented in the FT-IR. According to the elemental analyses, it was clearly shown the matching between the

theoretical and calculated values of C, H, and N. The melting points of the prepared compound were further matched with the literature [15].

The optimum conditions of the catalyst for the formation of N-Gly derivatives

The optimization parameters of RHAPrIM over the formation of N-Gly derivatives were studied to reach a high yield of the products. The following subtitle indicates these conditions.

Scheme 2. General reaction of the Schiff bases with α-chloroacetic acid over RHAPrIM

Table 1. The physical properties FT-IR analysis and elemental analysis of N-Gly derivatives prepared over RHAPrIM

| Compound | Mp (°C) | Elemental analysis (%) | | FT-IR (cm⁻¹) |
		Calculated	Found	
1	75-80	C: 64.81, H: 7.79, N: 6.88	C: 65.00, H: 7.11, N: 7.00	3070.78 (C-H aromatic) 2885.60 (C-H aliphatic) 1327.07 (C-N) 1687.77 (C=O) 2677.29 (-OH) 707.90 (C-Cl)
2	90-93	C: 57.77, H: 4.15, N: 7.05	C: 58.88, H: 5.18, N: 7.11	3061.06 (C-H aromatic) 2953.12 (C-H aliphatic) 1369.50 (C-N) 1606.76 (C=O) 2423.76 (-OH) 777.34 (C-Cl)
3	80-85	C: 64.22, H: 8.12, N: 5.01	C: 67.65, H: 7.99, N: 5.16	2958.90 (C-H aliphatic) 1384.94 (C-N) 1626.05 (C=C) 3421.83 (-OH) 758.96 (C-Cl)

The effect of time on the reaction

The reaction of Schiff base with α-chloroacetic acid over RHAPrIM occurred with 0.2 g of catalyst, at 90 °C and (0.0018 g, 0.01 mol) of Schiff base and (0.9 g, 0.01 mol) of α-chloroacetic acid in 15 mL of toluene as a solvent. During the first hour of the reaction, the yield was found to be 67%. After five hours, the yield of N-Gly derivatives reached to be 90%. However, it was observed that when the reaction time was increased over 5 hr, there was no change occurred in the yield. Therefore, 5 hr was chosen as the optimum reaction time, as displayed in Figure 1.

Effect of catalyst's mass

The reaction of Schiff base and α-chloro acetic acid was carried out by over amount of RHAPrIM (between 0.05 and 0.25 g), with other fixed parameters as constant. The amount of Schiff base was (0.0018 g, 0.01 mol) and (0.9 g, 0.01 mol) of α-chloroacetic acid in 15 mL of toluene. Figure 2 clearly depicts when the catalyst mass of RHAPrIM was increased from 0.05 to 0.25 g, the yield of the reaction increased

too from 25 to 90%. As the catalyst mass increased the availability of active sites increased too which led to an increase in the yield. In general, 0.25 g was found the optimum mass of the catalyst.

Effect of temperature

The temperature effect on the reaction of Schiff base with α-chloroacetic acid over RHAPrIM was demonstrated in Figure 3. In general, the temperature was studied as it would be above the boiling point of the used solvent. The reaction parameters were 0.25 g catalyst mass and 5 h reaction time. The reaction percentage was increased from 57 to 90% when the temperature was increased from 70 to 90 °C. The yield increased as temperature increased during the fact that the reducing of activation energy. 90 °C was chosen as the optimum reaction temperature.
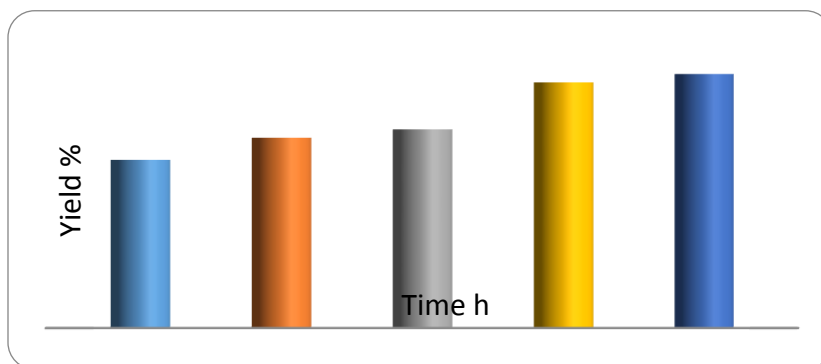

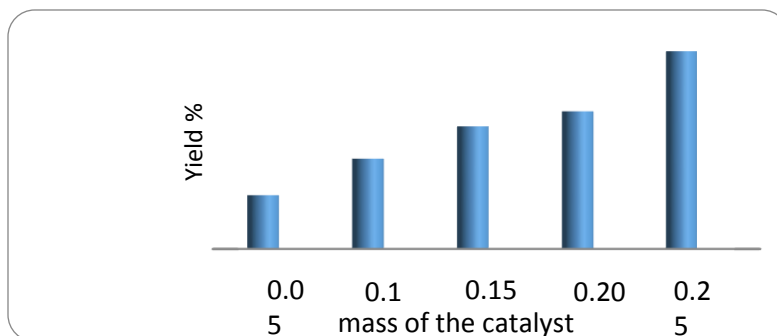**Figure 1.** Time effect on the reaction of Schiff base with α-chloro acetic acid over RHAPrIM

Figure 2. Mass of catalyst effect on the reaction of Schiff base with α-chloro acetic acid
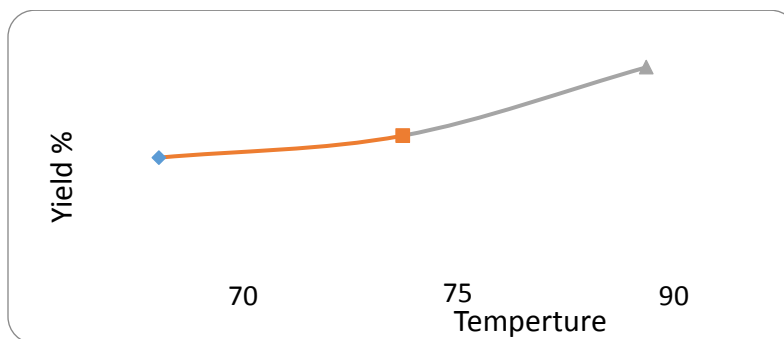

Figure 3. The temperature effect on the reaction over RHAPrIM

Solvents effect

The effect of the solvents used as a medium in the reaction of Schiff base with α-chloroacetic acid over RHAPrIM was listed in Table 2. The reaction was studied over RHAPrIM at the optimum time, mass, and temperature. Different solvents were used such as dioxane, nitrobenzene, toluene, and 1-butanol. The results of yield revealed that the order solvents could be as followed.

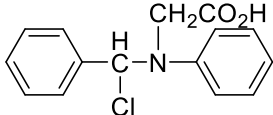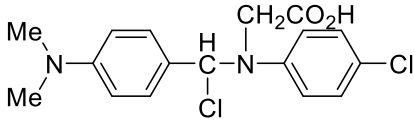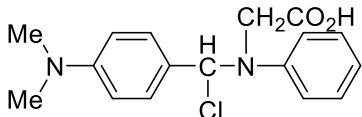Toluene > Dioxane > 1-Butanol > Nitro benzene

The N-Gly derivatives

To give the general applicability of the catalyst, different Schiff base was reacted with α-chloro acetic acid over RHAPrIM. The optimum time, mass of catalyst, and reaction temperature were fixed during the reaction. The results are presented in Table 3.

Table 2. The N-Gly derivatives yield over different solvents on the RHAPrIM surface

Solvents	Yield (%)
Toluene	90
Dioxane	71
1-Butanol	42
Nitro benzene	28

Table 3. The effect of different parameters on the reaction of Schiff base with α-chloro acetic acid over RHAPrIM

	Structure of derivative	Yield (%)
Variation of Schiff base derivatives		90
		73
		76

Conclusion

CPTES was immobilized with silica from rice husk ash in the form of sodium silicate by simple strategy. P-xylyl di-imidazolium chloride was reacted with the product of silica-CPTES to produce catalyst in a heterogeneous form. Elemental analysis, TGA/DTA, FT-IR and ^{29}Si, and ^{13}C-MAS NMR spectra characterized the catalyst and reported by our team in a different paper. The heterogeneous catalyst RHAPrIM was using successfully to catalyse the reaction of the Schiff base with α-chloroacetic acid. The product was a type of amino acid derivative (Glycine). The maximum N-Gly derivatives yield was 90%. The optimum catalyst conditions were 5 h as reaction time, 0.25 g mass of catalyst, 90 °C as the reaction temperature, and toluene as the best solvent.

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