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Short Communication

Zirconium(IV)-modified silica gel: Preparation, characterization and catalytic activity in the synthesis of some biologically important molecules

R.K. Sharma *, Chetna Sharma

Department of Chemistry, University of Delhi, Delhi- 110007, India

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1. Introduction

The catalysts which would be useful to make the organic transformations eco-friendly and economically viable are highly demanded by academic laboratories and industries [1]. In this respect, development of immobilized catalysts that allows the simple work-up procedure and easy separation from reaction products is challenging and important [2]. In fact, the last decade has witnessed a growing interest in the building up of organic-inorganic hybrid catalysts using several types of supports and several immobilization strategies [3–8]. The importance of zirconium as a homogeneous catalyst has already been cited in the literature in the number of biologically and pharmaceutically significant organic transformations [9-14]. Our present work is directed to immobilize, for the first time, zirconium complex onto the functionalized support thereby combining the properties such as catalyst selectivity and activity with the ease of separation and catalyst reuse. As the choice of support material plays a critical factor in the performance of the resulting supported reagent catalyst, we have chosen silica gel support due to its high surface area, excellent stability (chemical and thermal), good accessibility, and ease of functionalization of the surface groups [15,16].

In the present study, Zr-CAP-SG has been investigated for its catalytic activity in the number of significant organic transformations such as Pechmann condensation of phenols with β -ketoesters to yield coumarins, condensation of various 1,2-diamines with 1,2-diketone to give quinox-

E-mail address: rksharmagreenchem@hotmail.com (R.K. Sharma).

ABSTRACT

Zirconium modified silica gel was prepared by the grafting method and the resulting organic–inorganic hybrid material was found to be a highly effective catalyst for the range of organic transformations such as syntheses of coumarins, quinoxalines and 2,4,5-trisubstituted imidazoles. The low percentage of zirconium in the catalyst gave products in high turnover numbers; the catalyst was recovered after reaction, and reused. The structure of the catalyst was investigated and confirmed by surface area (BET), FT-IR, ED-XRF and elemental analyses, ¹³C-CPMAS spectral studies, molecular mechanics studies and inductively coupled plasma mass spectrometry technique (ICP-MS).

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alines, and one-pot multi-component synthesis of 2,4,5-trisubstituted imidazoles. The biological, pharmaceutical, medicinal, and therapeutic properties of coumarins [17], quinoxaline derivatives [18], and substituted imidazoles [19] have been well established in the literature. Although there are many synthetic routes to obtain these derivatives, they suffer from several limitations such as drastic reaction conditions, low product yield, tedious work-up procedures, the use of toxic metal salts as catalysts, and expensive reagents. The main disadvantage of almost all existing methods is that the catalysts are destroyed in the work-up procedure and cannot be recovered or reused [20,21].

2. Experimental

2.1. Materials

Zirconium oxychloride octahydrate (Aldrich), 3-aminopropyltriethoxysilane (Fluka), silica gel (Qualigens), and 5-chloro salicylaldehyde (Aldrich) were commercially obtained and used as such in this study. Starting materials and reagents used in the reactions were obtained commercially from Alfa Aesar and Spectrochem Pvt. Ltd. and used without purification.

2.2. Characterization techniques

The IR spectra were recorded on Perkin Elmer Spectrum 2000 Fourier transform infrared (FT-IR) spectrometer. Surface area analysis was carried out at 77 K by Model 2010, Micromeritics, USA. Elemental analysis was performed on an Elementar Analysensysteme GmbH VarioEL V3.00. ¹³C-CPMAS spectra were recorded on a Bruker DSX-300

^{*} Corresponding author. Tel./fax: +91 11 27666250.

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Table 1

Pechmann condensation of various phenols with β -keto ester using Zr-CAP-SG as the catalyst.^a



 $^a~$ Phenol (1 mmol), $\beta\text{-keto}$ ester (1 mmol) and 10 wt.% catalyst were stirred at 130 °C.

^b Isolated yields.

^c Recycling experiment.

NMR spectrometer at 75.47 MHz. The content of zirconium in the heterogenized catalyst was determined by an ICP-MS Agilent 75003 model number G3272A. Molecular Mechanics calculations were performed using Spartan'08, Wavefunction, Inc. [22]. Qualitative analysis of catalyst for heavy metals was performed by XRF using energy dispersive XRF spectrometer (Fischerscope X-ray XAN-FAD BC). ¹H NMR spectra for the products were recorded on Bruker 300 MHz instrument using TMS as internal standard. Melting points were recorded on a Buchi R-535 apparatus and are uncorrected.

2.3. Preparation of catalyst and its applications

The grafted catalyst was prepared by following the slightly modified method of Airoldi et al. [23] and was investigated for a number of

important organic transformations such as C–O bond formation reaction (Pechmann condensation for the synthesis of coumarin derivatives) (Table 1), C–N bond formation reaction (synthesis of quinoxaline derivatives) (Table 2) and multi-component synthesis of trisubstituted imidazoles (Table 3).

2.3.1. Preparation of [1,2-bis(5-chlorosalicylidene amino)-phenylene], CAP, 1

The complexing agent, **1** was prepared by the condensation reaction of o-phenylenediamine (0.54 g, 5 mmol) with 5-chloro salicylaldehyde (1.56, 10 mmol) in ethanol (10 mL) for 3 h. After the completion of the reaction, a yellow precipitate of the product obtained was filtered and dried (86%) and recrystallized from acetonitrile. ¹H NMR (d⁶-acetone, 300 MHz): δ (ppm) 8.92 (s, 1H), 8.91 (s, 1H), 6.98–7.67 (m, Ar–H). ¹³C

Table 2

Condensation of various 1,2-diamines with 1,2-diketone in ethanol at room temperature using Zr-CAP-SG as the catalyst.^a



Entry	R	Product	Time/h	Yield ^b /%
1.	Н	1a	1.5	92
2. ^c	Н	2a	1.5	90, 90, 89, 90, 88
3.	4-Me	3a	1.0	95
4.	Ethylene diamine	4a	4.5	86
5.	4-PhCO	5a	3.0	83
6.	4-Cl	6a	2.5	85
7.	Н	7b	1.7	89
8.	4-Me	8b	2.0	87

^a 1,2-diamine (1 mmol), benzil (1 mmol) and 10 wt.% catalyst were stirred in 2 mL of ethanol at room temperature.

^b Isolated yields.

^c Recycling experiment.

Table 3

One-pot condensation of various aldehydes with 1,2-diketone and ammonium acetate in acetonitrile at room temperature using Zr-CAP-SG as the catalyst.^a



 $^{\rm a}$ Aldehyde (1 mmol), benzil (1 mmol), ammonium acetate (2 mmol) and 10 wt% catalyst were stirred in 2 mL of acetonitrile at room temperature.

^b Isolated yields.

^c Recycling experiment.

NMR (d⁶-acetone 300 MHz): δ (ppm) 163.8 (C=N), 159.9 (C–O), 118.6 (Ar–C), 118.7 (Ar–C), 119.9 (Ar–C), 120.4 (Ar–C), 128. 3 (Ar–C), 131.7 (Ar–C), 132.9 (Ar–C). Elemental analysis: C₂₀H₁₄Cl₂N₂O₂: C, 62.35; H,

3.77; and N, 7.19. Found: C, 62.35; H, 3.66; and N, 7.27. IR (KBr): $v_{max} = 3445, 3366, and 1615 \text{ cm}^{-1}$.

2.3.2. Grafting procedure for silica, 2

Silica gel was functionalized using 3-aminopropyltriethoxy silane to yield aminopropyl silica gel (APSG) according to a reported procedure [16]. ¹³C CPMAS NMR analysis: 9.3 ($-Si-CH_2-$), 22.3 ($-CH_2-$), and 42.9 ($-N-CH_2-$) ppm. IR (KBr): $\nu_{max} = 3434$, 2924, 2851, 1630, 1083, and 798 cm⁻¹. A mixture of APSG (4 g) and ligand (1.54 g, 8 mmol), **1** was refluxed in a diglyme solution for 3 h at 140 °C under nitrogen [23]. It was then filtered off and washed thoroughly with acetonitrile and acetone. The material obtained was dried overnight at 90 °C. ¹³C CPMAS NMR analysis: 9.2 ($-Si-CH_2-$), 22.7 ($-CH_2-$), 41.1 ($-N-CH_2-$), 50.1 ($-N-CH_2-$), 59.1 ($-N-CH_2-$), 118.9 (Ar–C), 122.5 (Ar–C), 130.2 (Ar–C), 159.8 (C–O), and 163.1 (C=N) ppm. IR (KBr): $\nu_{max} = 3422$, 2927, 1641, 1096, and 801 cm⁻¹.

2.3.3. Preparation of catalyst, 3

The grafted silica gel, **2** (4 g) was stirred with zirconium(IV) oxychloride (0.258 g, 0.8 mmol) in acetonitrile for 2 h at 80 °C (Scheme 1). It was then filtered off and washed thoroughly with acetone until the washings were colourless. The catalyst thus obtained was dried in a vacuum oven overnight at 90 °C. Anal. Found: C: 9.53, H: 2.15, and N: 1.58. IR (KBr): ν_{max} = 3431 (-OH str.), 2922 (-CH₂- str.), 1637 (-C=N- str.), and 1092 (-Si–O–Si– str.) cm⁻¹. Surface area analysis: 141.93 m² g⁻¹. ICP-MS analysis: amount of zirconium: 0.17 mmol g⁻¹.

3. Results and discussion

3.1. Catalyst characterizations

The three signals at 9.3, 22.3 and 42.9 ppm observed in the ¹³C-CPMAS NMR spectrum of APSG due to -Si-CH₂-, -CH₂- and -N-CH₂-



Scheme 1. Synthesis of covalently anchored zirconium complex onto silica.







Fig. 2. A perspective view of the monomeric unit of CAP-SG.

groups, respectively, authenticate the synthesis of APSG. Moreover, the covalent binding of ligand **1** with APSG has been confirmed by the shifting of $-NH-CH_2-$ peak to 50.1 ppm and 59.1 (Fig. 1). The two values confirm that grafting occurred at two different points of attachment. Since the ¹³C NMR chemical shifts are far more sensitive to changes in electronic and steric effects, the possibility of these two different values due to different orientation of phenyl ring with

respect to the support cannot be ruled out. As a supporting evidence, energy minimization was carried out using MMFF force field (Fig. 2). The energy minimized structure of a monomeric unit supports the observation that the molecule is not symmetrical with respect to the support. In addition, other signals in the spectrum can be assigned to – C=N-(163.1 ppm), and -C-O-(159.8 ppm) and the peaks at 118.9 ppm, 122.5 ppm, and 130.2 refer to the aromatic carbons of the phenyl rings.

No significant changes are observed in the silica gel structure sensitive vibrations, after its modification with 3-aminopropyltriethoxy silane, which is an indication that its framework remained unchanged. The spectrum of APSG exhibits an additional band at about 2924 cm⁻¹ and 2851 cm⁻¹ due to the aliphatic ($-CH_2$) stretching of the propyl chain of the silylating agent, thus suggesting that the silica gel surface was functionalized with the linking agent. The infrared spectrum of the 1,2-bis(5-chlorosalicylidene amino)-phenylene exhibits two sharp bands at 3445 cm⁻¹ and 3366 cm⁻¹ attributed to the presence of two free hydroxyl groups. The band at 1615 cm⁻¹ is due to the C==N stretching vibration of the imine bond. The spectrum of chemically modified silica shows a large number of bands which merely appeared as shoulders due to its superimposition by a broad polymer band at 1092 cm⁻¹. The bands at 2922 cm⁻¹ and 1637 cm⁻¹ are assigned to aliphatic –CH₂ and C==N stretchings.

The decrease in the surface area of the catalyst [24] is found to be 40% which is indicative of the grafting of ligand and hence zirconium oxychloride onto the silica gel. Chemical analysis of APSG (Anal. Found: C: 5.28, H: 1.26, and N: 2.04) corresponds to 1.46 mmol/g of 3-aminopropyl groups based on the nitrogen percentage, whereas for the catalyst the loading of organic moiety onto the silica gel is only 13.2% enabling a theoretical capacity of 0.18 mmol g⁻¹ of Zr-CAP-SG. The metal loading of Zr-CAP-SG, was confirmed by ICP-MS and found to be 0.17 mmol/g. Further to support the above observation, the catalyst was subjected to energy dispersive X-rays (Fig. 3).

3.2. Catalytic studies

To investigate the catalytic activity of the organic–inorganic hybrid material different reactions were studied. The reactions did not proceed in the absence of the catalyst or only silica as the catalyst. However, Zr-CAP-SG served as an efficient catalyst for the reactions with high turnover numbers. As can be seen (see Supplementary data), ethanol clearly stands out as the solvent of choice for the synthesis of quinoxalines derivatives with its high reaction rate, high turnover number, selectivity, low cost, and environmental acceptability. However, acetonitrile proved



Fig. 3. XRF-spectrum of the catalyst (showing resolved peak of zirconium).

to be a better solvent for the preparation of substituted imidazoles since the reaction time period is least in this case. The Pechmann condensation of coumarins showed a drastic change in the reaction time period and product yield with increasing temperature. Therefore, we tried this particular reaction under neat conditions and at higher temperatures. For the other two reactions, there were not much significant changes observed in product yields or reaction time period with higher temperatures. As far as catalyst recovery is concerned, for every cycle it has been recovered, regenerated and recycled. There has been no loss in the amount of the catalyst after its recovery. It is worth mentioning here that for every cycle the catalyst has been tested for the reaction at microscale.

In order to verify whether the observed catalysis is truly heterogeneous or not, the catalytic reactions were carried out using Zr-CAP-SG as the catalyst under the conditions indicated in Tables 1, 2, and 3 and the solid Zr-CAP-SG was removed by filtration at about half the specified reaction time period. Then, the filtrate was allowed to react under the same conditions. No increase in the vield was observed. This suggests that the nature of the observed catalysis is truly heterogeneous.

4. Conclusions

In summary, we have reported the first example of a zirconium grafted onto the CAP-functionalized silica gel as an efficient and recyclable catalyst. The unique properties of the silica-supported catalyst allowed us to demonstrate a new synthetic methodology for the synthesis of coumarins, quinoxaline derivatives and substituted imidazoles. The significant advantages of our protocol are: mild reaction conditions, short reaction times, good yields, high TON, simple work-up procedure and involvement of an efficient and recyclable catalyst.

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Appendix A. Supplementary materials

Supplementary data to this article can be found online at doi:10.1016/i.catcom.2010.10.011.

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