Silica-bonded 1,4-diaza-bicyclo[2.2.2]octane-sulfonic acid chloride catalyzed synthesis of spiropyran derivatives

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Abstract:

In this research, a novel nanostructured heterogeneous catalyst, namely silica-bonded 1,4-diaza-bicyclo[2.2.2]octane-sulfonic acid chloride (SBDBSAC), as an acidic ionic liquid based on 1,4-diaza-bicyclo[2.2.2]octane ring bonded to silica has been prepared and fully characterized by several techniques such as fourier transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD), thermogravimetric analysis (TGA), differential thermogravimetric (DTG), scanning electron microscope (SEM), transmission electron microscopy (TEM) and energy dispersive X-ray analysis (EDX). The nanostructured catalyst has been successfully used as reusable nanostructured catalyst for green, simple and efficient synthesis of spiropyrans by the one-pot tandem Knoevenagel-Michael-cyclization reaction of isatin derivatives or acenaphthenquinone with barbituric acid derivatives, and 1,3-dicarbonyl compounds under aqueous media.

Keywords: Spiropyran, Silica-bonded 1,4-diaza-bicyclo[2.2.2]octane-sulfonic acid chloride, Nanostructured catalyst, Isatin, Barbituric acid, Aqueous media.

1. Introduction

Multi-component reactions (MCRs) achieve significant role in combinatorial chemistry because of the ability to prepare target compounds with more efficiency and atomic economy by the reaction of three or more compounds together in one single step. Additionally, MCRs increase simplicity and synthetic efficiency on the conventional organic transformations [1–5].

Spiropyrans including oxindoles are an important class of attractive heterocyclic compounds with useful biological properties such as spasmolytic, diuretic, anticoagulant, anticancer, and anti-anaphylactic activities [6-9]. Some catalysts have been applied for this transformation, including sodium stearate [9], sulfated choline based heteropolyanion [10], Protic guanidinium ionic liquid [11], 4-dimethylaminopyridine [12], [BMIIm]BF₄ [13], SBA-Pr-SO₃H [14], (SB-DBU)Cl [15], carbon-sulfonic acid [16], polyethylene glycol (PEG)-stabilized Ni nanoparticles [17], alpha-Amylase [18], ZnS nanoparticles [19], triphenylphosphine [20] and nickel oxide [21]. Therefore, considerable attention has been focused on the development of new methods for the synthesis of these compounds.

Recently, we have prepared a new category of ionic liquids and solid salts (with an organic cation), namely sulfonic acid functionalized imidazolium salts (SAFIS) [22-38]. In this class of salts, S-N bond formation in imidazole ring, as five member's heterocyclic compounds, was reported for the first time. These compounds have been successfully introduced as catalysts or reagent for the preparation of 6-amino-4-(4-methoxyphenyl)-5-cyano-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazoles [22], bis(indolyl)methanes [23], *N*-sulfonyl imines [24], 1-amidoalkyl-2-naphthols [25], various xanthene derivatives [26], 1-carbamatoalkyl-2-naphthols [27], 4, 4'-(arylmethylene)-bis (3-methyl-1-phenyl-1 H-pyrazol-5-ol)s [28], *N*-boc protected amines [29], hexahydroquinolines [30], nitroaromatic compounds [31,32]. In continuation of our

previous projects including the applications of acidic ionic liquids and solid salts in organic transformations, we have prepared, characterized an acidic ionic liquid based on 1,4-diaza-bicyclo[2.2.2]octane ring bonded to silica namely silica-bonded 1,4-diaza-bicyclo[2.2.2]octane-sulfonic acid chloride (SBDBSAC) in nano-size and applied it for the synthesis of spiropyrans by the one-pot tandem Knoevenagel-Michael-cyclization reaction of isatin derivatives or acenaphthenquinone with barbituric acid derivatives, and 1,3-dicarbonyl compounds under aqueous media (Figure 1) (Scheme 1).

Figure 1. The structure of silica-bonded 1,4-diaza-bicyclo[2.2.2]octane -sulfonic acid chloride (SBDBSAC).

Scheme 1. The preparation of spiropyran by the reaction of isatin derivatives or acenaphthenquinone with barbituric acid and 1, 3-dicarbonyl compounds using SBDBSAC.

2. Experimental

2.1. General

All chemicals were purchased from Merck or Fluka Chemical Companies. The known products were identified by comparison of their melting points and spectral data with those reported in the literature. Progress of the reactions was monitored by TLC using silica gel SIL G/UV 254 plates. The ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on a Bruker Avance DPX FT-NMR spectrometer (δ in ppm). Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes. **Thermogravimetric** (TG) and differential thermal gravimetric (DTG) were analyzed by a Perkin Elmer (Model: Pyris 1). TG/DTG analysis (0 to 600 °C, temperature increase rate of 10 °C. min⁻¹, nitrogen atmosphere). The crystal structure of synthesized materials was determined by an X-ray diffractometer (Italstructure ADP2000 XRD diffractometer) at ambient temperature.

2.2. Catalyst preparation

A mixture of 1,4-diaza-bicyclo[2.2.2]octane (0.56 g, 5 mmol), (3-chloropropyl)triethoxysilane (1.125 g, 5 mmol) and acetone (15 mL) in a 50 mL round-bottomed flask connected to a reflux condenser, was stirred for 12 hours under reflux conditions. In the next step, the obtained white precipitate, was filtered to separate from acetone, and reacted with silica (0.3 g, 5 mmol) in refluxed toluene (15 mL) for 8 hours. After removing of the solvent, the resulted product was added to a 50 mL round-bottomed flask in an ice water bath (0 °C), and a solution of chlorosulfonic acid (5 mmol) in chloroform (10 mL) was added dropwise to it, and stirred for 2 hours. Afterward, the residue was triturated with chloroform (3×10 mL), and dried under powerful vacuum at 90 °C to give silica-bonded 1,4-diaza-bicyclo[2.2.2]octane acid chloride (SBDBSAC) as a white precipitate in 95 % yield.

2.3. General procedure for the preparation of spiropyrans

A mixture of isatin derivatives or acenaphthenquinone (1 mmol), barbituric acid (1 mmol), 1, 3-dicarbonyl compounds (1 mmol), SBDBSAC (0.02 g) and H₂O (5 ml) was added to a in a 25 mL round-bottomed flask connected to a reflux condenser, and stirred under reflux conditions. After completion of the reaction, as monitored by TLC, the reaction mixture was cooled to room temperature. Methanol (20 mL) was added, stirred and refluxed for 3 min. Then, the resulting mixture was centrifuged for the separation of the catalyst from the product and remaining starting materials. After the separation of catalyst from the reaction mixture, methanol was removed and the solid residue (crude product) was triturated by a mixture of ethanol and water (9/1) to give the pure product.

3. Results and discussion

At first, 1,4-diaza-bicyclo[2.2.2]octane was reacted with (3-chloropropyl)triethoxysilane under reflux conditions to provide **I**. After that, **I** was reacted with silica in refluxed toluene for 8 hours to give **II**. At the end, silica-bonded 1,4-diaza-bicyclo[2.2.2]octane-sulfonic acid chloride (SBDBSAC) was synthesized *via* reaction of **II** with ClSO₃H in chloroform (Scheme 2).

Scheme 2. The preparation of silica-bonded 1,4-diaza-bicyclo[2.2.2]octane-sulfonic acid chloride (SBDBSAC).

Identification of SBDBSAC structure was achieved by FT-IR, XRD, TG, DTG, EDX, and SEM analysis.

In the IR spectrum of the catalyst (Figure 2), the peak related to O-H stretching of the SO_3H group was appeared at $2250\text{-}3600\text{ cm}^{-1}$. The vibrational mode of O- SO_2 was observed at 1318 cm^{-1} .

Figure 2. FT-IR spectrum of SBDBSAC.

The X-ray diffraction analysis (XRD) pattern of SBDBSAC in a domain of $0\text{-}90^\circ$ degree is shown in Figure 3. The XRD pattern showed diffraction lines of a high crystalline nature at about $2\theta \approx 9.1^\circ, 18.8^\circ, 19.4^\circ, 20.0^\circ$ and 26.6° . The crystallite size, which was calculated by Debye-Scherrer's formula [$D = K\lambda / (\beta \cos\theta)$], was 8.1 nm.

Figure 3. XRD diagram of SBDBSAC in comparison with other components of the catalyst.

The diagrams related to **thermogravimetric analysis** (TGA) of SBISAC are depicted in Figure 4.

According to the **thermogravimetric** (TG) and differential **thermogravimetric** (DTG) diagrams, weight loss of the catalyst was occurred in one step, after 280 °C.

Figure 4. Thermogravimetric (TG) and differential thermogravimetric (DTG) analysis of SBDBSAC at range of 0–600 °C, with a temperature increase rate of 10 °C.

The energy-dispersive X-ray spectroscopy (EDX) of the nanocatalyst (Figure 5) proved the presence of the expected elements in its structure, i.e. carbon, oxygen, nitrogen, sulfur, chlorine and silicon.

Figure 5. Energy-dispersive X-ray spectroscopy (EDX) of SBDBSAC.

The scanning electron microscope (SEM) micrographs of the catalyst showed that the particles have not completely agglomerated. Particles of the catalyst were observed in nano scale which is in good agreement with calculated size through to Debye-Scherrer's equation (Figure 6).

Figure 6. The SEM images of SBDBSAC.

To investigate the efficacy and the generality of the catalyst, different isatin derivatives or acenaphthenquinone was reacted with various 1,3-dicarbonyl compounds and barbituric acid derivatives under the optimized reaction conditions. The results are presented in Table 1. As it is shown in Table 1, all reactions proceeded efficiently to give the expected spiropyran derivatives in high yields and in short reaction times. Therefore, SBDBSAC was a highly efficient and general catalyst for the preparation of spiropyrans.

Table 1. The preparation of **spiropyran derivatives** using SBDBSAC as catalyst in water under reflux conditions.

Entry	1,2-dicarbonyl compound	Barbituric acid derivative	1,3-dicarbonyl compound	Product	Time (min)	Yield ^a (%)	Mp. °C (Lit.)
1					40	93	>300 (>300) ²⁷
2					30	94	290 dec. (293-295) ²⁷
3					55	91	>300 (>300) ²⁷
4					60	92	>300 (>300) ²⁷
5					70	88	290 (>300) ²⁷
6					90	89	>300 (>300) ²⁷
7					50	89	>300 (>300) ²⁷
8					45	95	287 dec (278-280) ²⁹

^a Isolated yield.

Table 1. (Continued)

Entry	1,2-dicarbonyl compound	Barbituric acid derivative	1,3-dicarbonyl compound	Product	Time (min)	Yield ^a (%)	Mp, °C (Lit.)
9					40	92	244-246 (245-247) ²⁷
10					60	90	>300 (>300) ²⁷
11					50	93	295 (>300) ²⁸
12					45	90	>300 (>300) ²⁷
13					65	87	>300 (>300) ²⁷
14					50	90	288-290 (288-289) ²⁸
15					40	95	290-292 (>300) ²⁷
16					60	91	290 (>300) ²⁸
17					60	93	>300 (>300) ²⁸

^aIsolated yield.

To achieve the optimization reaction conditions, at first, a mixture of isatin (0.147 g, 1 mmol), dimedone (0.14 g, 1 mmol) and barbituric acid (0.128 g, 1 mmol), as model reaction, was stirred in water (5 mL) in the presence of different amounts of SBDBSAC under reflux conditions. The respective results are presented in Table 2. As it can be seen in Table 2, 0.02 g of SBDBSAC was sufficient to catalyze the reaction under reflux conditions. In these reaction conditions, the expected spiropyran was obtained in 92% yield within 60 min (Table 2, entry 3). We also tested this obtained condition (0.02 g of SBISAC) in the present of different solvents (5 mL). As it is shown as Table 2, indicates that water is more suitable solvent in the synthesis of spiropyrans.

Table 2. Effect of different amounts of the catalyst and kinds of solvent on the reaction of isatin, dimedone and barbituric acid under reflux conditions.

Entry	Amount of Catalyst (g)	Solvent	Time (min)	Yield ^a (%)
1	0.005	H ₂ O	60	65
2	0.01	H ₂ O	60	72
3	0.02	H ₂ O	60	92
4	0.05	H ₂ O	60	92
5 ^b	0.02	-	120	43
6	0.02	EtOH	60	80
7	0.02	CH ₃ CN	60	30
8	0.02	n-Hexane	60	trace

^aIsolated yield. ^bThis reaction was carried out in the absence of solvent.

A plausible mechanism for the reaction is indicated in Scheme 3. Initially, the carbonyl group of isatin is activated by the acidic moiety of SBDBSAC (i.e. SO_3H). In the next step, 1,3-dicarbonyl compound reacted with **I** to afford **II** after removing of one molecule of H_2O . Then intermediate **II** as a Michael acceptor is activated by the catalyst, and reacted with another molecule of 1,3-dicarbonyl compound to give **III**. Finally, **III** was converted to **IV** (the desired product) by removing of H_2O .

Scheme 3. The proposed mechanism for the synthesis of spiropyran.

To study recyclability of SBDBSAC, the reaction of isatin (1 mmol), dimedone (1 mmol) and barbituric acid (, 1 mmol) was performed using SBDBSAC (0.02 g) under reflux condition. After completion of the reaction, the reaction mixture was cooled to room temperature. Methanol was added, stirred and refluxed for 3 min. Then, the resulting mixture was centrifuged for the separation of the catalyst from the product and remaining starting materials. The remained catalyst was washed with hot ethyl acetate (10 mL) and dried to use for the next run. Catalytic activity of SBDBSAC was restored within the limits of the experimental errors for 5 successive recycle runs.

4. Conclusions

In summary, we have prepared silica-bonded 1,4-diaza-bicyclo[2.2.2]octane-sulfonic acid chloride (SBDBSAC) as a nanostructured heterogeneous catalyst, and fully characterized it by several techniques including fourier transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD), thermogravimetric analysis (TGA), differential thermogravimetric (DTG), scanning electron microscopy (SEM) and Energy dispersive X-ray analysis (EDX). SBDBSAC was successfully tested for the multi-component condensation reaction between from isatin derivatives or acenaphthenquinone with barbituric acid derivatives, and 1,3-dicarbonyl compounds under reflux conditions to give spiropyrans. Short reaction time, high yield and reusability of the catalyst are some advantages of this work.

Acknowledgements

The authors gratefully acknowledge the Bu-Ali Sina University, Iran National Science Foundation (INSF) for financial support (The Grant of Allameh Tabataba'i's Award) to our research group and Sayyed Jamaledin Asadabadi University for providing support to this work.

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Graphical Abstract

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