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Sulfonated Porous Carbon (SPC): An efficient and recyclable solid acid catalyst for one-pot three-component synthesis of 2,3-dihydroquinazolin-4(1H)-ones under solvent-free conditions

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ABSTRACT

A simple and efficient procedure has been developed for the synthesis of 2,3-dihydroquinazolin-4(1H)-ones derivatives under solvent-free conditions. This method uses the condensation of isatoic anhydride, aldehydes, and amines in the presence of a catalytic amount Sulfonated Porous Carbon (SPC). One of the important advantages of the new method is that the SPC could be recycled and reused.

Keywords*: Heterogeneous catalysis, Sulfonated Porous Carbon, Solid acid, 2,3 dihydroquinazolin-4(1H)-ones*

1. Introduction

Quinazolinones are one of the important classes of heterocyclic compounds, which exhibit a wide range of pharmaceutical activities such as, antibacterial, antitumor, antifungal and anticonvulsant [1-6]. Thus, efficient synthesis of these compounds has been of great interest in recent years. Several methods have been reported in the literature for the synthesis of 2,3-dihydroquinazolinones. Despite advantage of success of their synthesis, unfortunately, many of these processes suffer limitations, such as drastic reaction conditions, low yields, tedious workup procedures and organic solvents [7-10].

The direction of science and technology has been shifted more towards eco-friendly and reusable catalysts in recent years. Therefore, green chemistry may be defined as a set of principles, which can reduce or eliminate the use or generation of hazardous substances throughout the life time of chemical materials. On the other hand, solid acid catalysts play a prominent role in organic synthesis under heterogeneous conditions. The more easily separation without resulting into problem of waste disposal and option of re-use of the solid acid catalysts render the processes employing solid acid catalysts as green processes. For the applications considered here, an ideal solid material should have high stability and numerous strong protonic acid sites [11-16]. Porous carbon materials and the products based on them can diffuse in many actual scientific applications. They may be used as supports for different catalytic processes, fuel cells and capacitors. Since porous carbon materials can fulfill most of the desirable properties required for a suitable catalyst support, their high surface areas and well developed porosities have attracted substantial attention. The major advantages of carbon materials include the stability in aggressive media at elevated temperature, feasibility of control parameters of the porous structure surface area in a broad range, and the physicochemical properties [17-21]. Moreover, two important aspects in this field are environmental and economical points of view because evolution of organic synthesis involving environmentally clean protocols and under solvent-free conditions has emerged as an area of great interest [22,24].

The purpose of this paper is to introduce a novel method for synthesis of 2,3-dihydroquinazolin-4(1H)-ones using sulfonated porous carbon (SPC) as a heterogeneous catalyst under solvent-free conditions (Scheme 1.).

2. Experimental

Melting points were measured on an Electrothermal 9100 apparatus. All chemicals were commercial products. Thin

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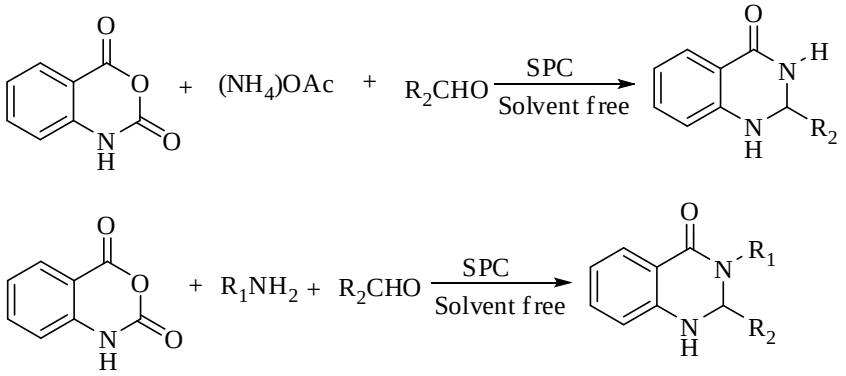

Scheme 1.

layer chromatography (TLC) was used to monitor all reactions and all yields refer to isolated products. The ^{1}H and ^{13}C -NMR spectra were recorded on a Bruker Avance AQS at 300 and 75 MHz, respectively.

2.1. Preparation of SPC

Pine wood powder was used as precursor to prepare of porous carbon material. In a typical procedure, wood powder (10 g) was impregnated with $ZnCl_2$ by immersion in aqueous solution of HCl (1.0 M, 50 ml) containing $ZnCl_2$ (20 g) under mechanical agitation at 25 ºC for 15 h. After that, the supernatant liquid was separated by filtration and the remaining solid was oven-dried at 80 ºC for 24 h. Then, the $ZnCl_2$-impregnated wood powder was placed in a boat like small size ceramic container and heated gradually from room temperature to 500 ºC. The heating gradient was not faster than 10 ºC min^{-1}. The heating time at maximum heat (500 ºC) treatment temperature was 1 h. Thereafter, the sample was washed by heating in the aqueous HCl solution (5 %, 100 ml) at 100 ºC for 1 h. Then, the resulting solid was filtered and rinsed with warm distilled water (50 ºC) to confirm that the wash solution is free of zinc ions. The resultant activated porous carbon material was finally dried at 80 ºC in an oven for approximately 24 h. Then, the activated porous carbon material (5 g) was heated for 15 h in oleum (18-24 wt% SO_3, 100 ml) at 150 ºC - 180 ºC under N_2 in order to introduce SO_3H. After heating and then cooling to room temperature, distilled water (400 ml) was added to the mixture. The black precipitate was filtered and repeatedly washed with boiling distilled water until impurities such as sulfate ions were no longer detected in the wash water. The sample was finally dried overnight in an oven at 80 ºC to afford the sulfonated acid catalyst [20,21,25].

2.2. General Experimental Procedure for the Preparation of 2,3- dihydroquinazolin-4(1H)-ones

A mixture of SPC (0.05 g equal to 0.22 mmol H^{+}), isatoic anhydride (1 mmol), primary amine or ammonium acetate (1.1 mmol) and aromatic aldehyde (1 mmol) were thoroughly mixed and the resulting mixture was heated at 70 ºC for the specified reaction time (see Table 2). The progress of reaction was monitored by TLC method (eluent: n-hexane/ethyl acetate:2/1). At the end of reaction 5 mL ethanol was added to the mixture, catalyst was removed by filtration and the resulting solution was concentrated under reduced pressure. Then, residue was recrystallized from ethanol to give the pure 2,3-dihydroquinazolin-4(1H)-ones. All of the obtained 2,3-dihydroquinazolin-4(1 H)-ones are known compounds in which the spectroscopic data were compared; however, spectral data for the following products has not been found.

The selected spectral data

2,3-dihydro-3-(4-Methoxyphenyl)-2-phenyl-1*H*-quinazolin-4-one (entry 10): White solid, 208-209 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ: 3.76 (s, 3H), 6.02 (s, 1H), 6.59 (d, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 9.0 Hz, 2H), 6.86 (t, *J* = 7.0 Hz, 2H), 7.00 (d, *J* = 9.0 Hz, 2H), 7.23- 7.29 (m,4H), 7.30-7.32 (m, 2H), 7.98 (dd, *J* = 7.0,1.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 55.8, 74.9, 114.0, 114.1, 116.0, 118.7, 126.2, 127.7, 128.4, 128.6,128.9, 132.8, 133.3, 133.6, 145.2, 157.2, 162.8; Anal. Calcd for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.49; N, 8.48. Found: C, 76.47; H, 5.41; N, 8.31.

2,3-dihydro-2-(4-Bromophenyl)-3-(4-methoxyphenyl)-1*H*-quinazolin-4-one (entry 11): White solid, 241-243 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ: 3.77 (s, 3H), 6.00 (s, 1H), 6.60 (d, *J* = 7.5, 1H), 6.76 (d, *J* = 9.0 Hz, 1H), 6.87 (d, *J* = 7.0 Hz, 2H), 7.00 (t, *J* = 9.4 Hz, 2H), 7.19- 7.29 (m, 3H), 7.35 (d, *J* = 7.6, 2H); 7.98 (dd, *J* = 7.0,1.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 55.9, 74.4, 114.6, 114.8, 116.9, 119.6, 122.9, 128.2, 128.6, 129.3, 131.8, 132.8, 134.0, 138.9, 145.0, 157.6, 162.8; Anal. Calcd for $C_{21}H_{17}$ Br N_2O_2: C, 61.63; H, 4.18; N, 6.84. Found: C, 61.49; H, 4.09; N, 7.02.

3. Results and discussion

First, we searched an efficient catalyst for the synthesis of 2,3-dihydroquinazolin-4(1H)-ones under solvent-free conditions. In an initial endeavor, isatoic anhydride, benzaldehyde and aniline were thoroughly mixed and the

Table 1. Optimization of the catalyst amounts for the synthesis of 2,3-diphenylquinazolin-4(1H)-one under solvent-free conditions at 70 ºC.

Entry	Amounts of SPC (g)	Time (min)	Yield (%)[a]
1	-	24 (h)	10
2	0.02	420	64
3	0.04	270	79
4	0.05	210	84
5	0.06	210	85

[a]Isolated yields.

resulting mixture was heated at 70 ºC. In the absence of acid catalyst, the yield of expected product was only 10% in duration 24 h after beginning of reaction.

Increasing the catalyst loading from 0.02 to 0.05 g was found to decrease reaction time substantially and the yield increased to 84%. Further increase of catalyst loading to 0.06 g increased the yield marginally (Table 1).

After optimizing the catalyst, in order to study the generality of this procedure, different types aldehydes and amines were reacted with isatoic anhydride and the corresponding 2,3-dihydroquinazolin-4(1H)-ones were obtained. The results are summarized in Table 2. As shown, a variety of substituted aromatic aldehydes, bearing either electron-donating or electron-withdrawing substituents, afforded the products in good yields. This method is also applicable for the reaction of ammonium acetate as ammonia source and different types aromatic aldehyde affording the corresponding 2,3-dihydroquinazolin-4(1H)-ones in good yields (Table 2 entry 15-18).

Table 3 compares the efficiency of the SPC with the efficiency of other catalysts in the synthesis of synthesis of 2,3-dihydroquinazolin-4(1H)-ones by some other researchers. The data given in Table 3 show that SPC can act as an effective catalyst with respect to reaction times and yields of the obtained products.

The reusability and recyclability of the catalyst (SPC) were checked for three catalytic cycles, the yields and reaction times remained the same (Table 1 entry 1).

4. Conclusion

One-pot three-component reactions of isatoic anhydride, aromatic aldehydes and primary amines or ammonium salts are efficiently catalyzed by SPC under solvent-free conditions. The method offers several advantages including high yield of products, recyclability of the catalyst, and easy experimental work-up procedure.

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Table 2. SPC catalyzed synthesis of derivatives of 2,3-dihydroquinazolin-4(1H)-one.

Entry	R_1	R_2	Time (min)	Yield (%)[a]
1 [b]	Ph	Ph	210	84,85,84,83
2	Ph	2-O_2N-C_6H_4	180	82
3	Ph	3-O_2N-C_6H_4	180	81
4	Ph	4-O_2N-C_6H_4	180	82
5	Ph	4-Me-C_6H_4	210	85
6	Ph	2-Cl-C_6H_4	180	81
7	Ph	4-Cl-C_6H_4	180	81
8	Ph	4-Br-C_6H_4	180	80
9	Ph	2,4-Cl_2-C_6H_4	150	81
10	4-CH_3O-C_6H_4	Ph	210	84
11	4-CH_3O-C_6H_4	4-Br-C_6H_4	210	79
12	$PhCH_2$	2-O_2N-C_6H_4	160	81
13	$PhCH_2$	4-O_2N-C_6H_4	160	85
14	$PhCH_2$	2-Cl-C_6H_4	180	78
15	$(NH_4)OAc$	Ph	180	80
16	$(NH_4)OAc$	4-Cl-C_6H_4	180	83
17	$(NH_4)OAc$	4-CH_3O-C_6H_4	180	81
18	$(NH_4)OAc$	4-O_2N-C_6H_4	180	86

[a]Isolated yields.

[b]The same reagent was used for each of the four runs.

Table 3. Comparison of the activity of various catalysts in the reaction of isatoic anhydride, aniline, and benzaldehyde**.**

Entry	Catalyst	Condition(Medium)	Time (h)	Yield (%)	Ref.
1	SPC (0.05g)	Solvent-free, 70 ºC	3.5	84	-
2	Montmorillonite K-10 (0.3 g)	EtOH, reflux	6.5	80	26
3	Silica sulfuric acid, 20 mol% (0.06 g)	Solvent-free, 80 ºC	5	80	27
4	$KAl(SO_4)_{21}2H_2O$ (alum, 0.2 g)	EtOH, reflux	7	78	28
5	$[Zn(PFO)_2]$ (0.027 g, 0.03 mmol)	H_2O/EtOH (1/3), reflux	6	82	29
6	Copolymer-PTSA (0.3 g)	EtOH, reflux	6.5	82	30
7	$Ga(OTf)_3$ (1 mol%)	EtOH, reflux	1	79	31
8	Acetic acid	Acetic acid, Reflux	2.5	79	32

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