

Cu(II)-Schiff base/SBA-15 as an efficient catalyst for synthesis of chromeno

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Abstract

Some chromeno[4',3'-b]pyrano[6,5-b]quinoline derivatives were synthesized by condensation of 2-amino-4-aryl-3-cyano-5-oxo-4*H*, 5*H*-pyrano-[3,2-*c*] chromenes and 1,3-cyclohexanedione in an environmentally benign and efficient method by Cu(II)-Schiff base/SBA-15 as an environmentally friendly heterogeneous and recyclable catalyst under solvent-free conditions in high yields and rates. These kinds of catalysts are built from mesoporous silica SBA-15 which was covalently anchored with Cu(II) Schiff base complex. The shorter reaction times, good yields, simple work-up procedure and environmentally friendly conditions are the main advantages of this method compared to the last one. The product was identified by its ¹H NMR, mass and IR spectra, which were compared to those reported previously.

Keywords: Chromeno-pyranoquinolines; coumarin heteroanalogues; malononitrile; Cu(II)-Schiff base/SBA-15.

Introduction

The various biological activities of coumarins fused with other heterocycles have inspired scholars to seek procedures and substrates to improve the feasibility of board families of these compounds. Accordingly, several biological activities have been proposed for compounds comprising both coumarins and coumarins fused to pyridine ring as well as dihydropyrano[*c*]chromenes. For instance, dihydropyrano[*c*]chromenes, containing coumarin nucleus, are present in promising drug candidates as spasmolytic, diuretic, anti-coagulant, anti-cancer, and anti-anaphylactic [1-3]. Moreover, coumarins joined to pyridines have been reported to possess

antiallergic [4], antitumor [5], and antidiabetic [6] activities. They have also been reported to have analgesic properties [7-12]. It is, then, evident from various reports that extensive efforts have been made on coumarins and pyridine derivatives.

Accordingly, the synthesis of novel coumarin fused to heterocycles derivatives and finding their new efficient methods for synthesis have been the main interest of respective scholars and researchers in recent years [13-18]. In line with this, we have already reported, the synthesis of novel chromeno[4',3'-b]pyrano[6,5-*b*]quinolone derivatives [15]. Therefore, herein, we wish to introduce a new efficient method using Cu(II)-Schiff base/SBA-15 catalyst for synthesis of

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these compounds. In our last report, we have made use of Cu(II)-Schiff base/SBA-15 for synthesis of chromeno[4,3-*b*]quinoline derivatives and impressive results were obtained [18].

These kinds of catalysts are built from mesoporous silica SBA-15 which was covalently anchored with Cu(II) Schiff base complex. There are few literatures about the application of these kinds of catalysts (silica supported Schiff base cobalt (II) (Co/SBA-15) and Copper (II) (Cu/SBA-15) complexes) for synthesis of heterocyclic compounds [19]. To the best of our knowledge, there are a few reports on the use of these kinds of catalysts for synthesis of derivatives of coumarins and our method is probably an important example of synthesizing these kinds of heterocycles with Cu(II) Schiff base complex as an efficient catalyst in solvent-free media which can be valuable to use or investigate for similar systems. This new procedure by solid-supported catalysts is generally faster, gives higher selectivity and yields, and typically requires easier work-up processes and simpler equipment than the extant methods.

Experimental

Materials and apparatus

¹H and ¹³C -NMR spectra were recorded in CDCl₃ on a Bruker 500 MHz spectrometer (Bruker, Rheinstetten, Germany). The IR spectra were recorded on Nicollet FT-IR magna 550 spectrometer (Nicollet, Madison, WI, USA) using KBr pellets. Electron-impact mass spectra were obtained using a Finnegan MAT TSQ-70 spectrometer (Finnegan Mat, Bremen, Germany). The purity of compounds was confirmed *via* thin layer chromatography (TLC) using different mobile phases.

Preparation of the catalyst Cu (II)-Schiff base/SBA-15

The Cu(II)-Schiff base complex was prepared using the pertinent literature procedure [20]. Activated silica gel SBA-15 (1.5 g) was suspended in a methanol solution of the Schiff base complex, and the mixture was stirred at room temperature for 24 h.

The solvent was then removed using a rotary evaporator, and the resulting green solid was dried at 80 °C overnight. The final product was washed with MeOH and deionized water until the washings were colorless to ensure that the noncovalently grafted complex and physically adsorbed metal species were removed. Further drying was carried out in an oven at 80 °C for 8 h. Moreover, to measure the amount of copper loaded into SBA-15, the catalyst (0.1 g) was digested with HNO₃ by stirring at room temperature for a week. Then, the mixture was filtered, and the total amount of copper in SBA-15 in the colorless sample was determined as 0.14 mmol/g by atomic absorption spectroscopy.

General procedure for synthesis of 8-amino-7-aryl-10,11-dihydro-7H,12H-chromeno[4',3'-b]pyrano[6,5-b]quinoline-6,9-diones (6a – l)

A combination of **4a – l** (1mmol), 1,3-cyclohexanedione (1 g, 5.4 mmol) and the catalyst (0.013 g, 0.00185 mmol), were thoroughly mixed and placed in the autoclave at 200-280 °C for a certain time (Table 1). After cooling, the mixture was washed with DMF (50 mL) and the catalyst separated by filtration, rinsed twice with MeOH, and followed by drying at 80 °C for 60 min, was reused for subsequent runs. Analytically, the pure products **6a–k** were obtained by evaporation of the solvent and recrystallization from EtOH. The yields and melting points are shown in Table 2. The products

were identified by comparison with the original samples [15].

Spectral and physical data for selected compounds

8-Amino-4-methyl-10,11 dihydro-7H,12H-chromeno[4',3'-b]pyrano[6,5-b]quinoline-6,9-dione (6l):

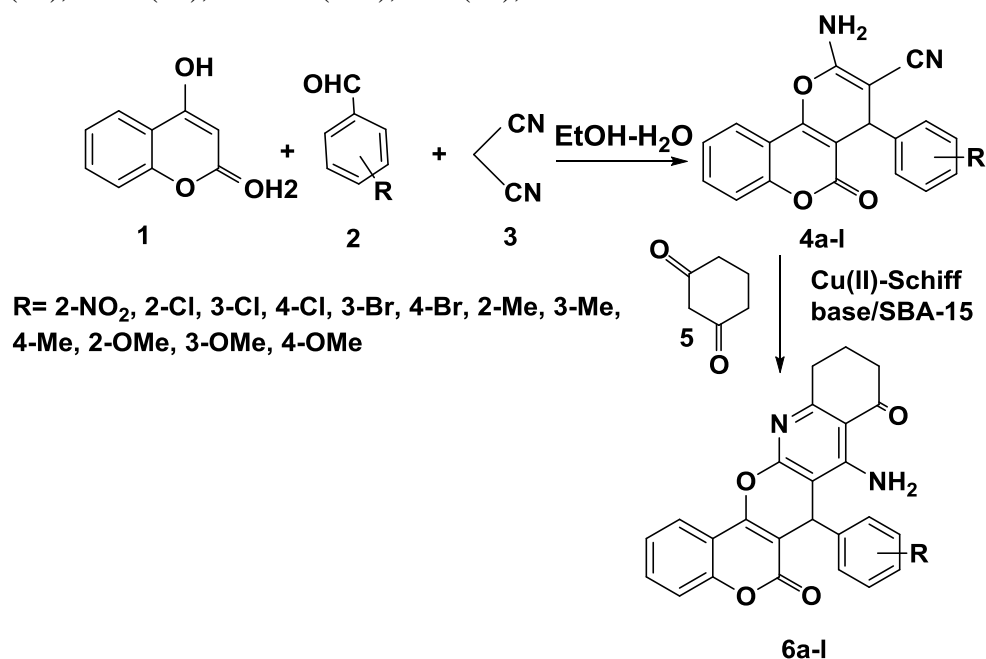
1.3g (57%), m.p. 220 °C. IR (KBr) ν : 3443 (NH₂), 3068 (C-H aromatic), 2955 (C-H aliphatic), 1733 (C=O) 1680(C=O) cm⁻¹. ¹H NMR (500 MHz, CDCl₃) δ (ppm): 2.13 m, 2H (H-11); 2.45 m, 2H (H-12), 2.78 m, 1H (H-10); 2.86 m, 1H (H-10); 4.97 s, 1H (H-7); 7.06 d, 2H, $J = 7.5$ (H-17, H-19); 7.28 d, 2H, $J = 7.5$ (H-16, H-20); 7.32-7.37 m, 2H (H-2, H-4); 7.56 t, 1H, $J = 7.5$ (H-3); 7.88 d, 1H, $J = 7.5$ (H-1). ¹³C NMR (75 MHz, DMSO-d₆) δ : 20.22, 21.05, 27.10, 32.86, 36.87, 106.92, 113.68, 116.46, 116.83, 122.38, 124.21, 128.45, 129.03, 130.02, 130.95, 132.11, 136.64, 139.76, 152.55, 153.75, 160.63, 163.43, 196.12. EI-MS: 425 (20) [M⁺+1], 409 (20), 354 (18), 333(40), 263 (100), 91(30),

64(20). Anal. Calcd. for C₂₆H₂₀N₂O₄: C, 73.57, H, 4.75, N, 6.60. Found: C, 73.55, H, 4.68, N, 6.51

Results and discussion

Recently, we have synthesized novel chromeno[4',3'-b]pyrano[6,5-b]quinoline derivatives, by condensation of 2-amino-4-aryl-3-cyano-5-oxo-4H, 5H -pyrano-[3,2-c]chromenes **4a-l** and 1,3-cyclohexanedione **5** in boiling acetic acid for 12 h in 35–78 % yield [15].

In continuation with our works using Cu(II)-Schiff base/SBA-15 [18] which are low in toxicity, highly stable towards humidity, recyclable, and air stable, herein, we introduce a simple, novel, and efficient protocol for the synthesis of chromeno[4',3'-b]pyrano[6,5-b]quinoline derivatives using the catalytic Cu(II)-Schiff base/SBA-15 in solvent-free conditions (Scheme 1). This catalyst is made by anchoring the copper complex to mesoporous silica SBA-15 [20,21] (Figure 1).



Scheme 1. Preparation of chromeno[4',3'-b]pyrano[6,5-b]quinolone derivatives **6a-l**

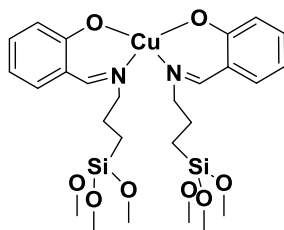


Figure 1. Structure of Cu(II)-Schiff base/SBA-15

The starting materials, 2-amino-4-aryl-3-cyano-5-oxo-4*H*,5*H*-pyrano[3,2-*c*]chromenes **4a – I**, were synthesized as shown in Scheme 1 [22, 23]. Initially, the condensation reaction of 2-amino-7(2-nitrophenyl)-3-cyano-5-oxo-4*H*,5*H*-pyrano-[3,2-*c*]chromenes **4g** and 1,3-cyclohexanedione **5** was picked out to optimize the reaction conditions such as temperature and quantity of the

catalyst (Table 1). We then found that, the maximum TON and TOF were obtained in the presence of Cu(II)-Schiff base/SBA-15 (0.0085 mmol) at 250 °C which is melting point of compound **4g** (Entry 8). Therefore, the best temperature for the synthesis of each compounds **6a-l** is the melting point of the starting compounds **4a-l**.

Table 1. The synthesis of 8-amino-7(2-nitrophenyl)-10,11-dihydro-7*H*,12*H*-chromeno[4',3'-*b*]pyrano[6,5-*b*]quinoline-6,9-dione **6g** catalyzed by Cu(II)-Schiff base/SBA-1

Entry	T(°C)	t (min)	Yield ^a (%)	Catalyst (mmol)	TON ^b	TOF ^c
1	250	13	76	0.0090	84	388
2	200	60	50	0.0090	55.5	55.5
3	150	-	-	0.0090	0	0
4	100	-	-	0.0090	0	0
5	250	13	76	0.0092	82	379
6	250	13	76	0.0089	85	393
7	250	13	76	0.0087	87	402
8	250	13	76	0.0085	89	412
9	250	25	60	0.0080	75	180

^aIsolated yield

^bTON=mmol of the product per mmol of the catalyst × 100

^cTOF= TON per reaction time(h)

Then, the reaction of a set of compounds **4a-l** with 1,3-cyclohexadione **5** was investigated, so that it would be possible to confirm the generality of the present method (Scheme 1). The results of the present study are depicted in Table 2. Thus, the desired products, chromeno[4',3'-*b*]pyrano[6,5-*b*]quinoline derivatives **6a-l** were obtained very fast, with high

yields and eco-friendly method (Scheme 2). The results also revealed that both the yields and the reaction times are relatively independent of arylaldehydes. Additionally, all the aforementioned catalyzed reactions delivered highly desirable product yields and short times, compared to the last method, in the absence of the catalyst (Scheme 1) (Table 2) [15].

Table 2. The synthesis of 8-amino-7-aryl-10,11-dihydro-7*H*,12*H*-chromeno[4',3'-*b*]pyrano[6,5-*b*]quinoline-6,9-diones **6a** – **1** catalyzed by Cu(II)-Schiff base/SBA-15

Entry	Comp	R	Temperature (°C)	m.p. (°C)	Time (min)	Yield ^{a,b} (%)	Yield ^c (%)	m.p. ^c (°C)
1	6a	2-OMe	260-270	>300	15	86	67	>300
2	6b	3-OMe	195-200	162-166	17	80	70	162
3	6c	4-OMe	230	150	15	75	78	146
4	6d	2-Cl	280	242-244	5	76	45	243
5	6e	3-Cl	230	225	4	85	76	220
6	6f	4-Cl	240-250	175	4	78	43	172
7	6g	2-NO ₂	250	270	13	76	45	275
8	6h	3- Br	260	260	10	70	56	260
9	6i	4-Br	248	250-254	11	85	50	254
10	6j	2-Me	276	270	3	90	35	270
11	6k	3-Me	250	>300	15	65	35	>300
12	6l	4-Me	240	230	17	80	57	220

^a Condition: Solvent-free system, catalyst (0.0085 mmol)

^b Isolated yield

^c Yields and m.p. refer to the literature [15], Conditions: Refluxing in acetic acid for 12h, without catalyst.

Furthermore, easy recovery of the catalyst by filtration, washing with ethanol and drying at 80 °C for 60 min, is another advantage of this method. As shown in Table 3, The recovered catalyst was reused for 6 times without

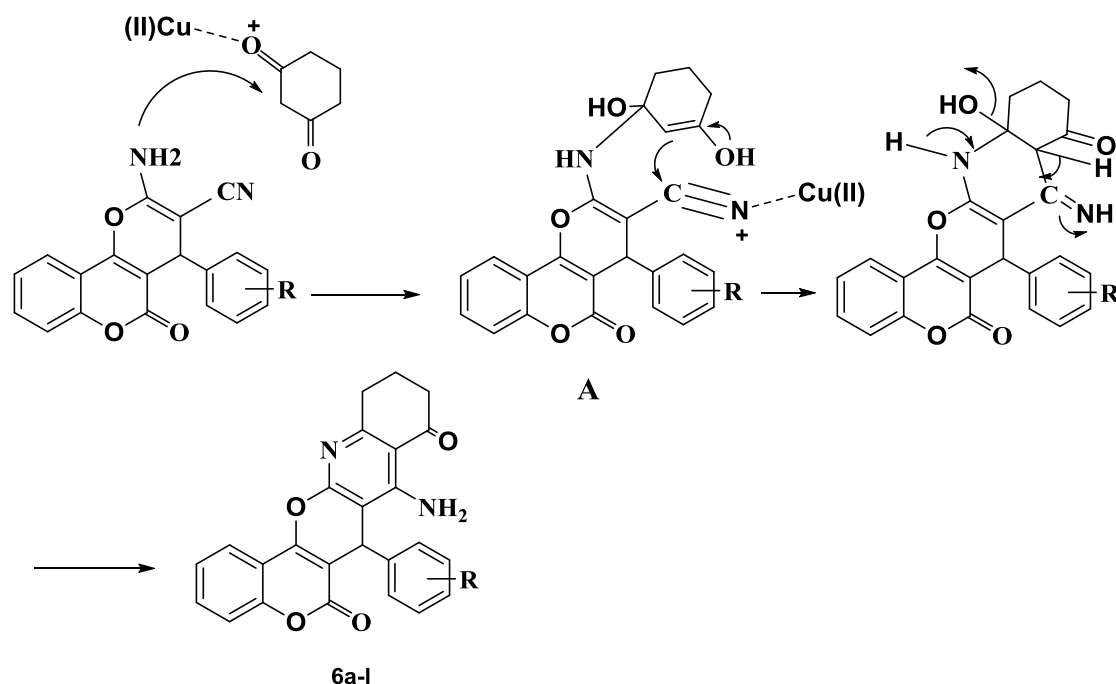
any significant drop in catalytic efficiency in terms of reaction yield. But, the yield drops to 70% in the seventh run which possibly comes from a leakage of Cu²⁺ from SBA-15 channels.

Table 3. Recycle study of the catalyst in the synthesis of compound **6g** under the optimized reaction conditions

Run	1	2	3	4	5	6	7
Reaction time (min)	13	13	14	14	14	14	17
Yield (%)	76	76	76	75	75	74	70
TON	89	89	89	88	88	87	82

A plausible mechanism for the synthesis of compound **6** in the presence of the catalyst is shown in scheme 2. Coordination of the carbonyl and nitrile groups in 1,3-

cyclohexadione and the intermediate A by the Cu²⁺ cation of the catalyst may increase electrophilicity of the carbonyl and nitrile group in both condensation steps.



Scheme 2. Possible mechanism pathway for the formation of **6**

Conclusion

In summary, we introduced a new application of Cu(II)-Schiff base/SBA-15 as an environmentally friendly heterogeneous catalyst for the synthesis of chromeno[4',3'-b]pyrano[6,5-b]quinoline derivatives, new groups of heterocyclic compounds derived from coumarin, under solvent-free conditions. Excellent yield of products, short reaction time and application of a non-toxic, easy to separate and recyclable catalyst making this methodology economically and environmentally acceptable.

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