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Efficient, convenient and reusable polyaniline-sulfate salt catalyst for the synthesis of quinoxaline derivatives

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Abstract

Biologically important quinoxaline derivatives were prepared in excellent yields using very low amount of reusable polyaniline-sulfate salt catalyst from various 1,2-dicarbonyls and aromatic 1,2-diamines. This methodology is also very much useful for the synthesis of new quinoxaline derivative using sterically hindered diamine.

Keywords: 1,2-Dicarbonyls; Aromatic 1,2-diamines; Polyaniline-sulfate salt; Reusability; Quinoxaline

1. Introduction

Quinoxaline derivatives are nitrogen containing heterocyclic compounds and their importance has been reported in the literature [1]. They possess well known biological activities including anti-viral, anti-bacterial, anti-inflammatory, anti-protozoal, anthelmintic, anti-cancer and as kinase inhibitors. Quinoxaline derivatives constitute the basis of many insecticides, fungicides, herbicides, as well as being important in human health and as receptor antagonists. Although rarely described in nature, synthetic quinoxaline moiety is a part of number of antibiotics such as echinomycin, levomycin and actinomycin which are known to inhibit the growth of Gram-positive bacteria and also active against various transplantable tumours. In addition, quinoxaline derivatives are reported for their application in dyes, efficient electroluminescent materials, organic semiconductors and DNA cleaving agents. These are useful as intermediates for many target molecules in organic synthesis and also as synthons.

Many synthetic routes have been developed for the synthesis of quinoxaline derivatives. Most common method is the condensation of aromatic 1,2-diamine with 1,2-dicarbonyl compound in refluxing ethanol or acetic acid [2]. However, many improved methods have been reported for the synthesis of quinoxalines using catalytic amounts of various metal precursors such as $Pd(OAc)_2$, $RuCl_2$-$(PPh_3)_3$-TEMPO, MnO_2, acids and zeolites [3]. In addition, microwave [4], solid phase synthesis [5], bi-catalyzed (bismuth and copper) oxidative coupling of peroxides and ene-1,2-diamines [6] were also reported. Very recently molecular iodine was used as catalyst for the synthesis of quinoxaline derivatives by Shivaji et al. [1a] in acetonitrile medium and by Rajesh et al. [1b] in dimethyl sulfoxide medium.

Many of these methods suffer from one or more limitations such as harsh conditions, low yields, long reaction times, critical product isolation procedures and co-occurrence of several side products. The main disadvantage of the existing methods is that the catalyst cannot be recovered and reused. In this paper work, we wish to report a facile, efficient and practical method for preparation of quinoxaline derivatives in excellent yields using cheaper and recyclable polyaniline-sulfate salt as a catalyst.

2. Experimental

2.1. Preparation of polyaniline-sulfate salt catalyst [7a]

In a 2 l round-bottomed flask, 700 ml of water was taken and 30 ml of H_2SO_4 was added slowly with stirring. To this mixture,

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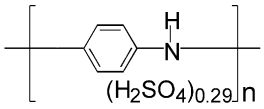
10 ml of aniline was added and the solution was kept under constant stirring at room temperature. To this solution, 250 ml of aqueous solution containing sodium persulfate (23.8 g) was added for 15–20 min duration. The reaction was allowed to continue for 4 h at room temperature. The precipitated polyaniline powder was filtered and washed with 51 distilled water followed by 500 ml of acetone. The polyaniline powder was dried at 100 °C till a constant weight.

2.2. General experimental procedure for the synthesis of quinoxialine derivatives

A mixture of 1,2-dicarbonyl (1 mmol), aromatic 1,2-diamine (1 mmol), 1,2-dichloro ethane (5 ml) was stirred in presence of polyaniline-sulfate salt catalyst (5 wt.% with respect to 1,2-dicarbonyl) at room temperature. The reaction was monitored by TLC. The reaction mixture was filtered in order to recover the catalyst and the filtrate was dried with sodium sulfate, concentrated in vacuum. The crude product was purified by column chromatography (eluent-95:5 hexane–ethyl acetate). All the products were characterized by ^{1}H NMR and mass spectra.

3. Results and discussion

In recent years, polyaniline salts have received considerable attention as a mild polymer based solid acid catalyst in organic synthesis [7]. Polyaniline-sulfate salt has excellent catalytic properties like recovery, reusability, stability, eco-friendly and it can be easily prepared [7]. Preparation of polyaniline-sulfate salt and its characterization are available in our recent report. The representative structure of polyaniline-sulfate salt (for simplicity) is given below:



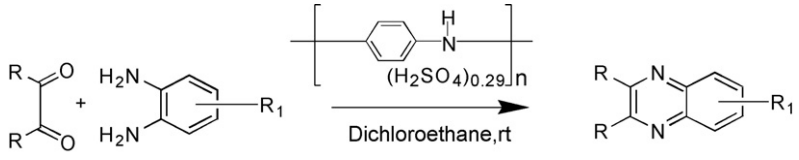
Simplified structure of polyaniline-sulfate salt

Polyaniline salt contains 23.3 wt.% of sulfuric acid, i.e. 0.29 unit per aniline unit. Conductivity and pellet density were found to be 0.02 S/cm and 1.22 g/cm^3.

In this work, the methodology of synthesis of quinoxaline derivatives is reported using very low amount of polyaniline based solid acid catalyst from the reaction of 1:1 mole ratio of 1,2-dicarbonyl and aromatic 1,2-diamine (Scheme 1). Polyaniline-sulfate salt catalyst consists of polyaniline base and sulfuric acid as dopant group. This sulfuric acid dopant present in polyaniline chain takes part in the reaction. The mechanism of this reaction is very similar to that of the protic acid or Lewis acid catalysed reactions [1a,1b].

Initially the reaction was conducted with benzil and *o*-phenylene diamine at room temperature without using catalyst and obtained very low yield even for a period of 12 h. However, quantitative yield of the product was obtained with the use of polyaniline-sulfate salt catalyst (5 wt.% with respect to benzil) within 20 min.

In order to evaluate the efficiency of this methodology, a number of 1,2-dicarbonyls and 1,2-diamines were further subjected to condensation using very low amount of polyaniline-sulfate salt (5 wt.%) (Table 1). When the electron-donating substituents present in diamine part, increased yields of products were observed, whereas the effect is reverse with the electron withdrawing substituents. On the other hand, electron-donating substituents with aromatic 1,2-diketone decreased the product yields and the effect is reverse with electron withdrawing groups.



Scheme 1.

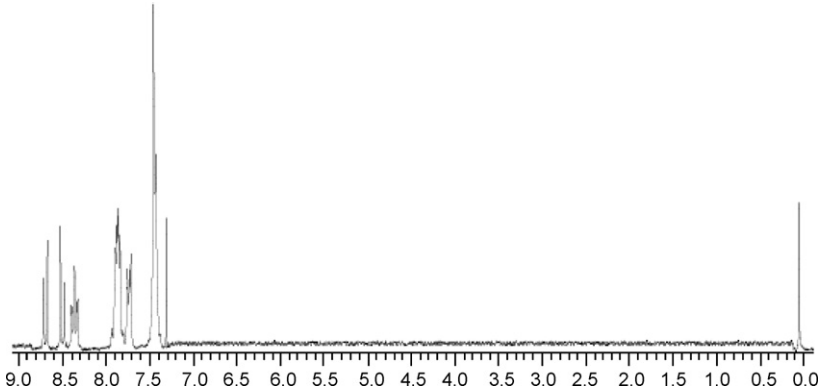


Fig. 1. NMR spectrum of 2,3-diphenyl-7,12-dihydro naphtho[2,3-f] quinoxaline-7,12-dione ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.69 (d, J = 9.33 Hz, 1H), 8.49 (d, J = 9.33 Hz, 1H), 8.35 (m, 2H), 7.86 (m, 4H), 7.73 (m, 2H), 7.45 (m, 6H).

Table 1
Synthesis of quinoxaline derivatives using polyaniline-sulfate salt catalyst

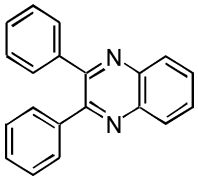
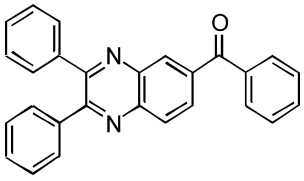
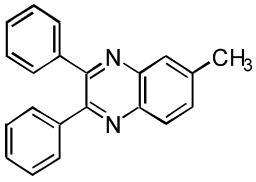
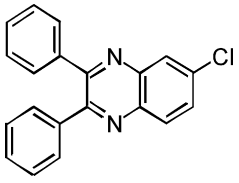
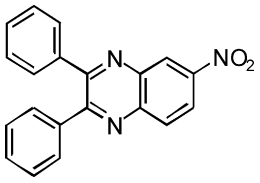
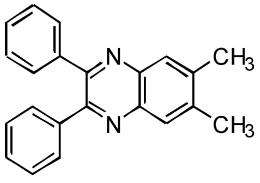
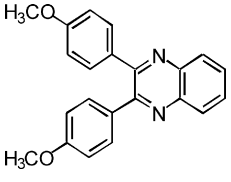
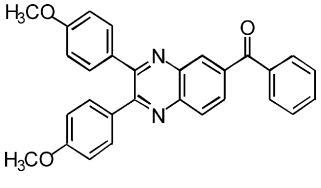
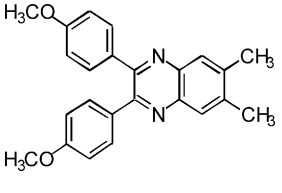
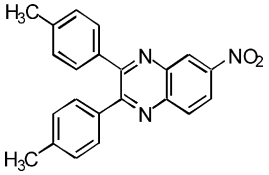
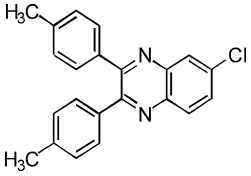
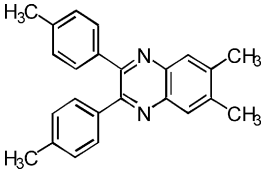
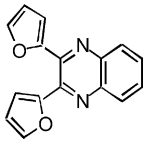
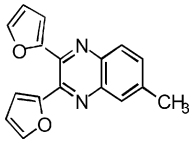
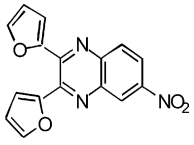
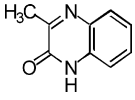
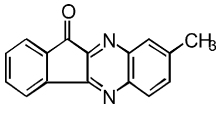
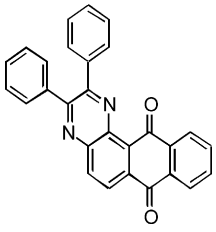
Entry	Product	Time	Yield (%)[a]
1		20 min	95
2		25 min	90
3		15 min	92
4		25 min	92
5		40 min	90
6		10 min	94
7		15 min	92
8		25 min	89
9		20 min	91

Table 1 (*Continued*)

Entry	Product	Time	Yield (%)[a]
10		1 h	86
11		30 min	88
12		15 min	92
13		10 min	92
14		20 min	93
15		35 min	95
16		30 min	85
17		40 min	90
18		45 min	93[b]
19		2 h	75

[a] Refers to isolated yield.
[b] The yield belongs to the overall yield of two regio isomers.

Table 2
Recyclability of polyaniline-sulfate salt catalyst

Entry	Benzil (mg)	Catalyst (5%) (mg)	Time (min)	Yield (%)[a]
1	1000	50	20	95
2	770	38.5	20	95
3	680	34	20	94
4	560	28	20	94
5	330	16.5	20	94
6	240	12	20	93

[a] Refers to isolated yield.

However, the variations in the yields were very little. On continuing of our interest, other 1,2-dicarbonyls such as furil (entry nos. 13–15), glyoxal (entry no. 16) were subjected for condensation reaction and obtained excellent yields.

We have also examined other than 1,2-diketones such as ethyl pyruvate (entry no. 17), ninhydrin (entry no. 18), and obtained the corresponding products in excellent yields. Authenticity of the products (1–18) has been confirmed by ^{1}H NMR and mass spectral data. Besides this, highly sterical 1,2-diamino anthraquinone was used for the first time in condensation reaction with benzil (entry no. 19). The reaction did not proceed at room temperature and however, under reflux condition it yields the corresponding product in 75%. The NMR spectrum of 2,3-diphenyl-7,12-dihydro naphtho[2,3-f] quinoxaline-7,12-dione (Table 1—entry no. 19, Brick red solid, mp 279–281 °C) is shown in Fig. 1.

Recyclability of the catalyst was also studied through a condensation reaction of benzil and *o*-phenylene diamine as model substrate. The catalyst was simply filtered from the reaction mixture and reused for five cycles. The reaction proceeded smoothly with a yield of 95–93% (Table 2). This result indicates that the activity of catalyst was not affected on recycling.

4. Conclusion

In conclusion, we describe a simple, efficient and eco-friendly method for the synthesis of various quinoxaline derivatives using polyaniline-sulfate salt. Easy synthesis of catalyst, stability of catalyst, uncomplicated handling, convenient work-up procedure, mild reaction conditions, versatility, recyclability, inexpensive and eco-friendly nature of the catalyst make this method a valid contribution to the existing methodologies.

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