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Green chemistry approaches for the synthesis of quinoxaline derivatives: Comparison of ethanol and water in the presence of the reusable catalyst cellulose sulfuric acid

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Abstract

Quinoxaline derivatives have been synthesized in high yields in the presence of cellulose sulfuric acid as an inexpensive, recyclable and biodegradable solid acid catalyst in H_2O or EtOH at room temperature. ***To cite this article: A. Shaabani et al., C. R. Chimie 12 (2009).***

Keywords: Quinoxaline; Cellulose sulfuric acid; Solid acid; Green chemistry

1. Introduction

Quinoxaline and its derivatives are an important class of benzoheterocycles displaying a broad spectrum of biological activities which have made them privileged structures in pharmacologically active compounds [1–4]. They have also been found applications as building blocks in the synthesis of organic semiconductors [5], rigid subunits in macrocyclic receptors or molecular recognition [6], and chemically controllable switches [7]. Recently, the synthesis of quinoxaline derivatives via the condensation of aryl 1, 2-diamines with 1, 2-dicarbonyl compounds in MeOH/AcOH [8] under microwave irradiation at 100 °C has been reported, but requires special instrumentation. In addition, improved methods have been developed for the synthesis of quinoxaline derivatives, including *o*-iodoxybenzoic acid [9], ceric(IV)ammonim nitrate [10], $Yb(OTf)_3$ [11], $H_6P_2W_{18}O_{62}\cdot 2H_2O$ [12] and oxone [13]. However, most of the traditional processes suffer from a variety of disadvantages, such as pollution, high cost, poor chemical yields, requirements for long reaction time, and tedious work-up procedures, which limit their use under the aspect of environmentally benign processes. Recently, some other methods for the preparation of quinoxaline derivatives have been reported [14–16].

At the commencement of the new century, a shift in emphasis in chemistry is apparent with the desire to develop more environmentally friendly routes to a myriad of materials. This shift is most apparent in the growth of green chemistry [17–19]. Green chemistry approaches not only hold out significant potential for reduction of by-products, a reduction in the waste produced and lowering of energy costs, but also in the development of new methodologies towards previously unobtainable materials, using existing technologies [20].

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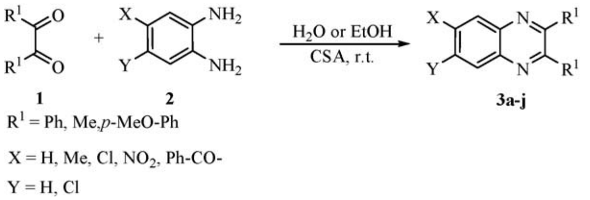
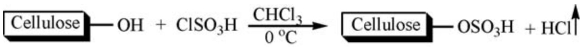


Scheme 1.



Scheme 2.

Biopolymers, especially cellulose and its derivatives [21], have some unique properties, which make them attractive alternatives for conventional organic or inorganic supports for catalytic applications. Cellulose is the most abundant natural material in the world and it has been widely studied during the past decades because it is a biodegradable material and a renewable resource. Recently, science and technology are shifting emphasis on environmentally friendly and sustainable resources and processes. In this regard, biopolymers are attractive candidates to explore for supported catalysis [22,23]. Several interesting biopolymers have been utilized as a support for catalytic applications, such as alginate [24], gelatin [25,26], starch [27] and chistosan [28] derivatives.

During the course of our studies toward the development of new routes to the synthesis of heterocyclic compounds using green reaction mediums [29–33], we herein disclose a valid and an efficient procedure for the synthesis of quinoxaline derivatives *via* condensation of 1,2-diketones: (1) with *o*-diamines; (2) in the presence of cellulose sulfuric acid (CSA) [34–36], as an inexpensive and biodegradable solid acid catalysts in H_2O or EtOH at room temperature (Scheme 1).

2. Results and discussion

The synthesis of 3a–j was accomplished as outlined in Scheme 1. Reaction of the appropriate 1,2-diketone: (1) with *o*-diamino-substituted benzene; (2) in the presence of CSA gave the known quinoxaline derivatives in high yields at room temperature. The catalyst is very active, stable to air and moisture, nontoxic and inexpensive. In addition, it can be quantitatively recovered by filtration and reused. Both aliphatic and aromatic 1,2-diketones afforded good yields. The results summarized in Table 1 clearly indicate the scope and generality of the reaction with respect to various 1,2-diketones and *o*-diamines. As can be seen from Table 1, in comparison of EtOH and H_2O as a solvent, EtOH is better solvent in view point of short reaction times and improvement of yields. Most of the reactions proceed very cleanly at room temperature and no undesirable side-reactions were observed, although the yields were highly dependent on the substrate used (spatially in H_2O). For instance, a substrate bearing a strong electron withdrawing group completely stopped in H_2O even after 24 h (Table 1, entries 3c and 3h).

Cellulose sulfuric acid is readily prepared [34–36] by the dropwise addition of chlorosulfonic acid to a $CHCl_3$ mixture of cellulose at 0 °C. It is important to note that this reaction is easy and clean without any work-up procedure since the HCl gas is evolved from the reaction vessel immediately. This white homogeneous, non-hygroscopic solid acid is very stable under reaction conditions (Scheme 2).

To illustrate the need for cellulose sulfuric acid for these reactions, the experiment (Table 1, entry 3a) was conducted in the absence of cellulose sulfuric acid. The yield in the absence of catalyst was about 20% after

Table 1
Synthesis of quinoxaline derivatives using CSA as catalyst in EtOH and H_2O.

Entry	R^1	X	Y	EtOH (time / yield (%)[a])	H_2O (time / yield (%)[a])
3a	Phenyl	H	H	60 min / 93 (92, 95, 90, 90)[b]	2.30 h / 80 (78, 80, 82, 80)[b]
3b	Phenyl	Me	H	75 min / 90	2.30 h / 72
3c	Phenyl	NO_2	H	6 h / 86	24 h / 0
3d	Phenyl	Cl	Cl	100 min / 90	24 h / 80
3e	Phenyl	Ph-CO-	H	3 h / 92	24 h / 83
3f	Me	Me	H	2 h / 86	2 h / 75
3g	Me	Cl	Cl	2 h / 91	2 h / 77
3h	Me	NO_2	H	2 h / 79	2 h / 0
3i	4-Methox phenyl	H	H	24 h / 85	24 h / 50
3j	4-Methox phenyl	Me	H	24 h / 81	24 h / 50

[a] Isolated yields.
[b] The yields of four subsequent runs by using the same recovered catalyst.