Available online at www.sciencedirect.com
ScienceDirect
Chinese Chemical Letters 20 (2009) 161–164
CHINESE CHEMICAL LETTERS
www.elsevier.com/locate/cclet

Keggin type heteropolyacids-catalyzed synthesis of quinoxaline derivatives in water

Tai Kun Huang, Lin Shi, Rui Wang, Xing Zhou Guo, Xiao Xia Lu *

Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu 610041, PR China

Received 3 July 2008

Abstract

Keggin type heteropolyacids was found to be an efficient and reusable catalyst for the synthesis of biologically active quinoxaline derivatives from the condensation of 1,2-diamine with 1,2-dicarbonyl compounds in excellent yields in water. This method provides a new and efficient protocol in terms of small quantity of catalyst, a wide scope of substrates, and simple work-up procedure.

Keywords: Keggin type heteropolyacids; 1,2-Diamines; 1,2-Diketones; Quinoxaline derivatives; Water

Quinoxalines are important compounds from both academic and industrial perspective because they are significant intermediates for the manufacturing of pharmaceuticals and advanced materials [1]. There is an increasing interest in developing environmentally benign reactions and atom-economic catalytic processes that employ 1,2-diamine and 1,2-dicarbonyl compounds for the synthesis of quinoxaline derivatives in recent years [2]. Reactions that are performed in water have attracted a great deal of attention in synthetic organic chemistry over past decades [3], because water is safe, cheap, and environmentally friendly. Despite a number of synthetic strategies have been developed for the preparation of quinoxalines, most of them are preformed in organic solvents, with the use of water as a sole medium being very rare [4]. Moreover, most of synthetic strategies for the synthesis of quinoxaline derivatives suffer from several drawbacks including the use of a large amount of catalysts, unsatisfactory product yields, and critical product isolation procedures. Especially the limited application of less-reactive aromatic diamine such as 4-nitrophenylenediamine. Therefore the search continues for a better catalyst for the quinoxaline derivatives in water in terms of a wide scope of substrates, economic viability and reusability.

Heteropolyacids (HPAs) are environmentally benign and economically feasible solid catalysts that offer several advantages such as excellent solubility in water, high catalytic activities and reactivates, ease of handling, cleaner reactions in comparison to conventional catalysts (less waste production), non-toxicity and experimental simplicity [5]. It is attractive that HPAs have hierarchical structure [6], which are important for the forming of active pseudoliquid phases and keeping high catalytic activities. HPAs are strong Brønsted acid and most of them are stronger in acidity than the usual inorganic acids (HCl, H_2SO_4, HNO_3, HBr), even stronger than $HClO_4$ and CF_3SO_3H. Both its structural

* Corresponding author.
E-mail address: xlua71@yahoo.com.cn (X.X. Lu).

1001-8417/$ – see front matter
doi:10.1016/j.cclet.2008.10.048

Table 1
Synthesis of quinoxalines under different catalysts and different conditions[a].

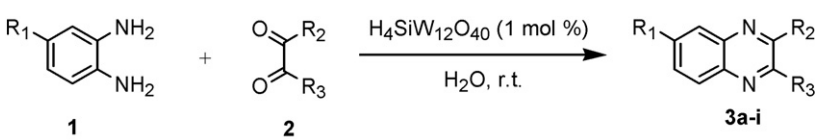
Entry	Catalyst (mol%)	Time	Solvent	Yield (%)[b]
1	NH_2SO_3H (1)	1 h	H_2O	42
2	Mont. K-10 (1)	1 h	H_2O	57
3	*p*-TsOH (1)	1 h	H_2O	60
4	$H_4SiW_{12}O_{40}$ (10)	1 h	H_2O	96
5	$H_4SiW_{12}O_{40}$ (5)	1 h	H_2O	95
6	$H_4SiW_{12}O_{40}$ (1)	1 h	H_2O	96
7	$H_4SiW_{12}O_{40}$ (0.5)	1 h	H_2O	72
8	$H_4SiW_{12}O_{40}$ (0.1)	8 h	H_2O	96
9	$H_4SiW_{12}O_{40}$ (1)	15 min	CH_3OH	100
10	$H_4SiW_{12}O_{40}$ (1)	15 min	CH_3CN	100
11	$H_4SiW_{12}O_{40}$ (1)	15 min	$CHCl_3$	100
12	$H_4SiW_{12}O_{40}$ (1)	15 min	AcOH	100

[a] Reaction conditions: 1,2-diaminobenene (1.0 mmol) and benzil (1.0 mmol) in solvent (3 mL) at room temperature.
[b] Isolated yield.

features [6] and synthetic potential [7] have been extensively studied. Due to strong catalytic activity as Brønsted acid, HPAs have been used extensively as catalyst in: esterification [7(a)], Friedel–Crafts reactions [7(b)], cyanosilylation [7(c)], ring-opening of epoxides [7(d)], and dehydration [7(e)].

In continuation of the studies on the new variants, of a one pot synthesis of quinoxaline derivatives and our ongoing green organic chemistry program that uses water as a reaction medium, Wells–Dawson type heteropolyacids ($H_6P_2W_{18}O_{62}$) which is ellipsoidal structure [8] as catalyst for synthesis of quinoxaline derivatives has been reported, however use of water as solvent in this reaction gave very low yields of products (30% after 24 h) [9]. Keggin type heteropolyacids ($H_4SiW_{12}O_{40}$) are roughly spherical and involves 4 threefold M_3O_{13} groups. The total assemblage contains 40 close-packed oxygens and has a tetrahedron pocket in its center for the heteroatom [10]. To the best of our knowledge, there are no examples of the use of Keggin type heteropolyacids as catalyst for the synthesis of quinoxaline derivatives. Following our previous work on the synthesis of quinoxaline derivatives [11], and in view of the importance of heterogeneous solid acids as reusable catalyst in organic synthesis, herein, we describe a green and efficient method for the synthesis of quinoxaline derivatives in high yields by the condensation 1,2-diamine with 1,2-dicarbonyl compounds catalyzed by Keggin type heteropolyacids in water (Scheme 1).

Initially, following the report by Heravi et al. [9], we attempted the condensation of *o*-phenylenediamine and benzil (PhCOCOPh) using 1 mol% different solid acids, such as NH_2SO_3H, Mont K-10 and *p*-TsOH, in place of Wells–Dawson type heteropolyacids, at room temperature in water for the synthesis of quinoxaline, only providing moderate yield of a condensation product **3a** after 1 h (Table 1, entries 1–3). Thus, using Wells–Dawson type heteropolyacids, NH_2SO_3H, Mont K-10 and *p*-TsOH, as catalyst in water, the reaction was slow with unsatisfactory yields. While using Keggin type heteropolyacids ($H_4SiW_{12}O_{40}$) as catalyst with similar substrates in water, to our surprise, the reaction proceeded smoothly after 1 h and afforded the products **3a** in 96% yield (Table 1, entry 6). In order to determine the optimum conditions, we examined the influence of the proportions of $H_4SiW_{12}O_{40}$ to substrate. The condensation was completed in the formation of quinoxaline ring using 1 mol% of $H_4SiW_{12}O_{40}$ after 1 h (Table 1, entry 6, 96%). Decreasing the amount of $H_4SiW_{12}O_{40}$ to 0.5 mol% resulted in lower yields (Table 1, entry 7, 72%), while increasing the amount of $H_4SiW_{12}O_{40}$ to 5 mol% showed no substantial improvement in the yield (Table 1, entry 5, 95%). We also observed that the reaction proceeded with 0.1 mol% of $H_4SiW_{12}O_{40}$, longer time (8 h) is typical to achieve comparable yields to those obtained with 1 mol% of $H_4SiW_{12}O_{40}$ (Table 1, entry 8, 96%). The reaction was also carried out in some organic solvents (Table 1, entries 9–12). Organic solvents stood out as the solvent of choice, with their fast



Scheme 1.