Iranian Journal of Organic Chemistry Vol. 3, No. 2 (2011) 629-633

$KAl(SO_4)_2.12H_2O$ as an efficient and reusable catalyst for the synthesis of quinoxaline in solvent-free condition

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Received: March 2011; Revised: March 2011; Accepted: April 2011

Abstract: 1,2-Diketones have been reacted in one-pot method with 1,2-diamines at room temperature with $KAl(SO_4)_2.12H_2O$ as a catalyst. Alum $KAl(SO_4)_2.12H_2O$ as an available and reusable catalyst is disclosed for the synthesis of Quinoxaline in improved yields.

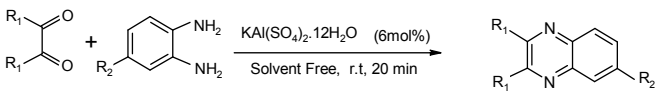
Keywords: Quinoxaline, $KAl(SO_4)_2.12H_2O$, Alum, Benzil, 1,2-Diamines.

Introduction

Among the various classes of nitrogen containing heterocyclic compounds, quinoxaline derivatives display a broad spectrum of biological activities and quinoxalines play an important role as a basic skeleton for the design of a number of antibiotics such as echinomycin, actinomycin and leromycin [1]. Quinoxalines have a variety of activities such as tranquilizing, antimycobacterial, cardiotonic, antidepressant and antitumor activities depending on the substitution pattern on the scaffold [2]. Synthesis of quinoxaline ring is still an important challenge. They have also many applications in dyes, pharmaceuticals and efficient electroluminescent materials [3]. The most common method for their synthesis relies on the condensation of an aryl 1,2-diamine with a 1,2-dicarbonyl compound in refluxing ethanol or acetic acid for 2-12h giving 34-85% yields [4]. Recently, the synthesis of quinoxaline has been catalyzed by $CuSO_4.5H_2O$, microwave irradiation, $H_6P_2W_{18}O_{62}.24H_2O$, Zn[(I)proline], Acidic alumina, NH_4Cl-CH_3OH, Sulfamic acid/MeOH, Molecular iodine, Metalhydrogen sulfated, Ni-nanoparticles, Montmorillonite K-10, Task-specific ionic liquid and Oxalic acid [5-17].

$KAl(SO_4)_2.12H_2O$ (alum) as a solid acid catalyst has been used in some organic reaction, such as Synthesis of some new oxindoles [18], Quinolines [19], some 4-substituted coumarins [20], 1,3,4-Oxadiazoles [21], Alkyl or aryl-14H-dibenzo[a,j] xanthenes [22], coumarins [23], trisubstituted imidazoles [24], 1,5-benzodiazepines [25] and etc.

Based on our previous studies on the use of hetrogenous catalysts for carring organic reactions [26,27], in the present research, we wish to describe a mild and efficient approach for the synthesis of quinoxalines using a catalytic amount of $KAl(SO_4)_2.12H_2O$ as a solid acid catalyst, under solvent-free conditions (Scheme **1**). This method appeared to be efficient and economical, with a wide range of applications.



Scheme 1:

Results and discussion

In continution of our investigation about application of solid acids in organic synthesis [28], we investigated the synthesis of quinoxalines in the presence of $KAl(SO_4)_2.12H_2O$ as a inorganic solid lewis acid. To optimize the reaction conditions, the reaction of benzil and ortho phenilendiamin was used as a model reaction (Table **1**). The efficiency of this acid is comparable with other catalysts such as $CuSO_4.5H_2O$, NH_4Cl,

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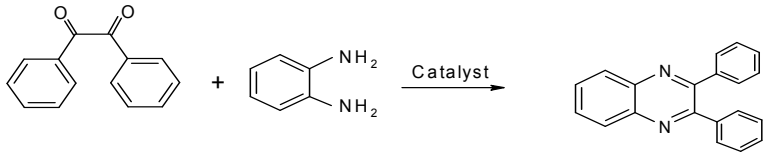
Sulfamic acid, Acidic alumina, $FeCl_3$, $SnCl_4$ and $SbCl_5$. According to the obtained data, NH_4Cl and sulfamic acid have more yield but NH_4Cl was applied (50mol%) more amount. $FeCl_3$ and $ZnCl_2$ were not applied because they are weaker lewis acid than alum. Since, $SnCl_4$ and $SbCl_5$ are liquid with a high specific gravity that fumes in air and reacts with the moisture to form HCl. The handling and the usability of $SbCl_5$ and $SnCl_4$ as a liquid form is laborious and solid acid is indeed preferable.

Table 1: Acid-catalyzed synthesis of 2,3-diphenylquinoxaline



Entry	Catalyst (mol%)	Temp. (°C)/ Solvent	Time(min)/ Yield(%)[a]	Ref.
1	$CuSO_4.5H_2O$(10)	25/H_2O	15/96	5
2	$CuSO_4.5H_2O$(10)	25/EtOH	8/97	5
3	NH_4Cl(50)	25/CH_3OH	7/100	10
4	Sulfamic acid(5)	25/CH_3OH	5/100	11
5	Acidic alumina	Microwave	5/85	9
6	$FeCl_3$ (6)	25/-	20/45	-
7	$ZnCl_2$(6)	25/-	20/40	-
8	$SnCl_4$(6)	25/-	20/45	-
9	$SbCl_5$ (6)	25/-	20/57	-
10	$KAl(SO_4)_2.12H_2O$(6)	25/-	20/93	-

[a]Isolated yield

After that, alum was selected as an efficient solid acid catalyst, the model reaction was done with varius amount of catalyst and varius condition. According to the obtained data, using the $KAl(SO_4)_2.12H_2O$ (6 mol%) under solvent free at 25 ºC is the best condition for the quinoxaline formation (Table **2**,entry 2). The catalyst was reused in subsequent runs without further purification. These results clearly show the advantages of our method over protic or lewis acid catalyzed quinoxalines synthesis.

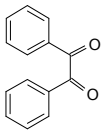
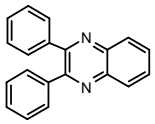
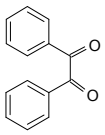
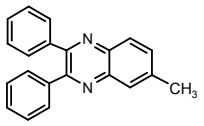
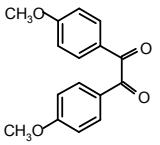
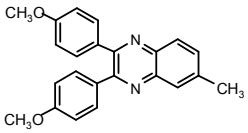
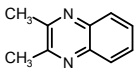
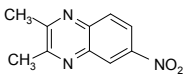
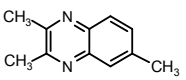
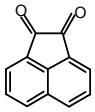
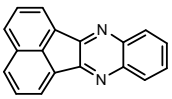
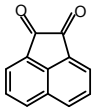
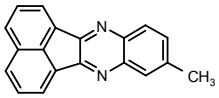
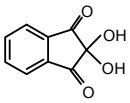
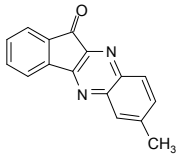
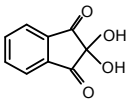
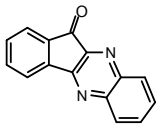
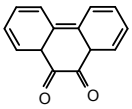
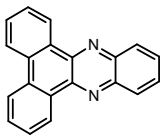
Table 2: Optimization of reaction condition.

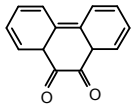
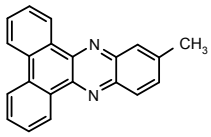
Entry	$KAl(SO_4)_2.12H_2O$ (mol%)	Temp. (°C)/ Solvent	Time(min)/ Yield(%)[a]
1	4	25/-	20/78
2	6	25/-	20/93
3	8	25/-	20/95
4	6	25/-	10/43
5	6	25/-	30/93
6	6	25/-	60/94
7	6	70/-	20/94
8	6	100/-	20/94
9	6	25/CH_2Cl_2	20/93
10	6	Reflux/EtOH	20/94
11	6	Reflux/H_2O	20/93
12	6, 2nd run	25/-	20/87
	6, 3rd run	25/-	20/82

[a]Isolated yield

Therefore, some 1,2-diketones and 1,2-diaminobenzenes were subjected to quinoxalines (Scheme **1** and Table **3**).

Table3: A recyclable and highly effective Alum catalytic system for the synthesis of quinoxalines at room temperature[a].

Entry	1,2-diketon	R^2	Product[b]	Yield(%)[c]	Ref	M.P(^oC)
1		H		93	12	126-128
2		CH_3		95	5	114-116
3		CH_3		96	5	125-127
4		H		92	11	102-104
5		NO_2		91	10	128-131
6		CH_3		94	10	76-78
7		H		92	-	242-244
8		CH_3		94	-	236-237
9		CH_3		93	29	177-179
10		H		92	29	221-225
11		H		93	-	226-228

12		CH_3		95	-	219-232

[a]Molar ratio of benzil, 1,2-diaminobenzene and $KAl(SO_4)_2.12H_2O$ (g) was 1:1:0.028.
[b] All products were identified by their melting points, IR, ^1H NMR, ^{13}C NMR spectra and CHN
[c] Isolated yield

Conclusion

$KAl(SO_4)_2.12H_2O$ as a solid acid has a high efficiency as catalyst of the quinoxaline synthesis under solvent-free conditions. This simple methodology offers several advantages including a simple work-up, opportunities for scale-up and improved yields.

Experimental

Melting points were measured by using the capillary tube method with a Barnstead Electrothermal melting point apparatus. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avans 500 MHz spectrometer using TMS as an internal standard ($CDCl_3$ solution). IR spectra were recorded from KBr disk on the Shimadzu IR-470 spectrometer. All products were characterized by spectra and physical data.

General procedure for the synthesis of 2,3-diphenylquinoxaline

A mixture of benzil (1 mmol), orthophenylendiamine (1 mmol) and $KAl(SO_4)_2.12H_2O$ (0.028 g) were placed in a round bottom flask. The materials were mixed at room temperature for 20 min (Table **3**). The progress of the reaction was followed by TLC. After the completion of the reaction, dichloromethan was added to the mixture and filtered to remove the catalyst. The recovered catalyst was washed with chloroform and dried in air. Thus recovered catalyst was reused for further reactions without significant loss of activity. By evaporation of the solvent, an oily residue or an impure solid was obtained. The solid was then crystallized with ethanol and then a milky to yellow solid was obtained. All the products (except entry 7, 8, 11, 12) are known compounds, which were characterized by IR and ^1H NMR spectral data and their mp, s compared with literature reports.

Acenaohtho [1,2-b] quinoxaline (entry 7). Cream solid, yield 92%, m.p.: 242-244 ^oC; IR (KBr): υ_{max} (cm^{-1}) 3040, 1622, 1571, 1480, 1297. ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.73(dd, J=3.4 Hz, 6.3 Hz, 2H), 7.78 (dd, J=7.1 Hz, 7.9 Hz, 2H), 8.03 (d, J=8.2 Hz, 2H), 8.17 (dd, J=3.4 Hz, 6.2 Hz, 2H), 8.35 (d, J=6.9 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) = 154.5, 141.7, 136.9, 132.2, 130.3, 130.0, 129.8, 129.6, 129.0, 122.2. Anal. Calcd. for $C_{18}H_{10}N_2$: C, 85.04; H, 3.94; N, 11.02 found: C, 84.8; H,3.89; N,11.01.

7-methylacenaphtho [1,2-b] quinoxaline (entry 8). Brown solid, yield 94%, m.p.: 236-237^oC; IR (KBr): υ_{max} (cm^{-1}) 3040, 2915, 1626, 1482, 1207. ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) = 8.36(d, J=6.6 Hz, d, J=6.6 Hz, 2H), 8.05 (m, 3H), 7.95 (S, 1H), 7.79 (d, J=7.4 Hz, d, J=7.6 Hz, 2H), 7.55(dd, J=1.3 Hz, 8.3 Hz, 1H), 2.61(S, 3H).^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) = 154.5, 153.8, 141.7, 140.1, 140.0, 136.7, 132.4, 131.7, 130.4, 129.8, 129.6, 129.5, 129.2, 129.0, 122.1, 122.0, 22.2. Anal.calcd. for $C_{19}H_{12}N_2$: C, 85.07; H, 4.47; N, 10.44, found: C, 84.9; H, 4.43;N, 10.40.

Phenantherene [1,2-b] quinoxaline (entry 11). Yellow solid, yield 93%. m.p.: 226-228 ^oC.
IR (KBr) υ_{max} (cm^{-1}): 3020, 1614, 1490, 1356, 1032. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 9.38 (dd, J=1.4 Hz, 7.9 Hz, 2H), 8.53 (d, J=7.9 Hz, 2H), 8.31 (dd, J=3.4 Hz, 6.4 Hz, 2H), 7.84 (dd, J=3.4 Hz, 6.5 Hz, 2H), 7.74 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) = 142.8, 142.6, 132.5, 130.7, 130.6, 130.1, 129.9, 128.3, 126.7, 123.3. Anal. Calcd. For $C_{20}H_{12}N_2$; C, 85.71; H, 4.28; N, 10. Found: C, 85.70; H, 3.90; N, 9.8.

7-methyl-Phenanthrene [1,2-b] quinoxaline (entry 12). Yellow solid, yield 95%. m.p.: 219-232 ^oC, IR (KBr) υ_{max} (cm^{-1}): 3010, 1622, 1499, 1354, 1206. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 9.39 (m, 2H), 8.56 (d, J=8.0 Hz, 2H), 8.21 (d, J=8.6 Hz, 1H), 8.09 (S, 1H), 7.78 (m, 4H), 7.68 (dd, J=1.8 Hz, 8.6 Hz, 1H), 2.68 (S, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) = 142.7, 142.6, 142.1, 141.2, 140.8, 132.8, 132.4, 132.2, 130.9, 130.8, 130.5, 130.4, 129.4, 128.4, 128.3, 128.2, 126.6, 126.5, 123.3, 22.5. Anal.calcd. for $C_{21}H_{14}N_2$: C, 85.71; H, 4.76; N, 9.52, found: C, 84.93; H, 4.67; N, 9.34.

Acknowledgements

We thank the Islamic Azad University of Yazd, for financial support of this investigation.

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