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Synthesis of quinoxaline derivatives catalyzed by PEG-400

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Abstract

Polyethylene glycol (PEG) was found to be an effective catalyst for the condensation of 1,2-diamines with 1,2-dicarbonyl compounds to afford the corresponding quinoxaline derivatives in excellent yields under mild reaction conditions.

Keywords: PEG-400; Quinoxaline derivatives; 1,2-Diamines; 1,2-Dicarbonyl compounds

Quinoxalines are very important compounds due to their wide spectrum of biological activities behaving as anticancer [1], antibacterial [2], and activity as kinase inhibitors [3]. Besides these, they are well known for their application in rigid subunits in macro cyclic receptors [4], electroluminescent materials [5], organic semiconductors [6] and DNA cleaving agents [7]. Considering the significant applications in the fields of medicinal, industrial and synthetic organic chemistry, there has been tremendous interest in developing efficient methods for the synthesis of quinoxalines. Improved methods have been reported via a condensation process catalyzed by $Pd(OAc)_2$ [8], MnO_2 [9], CAN [10], manganese octahedral molecular sieves [11], task-specific ionic liquid [12], Bismuth(III) [13] and so on. Although great success has been obtained, many of these processes suffer from drawbacks such as drastic reaction conditions, low product yields, tedious work-up procedures, using toxic metal salts as catalysts, long reaction time and relatively expensive reagents. Hence, the search for the better method, especially the readily available and green catalysts, is still being actively pursued.

As a non-toxic, inexpensive, thermally stable, recoverable and biologically acceptable reagent, polyethylene glycol (PEG) represents a very attractive medium for organic reactions [14]. To the best of our knowledge, the synthesis of quinoxaline using PEG-400 as catalyst has not so far been reported. In our continuous search for developing new processes using PEG as catalyst or solvent [15], in this paper, we wish to report a green and efficient method for the synthesis of quinoxaline derivatives in good to excellent yields by the condensation of 1,2-diamines with 1,2-dicarbonyl compounds catalyzed by PEG-400.

At the beginning of this work, the condensation reaction of 4-nitroenzene-1,2-diamine with benzil was employed as the model reaction to screen the suitable reaction conditions (Table 1). Among different catalysts and PEG species (Table 1, entries 1–11), we found PEG-400 was the best catalyst for the reaction. Furthermore, we studied the effect of temperature on the yields of the reaction (Table 1, entries 11–14), lowering or elevating the reaction temperature had

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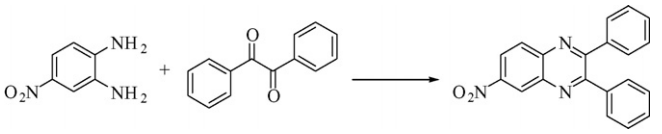
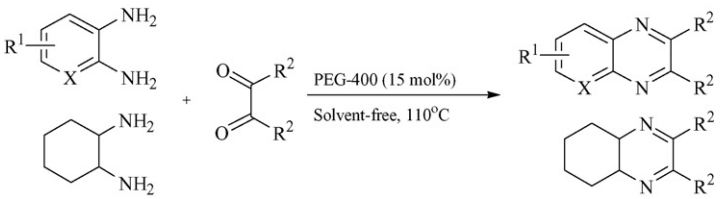
Table 1
Optimized conditions *via* the condensation of benzil and 4-nitroenzene-1,2-diamine.[a].



Entry	Catalyst	Temperature (°C)	Time (min)	Yield[b] (%)
1	HCl	110	240	20
2	H_2SO_4	110	240	32
3	CH_3COOH	110	240	35
4	$FeCl_3$	110	100	41
5	$ZnCl_2$	110	100	43
6	$CoCl_2$	110	100	55
7	$NiCl_2$	110	100	52
8	PEG-2000	110	50	75
9	PEG-10000	110	50	71
10	PEG-600	110	50	85
11	PEG-400	110	50	95
12	PEG-400	90	100	70
13	PEG-400	100	100	85
14	PEG-400	120	50	95

[a] *Reaction conditions:* 4-nitroenzene-1,2-diamine (1.0 mmol), benzyl (1.0 mmol), and catalyst (0.15 mmol) stirring at the appropriate temperature for the indicated time.
[b] Isolated yields.

Table 2
Synthesis of quinoxalines using different 1,2-diamines and 1,2-diketones.



R^1 = 4-NO_3, 4-CH_3, 5-Bz, 5-Br ; X = N, CH; R^2 = Ph, 2-Py, CH_3;

Entry	Amines	R^2	Products	Time (min)	Yield[b] (%)	Mp (°C)	
						Found	Lit.
1	Benzene-1,2-diamine	Ph	**2a**	10	100	129–130	126–127 [10]
2	4-Nitrobenzene-1,2-diamine	Ph	**2b**	50	95	190–191	187 [16]
3	(3,4-Diminophenyl)-(phenyl)methanone	Ph	**2c**	45	93	146	150–151 [17]
4	5-Bromopyridine-2,3-diamine	Ph	**2d**	30	95	150–151	149–150 [18]
5	4-Methylbenzene-1,2-diamine	Ph	**2e**	30	98	112	109–110 [16]
6	Cyclohexane-1,2-diamine	Ph	**2f**	15	92	170–171	167–169 [19]
7	Benzene-1,2-diamine	2-Py	**2g**	30	95	185–186	183–184 [20]
8	4-Methylbenzene-1,2-diamine	2-Py	**2h**	45	96	146	142 [21]
9	4-Nitrobenzene-1,2-diamine	2-Py	**2i**	60	93	191	193 [21]
10	(3,4-Diminophenyl)-(phenyl)methanone	2-Py	**2j**	60	94	164–166	–
11	Cyclohexane-1,2-diamine	2-Py	**2k**	15	90	188–189	
12	4-Methylbenzene-1,2-diamine	CH_3	**2l**	15	93	93	91 [22]
13	4-Nitrobenzene-1,2-diamine	CH_3	**2m**	20	90	136–137	134–135 [23]
14	Benzene-1,2-diamine	CH_3	**2n**	15	92	108	104–106 [24]
15	(3,4-Diminophenyl)-(phenyl)methanone	CH_3	**2o**	25	92	124	127 [25]

[a] *Reaction conditions:* 1,2-diamine (2 mmol), 1,2-dicarbonyl compound (2 mmol) and PEG-400 (0.3 mmol) stirring at 110 °C for the indicated time [26].
[b] Isolated yields.