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EFFICIENT SYNTHESIS OF QUINOXALINE WITH KIO_4 UNDER MILD CONDITIONS

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ABSTRACT

Efficient Synthesis of Quinoxalines derivatives with excellent yields using a catalytic amount of potassium periodate (KIO_4) at room temperature. The advantages of this synthetic protocol are a wide substrate range, easy handling and commercially available inexpensive catalyst.

Key words: Amine, Quinoxalines, Potassium periodate, Diketones.

INTRODUCTION

The development of simple, efficient, environmentally-benign and economically viable chemical processes or methodologies for widely used organic compounds is in great demand[1]. Quinoxaline derivatives are an important class of nitrogen containing heterocycles and they constitute useful intermediate in organic synthesis. Quinoxaline derivatives are well known in the pharmaceutical industry and have been shown to possess a broad spectrum of biological activities such as antibacterial, anti-inflammatory, antiviral and anticancer activity[2].

Research efforts have been focused on finding new catalysts to improve the yield of this condensation reaction. In addition to common Lewis acids, many other catalysts including I_2,[3-4] SA,[5] Montmorilinite K-10,[6] SSA,[7] $H_6P_2W_{18}O_{62}$. $24H_2O$[8], $InCl_3$[9], $MnCl_2$,[10] $CuSO_4.5H_2O$[11], CAN[12], p-TsOH[13], $Ga(OTF)_3$[14] and microwave[15,16] have been reported. Herein we report a simple, efficient process for the preparation of the biologically important quinoxaline derivatives through the reaction of 1,2-diamines and 1,2-diketones by using potassium periodate as a catalyst.

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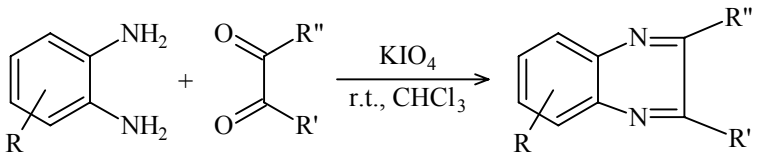

R', R": Phenyl, Alkyl.

Scheme 1

EXPERIMENTAL

General experimental procedure

A mixture of o-phenyldiamine (2 m mol), benzil (2 m mol), $CHCl_3$ (1 mL) and potassium periodate (0.1 m mol) was stirred magnetically at room temperature and the progress of the reaction was monitored by thin-layer chromatography (TLC). The reaction mixture was filtered and extracted with chloroform (3 x 30 mL). The combined $CHCl_3$ extracts were dried with Na_2SO_4 and concentrated under reduced pressure. In all the cases, the product obtained after the usual work up gave satisfactory spectral data.

Spectral analysis

Entry (1b): IR (KBr): 696, 772, 1211, 1346, 1580, 1660, 1675, 3059 cm^{-1}; ^1H NMR (300 MHz, $CDCl_2$): δ = 7.56 (m, 5H), 7.33 (m, 5 H); 8.0 (d, 2H, J = 8 Hz); 8.2 (m, 2H, J = 8 Hz); Anal. Calcd for $C_{20}H_{14}N_2$: C, 85.09; H, 5.02, N, 9.91 Found: C, 85.09; H, 5.00, N, 9.92.

Entry (4b): IR (KBr): 682, 772, 1226, 1574, 1622, 1660, 3052 cm^{-1}; ^1H NMR (300 MHz, $CDCl_2$): δ = 7.42-7.85 (m, 10 H), 8.05 (d, 2H, J = 7.2 Hz); 8.33 (s, 1H, J = 7.2 Hz); Anal. Calcd for $C_{20}H_{13}N_3Br$: C, 66.32; H, 3.65, N, 7.99 Found: C, 66.35; H, 3. 62, N, 7.99.

RESULTS AND DISCUSSION

We used a wide variety of compounds to which optimal reaction conditions were applied to prepare a wide range of quinoxalines. The results are summarized in Table 1. In order to expand the scope of this new protocol to synthesize quinoxaline from o-phenylenediamine and diketones, we investigated the reaction in the presence of potassium periodate (Table 1, entries 1-11). Results in Table 1, show that electron-donating groups at the phenyl ring of 1, 2-diamine favored the product with quantitative yields (Table 1, entries 2). In contrast, electron-withdrowing groups such as nitro, chloro and bromo groups afforded slightly lower yields (Table 1, entries 3-6, 8). Ethylene-1, 2-diamine, which was also reacted under similar conditions gave considerable yields (Table 1, entries 9, 10). Different 1,

2-diketones gave excellent yields of quinoxaline derivatives, while 1,2-dialkylketones afforded the reaction (Table 1, entries 11).

Table 1: Synthesis of quinoxaline in presence of KIO_4 at room temperature

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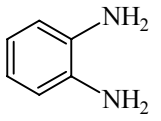
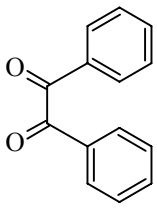
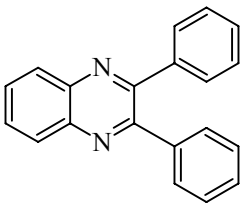
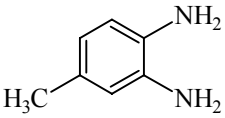
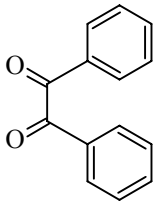
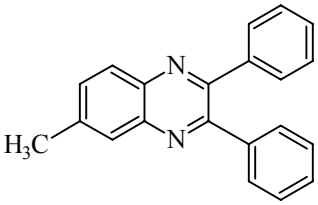
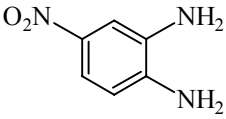
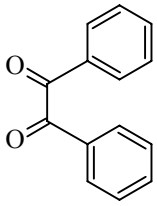
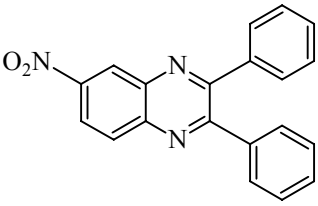
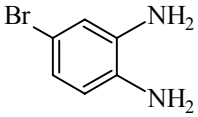
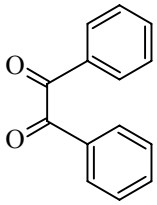
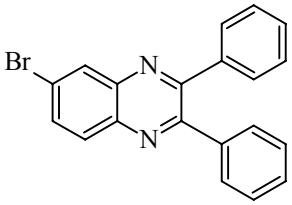
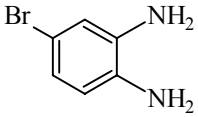
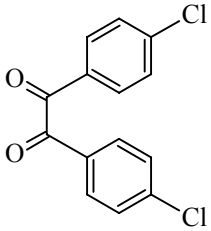
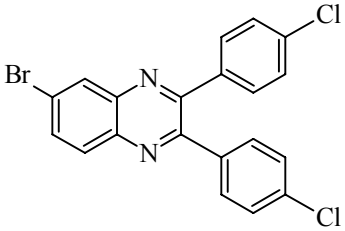
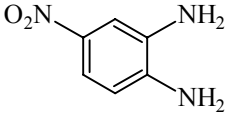
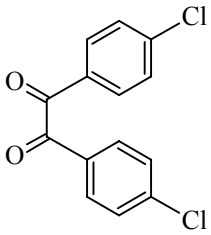
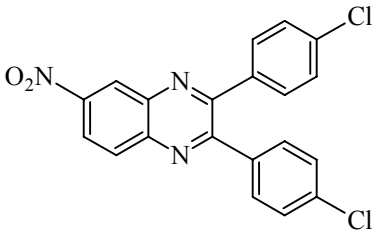
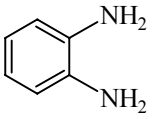
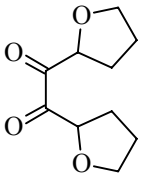
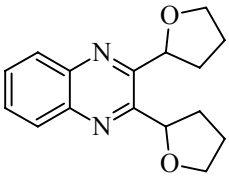
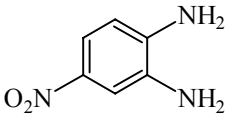
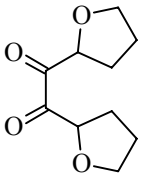
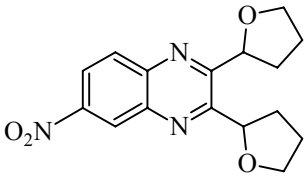
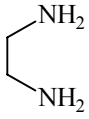
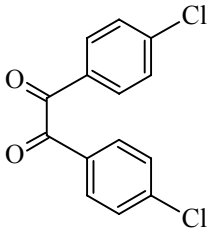
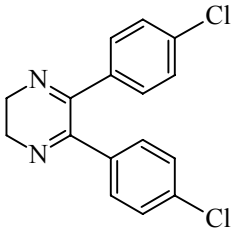
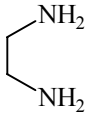
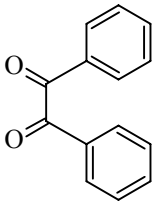
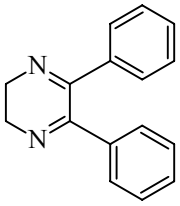
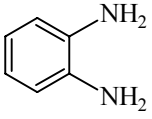
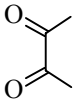
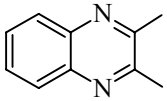
1				25	95
2				25	94
3				25	85
4				25	86
5				25	90

Cont…

Entry	1, 2-Diamine[a]	1, 2-Diketone	Product[b]	Time (min)	Yield[c] (%)
6				25	80
7				25	91
8				30	88
9				50	85
10				60	83
11				60	62

[a]The substrate was treated with 1,2-diketones (2 mmol) by using 0.1 mmol of KIO_4 under neat conditions at room temperature.

[b]All products were identified by their IR and ^1H NMR spectra

[c]Isolated yields.

In conclusion, this work describes a method in which KIO_4 is found as a highly efficient catalyst for the synthesis of quinoxaline derivatives. The advantages include low cost, ease of catalyst handling, mild reaction conditions and reactions carried out at room temperature with excellent yields.

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