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SHORT COMMUNICATIONS

Efficient One-Pot Synthesis of Quinoxalines in the Presence of Zinc Iodide as Catalyst*

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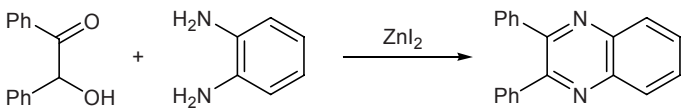
Quinoxaline and its derivatives constitute an important class of benzo-fused heterocycles with a broad spectrum of biological activity, which have made them privileged structural fragments of pharmacologically active compounds [1–4]. Quinoxaline derivatives are generally synthesized by condensation of arene-1,2-diamines with 1,2-dicarbonyl compounds in organic solvents under reflux (2–12 h); their yields range from 34 to 85% [5]. Some progress in the synthesis of quinoxaline derivatives was achieved with the use of bismuth-catalyzed oxidative coupling [6], tandem oxidation in the presence of $Pd(OAc)_2$ or $RuCl_2$–$(PPh_3)_3$–TEMPO [7] and MnO_2 [8], heteroannulation of nitroketene N,S-arylaminoacetals with $POCl_3$ [9], solid-phase synthesis over Synphase TM Lanterns [10], cyclization of arylimino oximes in boiling acetic anhydride [11], condensation of *o*-phenylenediamines with 1,2-dicarbonyl compounds in MeOH/AcOH under microwave irradiation [12], and molecular iodine-catalyzed cyclocondensation [13]. We have reported a procedure with the use of mercury iodide and lead oxide [14], and Heravi et al. recently described synthesis of quinoxalines under catalysis by $CuSO_4 \cdot 5H_2O$ and Zn[L-proline] [15].

Many of the above methods suffer from one or more limitations, such as harsh conditions, low yields, long reaction time, and laborious isolation procedures. Therefore, development of a mild, efficient, and versatile procedure for the synthesis of quinoxaline derivatives still remains strongly desirable.

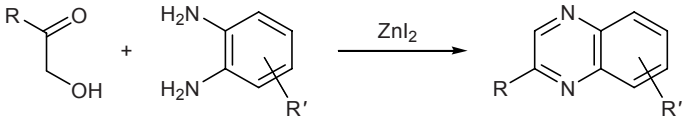
In continuation of our studies on the synthesis of various heterocyclic compounds [16], in the present communication we describe a simple, mild, and efficient procedure for the preparation of quinoxalines with the use of zinc iodide as catalyst. In the first step of our study, we examined the reaction of benzoin with *o*-phenylenediamine (Scheme 1) in the presence of ZnI_2 with a view to determine optimal conditions, such as solvent and amount of ZnI_2. Given below are solvent, reaction time (min), and yield (%) of 2,3-diphenylquinoxaline in the presence of 10 mol % of ZnI_2: acetonitrile, 50, 90; THF, 70, 75; ethanol, 30, 95; acetonitrile–water (1 : 1), 60, 88; ethanol–water (1 : 1), 30, 95. Thus the optimal conditions include aqueous ethanol (1 : 1) as solvent and 10 mol % of the catalyst (ZnI_2). Under these conditions we synthesized a series of substituted quinoxalines (Scheme 2). The substituents R and R′, reaction time (min), yield (% of the isolated product), and melting points (published data [7, 14] are given in parentheses) are listed below: Ph, H, 30, 92, 80–82 (81–82); Me, H, 30, 86, orange oily

Scheme 1.



* The text was submitted by the authors in English.

Scheme 2.



substance; 2-Fu, H, 45, 95, 102–104 (101–103); cyclohexyl, H, 45, 90, 44–46 (45–46); Ph, 4,5-Me_2, 45, 94, 121 (120–123); cyclohexyl, 4,5-Me_2, 45, 93, 67 (66–68); C_5H_{11}, 2,3-Me_2, 45, 89, orange oily substance; 2,4-$Cl_2C_6H_3$, H, 30, 84, 125–127 (124–126); 2,4-Cl_2-C_6H_3, 4,5-Me_2, 40, 90, 141–142 (140–142); 4-ClC_6H_4, H, 30, 85, 120–122 (118–119); 4-FC_6H_4, H, 30, 95, 126–129 (126–127).

Thus we have developed a simple, efficient, and ecologically safe procedure for the synthesis of quinoxalines from various α-hydroxy ketones and 1,2-diamines using inexpensive and readily accessible zinc(II) iodide as catalyst. In all the above syntheses, the solvent was aqueous ethanol which may be regarded as environmentally benign and conforming to the "green chemistry" principles. Mild reaction conditions, short reaction time, excellent yields, and easy workup make the proposed procedure a useful alternative to the existing methods.

Typical procedure for the synthesis of quinoxalines from *o*-phenylenediamines and α-hydroxy ketones. A mixture of 10 mmol of 2-hydroxy-1-phenylethanone, 10 mmol of benzene-1,2-diamine, and 2 mmol of zinc(II) iodide in aqueous ethanol was heated for 30–40 min at 80°C, the progress of the reaction being monitored by TLC. When the reaction was complete, the mixture was poured into ice water, and the precipitate was filtered off, washed with cold alcohol, and purified by column chromatography on silica gel (60–120 mesh) using petroleum ether–ethyl acetate (9 : 1) as eluent.

2,3-Diphenylquinoxaline. ^{1}H NMR spectrum, δ, ppm: 8.03 m (2H), 7.74 m (2H), 7.50–7.55 m (4H), 7.26–7.36 m (6H). Mass spectrum: *m*/*z* 281 $[M - H]^+$.

2-(2,4-Dichlorophenyl)quinoxaline. ^{1}H NMR spectrum, δ, ppm: 8.68 s (1H, 3-H), 7.90 m (2H, 5-H, 8-H), 7.60 m (2H, 6-H, 7-H), 7.34 d (1H, 3′-H), 7.32 d (1H, 2′-H), 7.20 s (1H, 5′-H). Mass spectrum: *m*/*z* 273 $[M - H]^+$.

The melting points are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 200 spectrometer (200 MHz for ^{1}H) using DMSO-d_6 as solvent and tetramethylsilane as internal reference. The mass spectra (electrospray ionization) were obtained on a Waters Micromass Quattro II instrument. All reagents used were of analytical grade and were not subjected to additional purification.

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