



Novel Synthesis of Some Quinoxaline Derivatives

Rajeev Kumar Karna

Assistant Professor, Department of Chemistry, R.B. Jalan Bela College, Darbhanga, Bihar, India

Abstract

Quinoxalines are nitrogenous compounds that are widely used in various industries like paint, pharmaceutical and medicine. By using of this synthetic method of these compounds based on condensation of Aryl-1,2-di amine with 1,2-di carbonyl in the Acidic condition, some new compounds was obtained from Quinoxaline family that for the first time some new catalysts was used for increasing of efficiency and reducing of process time. Used catalyst was $\text{CrCl}_2 \cdot 6\text{H}_2\text{O}$ compound that preparation of these catalysts is economically, cost-effective and saves time. All mechanisms were done in ethanol solvent at room temperature. However, all results suggest a mild and heterogeneous nature of these mechanisms, shorter time of reaction and higher yield.

Keywords: IR; NMR; Quinoxalines

Introduction

Heterocycles compounds are used in many various industries [1-3]. However most of heterocyclic compounds aren't extracted from nature source, but are synthesized. Almost all alkaloids that are used as drugs are formed from hetero aromatic molecules. Because these compounds cause to cancer, these chemicals must be removed from output materials of smokestack in factories [4-5]. Some of these compounds are used as pigment and some additive in food industry and sometimes are applicable in pharmaceutical industry [4]. Quinoxalines are a family of hetero aromatic ring.

Warfarin is derived from Coumarin that is anticoagulation. Prazosin compound is belonging to the anti-hypertensive that is Quinazoline family. Quinine structure which is known as an anti malaria drug [7-9]. However, Quinoxalines and derivatives which are called Benzopyrazine is the most important compound of nitrogen heteroaromatic. The combination of component family Benzo-Heterocycles to the floor and classified as very important intermediate compounds is in organic and inorganic chemistry [10]. Although these compounds are rarely found in nature, but many Quinoxaline derivatives are known in the pharmaceutical industry and wide area of biological activities including anti-virus, anti-diabetic, anti-HIV, antifungal, anti parasitic, anti-cancer, anti-bacterial and anti-depression has been reported in the literature for this compound [11-13].

Experimental

General Method

All materials in these experiments were obtained from Merck, Germany. All melting points and efficiencies have been reported related to the pure products. Synthetic compounds were compared with spectroscopic data and physical properties of real samples. Progress of reactions was with thin layer chromatography (TLC) at first till completion of reaction. Used TLC plates are G/UV254 nm-TLC-Grade silica gel. Infrared spectrums of the precursor and final products were recorded by IR-470 infrared

spectrophotometer equipped with Shimatzu companies' monitor. $^1\text{H-NMR}$ and $^{13}\text{CNMR}$ spectra of final products were recorded by NMR 400 MHz broker, Avance 2 model. For purifying, especially in the vacuum distillation, solvent removal and drying of products were used from a vacuum pump model OV-42N-250. For determination of melting point, the sample is powdered in a porcelain mortar, and then the melting point was measured by the UK company British Barnstead Electro thermal 9100 BZ.

Synthesis

Required amount of Lewis acid and 5 mL ethanol were added to mixture of derivatives of ortho-phenylen diamine (1.10 mol), aromatic 1,2-di ketone (1.00 mmol) as solvent to 25 mL flask equipped to magnetic stirrer in room temperature. All organics were dissolved in a solvent in the beginning of reaction. Progress of reaction was considered by using thin layer chromatography (TLC) in mixture of n-hexane and ethyl acetate. At the end, the mixture of reaction was heated till it was dissolved in hot ethanol and catalysts that wasn't soluble in ethanol, was separated by simple filtration. After cooling of solution, single crude product was obtained.

Results and Discussion

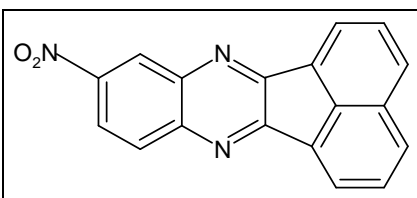
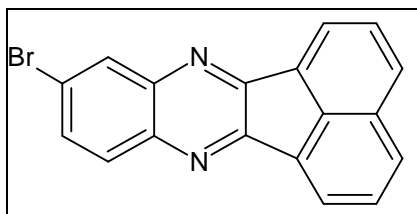
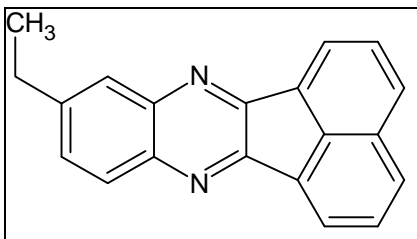
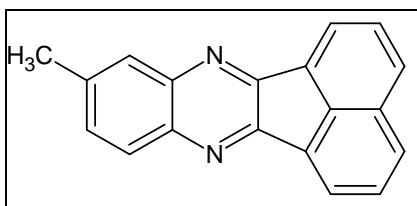
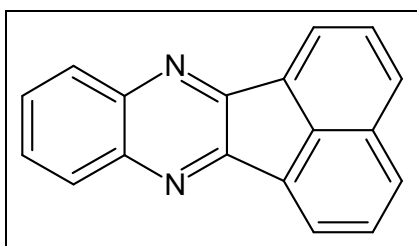
In all cases, ethanol was used as a solvent. In according to catalyst type, because of empty orbital was acted like a Lewis acid and activated carbonyl part of aromatic 1,2-di ketones. At this time, amine group because of non-bonding electron pair on nitrogen atom was done nucleophilic attack to carbon atom joint to oxygen.

This mechanism is repeated until the removal of two water molecules, Quinoxaline was obtained. Obviously, when there is electron withdrawing groups such as nitro and chlorine on carbon number 4 of aryl 1,2-diamine ring, because of being positive of reaction center namely nitrogen caused to reduction of reaction progress rate. On the other hand, electron donating groups like methyl on carbon atom number 4 of aryl 1,2-diamines because of hyper conjugation effect of methyl group accelerated reaction. But because the

methyl group relative to amine is in para position and relative to the other amines is in the meta position, therefore these two effects offset each other and significant difference in reaction rate compared with nonsubstituted aryl 1,2-diamine was not observed.

According to obtained results in the above tables, less reactivity of benzyl compound in comparison with other compounds is considerable that is because of trans formation of this molecule that was required initial energy for reaching to cis formation until nucleophiles attack was provided. Formation of two other di carbonyl was cis and required any initial energy and finally enough energy for reaching to less transition state and reaction rate was increased. This reaction was done in two steps, respectively nucleophilic attack and removal of water that using of large amounts of Lewis acid caused to difficulty passing of the first step of reaction. It's because of reaction between nucleophile (diamine) and Lewis acid and caused to limitation of nucleophilic attack.

On the basis of above facts following structures of the compounds are confirmed.



Conclusion

General and basically result was described below:

1. The reaction in ethanol solvent was done well that is a clean reaction, non-toxic and appropriate with environment. This solvent is inexpensive and doing of this reaction is economical. It can be used for industry, too.
2. Most reactions were done at room temperature and did not require to temperature conditions. So, the reaction was progressed at mild conditions that were not required to special device for applying of these conditions.
3. Reaction time was relatively short and reaction efficiency was relatively high.
4. The used catalysts against to some reported catalysts in some articles was not required to prior preparation for doing of reaction and are easily accessible with affordable price.
5. $\text{CrCl}_2 \cdot 6\text{H}_2\text{O}$ is a very good catalyst for the synthesis of Quinoxaline derivatives. One important feature of this catalyst is insolubility in ethanol that was made heterogeneous system for the reaction and other feature is using few values of catalysts.
6. Separation of the products was done by a simple filtering.

References

1. Husain A. Al-Tamany and MF Abnder Fattah, Orient J. Chem., 2010;26(2):421-427.
2. Mishra RM. Orient J. Chem. 2011;27(1):227-232.
3. Montazari N, Pourshamsian K, Fauladi M, Bayazi M. Orient J. Chem. 2012;28(1):399-404.
4. Badger GM. The Chemistry of Heterocyclic Compounds, Academic press, New York, 1961.
5. Joule A, Smith GF. Heterocyclic Chemistry, Methuen, Van Nostrand-Reinhold, New York, 1972.
6. Clough JM, Godfrey CRA. Chem. in Britain, 1995;31:466.
7. Krsti L, Sukdolak S, Soluji S. J. Serb. Chem. Soc, 2002;67:325.
8. Bolognesi ML, Budriesi R, Chiarini A, Poggesi E, Leonardi A, Melchiorr C. J. Med. Chem, 1998;41:4844.
9. Weinreb SM. Nature, 2001;411:429.
10. Porter AE. In Comprehensive Heterocyclic Chemistry, 1984;3:157.
11. Kim YB, Kim YH, Park JY. Bioorg. Med. Chem. Lett, 2004;14:541.
12. Sakata G, Makino K, Kurasawa Y. Heterocycles, 1998;27:2481.
13. Ali MM, Ismail MMF, El-Gabby MSA, Zahran MA, Ammar TA, Molecules, 2000;5:864.