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Condensation Reactions of Methyl Derivatives of Quinoxaline-1,4-Dioxide with 4,4'-Biphenyl Carboxaldehyde

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Autho's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

Aims: To synthesis new compounds via condensation reactions between 2-methyl quinoxaline-1,4-dioxide derivatives 4,4'-biphenyl carboxaldehyde.
Methodology: The Quinoxalines derivatives were prepared from 2-nitroaniline derivatives using the Beirut reaction, and the condensation reaction was carried out at room temperature in absolute methanol. Based on IR and NMR spectroscopic techniques, the structures of all products have been suggested. For their synthesis, suitable mechanisms have been suggested.
Results: In this work, condensation reactions involving 2-methyl quinoxaline-1,4-dioxide derivatives and 4,4'-biphenyl carboxaldehyde were performed.
Conclusion: The final compounds, we suppose, have considerable applications in fluorescent and chromophoric activities. In all known solvents, the products were just slightly soluble. Products have been subjected to sulfonation reactions, although with limited success.

Keywords: 2-methylquinoxaline-1,4-dioxid; 4,4'-biphenyl carboxaldehyde; 2-nitroaniline derivatives; Beirut reaction; condensation reaction.

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1. INTRODUCTION

The last few decades witness many publications and research about Quinoxaline derivatives and their biological activities [1], industrial processes, dyes, fluorescent, and many other uses.

Many of Quinoxalines were published in "Chemistry of Heterocyclic Compounds Series" several times since 1953 [2].

And several Quinoxaline and Quinoxaline-1,4-dioxide Derivatives have biological activities [3].

A recent review study (2021) shows reviews from the previous two decades for 'Novel Synthetic Routes to Prepare Biologically Active Quinoxalines and Their Derivatives.' [4], this study refers to Quinoxaline derivatives, which have a wide range of therapeutic applications and have become an important component in drugs used to treat cancerous cells, AIDS, plant viruses, and schizophrenia, indicating that they have a bright future in medicinal chemistry. Because of the current SARS-COVID 19 pandemic, another study (April 2019) looked at the effects of quinoxaline-1,4-dioxide, 2-methylquinoxaline-1,4-dioxide, 2-amino-3-cyanoquinoxaline-1,4-dioxide, 3-methyl-2-quinoxalinecarboxamide-1,4-dioxide, and 2-hydroxyphenazine-N,N-dioxide (2HF) in the migration, viability, and proliferation of nonmalignant and malignant cell lines [5].

The derivatives of Quinoxaline have important antimicrobial activity (against Bacterial and yeast strains) [6], also show antitumoral activity [7].

The Quinoxaline and Quinoxaline-1,4-dioxide derivatives show Antibacterial activity [8], (including such 2-Chloro-3-methylquinoxaline [9] and 2-hydroxy methyl-3-methyl quinoxaline-1,4-dioxide [10]) along with many others.

Furthermore, antifungal activity (such as 3-phenyl-7-triflouro methyl quinoxaline-1-oxide [11]) and others, antiviral activity (pyrroloquinoxaline derivatives [12]), antineoplastic (2-ciano quinoxaline-1,4-dioxide derivatives [13]), and many biological activities are present.

Some Quinoxaline 1,4-Di-N-Oxide esters have anti-Mycobacterium tuberculosis activity [14].

Recent research (2021), synthesis new Quinoxaline-1,4-Dioxides Derived from Beirut Reaction of Benzofuroxane with Active Methylene Nitriles [15].

A new fluorescent chemosensor based on quinoxaline has been successfully synthesized using a simple and environmentally friendly catalytic reaction of ortho-phenylenediamine (O-PDA) and acenaphthylene-1,2-dione [16].

And 6-nitroquinoxaline was used to produce some fluorescent quinoxaline derivatives [17].

In our study, we used the Beirut reaction [18] to synthesize quinoxaline-1,4 dioxide derivatives from benzofurazan oxide derivatives in alcohol [19], followed by condensation reaction with aromatic dialdehyde such as 4,4'-biphenyl carboxaldehyde (in a similar study the condensation of 2-methy quinoxaline-1,4-dioxide with benzaldehyde was performed [20]).

We made the 2-methyl quinoxaline-1,4-dioxide derivatives (were not commercially available) and then used aromatic dialdehyde in an alcoholic KOH condensation process (the result compounds may have fluorescent and chromophoric activities).

2. MATERIALS AND METHODS

2.1 Chemicals and Reagents

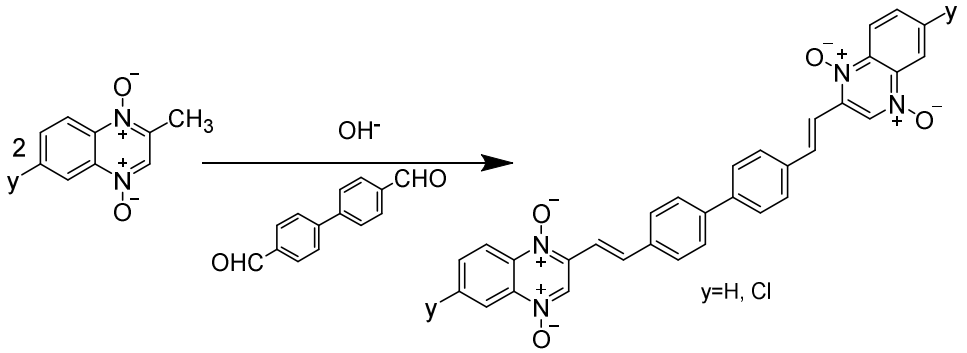
All chemicals used were laboratory reagent grade and were not purified further (Merck, Sigma-Aldrich), For thin-layer chromatography, a pre-coated silica gel plate (Merk Co. Inc, Kiesel gel 60 F256) was used.

2.2 Instruments

FT-IR spectrometer (Jasco, Japan), Rotary vaporer (4.91Model, Normschiff, Germany), Melting point meter (Bruker, 400MHz, CDCl3), Nuclear Magnetic Resonance (Bruker, 400MHz, CDCl3) (Electrothermal, with mercury thermometer).

3. RESULTS AND DISCUSSION

The purpose of this research was to perform a condensation reaction between 2-methyl quinoxaline-1,4-dioxide and (4,4'-biphenyl carboxaldehyde), Scheme 1.



Scheme 1.

A. Preparing Benzofurazan Oxide and 5-chloro benzofurazan oxide:

The oxidation of ortho-nitroaniline with sodium hypochlorite (commercial) in cooled ethanolic KOH produced Bezofurazan oxide (95 percent) [21] Scheme 2.

Melting Point (benzofurazan oxide) was 59-60 ○C.

Melting point (5-chloro benzofurazan oxide) was 43-45 ○C.

B. Preparation of 2-methyl quinoxaline-1,4-dioxide and 6-chloro-2-methyl quinoxaline-1,4-doixide via Beirut Reaction:

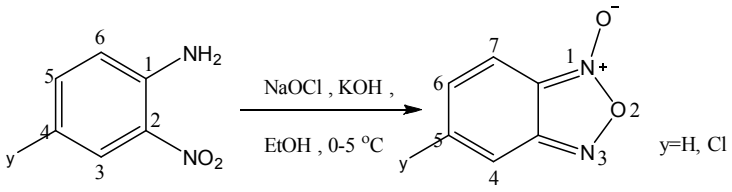
The pyrrolidine was added just after benzofurazan oxide and 5-chloro benzofurazan oxide were refluxed with acetone (acetonitrile solvent). Scheme 3

- 2-methyl quinoxaline-1,4-dioxide: Yield:59%, Meting point: 170-172 ○C and Rf=0.77 with Methanol: Chloroform (3:97).
- 6-chloro-2-methyl quinoxaline-1,4-doixide: Yield:62%, Meting point: 174-176 ○C and Rf=0.8 with Methanol: Chloroform (3:97).

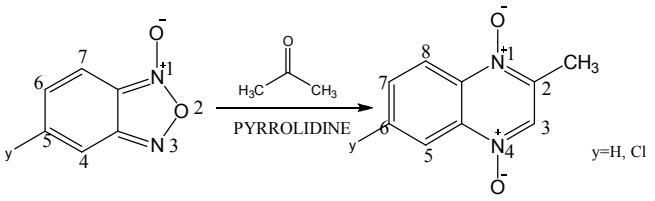
C. Condensation of 2-methyl quinoxaline-1,4-dioxide with 4,4'-biphenyl carboxaldehyde Scheme 4:

The reaction was carried out with 95% methanolic KOH (absolute methanol as a solvent) and allowed to stand for 24 hours (at room temperature). the result was dark yellowish, any Purification process was difficult because insoluble in common solvents (water, methanol, ethanol, benzene, ethyl acetate, petroleum ether, DMF, 1-propanol, 2-propanol, acetone, and others), but only sparingly soluble in chloroform.

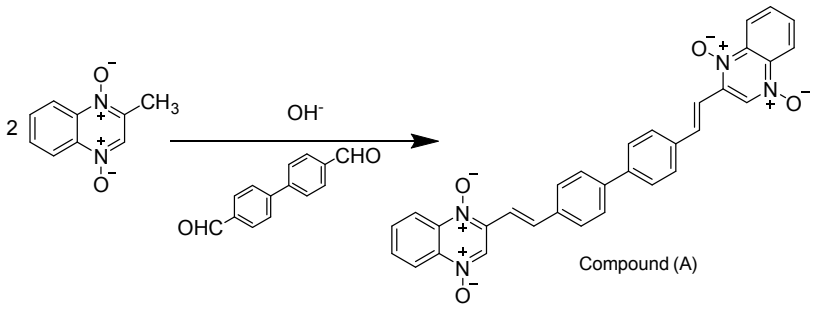
With yield: 57.8%, melting point>250 ○C(decompose).



Scheme 2.



Scheme 3.



Scheme 4.

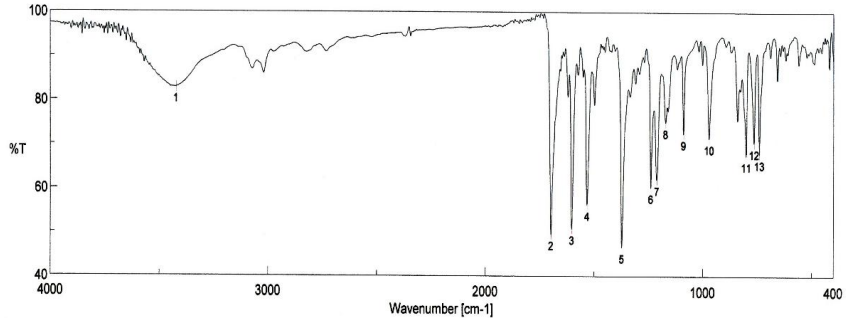


Fig. 1. FT-IR(KBr): the band around 3050cm-1 (sp2 carbons), the band around 1698cm-1(conjugated C=C), the strong band 1370cm-1 for N-O bond

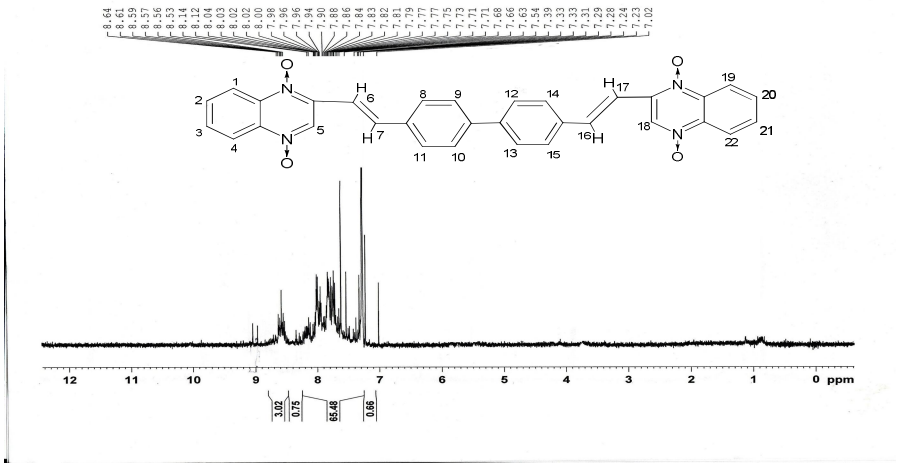
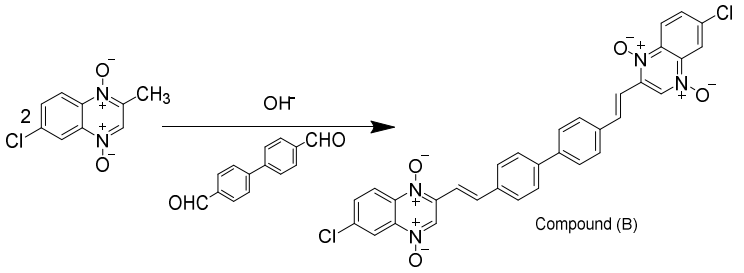


Fig. 2. 1H-NMR (CDCl3): δ=7.64ppm (s, 8H), 7.96ppm (d, 2H), 8.11ppm (d, 2H), 8.65(s, 2H)

D. Condensation of 6-Chloro-2-methyl quinoxaline-1,4-dioxide with 4,4'-biphenyl carboxaldehyde Scheme 5:

The reaction was carried out with 95% methanolic KOH (absolute methanol as a solvent) and allowed to stand for 24 hours (at room temperature). The result had a dark color, was insoluble in most common solvents (water, methanol, ethanol, benzene, ethyl acetate, petroleum ether, DMF, 1-propanol, 2-propanol, acetone, and others), but was only sparingly soluble in chloroform, making purification a difficult task.

with yield: 30.55%, melting point>230-233 ○C(decompose).



Scheme 5.

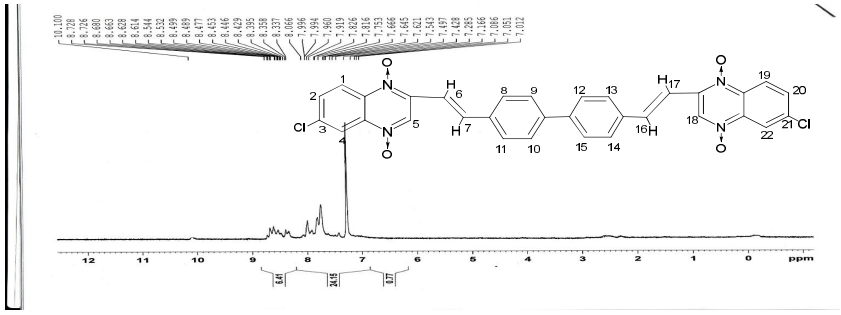
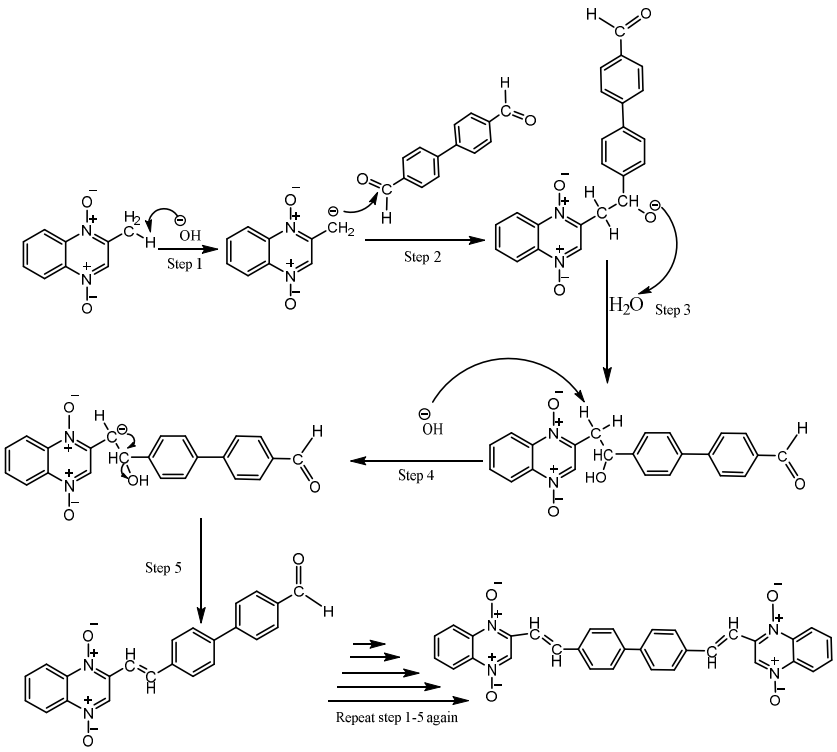


Fig. 3. 1H-NMR (CDCl3): δ=7.75ppm (d, =C-H), 7.9ppm (d, =C-H), 8.33ppm (d, Ar-H), 8.6ppm (m, Aromatic-protons)

The suggested mechanism of condensation reaction was:



Scheme 6.

4. CONCLUSION

We prepared 2-methyl quinoxline-1,4-dioxide and 6-chloro-2-methyl quinoxline-1,4-dioxide (these compounds were not commercially available) and used them to perform condensation reactions with 4,4'-biphenyl carboxaldehyde to obtain two products (A, B), which were identified by 1H-NMR and FT-IR, and a mechanism was suggested for them.

Because of their hard insolubility in common solvents but sparingly soluble in chloroform, we had difficulty purifying the final products.

5. RECOMMENDATIONS

Due to the resulting compounds are important as fluorescent and chromophores, we advise doing the condensation processes with quinoxaline derivatives and aromatic dialdehydes, which have more soluble functional groups.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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