DFT and Experimental Study of Synthesis a Quinoxaline Derivative Using Photocatalysis

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Abstract

The photocatalysis synthesis of 2-methylquinoxaline 1,4-dioxide (2MQOX) was investigated by the cycloaddition reaction of Benzofurazan oxide with acetone at 254 nm with yield 65% and the quantum yield was calculated (0.03).The structure of the resultant was elucidated by spectroscopic analysis (IR, UV, and ^{1}H,^{13}C NMR). A mechanism for the reaction was proposed using the density functional theory (DFT / B3LYP (6-311 + G (2d)). The molar ratio of reaction was 1: 1.

Keywords: quinoxaline**,** density functional theory**,** mechanism, spectroscopic analysis**.**

1. Introduction:

The study of quinoxaline and its quinoxaline 1,4-di-N-oxide derivatives has become a subject of interest in recent years due to their wide variety of biological activities as well as therapeutic applications. Since they are rare in nature, synthetic quinoxalines are included in various antibiotics such as echinomycin, levomycin and actinomycin[1], well-known to inhibit the growth of Gram-positive bacteria and are also active against transplant tumors [2]. Echinomycin, for example have quinoxalinyl moiety in their structure and also some known drugs, like Brimonidins, alleviates glaucoma symptoms[3]

They are important in industry due to their ability to inhibit the metal corrosion[4]. And also in the electroluminescent materials[5].

Numerous methods are available for the synthesis of quinoxaline derivatives which involve condensation of 1,2-diamines with α-diketones[6], 1,4-addition of 1,2-diamines to diazenylbutenes[7], cyclization–oxidation of phenacyl bromides and oxidative coupling of epoxides with ene-1,2-diamines[8].

Recent research groups have presented reports concerning the synthesis of different quinoxaline derivatives involving several green methodologies, including recyclable catalysts, microwave-assisted synthesis and reactions in aqueous medium[9].

In the present work 2-methylquinoxaline 1,4-oxide were prepared by the the cycloaddition reaction of Benzofurazan oxide with acetone using photocatalysis and the mechanism for the reaction was proposed using the density functional theory (DFT / B3LYP (6-311 + G (2d))[10, 11, [12].

2. Apparatus Section:

Quantum method (DFT / B3LYP (6-311 + G (2d))., GaussView5 and Gaussian09 programs.
spectrum NMR proton and carbon device 400 MHz model Bruker by Switzerland company, optical absorption spectrum infrared device model FT-IR-4100 from the Japanese company Jasco, UV/Vis spectroscopy (model: Optizen 2120 UV), rotar evaporator 4.91 model from the German company Normschiff, thin layer chromatographic of aluminum coated by Silica Gel 60F254 measuring 20 X 20 from the German company Merc, WD-9403E Hand Held UV Lamp from Beijing Liuyi Instrument Factory.

3. Chemicals Materials:

Benzofurazan oxide was prepared in the laboratory, pyrrolidine 99.0% (by SIGMA- ALDRICH),acitone 99.8% (by CHEM LAB), acetonitrile 99.9% (by panreac), ethanol 99.9% (by eurolab), methanol 99.99% (by ACROS ORGANICS).

4. Quantum-Chemical Study:

To judge the spontaneity of the reaction in the liquid state and the stability of the resulting compound, the energies of MO's, especially the energies of HOMO and LUMO of the reactants and resultant was analyzed as in the following two figures:

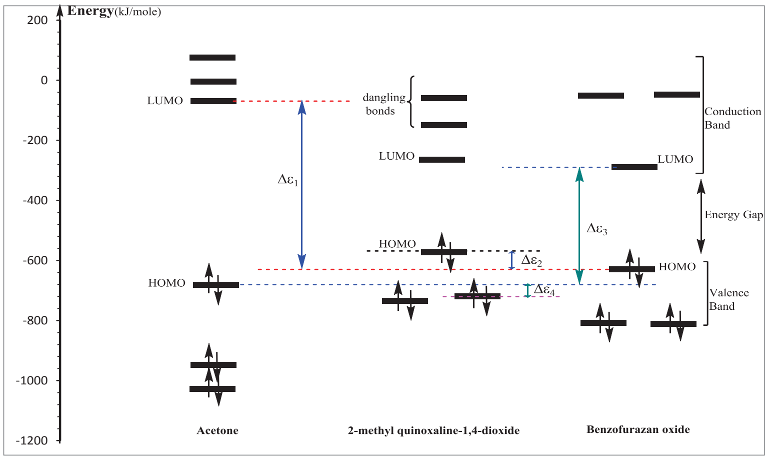


Figure 1: Molecular orbital energies for reactants and resultant when the reaction ratio (1: 1).

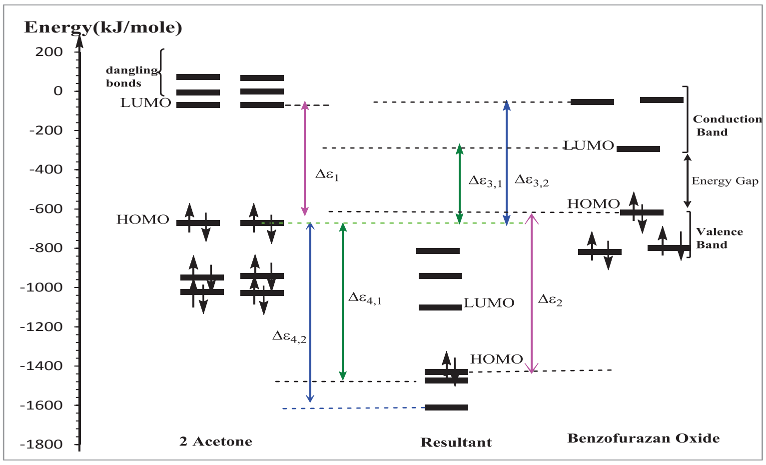


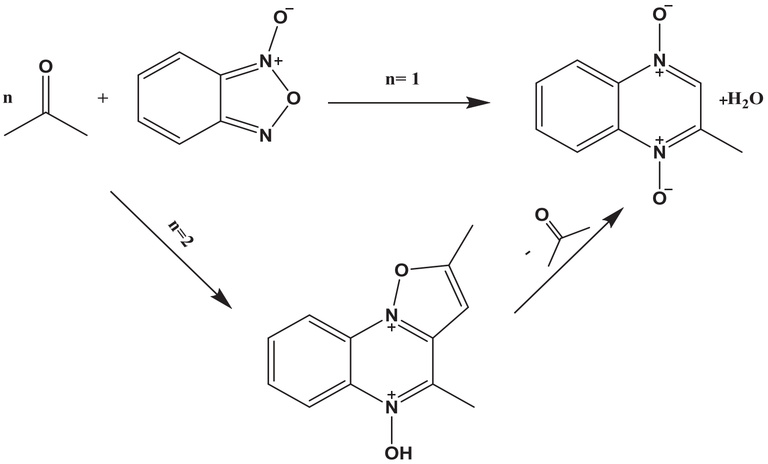
Figure 2: Molecular orbital energies for reactants and resultant when the reaction ratio (1: 2).

An analyze of MO's energy, especially the energies of the HOMO and LUMO orbitals in each of the reactants and resulting from the reaction in the ratio of 1: 1, shows that the energy difference between LUMO in acetone and HOMO in benzofurzan oxide is very large ($\Delta\varepsilon_1$ = 556.4463 kJ / mol) and therefore the interactions between them is very weak ($\Delta\varepsilon_2$= + 59.5461 kJ / mol). The energy difference between LUMO in benzofurazan oxide and HOMO in acetone is relatively large ($\Delta\varepsilon_3$ = 393.2196 kJ / mol) and therefore the interactions between them is relatively weak ($\Delta\varepsilon_4$ = -45.7097 kJ / mol).

We conclude from the above that the average energy difference between the HOMO and LUMO orbitals in reactants (474.8329 kJ / mol) is large and the interactions is weak (+13.8363 kJ / mol). This indicates that 2-methylquinoxaline1,4-dioxide can be formed, but the reaction is very slow, so we need hard conditions (temperature , photocatalyze,…..etc) to make the LUMO in acetone lower.

In the case of the ratio (2: 1), if we had the same discussion, the average energy difference between HOMO and LUMO in the reactants (709.3811 kJ / mol) is very large and the interactions is very strong (-3355.901 kJ / mol) this indicate to the stability of the resulting compound, which is likely to be the intermediate compound through which the reaction occurs. This explains the use of photocatalyze to accelerate the reaction.

Extrapolating the previous results, we find that the formation interaction of 2- methyl quinoxaline 1,4-dioxide is probably passed through an activated complex:



Depending on the energy scheme shown in Fig. 1, the wavelength of light needed to accelerate the reaction (λ = 252 nm) was calculated as follows:

$$\Delta E = N_A.h.\nu = N_A.h\,\frac{c}{\lambda} \Longrightarrow \lambda = \frac{N_A.h.c}{\Delta E}$$

Where Δ E: the average energy difference between HOMO and LUMO for reactants, which corresponds to the photon energy per mole of matter (474.83 kJ.mol^{-1})
h: Planck's constant (6.626 × 10^{-37} kJ.s.photon^{-1})
c: the speed of light in the vacuum (3 × 10^{8} m.s^{-1})
N$_A$: Avocadro number (6.022 × 10^{23})
a scan of energy have done for reactants and resultant by the distances between molecules of reactants in the previous probably reactions, the curve of energy is shown in scheme (3)

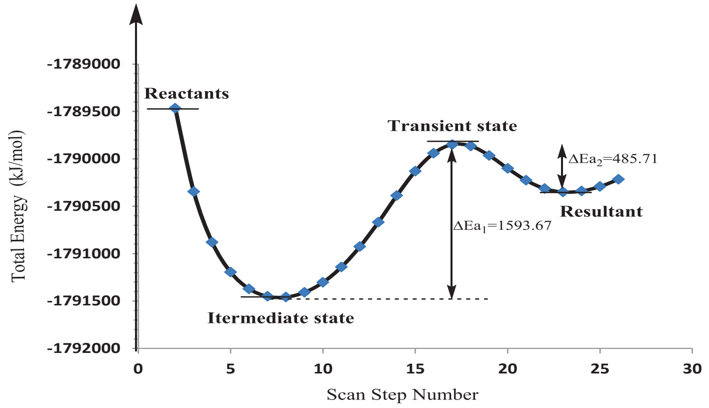
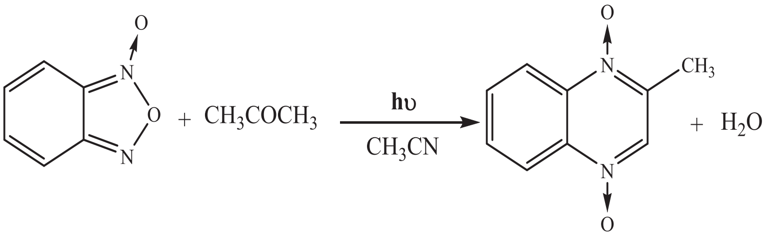


Figure (3): the formation stages of 2- methyl quinoxaline 1,4-dioxide molecule.

5. Experimental study:

- **Synthesis:**

2- methyl quinoxaline 1,4-dioxide is prepared using a monochromatic UV light that gives a light length of 254 nm. In a flat cell, 1.2ml acetone and 0.8 ml acetonitrile are applied and irradiated for five minutes. 0.068 g benzofurazan oxide and 0.08 ml pyrrolydine are added and continued for fifteen minutes, at room temperature (25^{0}C). the resulting precipitation is washed by ethanol in batches and left to dry in the air and re-crystallized using methanol. A precipitate is obtained with a yellow crystalline yield of 65% and a melting point of 183^{o}C.



- **Infrared Spectra:**

Spectrum of 2- methyl quinoxaline 1,4-dioxide is shown in figure (4). A weak absorption band at 3025 cm^{-1} is observed due to the vibration of the C-H bond in the aromatic ring, and another band at 2922cm^{-1} returns to the aliphatic C-H bond, strong absorption bands are noted at(1603 cm^{-1}, 1540 cm^{-1}, 1506 cm^{-1},1449 cm^{-1}) return to Ar (C=C, C=N) bonds, strong band at 1334cm^{-1} belonged to N-O bond.

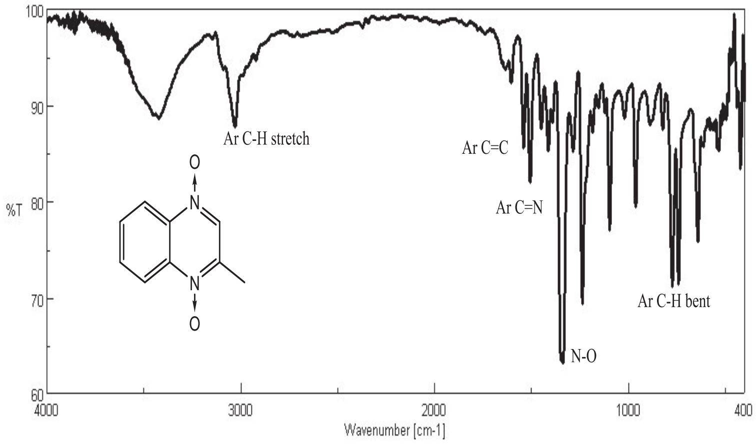


Figure (4):. IR absorption spectra of 2MQOX

- **^{13}C and ^{1}H NMR spectroscopic measurements:**

2-methyl quinoxaline 1,4-dioxide was further confirmed by ^{1}H-NMR spectroscopy, as shown in figure (5). the characteristic signal around (δ =2.59 ppm) belonged to protons in methyl group CH_3, and the signals around (δ = 8.56, 8.29, 7.82 ppm) belonged to aromatic protons see table (1).

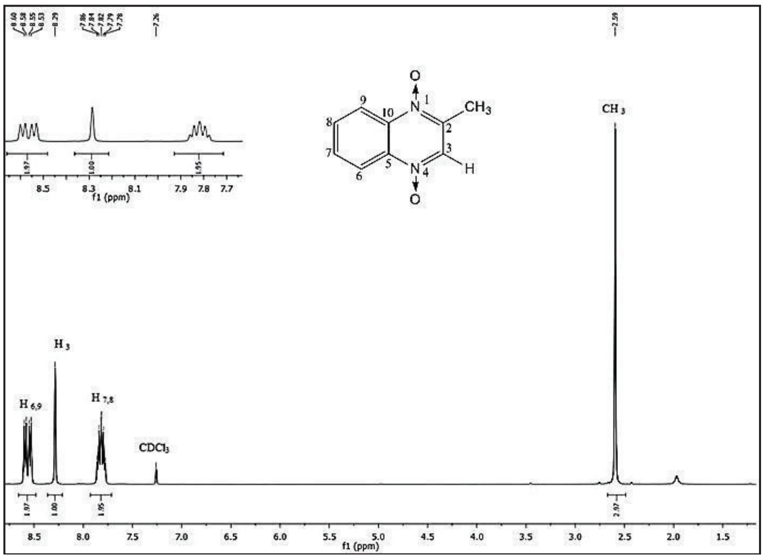


Figure (5): ^{1}HNMR spectrum of 2MQOX (400 MHz, CDCl3, δ_{TMS} = 0 ppm).

^{13}C-NMR spectroscopy exhibits signals at (δ =16.23 ppm), this signal assigned to carbon methyl group, and signals (δ = 141.65, 132.30, 137.62, 131.32, 120.71,138.84 ppm) belonged to carbon atoms in aromatic rings as shown in figure (6).

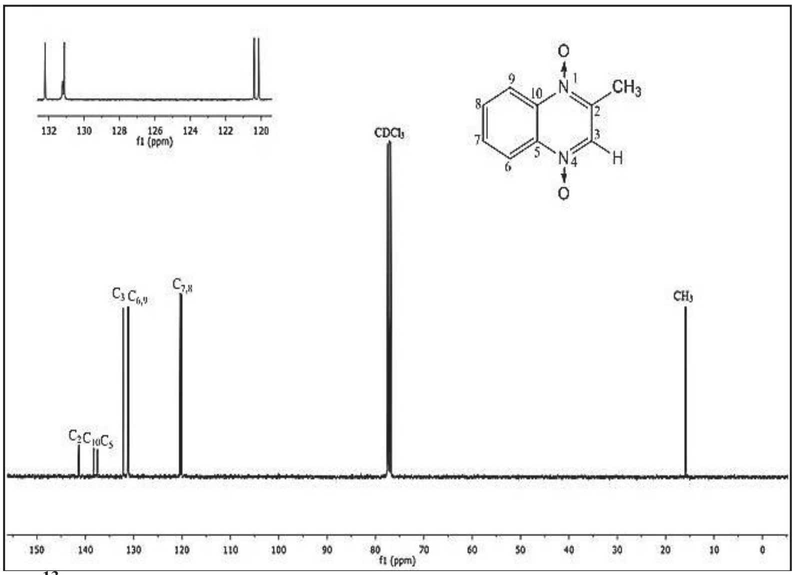
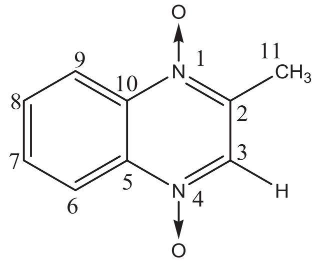


Figure (6): ^{13}CNMR spectrum of 2MQOX (100 MHz, CDCl3, δ_{TMS} = 0 ppm).

Table(3): ^{13}C and ^{1}HNMR spectroscopic measurements of 2MQOX:



.No	Hydrogen atom type	δ_C	δ_H
1	------		----------------
2	------	141.65	----------------
3	aromatic	132.30	8.29 (s,1H)
4	------		----------------
5	------	137.62	----------------
6	aromatic	131.32	8.56 (dd, 2H, J^2=19.6, J^3=8.3 Hz)
7	aromatic	120.71	7.82 (m, 2H)
8	aromatic	120.71	7.82 (m, 2H)
9	aromatic	131.32	8.56 (dd, 2H, J^2=19.6, J^3=8.3 Hz)
10	------	138.84	----------------
11	CH3	16.23	2.59 (s, 3H)

- **Electronic spectral data:**

The electronic spectra of the resulting compound in acetonitrile solution has three bands at (226nm), (262 nm) and (394 nm), assigned to ($\pi \rightarrow \pi^*$) and ($n \rightarrow \pi^*$) transition, due to nitrogen atom and oxygen atom in the compound.

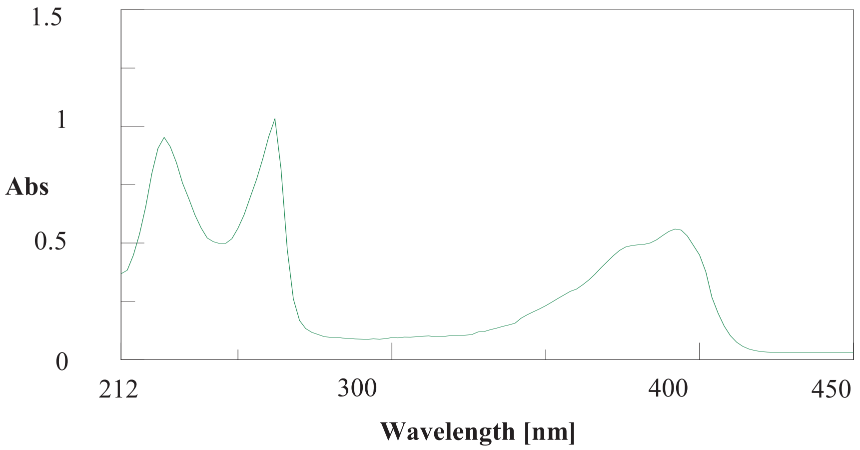


Figure (7): UV spectra of 2-methylquinoxaline 1,4-dioxide.

- **The quantum yield:**

The quantum yield and the intensity of absorbed light were calculated according to Table (2)

Table (2): The quantum yield, the intensity of absorbed light and the number of moles.

n(mol)	3.23×10^{-4}
I_a (photon.s^{-1})	76.73×10^{17}
ϕ	0.03

Where n is the number of moles and is calculated from the relationship:

$$n = \frac{m}{M}$$

I_a absorbed light intensity (number of photons absorbed per second) calculated from the relationship:

$$I_a = \frac{E}{E_{photon}} = \frac{E}{h\,.\,\bar{\upsilon}\,.\,c} = \frac{E\,.\,\lambda}{h\,.\,c}$$

Quantum yield is calculated according to the following relationship:

$$\phi = \frac{N_A\,.\,n}{I_a\,.\,t}$$

Where h: Planck constant (6.626×10^{-34} J.s.photon^{-1})
c: the speed of light in the vacuum (3×10^{8} m.s^{-1})
N_A: Avocadro number (6.022×10^{23} mol^{-1})
t: reaction time in second.
M: the mass of the resulting material and its unit (g.mol^{-1}), m: the quantity of the resulting material and its unit (g)
E: The photo source energy is equal (6 J.s^{-1}), E_{photon}: photon energy

6. Summary and conclusions:

The Synthesis of 2-methylquinoxaline 1,4-dioxide were carried out by the the cycloaddition reaction of Benzofurazan oxide with acetone using photocatalysis and the molar ratio of reaction was 1: 1. also the quantum yield was calculated. A mechanism for the reaction was proposed using the density functional theory (DFT / B3LYP (6-311 + G (2d)).

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