Каутар Ганум

факультет наук

Химический факультет Университета Аль-Баас

Хомс, Сирия

Аднан Кодлаа

факультет наук

Химический факультет Университета Аль-Баас

Хомс, Сирия

Джумаа Мерза

Фармацевтический факультет

Арабский частный научно-технический университет

Хама, Сирия

Kawthar Ghanoum

Faculty of Sciences

Department of Chemistry, Al-Baath University

Homs, Syria.

Adnan Kodlaa

Faculty of Science

Department of Chemistry, Al-Baath University

Homs, Syria

Joumaa Merza

Faculty of pharmacy at AUST University

Hama, Syria

QUANTUM AND EXPERIMENTAL STUDY OF SYNTHESIS A QUINOXALINE DERIVATIVE

Abstract: *In this paper, the synthesis of QBCl from 2-methylquinoxaline 1,4-dioxide (Q) and benzoyl chloride (ClB) using the density functional theory DFT/B3LYP(6-311++G(2d,p)) and time depended density functional theory TD-DFT/B3LYP(6-311++G(2d,p)) was reported by finding the optimal structure for the product. The lengths of the bonds and angles of the product were measured. The structure of the product was elucidated by spectroscopic analysis (IR, UV, and ^{1}H NMR)., The solubility of the product molecule was studied.*

Keywords: *quinoxaline, solubility, spectroscopic, analysis, density functional.*

Аннотация: *В этой статье синтез QBCl из 2-метилхиноксалина, 1,4-диоксида (Q) и бензоилхлорида (ClB) с использованием теории функционала плотности DFT / B3LYP (6-311 ++ G (2d, p)) и зависимости от времени Теория функционала плотности TD-DFT / B3LYP (6-311 ++ G (2d, p)) была представлена путем нахождения оптимальной структуры продукта. Были измерены длины связей и углы продукта. Строение продукта было выяснено с помощью спектроскопического анализа (ИК, УФ и 1H ЯМР). Растворимость молекулы продукта была изучена*

Ключевые слова: *хиноксалин, растворимость, спектроскопический, анализ, функционал плотности.*

1- Introduction:

Photochemistry is a very effective and powerful method for converting simple substances into complex products, opening new horizons especially for the pharmaceutical industry, where the reactants are activated directly without catalysts or initiators, which makes photochemistry more Attractive for modern green chemistry [**1**].

Some of the main applications of photochemistry are polymerization, photohalogenation, photosulfonization, photolysis, photooxidation and photoaddition reactions [**2**].

Because of the importance of the addition reactions and their applications, in this research we carried out the photoaddition reaction of 2-methylquinoxaline **[3]**.

Interest in quinoxaline derivatives has increased in recent times, especially quinoxaline dioxide derivatives due to its importance in pharmacological applications and medicinal properties as effective antibiotics against some germs [**4**]. Some of them are also known as an inhibitor of bacterial growth and some types of fungi and tuberculosis [**5**], Antitumoral activity [**6**]. The applications of quinoxaline derivatives did not stop on the medical side but were used in useful fields in the industry such as dyes and electro-luminescent materials [7, 8] quinoxaline derivatives were used as inhibitors Corrosion of metals in an acidic solution [**9**]. Because of the importance of quinoxaline derivatives, in the present work a quinoxaline derivative was synthesized and confirmed by using infrared, ultraviolet and nuclear magnetic resonance spectroscopy.

2- **Apparatus:**

Quantum method (DFT / B3LYP (6-311 ++ G (2d, p)), GaussView06 and Gaussian09 programs. spectrum NMR proton and carbon device 400 MHz model Bruker by Switzerland company, , T80+ UV/Vis spectroscopy (PG Instruments Ltd), 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. Silica gel dedicated to Merck chromatographic columns

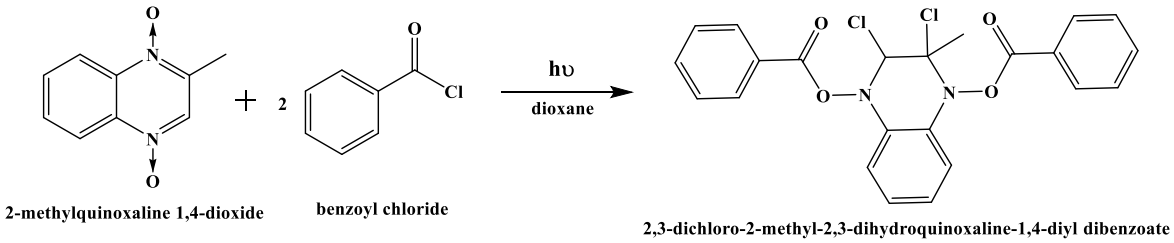
3- Chemicals Materials:

2- methyl quinoxaline 1,4-dioxide was prepared in the laboratory, benzoyl chloride 99% (by SIGMA- ALDRICH), dioxane 99.5% (by POCH), hexane 99.5% (by Euro lab), Ethyl acetate 99% (by Merck).)

4- **Synthesis:**

2- methyl quinoxaline 1,4-dioxide was reacted with benzoyl chloride using a monochromatic UV light that gives a light length of 254 nm for (15min) at room temperature, as (0.0176g) of 2- methyl quinoxaline 1,4-dioxide and (0.023 ml) of

benzoyl chloride were placed in a glass dish, (5ml) of dioxane was added as a solvent and then the mixture was irradiated for (15min) at room temperature (25^0C), and a purified product was formed using a chromatographic column containing a fixed phase of silica gel and a moving phase consisting of a mixture (ethyl acetate and hexane at a ratio of 80:20), after purification, a yellow precipitate was obtained with a yield (70%), as shown in the following equation:

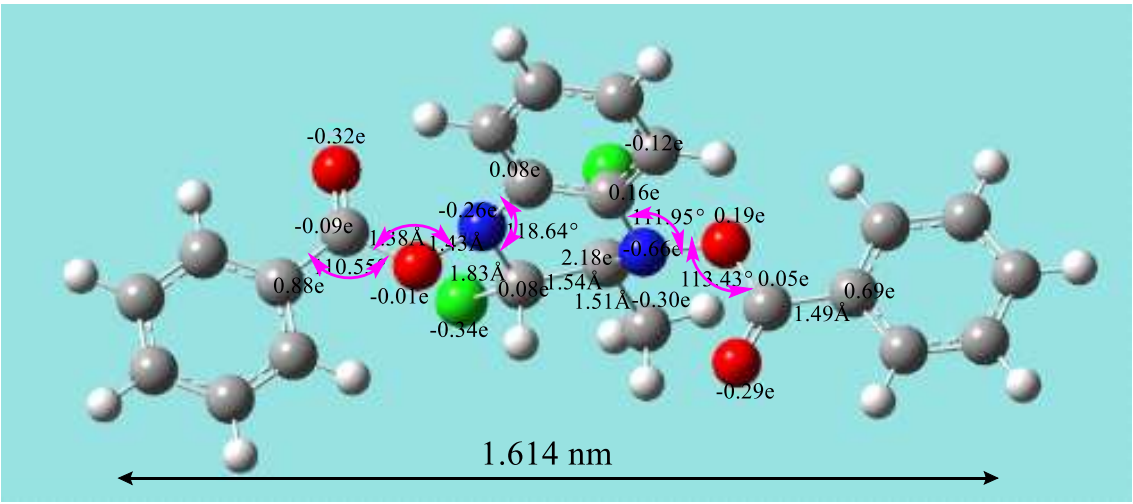


2-methylquinoxaline 1,4-dioxide benzoyl chloride 2,3-dichloro-2-methyl-2,3-dihydroquinoxaline-1,4-diyl dibenzoate

5- Results and discussion:

Structural and spectral characteristics of QBCl:

The structural and electronic properties of (QBCl) were studied in gas phase. Where the optimal structure for this compound was found in the ground state and the following figure includes this structure with the distribution of elemental charges Q and bond lengths in addition to some angles.



QBCl

Figure 1: The optimal structure of QBCl in ground state.

Also, quantum IR spectrum of (QBCl) was found as shown in figures (2), absorption band appears at (3100 cm^{-1}) belonged to the stretching vibration of the bond C-H in

the aromatic rings, and the band at (2925 cm^{-1}) returns to the aliphatic C-H bonds, a strong absorption band is observed at (1682 cm^{-1}) belonged to the carbonyl group C = O, the absorption bands at (1594, 1091, 1325, 760 cm^{-1}) return to: Ar (C = C), N-O, C-N, C-Cl, respectively.

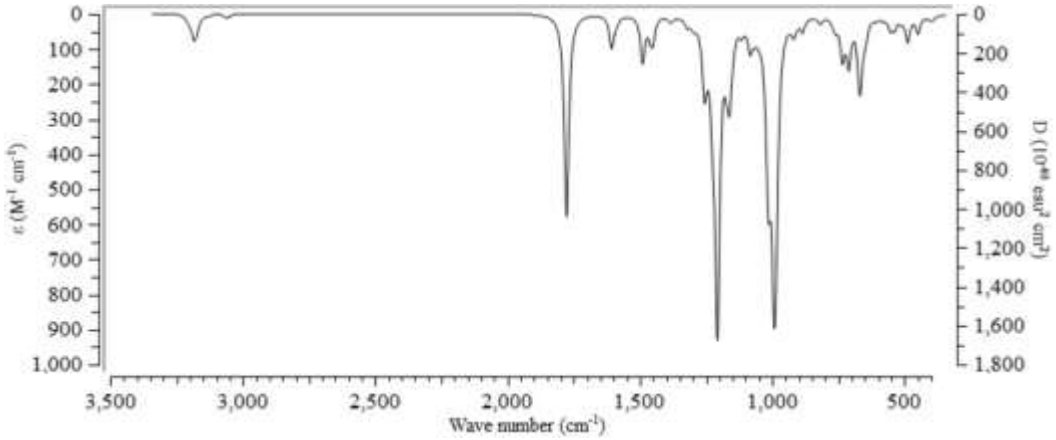


Figure 2: Quantum IR spectrum of QBCl.

And the absorption spectrum of visible and ultraviolet (UV-Vis) radiation of the product in methanol was studied, there are two bands at (240 nm) and (270 nm) assigned to ($\pi \rightarrow \pi^*$) transition in the aromatic rings and the band at (320 nm) assigned to ($n \rightarrow \pi^*$) transition due to carbonyl group C = O as shown in Figure 4.

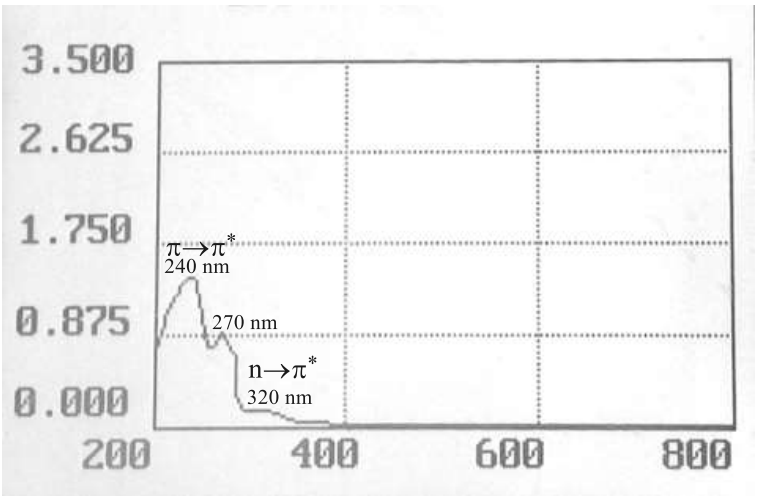


Figure 3: Absorption spectrum of QBCL.

The resulting compound was further confirmed by ^{1}H-NMR spectroscopy, as shown in figure. The signal of the methyl group protons appears at the displacement (δ = 2.06 ppm, s, 3H), the signal around (δ = 3.67 ppm, s, 1H) belonged to the third

aliphatic proton H_3, while the aromatic ring protons appear in the field (δ = 7.4-8.2ppm, m, 14H).

^{13}C-NMR spectroscopy exhibits signal at (δ = 20.54ppm) assigned to the methyl group carbon, signals appear in the field (δ = 128.32-133.78 ppm) belonged to carbon atoms in aromatic rings and the carbonyl carbon signal appears at (δ = 171.77ppm), signals of (C_3, C_2) carbon atoms appear in the spectrum at (51.46, 29.98ppm), respectively.

Study of the solubility and distribution coefficient of QBCl:

The dissolution of the product was studied in water, cyclohexane and chloroform by calculating the change of Gibbs free energy when moving from the gaseous phase to the aqueous phase and the organic phase. Also the change of free Gibbs energy for transit from the aqueous phase to the organic phase (cyclohexane, chloroform) and the distribution coefficient of the compound in the mixture (water, cyclohexane) and (water, chloroform) was studied, as shown in the following table.

Table (1): Distribution coefficient and free Gibbs energy of QBCl in the studied solvents:

	ΔG (eV)		$\Delta G_{transfer}$ (eV)	LogP
gas → H_2O	-0.522	H_2O → cyclohexane	0.196	3.313
gas → cyclohexane	-0.718	H_2O → chloroform	0.479	8.106
gas → chloroform	-1.002	Cyclohexane→chloroform	0.283	4.794

Where it was found that the compound dissolves well in chloroform and does not dissolve in water and has a weak dissolution in the cyclohexane. Comparing the coefficient of distribution in mixtures from previous solvents, it was found that the best coefficient is in the case of (chloroform, cyclohexane) where the substance is well transported to chloroform, and this feature can be used and experimented with pharmacological applications.

6- Summary and Conclusions:

- Finding the wavelength of light absorbed by the molecule and necessary for the reaction to take place.
- Finding the structural and spectral properties of the product and calculating the distribution coefficient for it, as it was found that it dissolves well in chloroform. This feature can be used and experimented with pharmacological applications.

References:

[1] Aillet T., Loubiere K., DechyCabaret O., Prat L., **Photochemical synthesis of a "cage" compound in a microreactor: Rigorous comparison with a batch photoreactor**, Chemical Engineering and Processing: Process Intensification, Vol. 64 (2013) pp. 38-47.

[2] Hook B., Dohle W., Hirst P., Pickworth M., Berry M., Booker-Milburn K., **A Practical Flow Reactor for Continuous Organic Photochemistry**, Journal of. Organic. Chemistry, Vol. 70(2005) pp. 7558-7564.

[3] Ghanoum K., Kodlaa A., Merza J., **Quantum Chemical Study of Photochemical Properties of some Unsaturated Compounds,** Journal of Al-Baath university , Vol. 41(2019) pp147-172.

[4] El-Zahabi H., **Synthesis, Characterization, and Biological Evaluation of Some Novel Quinoxaline Derivatives as Antiviral Agents**, Archiv der Pharmazie,Vol.350 (2017) p.1700028.

[5] Vieira M., Pinheiro C., Fernandes R., Noronha J., Prudêncio C., **Antimicrobial activity of quinoxaline 1,4-dioxide with 2- and 3-substituted derivatives**, Microbiological Research, Vol.169 (2014) pp.287-293.

[6] Ismail M., Amin K., Noaman E., Soliman D., Ammar Y., **New quinoxaline 1, 4-di-N-oxides: Anticancer and hypoxia-selective therapeutic agents**, European Journal of Medicinal Chemistry,Vol. 45(2010) pp.2733-2738.

[7] Aguiar L.d.O., Adalberto S.L., Bechtold I.H., Curcio S.F., Cazati T., Alves T.V., **Molecular 5,8-π-extended quinoxaline derivatives as chromophores for photoluminescence applications,** Journal of Molecular Liquids, Vol. 296 (2019) p.111763.

[8] . Rajalakshmi A.V., Palanisami N., **Y-shaped ferrocene/nonferrocene conjugated quinoxalines for colorimetric and fluorimetric detection of picric acid,** Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, Vol.228 (2020) p.117812.

[9] Fu J., Zang H., Wang Y., Li S., Chen T. , Liu X., **Experimental and Theoretical Study on the Inhibition Performances of Quinoxaline and Its Derivatives for the Corrosion of Mild Steel in Hydrochloric Acid**, Industrial & Engineering Chemistry Research, Vol. 51(2012) pp.6377-6386.