Experimental and Theoretical Analysis of Solvents Effect on A Derivative of Carbothioamide

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ABSTRACT

The titled molecules are an optically pure anti-cancer agent and also plays a vital role as an important staritng material for developing medicines that can cure many diseases. Synthesis of carbothiomide is a subject of deep chemical and biochemical research due to its medicinal value and can also use as a starting material for many important compounds. In this work 2,2'-[(2R,3R)-2,3-dihydroxy-1,4-dioxobutane-1,4-diyl]bis(N-P-tolyhydrazine-1-carbothioamide was synthesized experimentally in the laboatory and then characterized. The structure was later designed and optimized by Gaussian 09 package using ab initio method. To obtain the minimum energy of the titled structure, many basis set in density functional theory (DFT) and Hatree-Fock (HF) were used in geometry optimization. The molecule was characterized using spectroscopic methods such as 1H-NMR, 13C-NMR, FT-IR to determine the molecular dynamics as well as their optical and electrical properties. The energy difference between the HOMO and LUMO was computed. The HOMO and LUMO was found to be -0.15064 and -0.035472 eV respectively. The bandgap was also found to be -3.133 eV. The optimized titled structure then undergoes spectroscopic calculations to determine the theoretical spectroscopic parameters. A comparison was also studied between the theoretical and experimental datas. Finally, the effect of polar and non-polar solvent (DMSO and CCl4) on the optimized titled compound is analysed. It was found that the bandgap responds to the addition of solvent due to the involvement of the molecules in the solvent. The polar solvent has highest bandgap values due to the fact that the titled molecule is polar and its molecules can interact more easily with polar solvent that non-polar solvent. This result indicate that polar solvent can be used to increase the effectiveness of the titled molecule in terms of medicinal value.

ARTICLE INFO

1 Introduction

Thioamides are one of the important functional group in the organic chemistry as they have many fascinating biological activities such as anticonvulsant, antioxidant, and antifungal activities[1-2]. Majority of the members of thioamides class are strong inhibitors of dehydrogenase and phosphoglycerate[3]. Additionally, they serve as intermediates in the synthesis of some organic materials such as synthesis of heterocyclic compounds and other starting materials[4-6]. The titled molecule also serve as a starting materials of many organic compounds such as enamines, amidines and their vinylogs and other heterocyclic organic compounds[7]. Natural chiral compounds provides an option for the synthesis of enantiomerically pure compounds[8]. Enantiomerically

pure 1,2 diols are crucial intermediates in the production of natural products and active biological compounds[9]. They can easily be change into chiral epoxides, aziridines, and amino acohols[10,11]. Optically active compounds can easily modify another compound that is optically active without breaking or changing any covalent bond that is attached to the asymmetric carbon. The configuration remained the same without changing[12,13]. Have investigated the effect of hydorgen on the halogen on the heterocyclic diols compound and discovered that their bandgap is very sensitive when doped with halogens [14]. In the present paper, we have investigated the preparation and characterization of chiral 2,2'-[(2R,3R)-2,3-dihydroxy-1,4-dioxobutane-1,4-diyl]bis(N-P-tolyhydrazine-1-carbothioamide using (2R,3R)-2,3-dihydroxybutanedihydrazide (1) as a starting material. In light of the studies conducted on the synthetic chemistry of carbothioamide during last 20 years, we have also partly contributed to this progress by developing a new chiral carbothioamide synthesis which has an optical property. The compound was first synthesized experimentally in the laboratory and analyzed using using the spectroscopic method (FT-IR and NMR) to verify its purity. Furthermore, the compound is again designed in Gaussian softwares package, optimized, and the spectrospic properties were again calculated. The comparison between the experimental and theoretical datas prove a strong correlation and the accuracy of the basis set that was considered in the DFT (density functional theory).

2 Experimental Procedure

The reaction in figure 1 was carried out at standard temperature and pressure (STP). 10 mmol of (2R,3R)-2,3-dihydroxybutanedihydrazide **(1)** was added to the reaction flask follwed by 50 ml of absolute ethyl alcohol. After the reflux process started, 20 mmol tolyl isothiocynate was added. The reaction was left to cotinue, after 4 hours solid 2,2'-[(2R,3R)-2,3-dihydroxy-1,4-dioxobutane-1,4-diyl]bis(N-P-tolyhydrazine-1-carbothioamide began to form in the reaction. The crystal solid of the formed compound was filtered off, dried and collected.
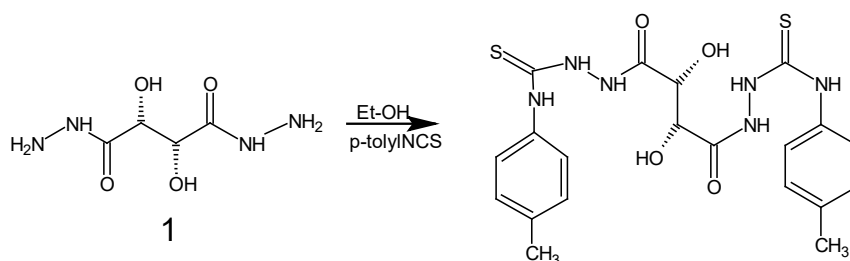
Figure 1. The structural chemical reaction of 2,2'-[(2R,3R)-2,3-dihydroxy-1,4-dioxobutane-1,4-diyl]bis(N-P-tolyhydrazine-1-)carbothioamide.

3 Theoretical Techniques

The B3LYP/6-311G basis set of the density functional theory in the Gaussian softwares is one of the accuracy and suitable basis set for the simulation of organic multi-electron compound. In this work, B3LYP functional was choosen together with the 6-311G to achieve molecular optimization. The method is used by most of the schorlars to detemine the energies of a covalent systems as well as their geometries. The gorund-state geometry optimization of the titled molecule was done with different basis set such as STO-3G, 3-21G, 6-31G, 6-31G*, 6-311G, LanL2DZ, LanLMB, and SDD. The NMR and FT-IR calculation was obtained from the optimized structure and the replotted with the Origin graphing and analysis softwares. Furthermore, the plot of the HOMO and LUMO is by three dimensional mapping in the Gaussian 09 softwares package. The energy difference (band-gap) of the HOMO and LUMO was also computed. All simulations and calculations in this research paper was implemented by the Gaussian 09 software package and Origin graphing and analysis software package. Theoretical results were given in the this section in table 1,2 and figures 5-7 respectively. Additionally, some of the theoretical results (Table 3-5, Figure 5-7) were also shown in the results and discussion section.

**Table 1.** Comparison showing optimization of basis set for Hatree-Fock versus DFT

Basis set	Hatree-Fock (eV)	DFT (eV)
STO-3G	0.47722504	1.87044190
3-21G	6.86689991	3.64031623
6-31G	7.19786205	2.39527258
6-31G*	7.17986205	2.39527258
6-311G	7.83364247	3.26137850
LanL2DZ	7.41250704	5.40120704
LanL2MB	2.40275670	2.97108481
SDD	7.75335401	3.44735868

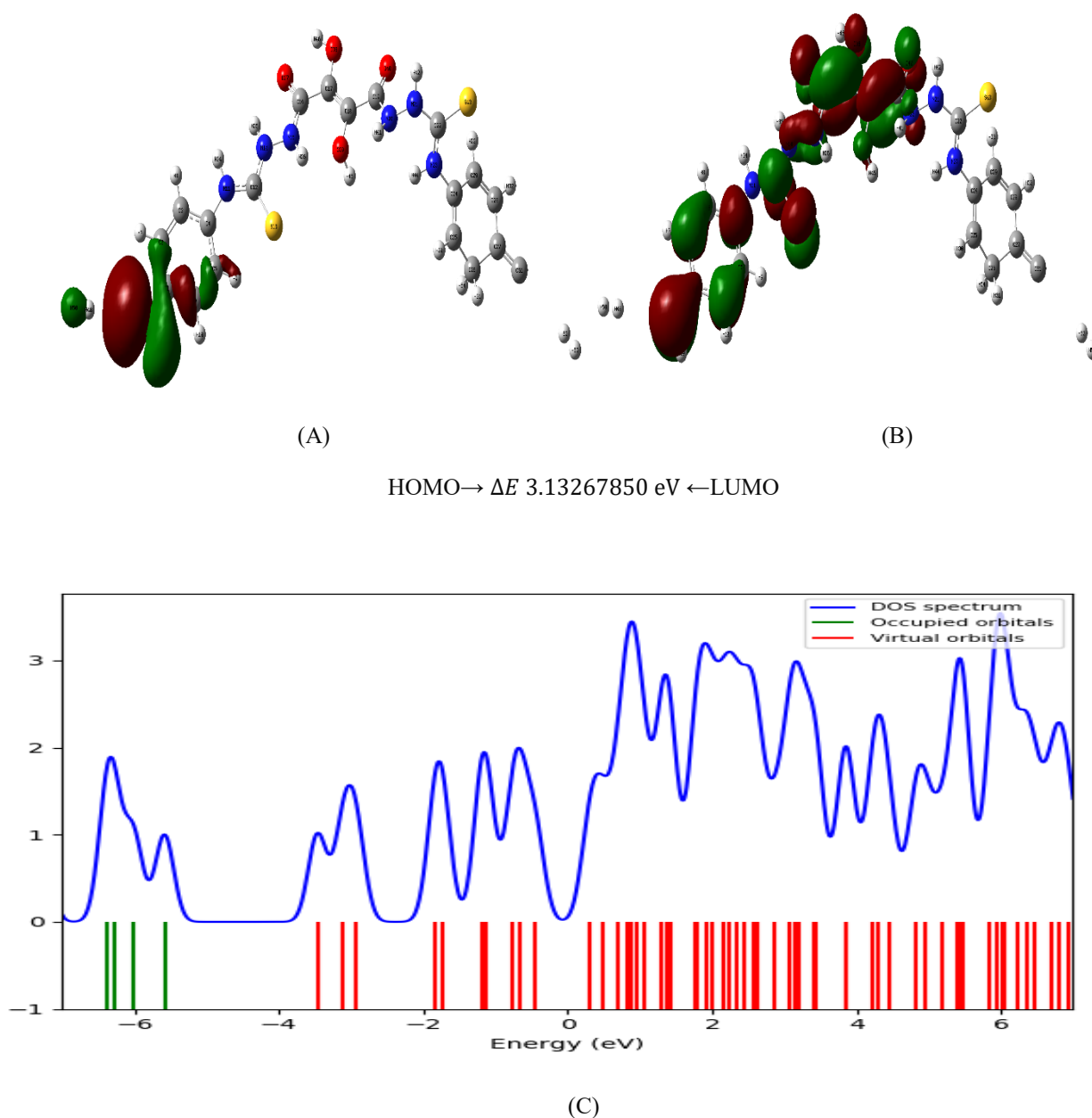**Table 2.** Comparison showing the effect of the solvent on the bandgap with the same basis set

Solvent	Basis set	Bandgap energy (eV)
DMSO	6-311G	4.645026248
CCl$_4$	6-311G	3.750673404
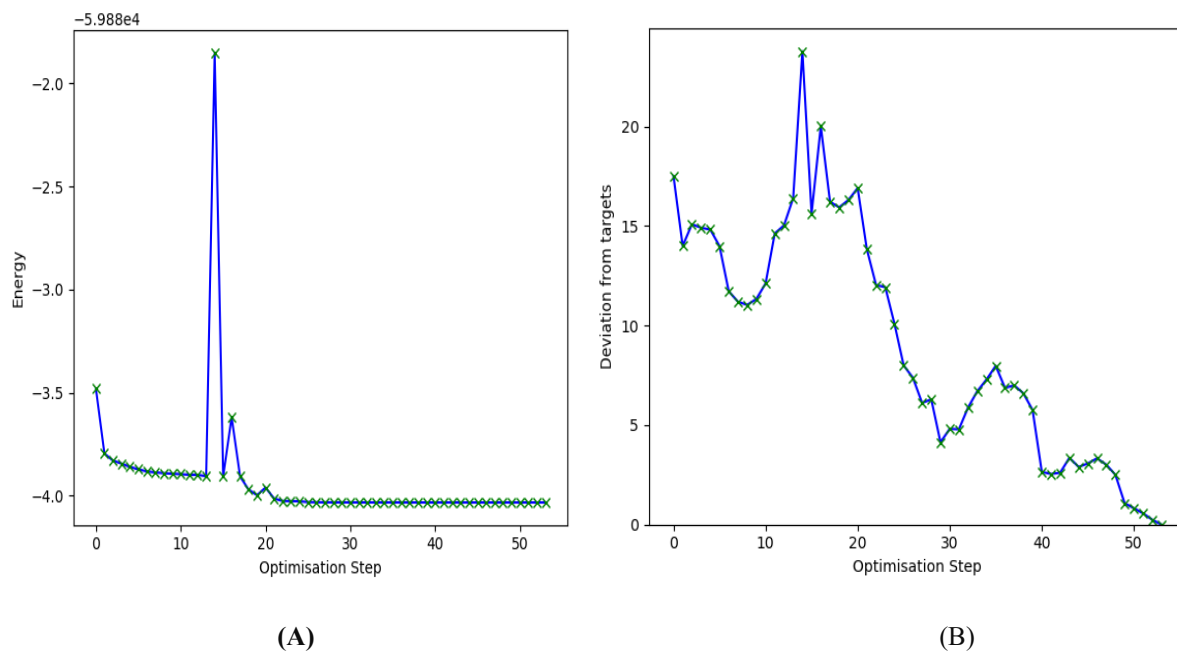
(A)   (B)

Figure 2. (A) and (B) The geometry optimization steps
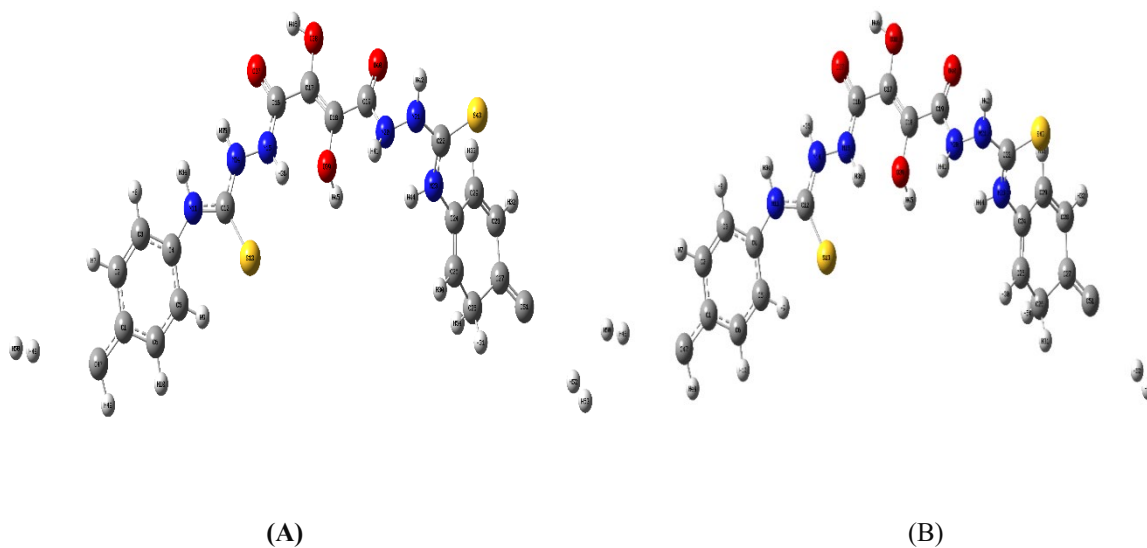
(A)   (B)

Figure 3. (A) and (B) the stable structure

(A)   (B)

HOMO→ ΔE 3.13267850 eV ←LUMO

(C)

Figure 4. The 3-D mapping of (A) HOMO and (B) LUMO (C) Density of state of the titled compound

4 Result and Discussion

4.1 FT-IR Spectroscopy

The IR spectra were measured with Perkin–Elmer Spectrum One FTIR spectrophotometer. The vibrational frequency in this theoretical research part was computed using the B3LYP/6-311G functional along with DFT(density functional theory) method. There are five important peaks associated with the titled molecule. The highest peaks are attributed to hydrogen bonding (O-H and N-H) which absorbed at about 3365-3100 cm^{-1} experimentally and then absorbed at about 2950-3050 cm^{-1} theoretically. The closeness in the two values (table 3) is as a result of the accuracy of the basis set selected to optimize the titled structure. Another absorption ocurred at 3072-3107 cm^{-1} which is attributed to aromatic ring hydrogen, 2800-2930 cm^{-1} also attributed to carbon hydrogen stretching, 1267 cm^{-1} attributed to carbon sulphur (C=S) bond.

Table 3. Comparison between the experimental and theoretical FT-IR

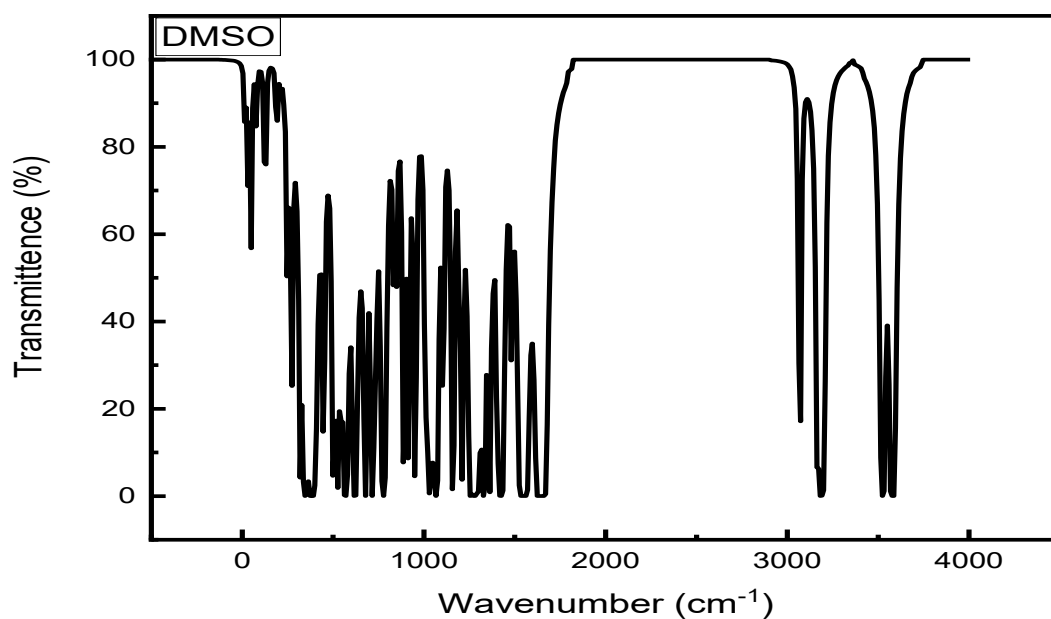| Experimental Peaks (cm^{-1})	Theoretical peaks (cm^{-1})	Vibrational mode	Bonding mode
3352–3236	3365-3100	Hydrogen bonding mode	O-H, N-H
3072–3107	2950-3050	Ar-H stretching vibration	Ar-H
2870–2914	2800-2930	C-H stretching vibration	C-H
1677	1580	NH-C-O stretching vibration	NH-C=O
1267	1255	C=S scissoring vibration	C=S

(A)
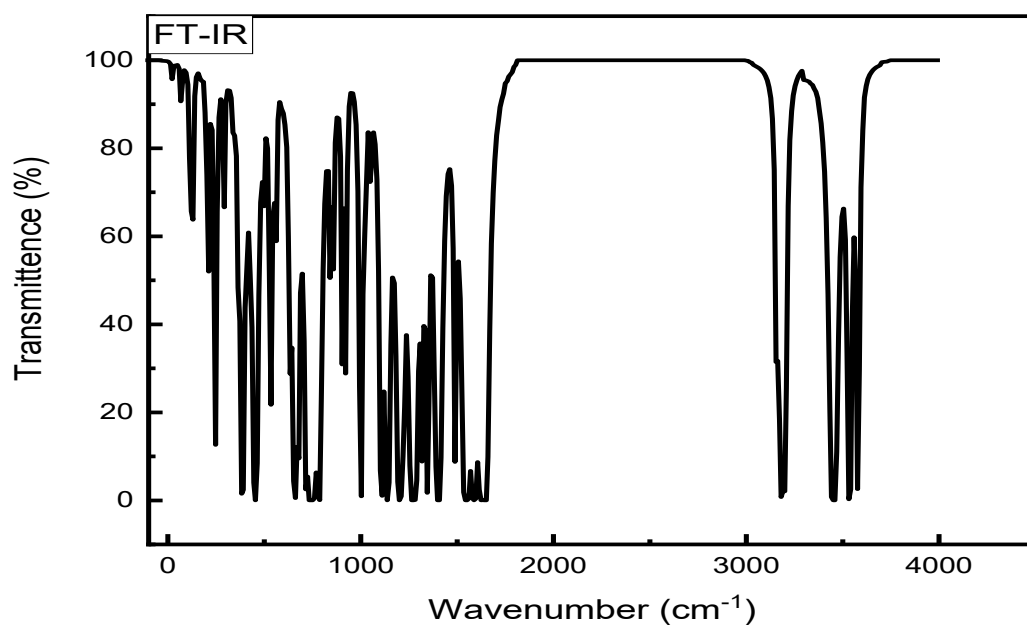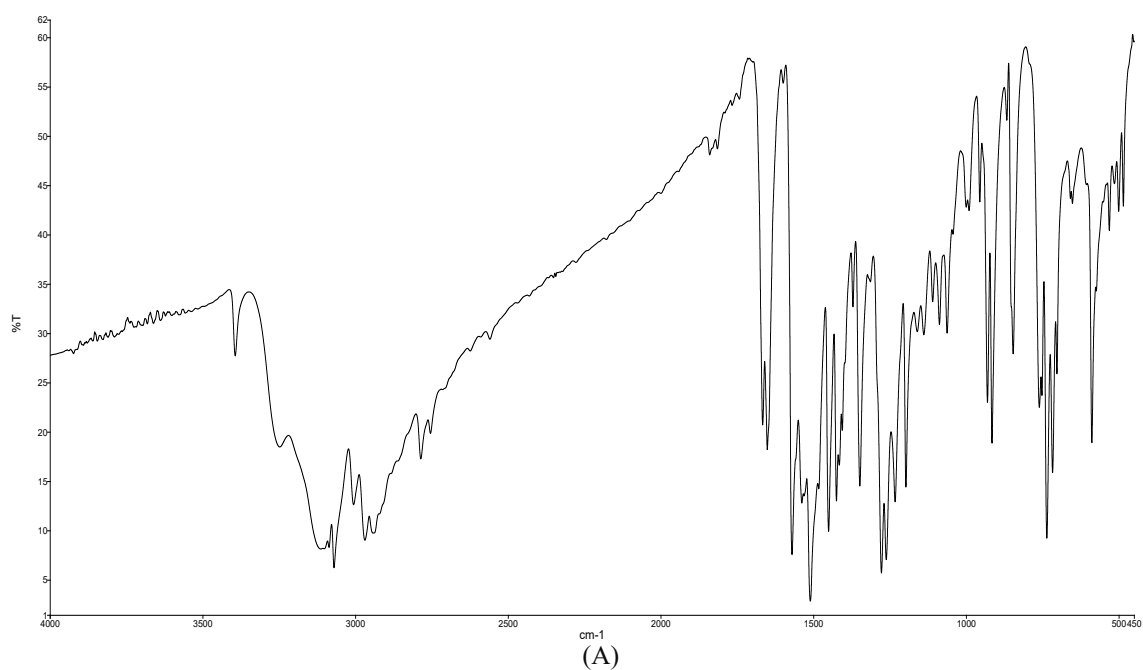
(B)
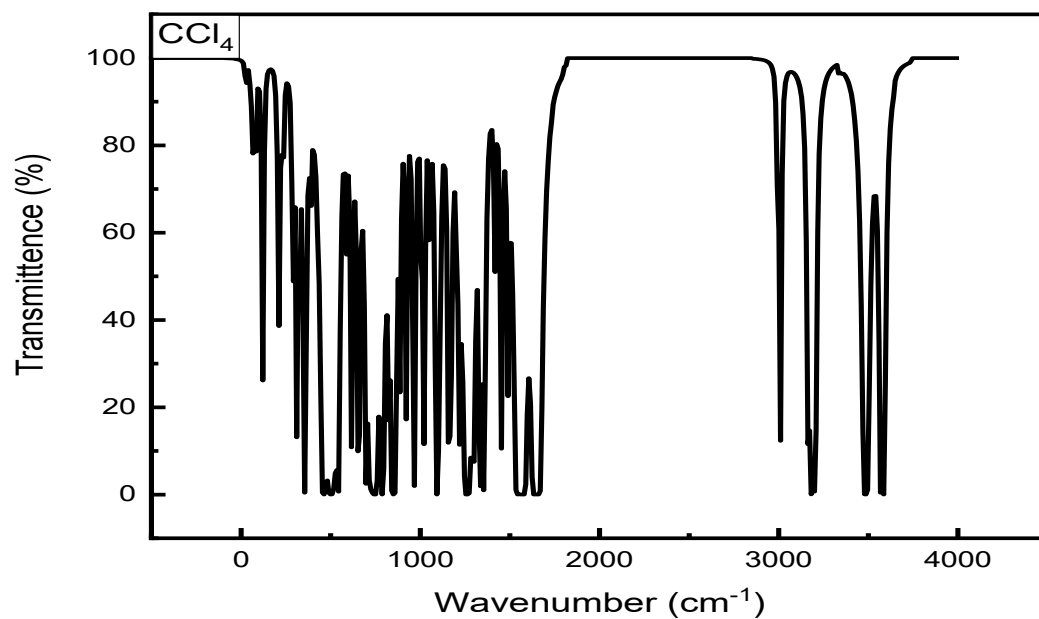
(C)

(D)

Figure 5. (A) experimental FT-IR (B) theoretical FT-IR (C) theoretical FT-IR when solvated with CCl_4 (D) theoretical FT-IR when solvated with DMSO

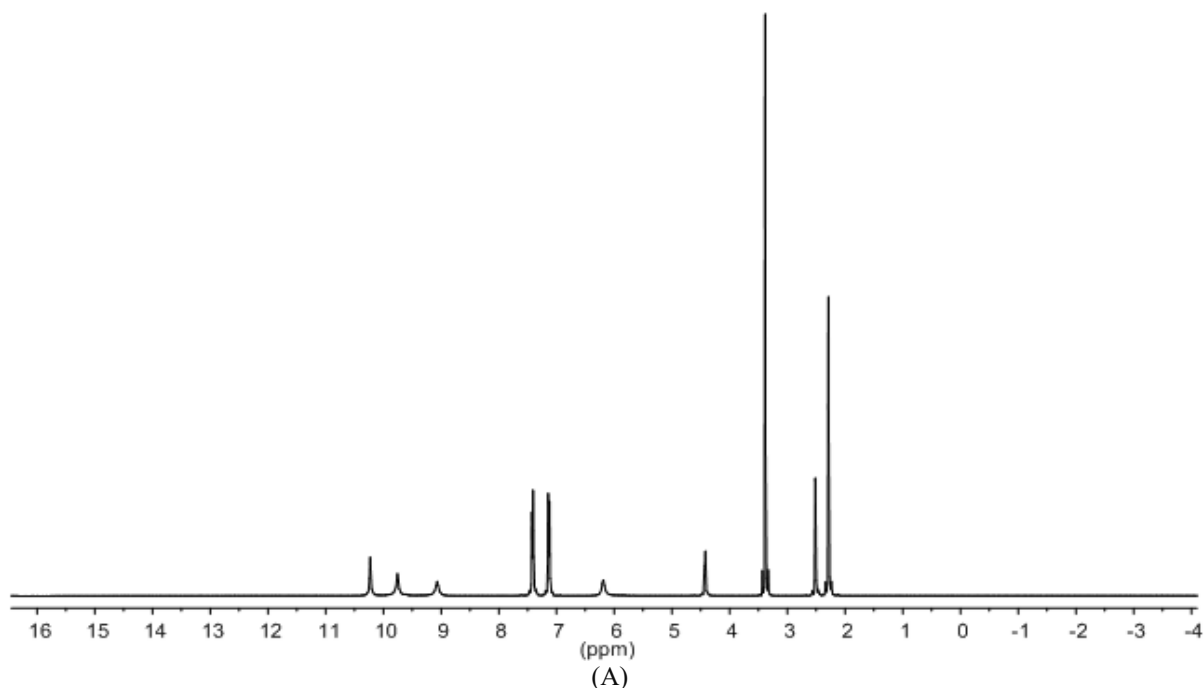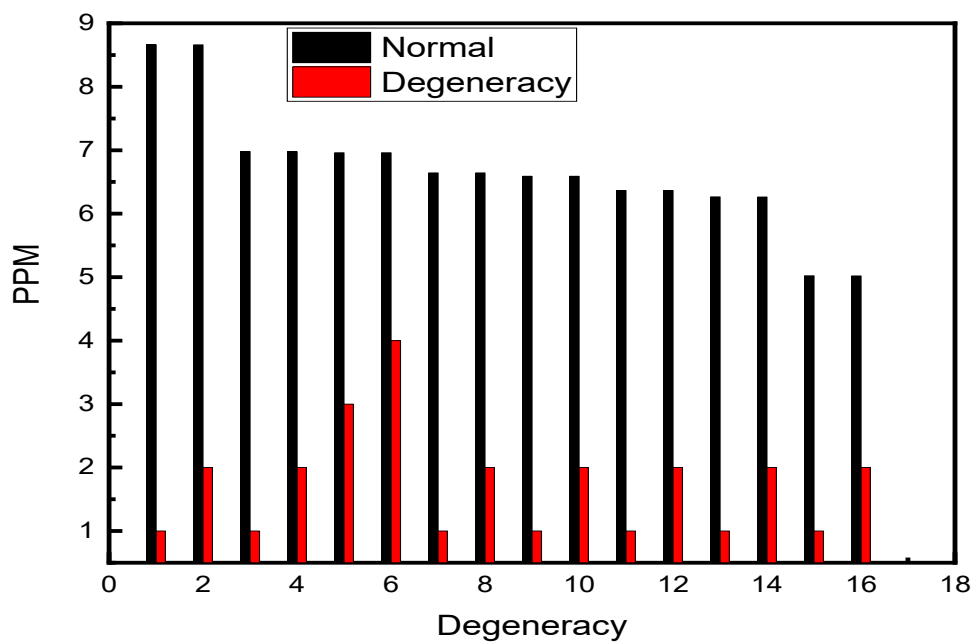### 4.2 Proton NMR (^{1}H-NMR)

The proton NMR spectra was obtained from Bruker AC-400 NMR spectrometer operating at 400 MHz for ^{1}H. The molecule was dissolved in DMSO-d_6 and chemical shifts were referenced TMS. The NMR was again determined theoretically using the Gaussian 09 software package using TMS as a reference. Table 4 shows the comparison between the theoretical and experimentally obtained result. There are eight absorption peaks present at different location depending on the chemical enviroment. The two hydrogren with the highest peak are the protons directly attached to the nitrogen atom and they have absorbtion at

about 180.16 ppm when determined experimentally and at the same peaked at about 182.20 ppm when calculated theoretically. This explains that the basis set that is selected is in agreement with literature. As the solvation took place, the two hydrogen shifted to another chemical enviroment to indicate the effect of both the solvents. The two hydyrogen with the highest peak that are bonded to nitrogen go to downfield at about 160 ppm when solvated with DMSO and also change to 165 ppm when CCl$_4$ is added. The solvation dont have much effect on aromatic hydrogen due to the fact that aromatic compounds has rings that is resonating.

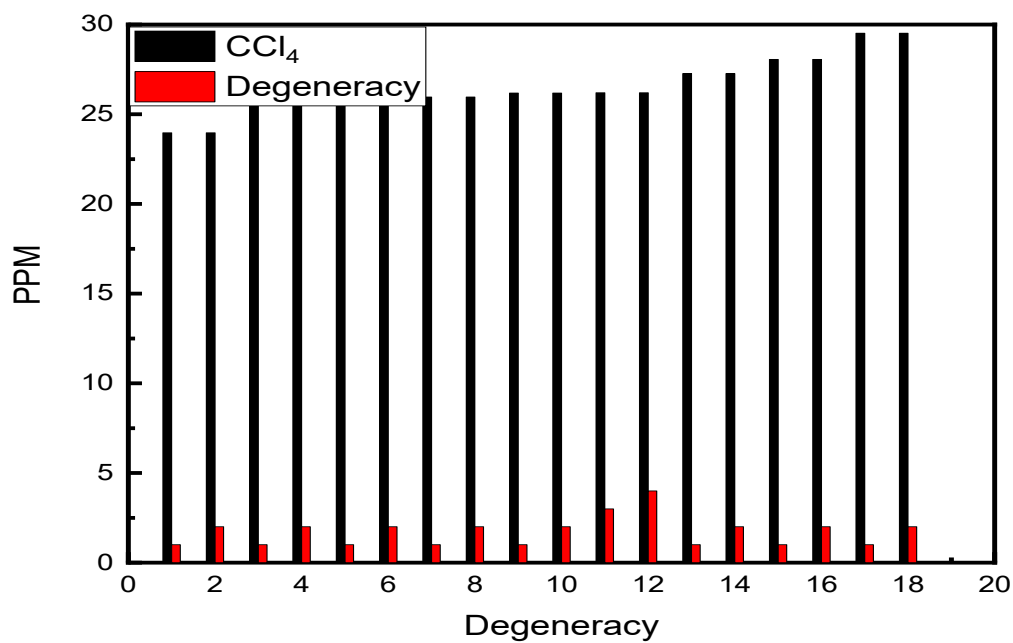**Table 4.** Comparison between experimental and theoretica^l H-NMR

S/N	Hydrogen position	Experimental peaks (ppm)	J-coupling (Hz)	Theoretical peaks (ppm)
1	s, 6H,2XAr-CH$_3$	2.29	4.81	2.94
2	d, 2H, 2XCH	4.43	5.21	4.33
3	br, 2H, 2XOH	6.19		6.85
4	d, 2H, Ar-H	7.13	7.67	7.43
5	d, 4H, Ar-H	7.42	8.30	7.51
6	s, 2H, NH-<u>NH</u>-C=O	9.07	8.20	9.17
7	s, 2H, <u>NH</u>-NH-C=O	9.76		9.83
8	s, 2H, NH-C=S	10.76		11.01

(A)
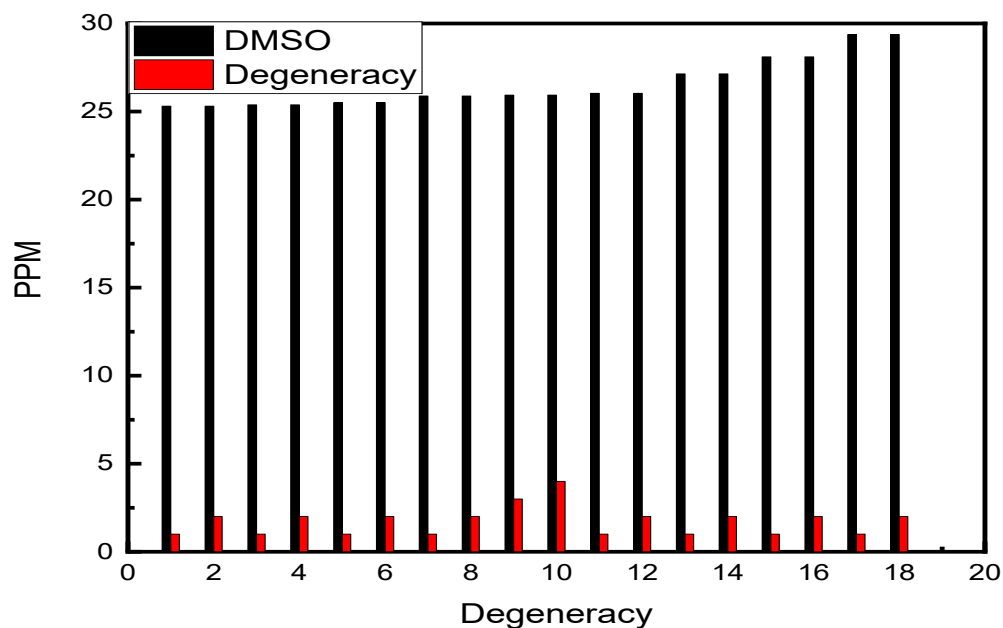
(B)

(C)

(D)

Figure 6. H-NMR (A) experimental (B) theoretical (C) solvated with CCl$_4$ (D) solvated with DMSO

4.3 Carbon NMR (^{13}C-NMR)

The ^{13}C spectra were taken on Bruker AC-400 NMR spectrometer operating at 100 MHz for ^{13}C. The molcule was dissolved in DMSO-d_6 and chemical shifts were referenced to TMS. The NMR was again determined theoretically using the Gaussian 09 software package using TMS as a reference. Table 5 give the comparison between the theoretical and experimental obtained data. There are seven absorption peaks present at different location depending on the chemical enviroment. The two carbonyls are the carbons with the highest absorbtion at about 180.16 ppm when determined experimentally and at the same

peaked at about 182.20 ppm when calculated theoretically. This is an indication that the two carbonyls are in the same chemical enviroment which is absolutely true because the tittled molecule is a symmetric molecule. Also, the closeness in the values of experimental and theoretical result is attributed to the accuracy of the B3LYP/6-311G basis set. The following carbons absorbed at 73.38, 125.13, 126.28, 128.61, 139.33, and 171.67 ppm when experiment was carried out and also absorbed at about 126.80, 128.00, 131.00, 139.00, 145.50, and 165.80 ppm theoretically respectively. The agreement between the comparison describe the sophistication of the method, functional and the basis set that is used

Table 5. Comparison between experimental and theoretical ^{13}C-NMR

S/N	Carbon position	Experimental peaks (PPM)	Theoretical peaks (PPM)
1	2C, H- C-O	21.02	81.80
2	2C, H-C-C-N	73.41	123.50
3	2C, H-C-C-N	123.19	126.50
4	2C, H-C-N	129.05	139.00
5	2C, H-C-C	134.55	137.50
6	2C, C-N	136.76	168.80
7	2C, C=O	171.50	188.20

(A)

(B)
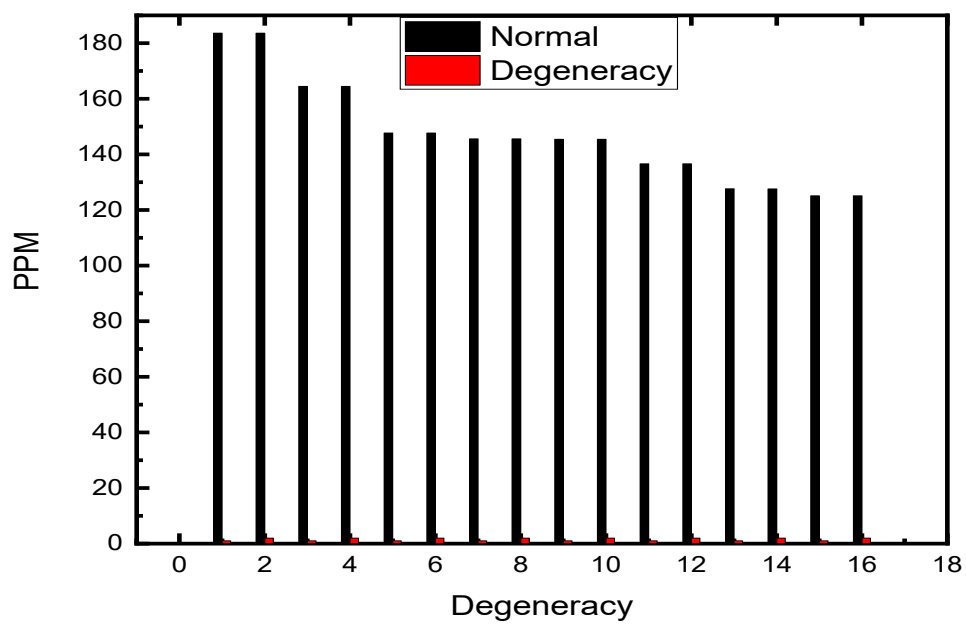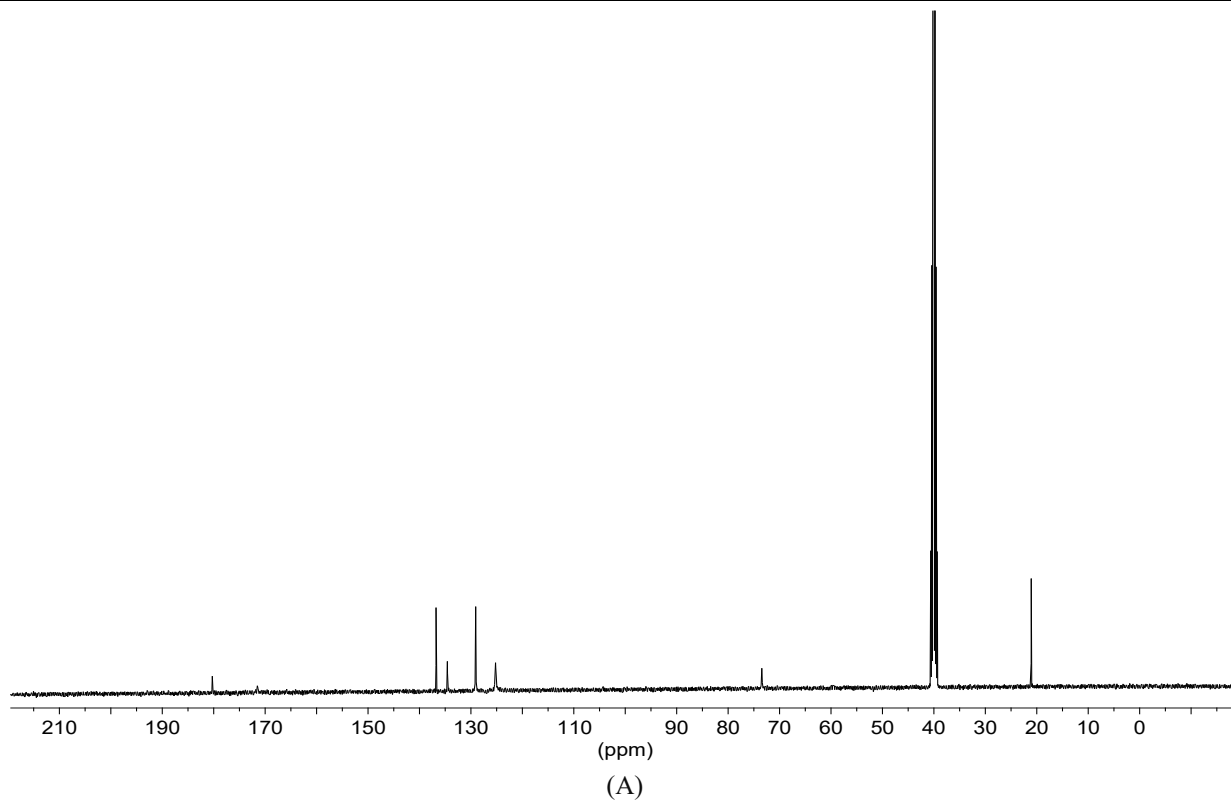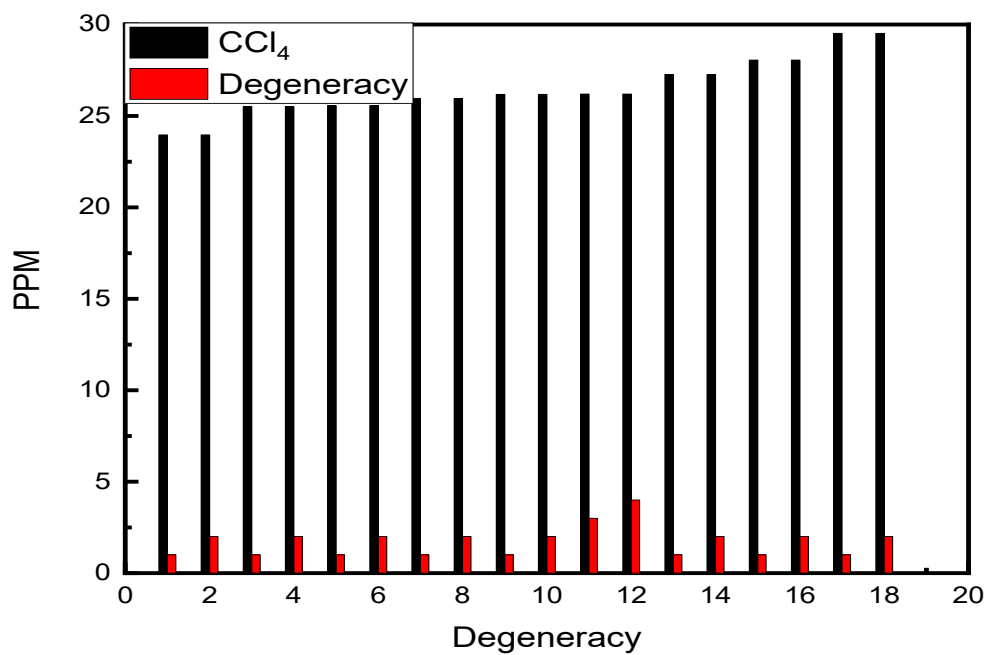
(C)
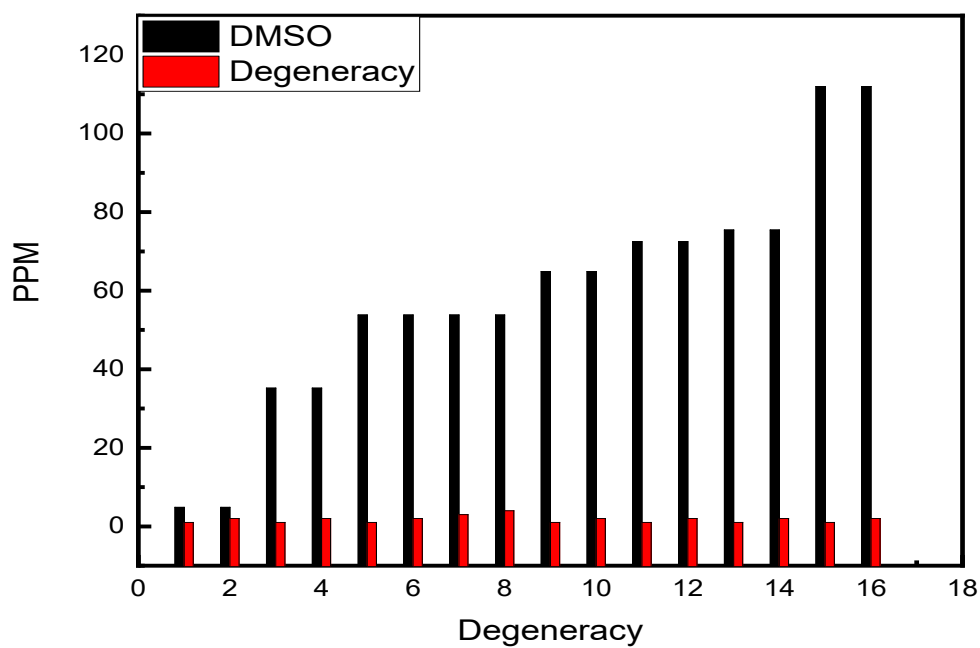
(D)

Figure 7. ^{13}C-NMR (A) experimental (B) theoretical (C) solvated with DMSO (D) solvated with CCl$_4$

Conclusion

In this paper, the titled molecule is prepared in the laboratory using experimental method and characterized using spectroscopic methods to determined the structure and purity of the synthesized molecule. The same structure was designed, edited and optimized theoretically. The optimized titled structure then undergoes spectroscopic calculations to determined the theoretical spectroscopic parameters. A comparison was also studied between the theoretical and experimental datas. Finally, the effect of polar and non-polar solvent (DMSO and CCl_4) on the optimized titled compound is analysed. It was found that the bandgap respond to the addition of solvent due to the involvement of the molecules in the solvent. The polar solvent has highest bandgap values due to the fact that the titled molecule is polar and its molecules can interact more easily with polar solvent that non-polar solvent. This result indicate that polar solvent can be use to increase the effectiveness of the titled molecule in terms of medicinal value.

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