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Solvents Effect on 4-phenyl-5-(2-thienyl)-2,4-dihydro-3H-1,2,4-triazol-3-thion Molecule: Experimental and Theoretical Study

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ABSTRACT

In this study 4-phenyl-5-(2-thienyl)-2, 4-dihydro-3H-1,2,4-triazol-3-thion was synthesized using experimental method and later characterized using spectroscopic methods. The titled molecule was then designed, optimized and characterized with theoretical first principal method. The result compared and the molecule is solvated with polar and non-polar solvent to see the effect of their interaction and changes that occurs in the spectroscopic results.

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Introduction

Researches have indicated that most of the aromatic five-membered rings with heteroatoms such as 1,3,4-oxadiazole, 1,3,4-thiazoles, 1,2,4-triazole rings systems and their derivatives were given much attention due to their use as a starting materials for many heterocylic organic complex molecules that posseses many pharmacological activities like anti-microbial, analgesic, anti-inflammatory, anti-cancer and anti-oxidant properties. Drugs of nowadays such as Ribavarin (anti-viral), Rizatriptan (anti-migraine), Alprazolam (anxiolytic agent), Fluconazole and Itraconazole (anti-fungal agents) posses five membered ring with heteroatoms in them. Recent understanding of Mannich bases showed that it posesses biological properties such as anti-fungal, anti-bacteria, anti-inflammatory and anti-malarial function. [1-7]

In this research, 4-phenyl-5-(2-thienyl)-2, 4-dihydro-3H-1,2,4-triazol-3-thion was synthesized using experimental method and later characterized using spectroscopic methods. Many studies have shown that Mannich bases have possess potent biological characteristics such as antibacterial, antifungal, anti-inflammatory, antimalarial and pesticide properties [8-11]. Few Mannich bases derived from 1,2,4-triazoles carrying N-methylpiperazine substituent were biologically active [12,13]. 4,5-Substituted products containing 1,2,4-triazole in their molecules seem to be suitable candidates for further chemical modifications and might be of interest as pharmacologically activecompounds and ligands useful in coordination chemistry [14]. Derivatives of 4,5-disubstituted 1,2,4-triazole were synthesized by intramolecular cyclization of 1,4-disubstituted thiosemicarbazides [15]. In addition there are some studies on electronic structures and thiole-thione tautomeric equilibrium of heterocyclic thione derivatives [16-19].

Experimental Method

The experiment set up started with a three-mouth test flask with a volume of 250 ml which was equipped with a thermometer and reflux. 70 mmol of 2-thiophenecarboxylic acid hydrazide and 100 ml of ethyl alcohol were added to the reaction flask. Reflux was expected. After reflux, 70 mmol of phenylisothiocyanate was added. Solid (thiosemicarbazide) formation was

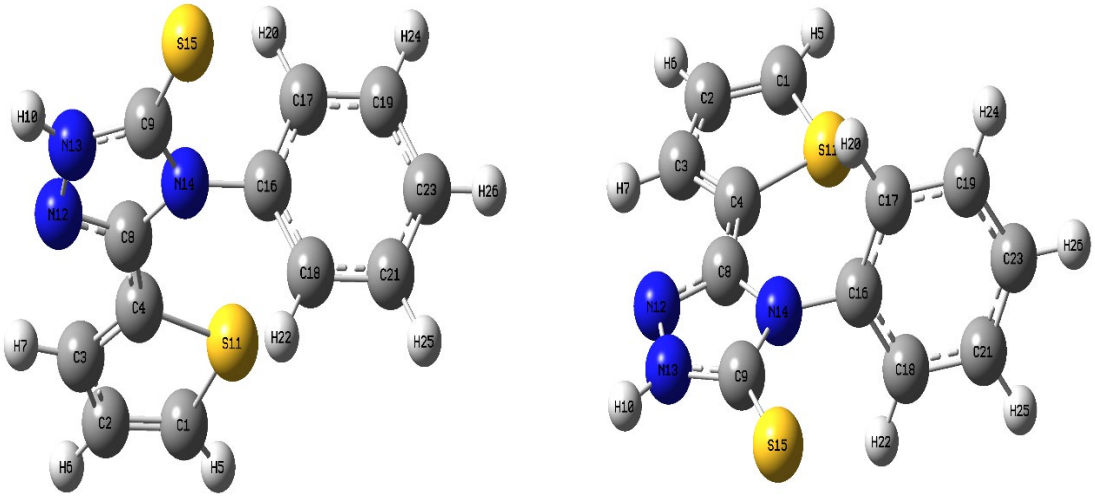
observed. After 4 hours, 4 g of KOH, which we weighed and prepared before, was added and slowly dissolution started. After a few hours the reaction was stopped. The pH was adjusted to 3-4 with HCl. The solid formed was filtered off. The resulting solid filtrate was washed with cold water and crystallized with alcohol. The structure of the obtained product was elucidated by IR and ^{1}H-NMR. The three-dimensional molecular model of 4-phenyl-5-(2-thienyl)-2,4-dihydro-3H-1,2,4-triazole-3-thion is shown in Fig 1.

Theoretical Method

In this research Gaussian 09 view was used to optimize the titled structure uisng Hatree-Fock (HF) and Density functional theory (DFT). In the molecular optimization, DFT method was used with 6-311G basis set and B3LYP functionals were selected due to its accuracy with the literature.

Table 1. Comparison Showing Optimization of Basis Set For Hartree-Fock Versus DFT

Basis set	Hartree-Fock (eV)	DFT (eV)
STO-3G	0.884914728	1.422067764
3-21G	6.067870086	3.760887594
6-31G	6.166103240	3.735308878
6-31G*	6.166103240	3.735036764
6-311G	6.433591302	3.748370350
LanL2DZ	6.514681274	3.641973776
LanL2MB	2.823999092	3.776398092
SDD	6.471959376	3.654218906



(A) (B)

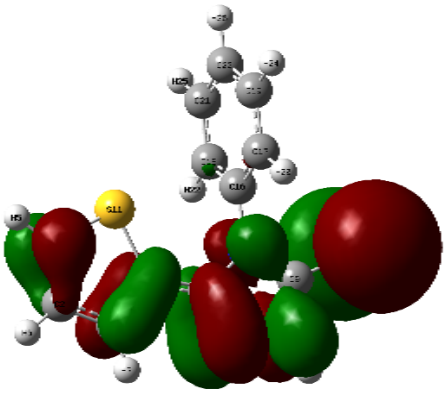
Fig 1. Optimized Molecular Structure of The Titled Molecule

Result And Discussıon

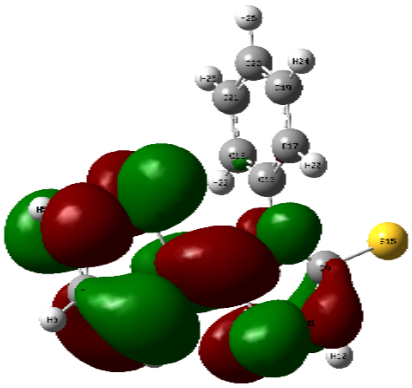
The titled molecule has 68 molecular orbitals. These molecular plays very important role in the determination of electrical and magnetic properties of a molecule. The calculations show that the title compound has 68 occupied molecular orbital. Both the highest occupied molecular orbital (HOMO) and the lowest-lying unoccupied molecular orbital (LUMO) are mainly delocalized on the benzene ring. As seen from Fig 2. Both in the HOMO and LUMO electrons are delocalized on the 4 membered rings. The HOMO–LUMO energy values of the titled molecule are shown in Fig 2. HOMO–LUMO energy gap can be to determine correlations for chemical and biological systems.

Table 2. Comparison Showing The Solvent Effect

S/N	Solvent	Basis set	Bandgap (eV)
1	Normal	6-311G	3.748370350
2	CCl_4	6-311G	3.896400366
3	DMSO	6-311G	4.088784964

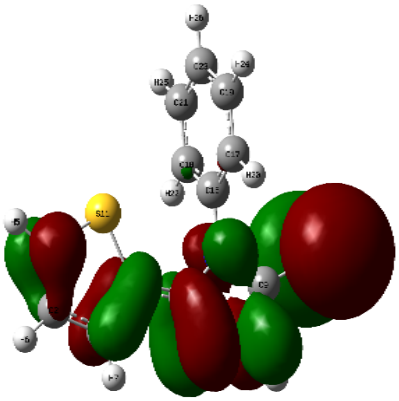


(A)



(B)

HOMO→ 3.748370350 eV ←LUMO



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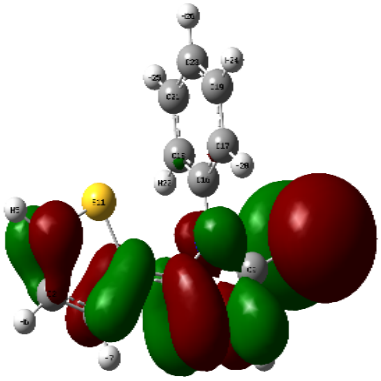
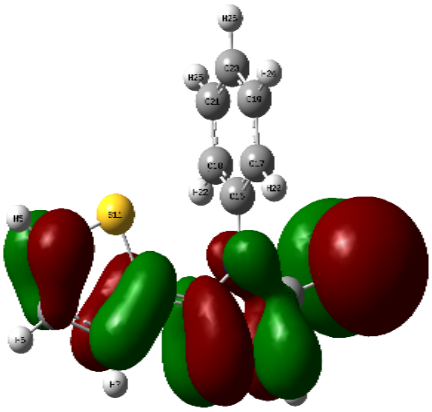


(D)

HOMO→ 3.896400366 eV ←LUMO



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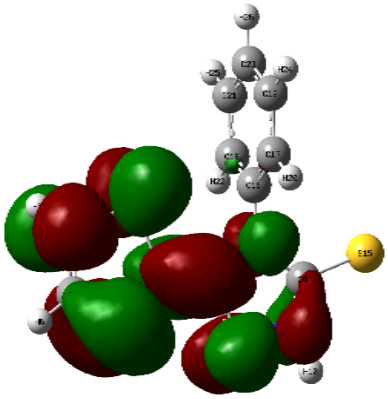
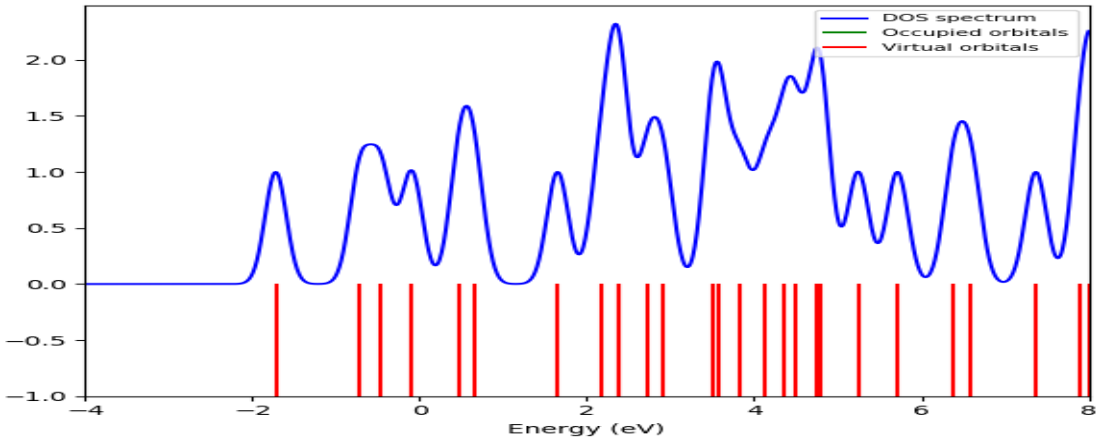


(F)

HOMO→ 4.088784964 eV ←LUMO

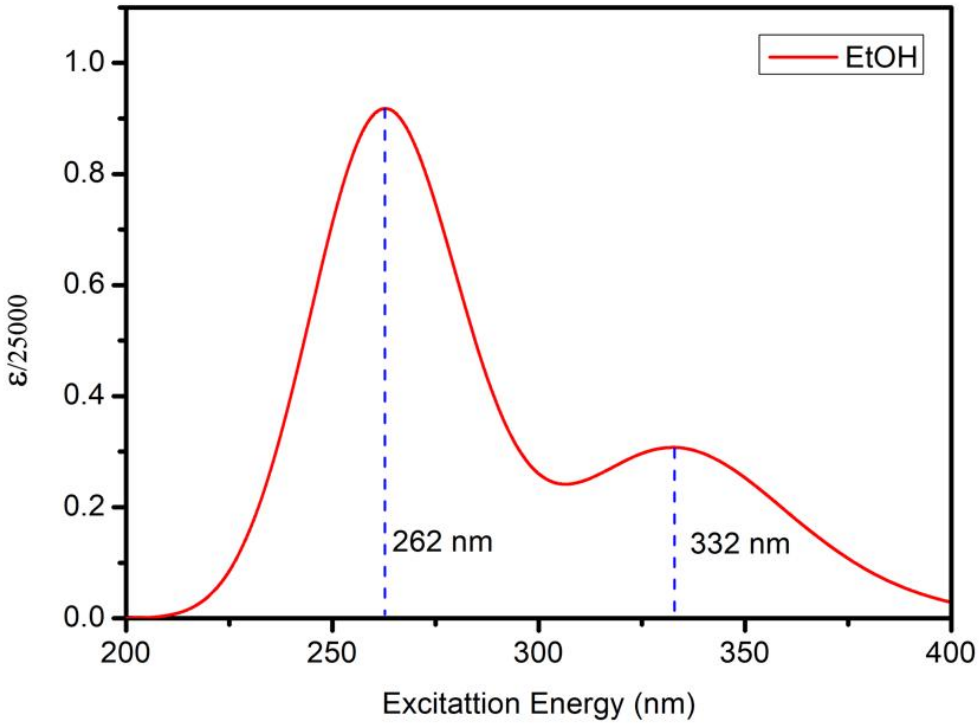


(G)

Fig 2. The 3-D mapping of HOMO and LUMO (G) Density of state of the titled compound

Ultraviolet Spectroscopy

One of the prominient method in spectroscopic analysis of an organic molecule is ultraviolet spectroscopy due to its accuracy and easiness. It is use to measure the absortion rate of a molecule. In Fig 3. The CCl_4 solvent has the highest absorbtion with around 27000 cm followed by DMSO with absorbtion around 25000 cm and finally the vacuum (with no solvent) which has a peak around 22000 cm theoretically and 22350 cm experimentally with a wavelength a 262 nm. The peak around 232 cm is attributed to second excitaiton states of the molecule. The changes wavelengths and intensities of the titled molecules is due to the fact that the solvents differs in polarity. One is polar (DMSO) and another is non-polar (CCl_4).



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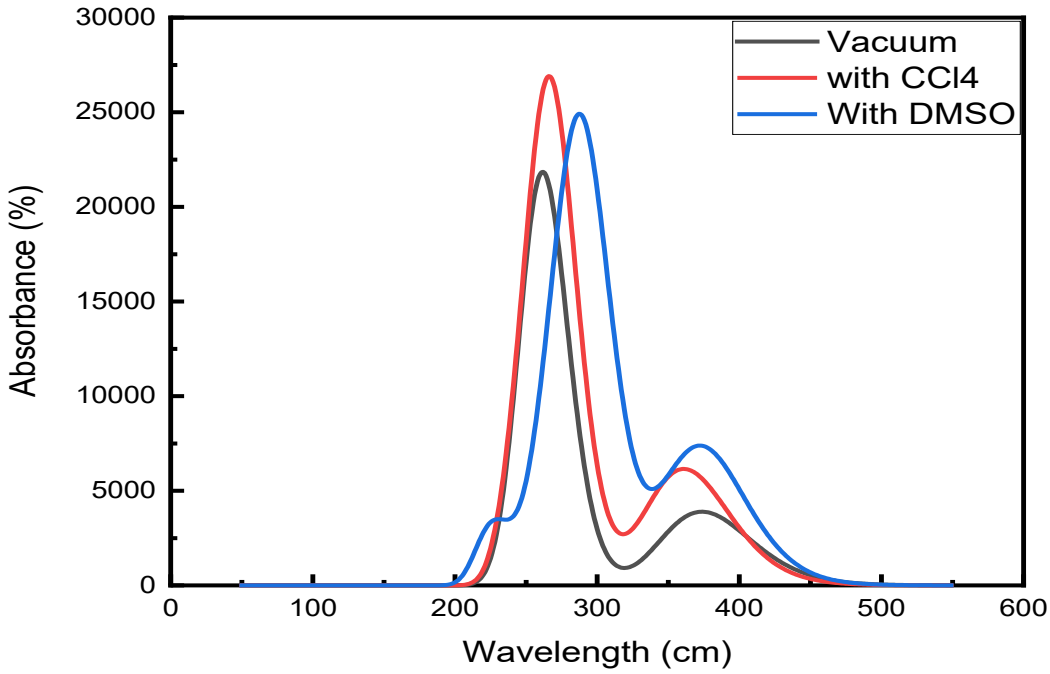
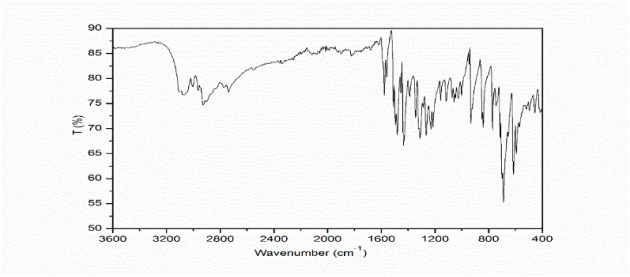


(B)

Fig 3. Ultraviolet Spectroscopy (A) Experimental FT-IR (B) Theoretical FT-IR

Fourier-Transform Infrared (FT-IR)

FT-IR is one of the spectroscopic techniques that can be use by the reseachers to analyze the functional group present in a particular molecular. In this experimental analysis, the presence of aromatic ring can only be known by C-H and C-C=C related vibrations and the C-H stretching occurs at about 3000 cm^{-1}. In this research, the peak at about 3025-3062 cm^{-1} is attributed to C-H streching in the benzene ring which very close to the literature due to the richness of 6-311G/B3LYP method. The aliphatic C-H stretching occurs at about 2867-2973 cm^{-1}. The aromatic C-H plane bending also is present at about 1000-1300 cm^{-1} which is close to the experimental aliphatic C-H plane bending that happens at about 900-1380 cm^{-1}. All the peaks below 1000cm-1 are considered to be in the finger print region where many functional in the molecule are present.



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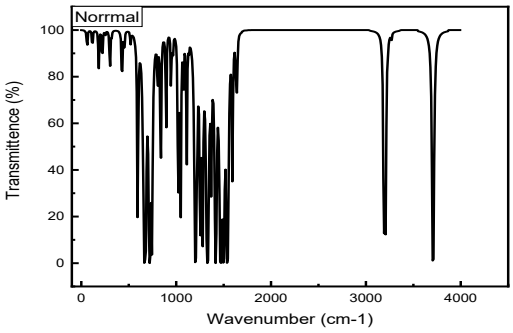

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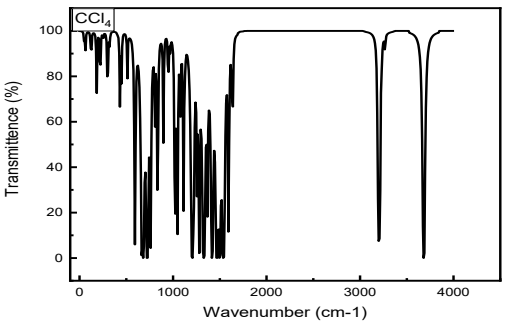

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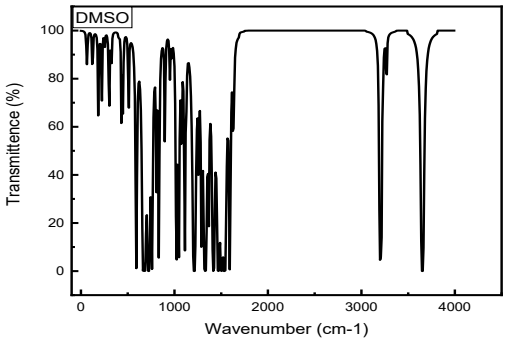
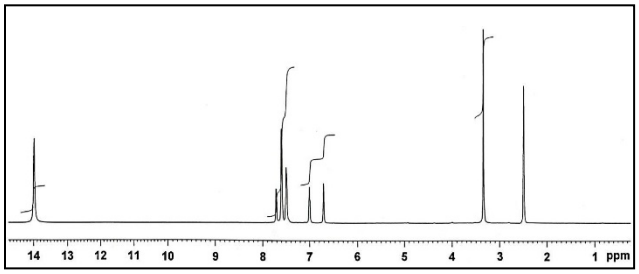


(D)

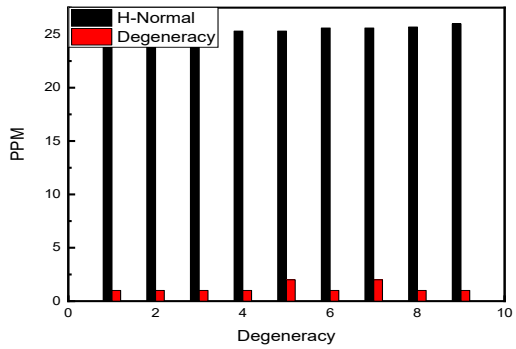
Fig 4. (A) Experimental FT-IR (B) Theoretical FT-IR (C) Theoretical FT-IR When Solvated With CCl_4 (D) Theoretical FT-IR When Solvated With DMSO

Nuclear Magnetic Resonance (^{1}H-NMR)

The absorbtion around 2.5-2.8 ppm is attributed to the hydrogens present in sulphur rings and it absorb in the downfield because they are far from sulphur and electrons cant be withdrawn easily due to inductive effect.



(A)



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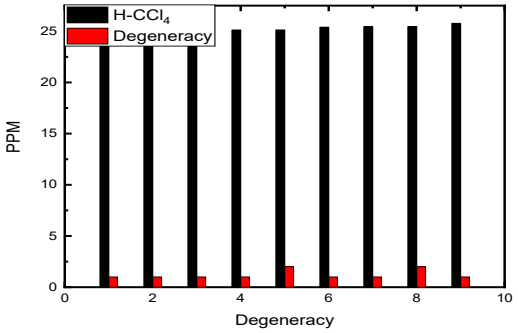

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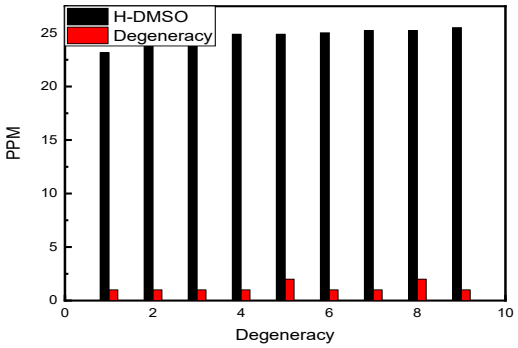
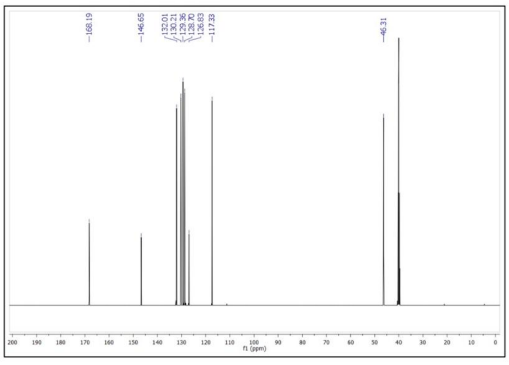


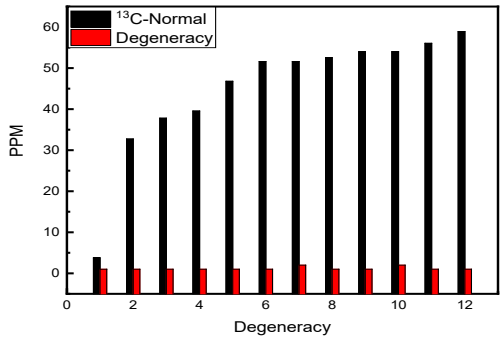
(D)

Fig 5. ^{1}H-NMR (A) Experimental (B) Theoretical (C) Solvated With CCl_4 (D) Solvated With DMSO

Nuclear Magnetic Resonance (^{13}C-NMR)



(A)



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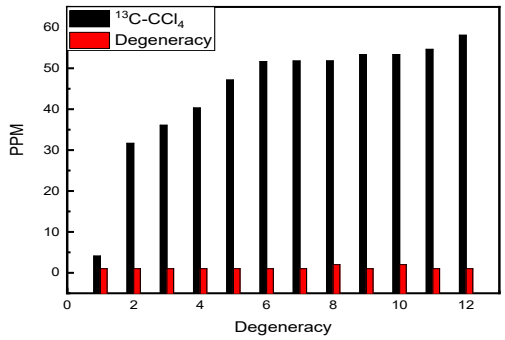

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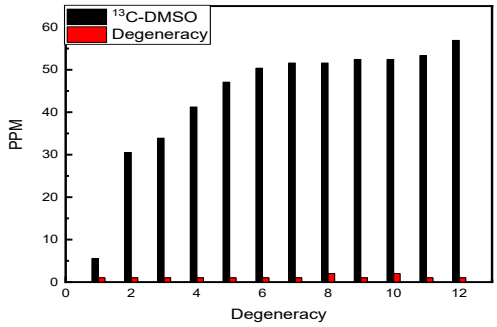

(D)

Fig 6. ^{13}C-NMR (A) Experimental (B) Theoretical (C) Solvated With DMSO (D) Solvated With CCl_4

Conclusion

In the current study, 4-phenyl-5-(2-thienyl)-2, 4-dihydro-3H-1,2,4-triazol-3-thion was synthesised experimentally and characterized by spectroscopic methods for the determination of the structure and purity of the synthesized molecule. The solvent effects on the molecules were theoretically explored. The optimized structure of the synthesized compound then underwent spectroscopic calculations to determine the theoretical spectroscopic parameters. A comparison was also performed between the theoretical and experimental datas. Finally, the effect of polar and non-polar solvent (DMSO and CCl4) on the optimized compound was analysed. It was found that the bandgap responded to the addition of solvent due to the involvement of the molecules in the solvent. The polar solvent had highest bandgap values due to the fact that the molecule is polar and it can interact more easily with polar solvent in comparison to non-polar solvent. This result indicate that polar solvent can be used to increase the effectiveness of the synthesised molecule in terms of medicinal value.

Acknowledgments

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