



Determination of ^1H and ^{13}C Nuclear Magnetic Resonance Chemical Shift Values of Glyoxime Molecule with Experimental and Theoretical Methods

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Abstract

In this study, the conformational analysis was performed by the semi-empirical PM3 method to determine the molecular structure of the glyoxime molecule. Each of conformer was optimized using the Density Functionals Theory (DFT) with DFT / B3LYP / 6-311G ++ (d, p) method basis set combination. As a result of the optimization, the most stable structure was determined according to the energy order. The chemical shift values of ^1H and ^{13}C , which were Nuclear Magnetic Resonance (NMR) parameters of this stable structure, were calculated in liquid phase and gas phase using DFT method and six different basis sets. Furthermore, the effect of intermolecular hydrogen bonding on ^1H chemical shift values was investigated by dimer molecular modeling at the level of B3LYP / 6-31G ++ (d, p) in the DFT method. Also, the ^1H and ^{13}C chemical shift values of the glyoxime molecule were determined experimentally. Structural analyzes of the glyoxime molecule were made by comparing the calculated NMR parameters with the experimental NMR parameters.

Keywords: Glyoxime, Nuclear magnetic resonance, Density functional theory, Hydrogen bonding.

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Gliksim Molekülünün ^1H ve ^{13}C NMR Kimyasal Kayma Değerlerinin Deneysel ve Teorik Metotlar ile Belirlenmesi

Özet

Bu çalışmada gliksim molekülünün moleküler yapısını belirlemek için konformasyon analizi yarı deneysel PM3 metodu ile yapılmıştır. Elde edilen konformasyonlar Yoğunluk Fonksiyonelleri Metodu (DFT) kullanılarak DFT/B3LYP/6-311G++(d,p) metot baz seti kombinasyonu ile optimize edilmiştir. Optimizasyon sonucunda enerji durumuna göre en kararlı yapı bulunmuştur. Bu kararlı yapıya ait Nükleer Manyetik Rezonans (NMR) parametreleri olan ^1H ve ^{13}C kimyasal kayma değerleri, DFT metodu ve 6 farklı baz seti kullanılarak sıvı fazda ve gaz fazında hesaplanmıştır. Ayrıca moleküller arası hidrojen bağının, ^1H kimyasal kayma değerlerine etkisi DFT metodunda B3LYP/ 6-31G++(d,p) seviyesinde dimer moleküler modellenmesi yapılarak incelenmiştir. Aynı zamanda gliksim molekülünün ^1H ve ^{13}C kimyasal kayma değerleri deneysel olarak da tespit edilmiştir. Hesaplanan NMR parametreleri ile deneysel NMR parametreleri karşılaştırılarak gliksim molekülünün yapı analizleri yapılmıştır.

Anahtar Kelimeler: Gliksim, Nükleer manyetik rezonans, Yoğunluk fonksiyonelleri teorisi, Hidrojen bağı.

1. Introduction

The Nuclear Magnetic Resonance (NMR) technique was a spectroscopic method used in natural sciences. The NMR technique helps explain the structures of the molecules by giving information about the electrons around nuclei that have non-zero nuclear spin [1,2]. Ab-Initio calculations give reliable results to define the molecular structures and NMR coupling constants for small and medium-sized molecules [3-11].

Some of the oximes have local anesthetic effects, while others have antimicrobial properties. Oxime derivatives with antimicrobial properties were used as

antibiotics in the health field [12-17]. Furthermore, some oxime derivatives have parasiticidal properties [18,19]. In addition, oximes were used in arrhythmia, intraocular pressure reduction, and in the treatment of some psychiatric disorders [20-22].

In this study, the most stable structure of the glyoxime molecule was determined by the theoretical calculations. The ^1H and ^{13}C chemical shift values of the most stable structure were calculated. The ^1H and ^{13}C chemical shift values of the glyoxime molecule were determined experimentally. Calculated chemical shift values were compared with experimental values. The effect of intermolecular hydrogen bonds on ^1H chemical shift values was investigated by theoretical calculations. As a result, the structure of the glyoxime molecule had been determined using the theoretical and experimental values.

2. Materials and Methods

2.1. Synthesis

The glyoxime sample used in the study was synthesized in chemistry department of Selcuk University Science Faculty. The synthesis method was carried out according to the literature [23]. Accordingly, 55 grams (1.37 mol) of NaOH are dissolved in 150 ml of water in ice bath and 139 gram (2 mol) of NH_2OHHCl is added. 1 mol 40% aqueous Glyoxal was slowly added to this cooled solution with ice bath and stirred for 15 minutes. The mixture, kept at room conditions overnight, was cooled to about 0°C and the resulting white precipitates were filtered, washed with cold water and dried in vacuum.

2.2. The measured ^{13}C and ^1H Chemical Shift Values of the Glyoxime Molecule

The ^1H and ^{13}C NMR spectra of the glyoxime molecule were recorded at room temperature in DMSO-d 6 solution using Varian 400 MHz NMR spectrometer in chemistry department of Selcuk University Science Faculty. Tetra methyl silane (TMS) was used as a reference sample in NMR measurements. The experimental chemical shift values were found with reference to the coupling constant values of the TMS molecule.

2.3. Computational Details

The correct determination of the NMR parameters of the glyoxime molecule depends on the knowledge of the molecular structure of the glyoxime molecule. Conformational analysis may be considered as the first step in the process of determining the molecular structure. Conformational space scanning of the glyoxime molecule was performed using the Spartan02 program and the PM3 semi-empirical method [24]. Conformational analysis of the glyoxime molecule was performed by giving 10° degree rotations to the single bonds. Optimization and harmonic frequency calculations for each of the 56 conformers obtained as a result of the conformational analysis were made using the DFT/B3LYP/6-311++G(d,p) method and basis sets [25]. According to the result of the harmonic frequency calculations, all points correspond to the local minima. Accordingly, the points found as a result of harmonic frequency calculations show stable regions on the potential energy surface. According to the results of these calculations, the most stable structure was determined by ordering the energies of the conformers. The ¹H and ¹³C experimental chemical shift values of the glyoxime molecule were determined relative to the ¹H coupling constant values of the Tetra methyl silan (TMS) molecule. In the theoretical calculations, the ¹H and ¹³C chemical shift values of the glyoxime molecule were also calculated relative to the ¹H and ¹³C coupling constant values of the TMS molecule. ¹H and ¹³C chemical shift values calculated as

$$\delta^H = \sigma_{TMS}^H - \sigma_{sample}^H$$

$$\delta^C = \sigma_{TMS}^C - \sigma_{sample}^C$$

In these equations δ^H : The chemical shift value of a hydrogen atom, σ_{TMS}^H : The coupling constant for the hydrogen atoms in the TMS molecule σ_{sample}^H : the coupling constants of the hydrogen atoms in the sample, δ^C : The chemical shift value of a carbon atom, σ_{TMS}^C : The coupling constant for the carbon atoms in the TMS molecule, σ_{sample}^C : the coupling constants of the carbon atoms in the sample.

Molecular coupling constants were calculated using DFT / B3LYP method and six different basis sets, for the determination of ¹H and ¹³C NMR chemical shifts of the

most stable structure of the glyoxime molecule in gas and solution phases. The ^1H and ^{13}C coupling constants of the TMS molecule were calculated for six basis sets and the chemical shift values were theoretically determined as described above. In addition, a dimer model of the glyoxime molecule was performed to study the effect of hydrogen bonding on ^1H chemical shift values. The DFT / B3LYP / 6-31 ++ G (d, p) method and basis set combination was used for dimer modeling. Both optimization and harmonic frequency calculations were performed with Gaussian03 program. ^1H and ^{13}C chemical shift values were calculated with the same program [26].

3. Results and Discussions

The property to be examined by a spectroscopic method in a molecule is closely related to the molecular structure. For this reason, while a spectroscopic property of a molecule is calculated, it is first necessary to know the molecular structure of the molecule.

The schematic representation of the most stable structure obtained as a result of the optimization process performed with the combination of the DFT / B3LYP/6-311++G(d,p) method base set was given in Figure 1. When the structure of the glyoxime molecule was examined, it can be said that the molecule was symmetrical and had C_{2h} symmetry.

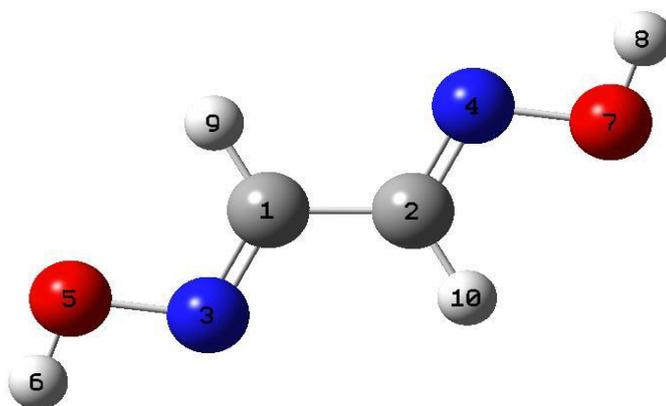


Figure 1 Schematic representation of the most stable structure of the glyoxime molecule [27]

Some bond lengths and bond angle values calculated in this work and X-ray study results were shown in Table 1 for the glyoxime molecule.

Table 1 Some bond length and bond angle values of molecule for X-ray structure and the calculated most stable structure [27]

Bond length	Calculated (Å)	X-ray structure (Å)
R(1,2)	1.4517	1.4528
R(1,3)	1.29086	1.2849
R(1,9)	1.09067	1.0926
R(2,10)	1.09067	1.0926
R(3,5)	1.39187	1.3854
R(4,7)	1.39187	1.3854
R(5,6)	0.96	0.9947
Bondangles (degree)	(°)	(°)
A(2,1,3)	117.635	118.00
A(2,1,9)	120.270	120.51
A(3,1,9)	122.095	121.49
A(1,2,10)	120.270	120.51
A(4,2,10)	122.095	121.49
A(2,4,7)	110.650	112.31
A(3,5,6)	102.448	104.76
D(3,1,2,4)	179.965	179.63
D(9,1,2,10)	179.907	179.16
D(2,1,3,5)	179.981	178.79
D(1,2,4,7)	179.982	178.79
D(1,3,5,6)	179.986	164.24

The calculated bond length and bond angle values for the glyoxime molecule were in good agreement with the values obtained from the X-ray spectrum. Therefore, the modeled structure that is theoretically determined could be used to calculate the chemical shift values of ^1H and ^{13}C of the glyoxime molecule. The chemical shift values of ^1H and ^{13}C of the glyoxime molecule were calculated in gas phase and liquid phase with 6 different basis sets in order to examine the effect of basis set and calculated environment in the calculation of chemical shift values.

The ^1H and ^{13}C NMR spectra of the glyoxime molecule were recorded in the DMSO- d_6 solution at room temperature for evaluating which basis sets were more

effective in chemical shift calculations in the glyoxime molecule. The recorded NMR spectra were given in Figure 2 and Figure 3.

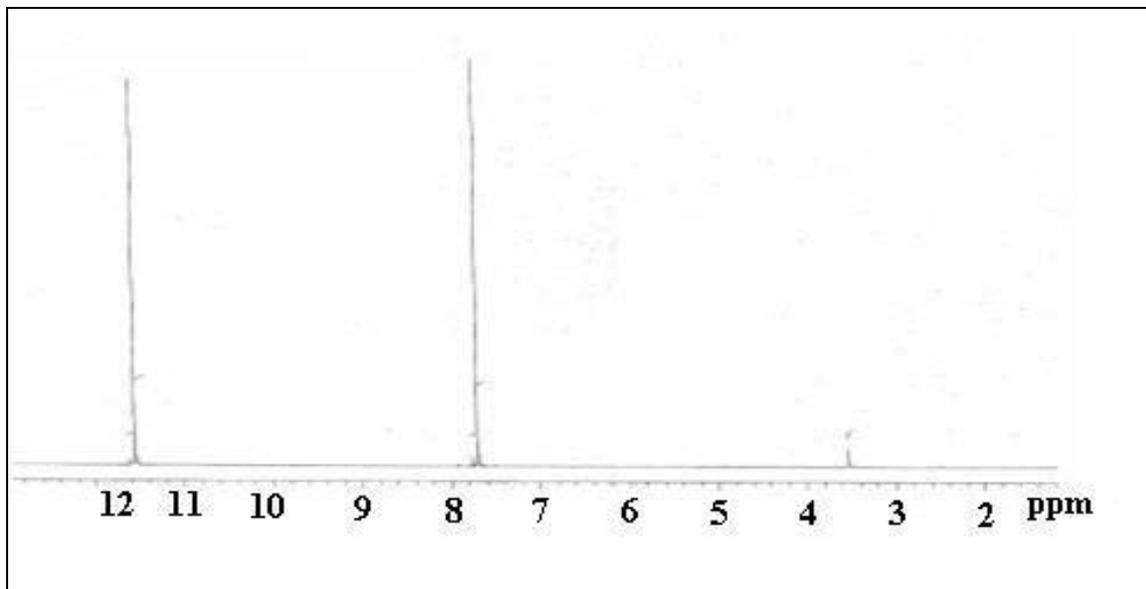


Figure 2 The ¹H chemical shift spectrum of glyoxime molecule in the DMSO-d₆ solution [27]

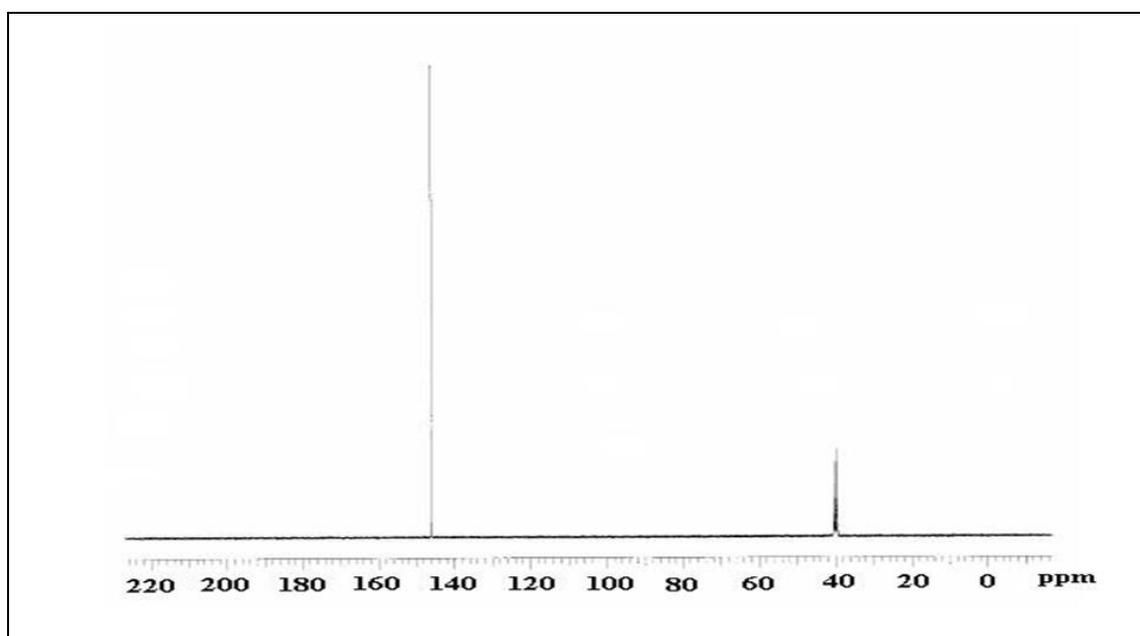


Figure 3 The ¹³C chemical shift spectrum of glyoxime molecule in the DMSO-d₆ solution [27]

Experimentally measured chemical shift values and chemical shift values calculated with 6 different basis sets in gas phase and liquid phase were given in Table 2.

Table 2 The calculated and measured chemical shift values of ^1H and ^{13}C for the glycoside molecule in gas phase and liquid phase [27]

Gas phase	H9 and H10 (ppm)	H6 and H8 (ppm)	C1 and C2 (ppm)
6-31G(d,p)	7.92	6.66	143.08
6-31+G(d,p)	8.16	6.69	146.30
6-311+G(d,p)	8.18	6.74	157.58
6-311G(d,p)	8.10	6.53	155.16
6-31++G(d,p)	8.16	6.69	146.30
6-311++G(d,p)	8.21	6.74	157.58
Liquid Phase (DMSO- d_6)			
6-31G(d,p)	8.16	8.32	144.69
6-31+G(d,p)	8.45	8.62	148.72
6-311+G(d,p)	8.50	8.40	160.29
6-311G(d,p)	8.36	8.21	157.18
6-31++G(d,p)	8.48	8.67	148.72
6-311++G(d,p)	8.47	8.47	160.29
Experimental (ppm)	7.7	11.5	146.07

The experimentally determined ^{13}C chemical shift values of the glyoxime molecule were 146.07 ppm as seen in Table 2. Considering the molecular structure of the glyoxime molecule, it was expected that carbon atoms will give a single peak. The chemical shift values of the carbon atom 1 and carbon atom 2 given in Figure 1 calculated with three base sets of 6-31G(d,p), 6-31+G(d,p) ve 6-31++G(d,p) were well matched to the experimental values both in gas phase and liquid phase. When the experimental ^1H NMR spectrum of the glyoxime molecule is examined, two distinct singlet peaks were observed.

These peaks were observed at 11.5 ppm and 7.7 ppm. The chemical shift corresponding to 11.5 ppm is thought to be the OH hydrogen of the molecule and the chemical shift corresponding to 7.7 ppm is thought to be the hydrogen bound to the carbon atoms. The difference between experimental values with calculated chemical shift values for 6 different basis set in solution and gas phase of H9 and H10 atoms was

less than 1 ppm. Therefore, the calculated chemical shift values and the experimental chemical shift values were in good agreement for H9 and H10 atoms. The difference between the experimental chemical shift values for H6 and H8 atoms and the chemical shift values calculated with 6 different base sets was about 5 ppm in the gas phase and about 3 ppm in the solution phase. According to these results, the theoretical chemical shift values were not in good agreement with experimental chemical shift values, for H8 and H6 atoms.

According to the literature research, chemical shift values of hydrogen atoms with hydrogen bonding were larger than chemical shift values of hydrogen atoms without hydrogen bonding [29,30]. Theoretical calculations show that the chemical shift values of OH hydrogens did not match the experimental chemical shift values since a single molecule approach was employed in solution. The glyoxim molecule was modeled as a dimer in solution to calculate the effect of the hydrogen bond on the ^1H chemical shift value, which was theoretically calculated. A schematic representation of the dimer molecular model was shown in Figure 4.

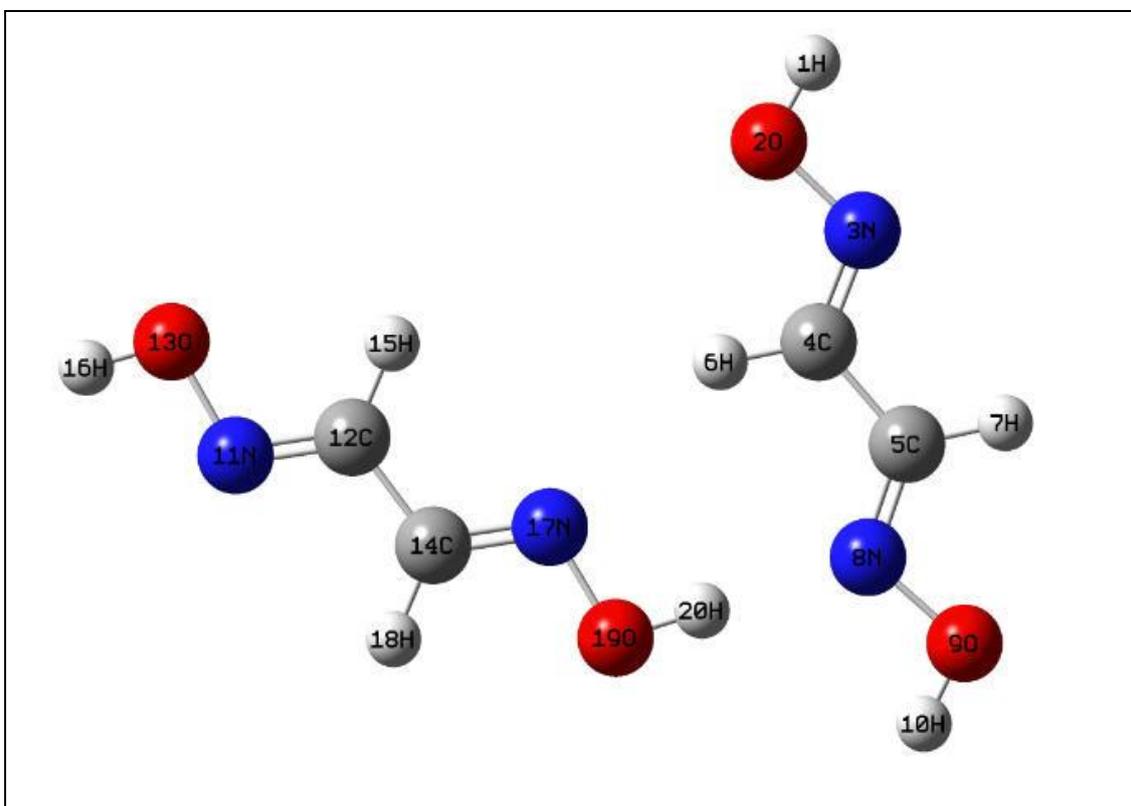


Figure 4 Schematic representation of the dimer modeling for glyoxime molecule [27]

The stable structure of the dimer model was calculated by the DFT / B3LYP / 6-311 ++ G (d, p) method basis set combination. The ^1H chemical shift values of the molecular dimer model were calculated in solution phase using the DFT/B3LYO/6-31++G(d,p) method and basis set combination. When Table 2 was examined, it appears that this method and basis set combination were suitable for the calculation. According to the results of the calculation, the chemical shift value of the hydrogen-bonding H atom was calculated as 11.3 ppm . This theoretical value was in very good agreement with the experimental value. Accordingly, the intermolecular hydrogen bonding significantly affect the ^1H chemical shift values, for the glyoxime molecule and this situation had been supported by the theoretical calculations.

Conclusions

In this study, the ^1H and ^{13}C chemical shift values of the glyoxime molecule were determined theoretically and experimentally. The experimental ^{13}C chemical shift values of the glyoxime molecule were consistent with theoretical calculated in the solution phase. However, it had been observed that the ^1H chemical shift values for the hydrogen atoms, which were formed hydrogen bonding, do not agree with the experimental values. Theoretical calculations had been carried out by using a dimer molecule approach instead of a single molecule approach for resolve this disagreement. It had been seen that theoretical and experimental values agree with each other as a result of the dimer molecular approach.

Accordingly, instead of the single molecule approach for ^1H chemical shift calculations in oxime molecules, at least a dimer molecule approach should be made and the hydrogen bond effect should be taken into account. If the calculations were performed in solution phase, both ^1H and ^{13}C chemical shift calculations would agree with the experimental values for oxime molecules.

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