

The computational analysis on NLO properties and molecular

docking studies for some cyclophosphazenes compounds

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Abstract- The hexakis-[30-(10,20,30-thiadiazol-40-yl)phenoxy] (5) and hexakis-[50-oxy-20-methylbenzothiazole] (6) cyclotriphosphazene derivatives were synthesized by Çiftçi et al. in 2017. The structural parameters for the compound (6) and the fluorescence properties for (5) and (6) were obtained experimentally. In this study, we researched to (5) and (6) compounds with computational chemistry method. The two compounds are optimized at B3LYP/6-31G(d,p) level in gas phase. The calculated bond length and bond angles are compared with experimental values. Also, nonlinear optic properties (NLO) are examined by using some quantum chemical parameters. Finally, the investigation for anticancer activity are made in molecular docking program. The binding energy and binding mode examined between the mentioned compounds with target protein. The target protein is determined as E. coli (PDB ID: 3T88).

Keywords- Cyclophosphazenes compounds, DFT, NLO properties, Molecular docking

1. Introduction

Cyclophosphazenes are inorganic heterocyclic compounds based on -P = N-repeat units. These compounds have been used in the preparation of functional materials in technology (such as organic light emitting diodes (OLED), fluorescent chemosensors), and in medical areas (such as anticancer agents and antimicrobial agents) [1,2]. Small ring heterocycles containing nitrogen and sulfur atoms are popular in recent research due to their synthetic diversity and therapeutic significance [3]. Non-linear optical materials have been tempted in recent years in terms of potential applications such as optical communications, optical computers, optical switching and dynamic imaging process. The molecules exhibit significantly NLO properties due to delocalized π electron moving along the molecule. NLO materials are categorized as semiconductor multilayer structures. Therefore, a wide variety of molecular systems inorganic, organic and organometallic were investigated for NLO activity.

1. Calculation methods

The structures of (5) and (6) compounds were drawn by Gaussian package programs GausView 5.0.8. All caltulations were made in Gaussian IA32W-G09RevA.02 and Gaussian AS64L-G09RevD.01 [4-6]. The cyclophosphazenes compounds were optimized by using B3LYP/6-31G(d,p) level in gas phase.

Non-linear optical (NLO) properties of cyclophosphazenes compounds were calculated in gas phase. NLO properties were compared to some quantum chemical parameters. These parameters are the highest occupied molecular orbital (E_{HOMO}), energy of the lowest unoccupied

molecular orbital (E_{LUMO}), ionization energy (I), electron affinity (A), energy gap (EGAP), absolute hardness (η), absolute softness (σ), optical softness (σ_0), absolute electronegativity (χ), chemical potential (CP), additional electronic charges (ΔN_{Max}) and polarizability (α), anisotropic polarizability ($\Delta \alpha$) and the first hyperpolarizability (β 0). Urea references material has been used in the determination of NLO properties. Therefore, these parameters are compared with those of ureas. These parameters were calculated according to Eq. (1) – (16).

$$I = -E_{HOMO} \tag{1}$$

$$A = -E_{LUMO} \tag{2}$$

$$E_{GAP} = E_{LUMO} - E_{HOMO} \tag{3}$$

$$\eta = \frac{I - A}{2} = \frac{E_{LUMO} - E_{HOMO}}{2} \tag{4}$$

$$\sigma = \frac{1}{\eta} \tag{5}$$

$$\chi = \frac{|I+A|}{2} = \frac{|-E_{HOMO} - E_{LUMO}|}{2}$$
(6)

$$CP = -\chi \tag{7}$$

$$\omega = \frac{CP^2}{2\eta} \tag{8}$$

$$N = \frac{1}{\omega}$$
(9)

$$\Delta N_{max} = -\frac{CP}{\eta} \tag{10}$$

$$S = \frac{1}{2\eta} \tag{11}$$

$$\mu = (\mu_x^2 + \mu_y^2 + \mu_z^2)^{\frac{1}{2}}$$
(12)

$$\alpha = \frac{1}{3}(\alpha_{xx} + \alpha_{yy} + \alpha_{zz}) \tag{13}$$

$$\Delta \alpha = \frac{1}{\sqrt{2}} \left[(\alpha_{xx} - \alpha_{yy})^2 + (\alpha_{yy} - \alpha_{zz})^2 + (\alpha_{zz} - \alpha_{xx})^2 + 6\alpha_{xz}^2 + 6\alpha_{yz}^2 + 6\alpha_{yz}^2 \right]^{\frac{1}{2}}$$
(14)

$$\sigma_o = \frac{1}{E_{GAP}} \tag{15}$$

$$\beta_0 = \left[(\beta_{xxx} + \beta_{xyy} + \beta_{xzz})^2 + (\beta_{yyy} + \beta_{yzz} + \beta_{yxx})^2 + (\beta_{zzz} + \beta_{zxx} + \beta_{zyy})^2 \right]^{\frac{1}{2}}$$
(16)

2. Result and discussion

2.1. The structures of cyclophosphazenes compounds

The cyclophosphazenes compounds are optimized at B3LYP/6-31G(d,p) level in gas phase. 2D structure are shown in Figure 1.



Figure 1. 2D structure of cyclophosphazenes compounds.

2.2.Structural parameters of cyclophosphazenes compounds

Experimental parameters are available for (6) compound. The structural parameters are calculated at the B3LYP/6-31G(d,p) level. For the (6) compound, the calculated bond lengths and bond angles were compatible with the experimental data. The experimental bond lengths and bond angles are not available for (5) compound. Structural parameters were proposed as a result of the calculation for the (5) compounds. According to Table 1, the bond lengths and bond angles are the cyclophosphazene ring and its periphery.

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Bond lengths (Å)					
(6) comp.	Exp.	Calc.	(5) comp.	Calc.	
N1-P1	1.5763	1.6060	N1-P1	1.5939	
N2-P1	1.5757	1.5972	N2-P1	1.5935	
N3–P3	1.5762	1.5940	N3–P3	1.5961	
O2–P1	1.5840	1.6119	O2–P1	1.6290	
N1-P3	1.5785	1.5937	N1-P3	1.6316	
N2-P2	1.5779	1.5940	N2-P2	1.6064	
N3-P2	1.5829	1.6056	N3-P2	1.5968	
O4–P2	1.5920	1.6269	O4–P2	1.6239	
O1–P1	1.5945	1.6235	O1–P1	1.6316	
O3–P2	1.5815	1.6101	O3–P2	1.6110	
O5–P3	1.5807	1.6288	O5–P3	1.6096	
O6–P3	1.5863	1.6315	O6–P3	1.6270	
Bond angles (°))				
P1-N1-P3	120.29	121.50	P1-N1-P3	121.42	
P3-N3-P2	121.63	121.30	P3-N3-P2	123.19	
N2-P1-N1	118.53	117.32	N2-P1-N1	119.31	
N3-P3-N1	117.64	117.50	N3-P3-N1	117.42	
N2-P2-N3	117.38	117.50	N2-P2-N3	117.27	
P1-N2-P2	121.89	123.05	P1-N2-P2	121.42	

Table 1. Selected bond lengths	(Å) and bond angles	(°) for ((5)) and ((6))
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2.3. NLO properties

NLO properties are the most essential feature in optical devices and telecommunication materials. In cyclophosphazenes compounds, π molecules reveal the presence of NLO properties due to electron delocalization. NLO properties can be determined numerically by computational chemistry methods. These numerical data are obtained by quantum chemical descriptors and form a criterion for the studied compounds. Urea is often used as a reference in these studies. Therefore, urea is calculated at the same level and given. The calculated quantum chemical identifiers are given in Table 2.

same level of theory in gas phase				
Parameters	Urea	(5)	(6)	
E _{HOMO} ^a	-6.899	-6.370	-6.139	
E_{LUMO}^{a}	1.070	-1.346	-1.086	
I ^a	6.899	6.370	6.139	
A^{a}	-1.070	1.346	1.086	
$E_{GAP}{}^{a}$	7.968	5.024	5.053	
η^{a}	3.984	2.512	2.527	
σ^{b}	0.251	0.398	0.396	
$\sigma_{O}{}^{b}$	0.125	0.199	0.198	
χ^{a}	2.914	3.858	3.613	
CP ^a	-2.914	-3.858	-3.613	
ω	1.066	2.962	2.583	
Ν	0.938	0.338	0.387	
ΔN_{Max}	0.732	1.536	1.430	
S	0.251	0.398	0.396	
μ	1.6955	2.6996	0.5843	
α^{c}	2.9522	68.84134	79.0509	
$\Delta \alpha^{c}$	10.7676	178.3952546	2.29×10^{1}	
β_0^d	4.3100	202.4483696	2.88×10^{1}	
^a in eV				
^b in eV ⁻¹				
^c in Å ³ .				
^d in cm ⁵ /esu.				

Table 2. Calculated quantum chemical parameters a	it
same level of theory in gas phase	

HOMO energy, which is the chemical parameter of quantum, is the first basic parameter in determining the activity and NLO properties of molecules. If HOMO's energy level is high, the electrons in HOMO move more easily, and the activity of the molecules of the NLO increases with the increase in electron mobility. According to the HOMO energy level, the NLO activity sequence should be as follows:

(6) > (5) > Urea

The other quantum chemical parameter is LUMO energy. The low value of LUMO means that the electrons can be easily fixed in LUMO. Therefore, the NLO activity of the molecules increases with the decrease of the LUMO energy level. According to the LUMO energy level, the NLO activity sequence should be:

(6) > (5) > Urea

The other parameter is the energy gap between LUMO-HOMO. Reduction of the energy gap means increased electron mobility and the NLO feature increases. According to EGAP, the activity sequence of NLO should be as follows:

(5) > (6) > Urea

Chemical hardness and softness are the parameters derived from HOMO and LUMO energy. If the softness of a chemical species increases or hardness of a chemical species decreases, the polarizability of the electrons in the molecule can be increased. An increase in polarizability in the molecule means an increase in NLO activity. In terms of these explanations, the ranking of the NLO activity should be as follows:

(5) > (6) > Urea

The optical softness is one of the important parameters in determination NLO activity. The increasing of optical softness means the increasing of NLO properties. The NLO activity ranking should be:

(5) > (6) > Urea

Absolute electronegativity and chemical potential are parameters associated with NLO properties. Electron delocalization increases with the decrease of absolute electronegativity. In addition, there is a direct correlation between NLO proporties and chemical potential. According to these parameters, the NLO activity ranking of the specified compounds should be as follows:

Urea > (6) > (5)

The other identifier is electronic charge. Electronic charge is related to the polarization of the molecule. As in the parameters of hardness and softness, the NLO property increases as the electronic charge increases. As a result, the NLO activity of the molecule must be as follows::

(5) > (6) > Urea

Other parameters are polarization, anisotropic polarization and hyperpolarized availability of molecules. In fact, the relationship of NLO properties with quantum chemical parameters has been first discussed with these parameters. NLO features are increasing with the increase of these identifiers. NLO activity ranking should be:

(6) > (5) > Urea (in α and $\Delta \alpha$)

 $(6) > (5) > Urea (in \beta)$

According to the ranking above, the NLO properties of the related compounds are better than those produced. The (6) compound can be considered as the best NLO material. The results were graphically given in Figure 2, according to the polarization, anisotropic polarization and hyperpolarized availability.



Figure 2. The graphically results of NLO proporties

2.4. Molecular docking

In recent years, molecular docking studies in anti-cancer and anti-bacterial studies have attracted great attention. The binding energy obtained by molecular docking between computational chemistry methods can be correlated with the experimentally determined half maximum inhibitory concentration (IC50) [7]. This feature is the main goal in the development of new and more effective drugs. In this study, docking studies were calculated for compounds in order to predict their affinity to bacterial protein DNA, from E. coli. The structure representing Crystal structure of Escherichia coli MenB in complex with substrate analogue, OSB-NCoA (PDB ID:3T88) was chosen as the target protein and the studied compounds are docked with target protein in DockingServer. The binding mode for each ligand-protein complex, secondary chemical interactions, and potential interactions with amino acid residues at the site of binding were investigated. The determined binding mode for compounds (5) and (6) is pictured in Figure 2. The analysis of the positional poses and the interaction energies for the studied compounds are shown in Table 3. The score values showed that the binding positions of (6) were weaker than (5). In addition, although the H-bond is not present in the molecule (5), the binding energy is higher. This shows that polar interactions in nonoptimal ligand enzyme interactions play an active role.

Componds	$\Delta G_{ ext{bind}}$	N-H···X	Polar contacts	Hydrophobic
				contacts
(5)	-4.94 kcal/mol	-	ARG45, GLN88,	ILE131
			LYS89, GLN189	
(6)	-0.58 kcal/mol	N-H···GLN43	ARG45, LYS89	TYR129

Table 3. Binding free energy (ΔG_{bind}), intramolecular hydrogen bonds (N-H···X), polar and hydrophobic contacts in the investigation compounds



Figure 3. The binding modes of (5) and (6)

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