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Theoretical study of Z- and E-isomers of some hemithioindigo-based peptide-switches

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ABSTRACT

Quantum chemical calculations of some hemithioindigo-based peptide-switches have been performed with the aim to demonstrate their cis (Z) and trans (E) properties and to describe the change of their quantum quantities as a result of the Z/E isomerization of these compounds. The effects of substituents, especially their nature and position of the substituents, with changing meta/para-substitution-pattern at the stilbene-part of the molecule, on electronic, optical, spectroscopic and other properties of these molecules, have been characterized with DFT and TDDFT methods The results of this work show that compound c with the strongest electron donating group (amino-group) in the para position of the stilbene-part, especially the E-isomer of this compound, has the convenient quantum properties. This compound shows higher NLO properties, higher chemical softness, higher absorption maximum wavelength, higher electrostatic potential values and in contrast, lower HLG, lower chemical hardness and lower thermodynamic properties, which these results are in agreement with the experimental results.

1. Introduction

Photo-switchable molecules that exist in two – or sometimes more – molecular states with various physical properties and undergo reversible structural changes from one state into the other by simple light radiation, have been employed in different fields ranging from material science to biology [1–5]. Nowadays, photoswitches have been used in different biological functions such as ion transport [4–7], biocatalysis [5,8,9], cell adhesion [5,10] and protein folding [4,5,11,12]. The structure of bio-molecules containing molecular-switches can be altered using light which causes new applications in biology and medicine. So, the biological activity of these molecules is changed by light-triggering [5,13]. Therefore, molecular switches have some important applications in the field of biological sensing and molecular machines, with supplementary advantages of being biodegradable and biocompatible for in vivo applications [14]. Most studies have been focused on chemical alteration of nucleotides, proteins, peptides and lipids containing azobenzene as a popular reversible photoswitch [4–11]. Several types of compounds based on azobenzene-based amino acids such as APB ((4-amino)phenylazobenzoic Acid), AMPB ((4-aminomethyl) phenyla-zobenzoic acid) and AMPP (3-(3-aminomethyl) phenylazo]phenylacetic acid) [13–19] have been used for specific biological systems. Azobenzene molecule can induce the strong geometrical changes of these bio-molecules through isomerization around N=N double bond in response to light radiation, while photoswitching of dithienylethenes or spiropyranes causes the considerable changes of electronic properties [1,15,20,21]. However azobenzene derivatives are well known, but because of the stability of azobenzene chromopeptides intensely depend on their chemical environments, the use of azobenzene photoswitch inside living organisms or in vivo/vitro studies may be restricted. Hence, it is necessary to search for substitute switching molecules [13,15]. In this context, new photoswitches with convenient optical properties have been considered. Compared to the most popular photoswitches such as azobenzenes, dithienylethenes or spiropyranes, hemithioindigos (HTIs) have preferable and very interesting physical and photophysical properties. HTIs have been known as an interesting class of photoswitches because of the frequent reversibility of the isomerizations or the thermal stability of the photochromic states, in addition to their other useful properties [1,4,5,22].

Hemithioindigos are asymmetrical molecules comprising of a thioindigo part, which is linked to a stilbene part through a central C=C double bond which this double bond causes that HTIs can be switched by light radiation between the thermodynamically most stable Z-isomer and the metastable E-isomer. The most fascinating

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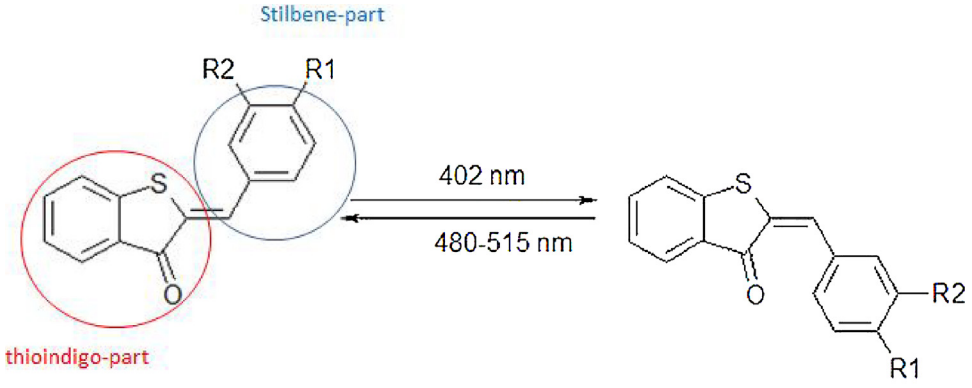
property of HTIs is photoisomerization in both Z–E and E–Z instructions through visible light which is more beneficial compared to the application of UV light for azobenzenes isomerization. The Z-isomer and E-isomers of HTI show absorption maxima at λ_{max} of 430 nm and 460 nm, respectively [1,2,23–25].

One category of the chromopeptides based on hemithioindigo is hemithioindigo (HTI)-based ω-amino acids which can work as peptide-switches, has been established with a linear- and cyclic-peptide structure. They are beneficial for the light variation of protein structure and related biological systems with great spatial and temporal regulation [13,15,24,26]. Recently, some of new HTI-based ω–amino acids have been synthesized where an alternation in the replacement-part of the stilbene-fragment of the molecules leads to molecular-photoswitches with optimized properties for primary investigations in protein folding. The structures of these molecules have been shown in Fig. 1, which different substituent groups have been exchanged in the para (R1) and meta (R2) positions. Fig. 1 shows that the HTI-peptides can isomerize around their central C=C double bond upon UV–vis-illumination. In this group of HTI-compounds, the carboxy group is constantly linked to the thioindigo-part and different amino-groups, which are electron donating groups, are linked to the stilbene-part in the para (R1)- or meta (R2)-positions. These two binding locations provide significant changes when the HTI-amino acid is applied as a switchable trigger for various protein and peptide structures. These compounds can be classified into two groups: a and b are known as “Normal” HTIs which have a methylene-piece that forbids direct contact of the amino-group with the chromophore. The c, d and e compounds which are known as “electron-rich” HTIs, have an amino or NHBoc groups that directly linked to the stilbene-portion. These HTIs compounds have been known as important photo-switchable trigger components [13].

Because of these HTI peptide-switches have not been studied by quantum computational methods to date, quantum chemical calculations have been performed on both Z- and E-isomers of these structures to describe the effects of different substitutions on the R1 and R2 positions of both Z- and E-isomers of these peptides and to compare some of the computed quantum parameters of these structures in order to description and correlation between the experimental biological properties of Z- and E-isomers of these HTI-peptides and their quantum parameters. The geometrical structure, electronic properties, nonlinear optical properties, electronic absorption spectra, MEP analysis, thermodynamic properties and other molecular properties of Z- and E-isomers of these HTI-peptide-switches on the basis of density functional theory (DFT) and time-dependent DFT (TDDFT) methods, are the main purpose of this work.

2. Computational methods

In this work, quantum chemical calculations on Z- and E-isomers of some of the HTI-peptide-switches have been performed by DFT and TDDFT methods. With the purpose of more understand the effects of various substituents on the electronic, optical and spectroscopic properties of this class of compounds, three hemi-thioindigo derivatives have been studied theoretically. The substituent groups are changed by substituting the R1 and R2 positions of these isomers that shown in Fig. 1. All calculations in this study, have been performed using Gaussian 09 package [27]. All the ground states structures have been optimized by DFT [28] with the Becke’s three-parameter hybrid function (B3) and the Lee–Yang–Parr nonlocal correlation function (B3LYP) [29–31] and 6-311 + G(d,p) basis set. 6-311 + G(d,p) basis set has been used with the aim of obtaining more exact results by using triple split valence basis set beside the polarization fnctions ((d,p) or (**)), which adds p functions to hydrogen atoms in addition to the d functions on heavy atom and diffuse function (+) which adds diffuse functions to the heavy atoms. These compounds have been dissolved in methanol [13]. Therefore, the solvent effects were simulated by the conductor polarizable continuum model (CPCM) [32–34]. The optimized structures were used in the frequency calculations at the same method to confirm that the optimized structures reach a stationary point and to calculate polarizability, hyperpolarizability and thermodynamic parameters of these molecules. The natural population analysis (NPA) and Molecular electrostatic potential (MEP) analysis of these compounds were computed at the same level. Also, the linear response time-dependent DFT (LR-TDDFT) method with the long-range-corrected CAM-B3LYP/6-311 + G**



a : R1=CH_2NH_2 , R2=H (Normal-HTIs)

b : R1=H , R2=CH_2NH_2 (Normal-HTIs)

c : R1=NH_2 , R2=H (amino-substituted HTIs)

d : R1=NHBoc , R2=H (amino-substituted HTIs)

e : R1=H , R2=NHBoc (amino-substituted HTIs)

Fig. 1. Structure of the examined HTI-peptide switches. Compounds have been described in Ref. [13].