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Symmetry adapted cluster–configuration interaction calculation of the photoelectron spectra of famous biological active steroids

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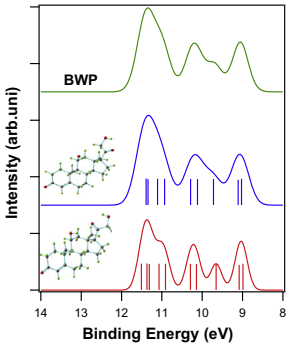
HIGHLIGHTS

- Gas phase ionization energies of important steroids were calculated.
- Population ratios of conformers of each steroid were calculated in the gas phase.
- Ten ionization energies were calculated for each steroid.
- The spectral bands of each steroid were assigned by NBO calculations.
- The calculated photoelectron spectra were in good agreement with the experiment.

GRAPHICAL ABSTRACT



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ABSTRACT

The photoelectron spectra of some famous steroids, important in biology, were calculated in the gas phase. The selected steroids were 5α-androstane-3,11,17-trione, 4-androstane-3,11,17-trione, cortisol, cortisone, corticosterone, dexamethasone, estradiol and cholesterol. The calculations were performed employing symmetry-adapted cluster/configuration interaction (SAC–CI) method using the 6-311++G(2df,pd) basis set. The population ratios of conformers of each steroid were calculated and used for simulating the photoelectron spectrum of steroid. It was found that more than one conformer contribute to the photoelectron spectra of some steroids. To confirm the calculated photoelectron spectra, they compared with their corresponding experimental spectra. There were no experimental gas phase He—I photoelectron spectra for some of the steroids of this work in the literature and their calculated spectra can show a part of intrinsic characteristics of this molecules in the gas phase. The canonical molecular orbitals involved in the ionization of each steroid were calculated at the HF/6-311++g(d,p) level of theory. The spectral bands of each steroid were assigned by natural bonding orbital (NBO) calculations. Knowing the electronic structures of steroids helps us to understand their biological activities and find which sites of steroid become active when a modification is performing under a biological pathway.

Introduction

Generally, steroids are known as hormones in biology. Hormones are materials which are produced at one site in the body of organism and acts at the other site. All steroid hormones are derived from cholesterol by a number of precise modifications to the cholesterol structure, with different series of modifications occurring in different pathways [1]. The main skeleton of molecular structure of steroid is composed of the ring system of three cyclohexanes and one cyclopentane in a fused ring system and different functional groups can be attached to this fused ring system [2] (see Scheme 1). The biological activities of steroids depend on

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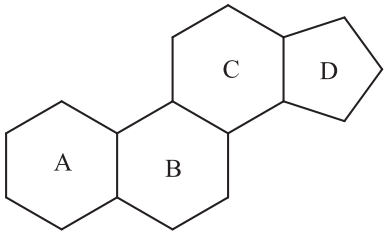

Scheme 1. Simple basic molecular structure of steroids considered in this work.

their structures [3–5] so that a little change in their molecular structures vary the number of populated conformers of steroid in the gas phase and yields dramatic changes of intensity and modes of action [6]. Change in the action of steroid has direct correlation with its electronic structure. Another important aspect of steroids which has direct correlation with their electronic structure is finding the region of steroid which can be attacked in biological pathways.

One of the best methods to obtain information about the electronic structures of molecules is photoelectron spectroscopy. Among the considered steroids in this work, there are only the experimental gas phase He—I photoelectron spectra for 5α-androstane-3,11,17-trione [7], corticosterone [8] and a thin film of cholesterol on hydroxypropionitrile solution running down a tungsten rod [9] in the literature. There are a limited number of theoretical works on the electronic structure of steroids in the literature which they use semi-empirical methods for calculating the ionization and molecular orbital energies of different series of steroids [7–15]. The semi-empirical methods used in this context are AM1, MNDO and HAM/3. The only *ab initio* calculation on the electronic structure of steroids is related to the work of Pasa-Tolic et al. [9]. which performed simple *ab initio* calculations on 5α-androstane steroid by self-consistent field (SCF) method using a very small basis set (STO-3G). It should be mentioned that the electronic correlations which are important in the energy order of molecular orbitals of each compound are absent in the computational methods used for the steroids in the literature. The selected steroids in this work are 5α-androstane-3,11,17-trione, 4-androstane-3,11,17-trione, cortisol, cortisone, corticosterone, dexamethasone, estradiol and cholesterol. One of the motivations for calculating the ionization energies of the steroids in this work is that the electronic structure of steroid is an important factor in determining its biological activities. Therefore, calculating the ionization energies of steroids and assigning their photoelectron spectra helps us to understand their electronic structures and find the most probable ionization sites in them relevant to their biological activities. The other motivation is that there is no report, experimentally and theoretically, on the gas phase ionization energies of some considered steroids in this work

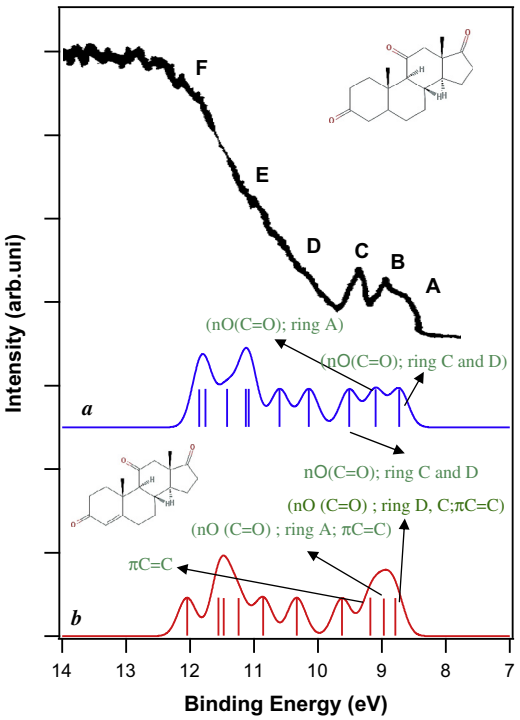

Fig. 2. (a) The experimental He—I photoelectron spectrum of 5α-androstane-3,11,17-trione [6] (black solid line) compared with its calculated photoelectron spectrum obtained using SAC–CI SD-R/6-311++G(2df,pd) level of theory (blue solid line). The calculated spectrum has been shifted as +0.8 eV (see '5α-Androstane-3,11,17-trione'). (b) Red trace shows the simulated photoelectron spectrum of 4-androstene-3,11,17-trione obtained at the same level of theory. Vertical lines show the energy position and intensity of the calculated ionization bands. The arrows in the figure show the assignment of the selected ionization bands. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

except for 5α-androstane-3,11,17-trione and corticosterone. Some of the steroids have a lot of conformers in the gas phase and using the theoretical calculations with the aid of the experimental photoelectron spectrum, it is possible to understand which conformers have dominant contributions in the spectrum of steroid and are responsible for the biological activity of steroid.

The gas phase experimental and theoretical information on the fundamental properties of biological molecules are very important in understanding many biological phenomena and providing insight into the physicochemical origin of the properties of biological molecules. One of the most important physicochemical properties of biomolecules is their ionization potentials which are useful quantum mechanical diagnostics for oxidative potentials of these

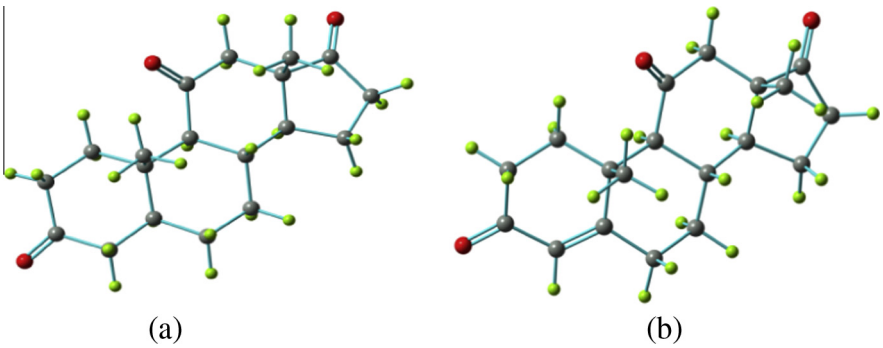

Fig. 1. The molecular structures of (a) 5α-androstane-3,11,17-trione and (b) 4-androstene-3,11,17-trione.