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Ionization energies and photoelectron spectra of fat-soluble vitamins in gas phase: theoretical study

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ABSTRACT

The electronic structures and photoelectron spectra of several fat-soluble vitamins including A (all-*trans*-retinol and its two derivatives (13-*cis*-retinoic acid and all-*trans*-retinoic acid)), D2, D3, E (consisted of α-Tocopherol, β-Tocopherol, γ-Tocopherol, δ-Tocopherol) and K were studied, theoretically in this work. For this purpose, the vertical ionization energies of these compounds, considering the electron correlations, were calculated in the gas phase. The direct symmetry adapted cluster/configuration interaction method which employs the single and double excitation operators (Direct-SAC-CI SD-R) and D95(df,pd) basis set was used for the calculations. It was found that more than one conformer contribute in the photoelectron spectrum of vitamin A, all-*trans*-retinoic acid, D2 and D3 which shows that there is more than one biological active form for these vitamins. The photoelectron spectrum of each vitamin was simulated, assigned and the previous assignments, reported in literature, were revisited. It was found that the ionization of vitamin D from HOMO-2 and the lone electron pairs of oxygen atom do not take place below 10 eV. Also, the first ionization band of vitamin E was assigned to the ionization from $\pi_{C=C}$ and $\pi^*_{C=C}$ of its aromatic ring unlike the previous assignment that this ionization band is related to the lone electron pair of oxygen atom. In addition, it was found that the ionization of vitamin A and its derivatives from the lone electron pairs of oxygen atoms does not occur below 11 eV in the gas phase.

Keywords: Ionization Energy; Fat-Soluble Vitamins; SAC-CI; photoelectron spectrum; Vitamin A; Vitamin E; Vitamin K

Introduction

Vitamins are important micronutrients that our body needs to them in small amounts for different activities throughout the human body[1]. They are divided into two groups: water-soluble involved B-complex and C vitamins and fat-soluble vitamins included A, D, E and K[2]. Vitamin A has main role in different biologic processes related to growth, cellular differentiation and interactions of cells with each other or with the extracelluar matrix[3]. Vitamins D are classified as steroid hormones because their molecular structures and biological activities are similar to steroids[4]. The most well-known of those vitamins regulate the activity of Ca^{+2} and PO_4^{-3} in the gut and kidneys[5]. Vitamin D3 is converted to 1,25-$(OH)_2D_3$ which represents an active form of the vitamin and is a recognized nuclear receptor[5]. Vitamin K is an essential cofactor for producing proteins that bind calcium, supporting cardiovascular and bone health[6]. Vitamin K2 is more efficient than K1 because it remains in body longer and is active in more tissues[7]. Vitamin E benefits the body by acting as an antioxidant and protecting vitamins A and C, red blood cells and essential fatty acids from destruction[8]. Vitamin E serves as an antioxidant, protecting the body from damage due to free radicals also is important for protecting cell membranes [9]. Vitamins are extremely sensitive to light. Water–soluble light sensitive vitamins include C, B12, B6, B2 and B9[10] and fat-soluble light sensitive vitamins include A, K and E [9].Most studies, regarding the interaction of light with vitamins, are related to the wavelength of 290-700 nm which include both ultraviolet (UV) and visible light [9]. For example, Kagan et al.[11] investigated the effect of UV light on vitamin E and found that this vitamin may act in two conflicting manners upon solar illumination in skin: in addition to its antioxidant function as a peroxyl radical scavenger, it may act as an endogenous photosensitizer, enhancing light-induced oxidative damage[10].

The intrinsic properties of biomolecules, which are hidden in the complex media of natural biological systems, can be revealed by theoretical and experimental studies in an isolated environment conducted in gas phase[12]. In this case, a detailed understanding of the structures, dynamics of biomolecules and distinction between intrinsic properties and those due to environmental interactions can be obtained. For example, the effect of bulk hydration and the interaction of other ions in the biological environment causes to large change in the electronic structure of biological molecule which in turn has effect on its different chemical and physical properties of the molecule. Change in the electronic structure of molecule in the biological media is accompanied with the change in their orbital energies and possibly reordering the orbital energies. This has effect on the vertical ionization energy and vertical excitation energy of molecule. Comparing the valence ionization and excitation spectrum of a biomolecule in gas phase with that in solutions provides enables an understanding of how the biomolecule bonds and interacts with its surroundings. For example, Ghosh et al. studied the effect of hydration on the vertical ionization energy of thymine, theoretically[13]. They found that microsolvation reduces the ionization energy by about 0.1 eV per water molecule, while the first solvation shell increases the ionization energy by 0.1 eV compared to gas phase. As an another example, Slavicek studied theoretically and experimentally the effect of water solvent on the vertical ionization energy of cytidine and deoxythymidine and compared it with the gas phase[14].They reported that upon bulk hydration, the ionization potential of the base becomes insensitive to the presence of the sugar and phosphate unlike to what is seen in the gas phase. Based on these explanations, the ionization energies of biomolecules in the gas phase is very important.

Knowing the gas phase ionization energies of vitamins is one of the most important and fundamental properties of these biological molecules which could be used for understanding

some of the biological phenomena that they contribute. For example, the vertical ionization energies of different forms of vitamin *E* can be used as a diagnostic value for the variation of the activation energy of antioxidant reaction of this vitamin.[15] In addition, measuring the ionization energies of vitamins provide information about the oxidative potential of these molecules and can be used as a scale for comparing their oxidation potential when contribute in electrochemical reactions. The assignment of the photoelectron spectra of vitamins is also important for unraveling the mechanism of damage of vitamin due to photoionization because it determines the place of ionization in the vitamin molecule. Knowing the place of ionization in the different ionic state of vitamin allow us to obtain information about how the vitamin is fragmented in its excited ionic states after ionization.

One of the best methods for measuring the ionization energies of molecules in the gas phase is photoelectron spectroscopy[16,17,18]. The most challenging part of gas phase photoelectron spectroscopy, especially in large biomolecules, is decomposing and degradation of the sample before reaching to the gas phase. In this case, calculating the gas phase ionization energies and photoelectron spectra of biomolecules with a very accurate computational method is useful and provides information about the ionization in the gas phase. Although, there are many experimental studies on the interaction of UV light with vitamins in solution but, there are a limited number of studies in literature related to the ionization of vitamins in the gas phase using UV and X-ray light. Jericevic et al[19]. Recorded the He-I photoelectron spectra of some derivatives of vitamin A including *trans*-retinoic acid, *trans*-retinal, and β-carotene in the gas phase. Katsumata et al. recorded the first He-I photoelectron spectrum of vitamin A in the gas phase[20]. Novak et al. have been studied the electronic structures of vitamin D2 and D3 using photoelectron spectroscopy technique[5] and found that vitamins D have steroid structures because

of the similarity of their photoelectron spectra with the spectra of steroids. There are no high level theoretical calculations on the ionization energies and photoelectron spectra of vitamin D and its derivatives in literature. Nagaoka et al. recorded the He-I photoelectron spectrum of vitamin E and its derivatives. There is no experimental photoelectron spectrum for vitamins K in literature. The aim of this work is to calculate the vertical ionization energies of fat-soluble vitamins including A (all-*trans*-retinol and its two derivatives (13-*cis*-retinoic acid and all-*trans*-retinoic), D2, D3, E (consisted of α-Tocopherol, β-Tocopherol, γ-Tocopherol, δ-Tocopherol) and K, considering electron correlations, to study their electronic structures, simulate and assign their photoelectron spectra.

COMPUTATIONAL METHOD

The Direct SAC-CI-SD-R method considering the single and double excitation operators was employed in this work. Direct SAC-CI method is another version of SAC-CI-SD-R which uses a direct configuration interaction like algorithm that is combined with the perturbation selection technique is efficient especially for large molecules[21,22,23,24,25,26,27]. An advantage of this method is that the computational time becomes shorter compared to the standard version of SAC-CI code. It should be mentioned that the direct version of SAC-CI predicts the relative energies of ionization bands very well and this has been confirmed by calculating the ionization energies and photoelectron spectra of caffeine, xanthine and hypoxanthine in our previous work[28]. The active space, consisted of the same number of unoccupied orbitals, was employed in the calculations for all compounds and only 1s orbital was frozen as core orbital. The calculated SAC wave function, as the wave function of ground electronic state, was chosen for the SAC-CI calculations. The D95(df,pd) basis set was used for the calculations. It is notable that the absence

of the diffuse functions in the basis set has been compensated by adding more polarization functions to the basis set. Geometries of the conformers of each vitamin were optimized at the B3LYP/6-31+G(d) level of theory and their standard Gibbs free energies were calculated at the same level of theory to obtain their Boltzmman population ratios (BPR) in the gas phase. The calculated BPR of the conformers of each vitamin were used for simulating its photoelectron spectrum. The ionization cross sections were calculated using the monopole approximation[29], which allows the correct estimation of the relative intensities of ionization bands. Furthermore, natural bonding orbital (NBO) calculations using Gaussian NBO (version 5)[30] were performed at the Hartree-Fock (HF) level of theory using D95(df,pd) basis set to determine the localization of the canonical molecular orbitals at the ground electronic state for the spectral band assignment. All of the calculations were performed using the Gaussian Quantum Chemistry Package[31].

Result and discussion

Vitamin D

In this part, the results of the calculations for vitamin D2 and D3 are presented. Generally, there are twenty and eight conformers for vitamin D2 and D3, respectively. Thermochemistry calculations, performed in this work, showed that only two and three conformers are populated in the gas phase for vitamin D2 and D3 at 406 K, respectively (Figure 1). These conformers are also responsible for the biological activity of vitamin D2 and D3 in solution. Figure 1 shows that there are three distinct moieties within the molecular structure of vitamin D including the rings of molecule, side chain and C=C bonds[5]. The population ratios of conformers have also been reported in Figure 1. The selected temperature for the thermochemistry calculations is equal to the temperature selected by Novak et al[5] for sublimating of vitamins D to record their photoelectron spectra. Table S1 reports the calculated HF energies

of molecular orbitals of conformers of vitamin D2 and D3 obtained from HF calculations using D95(df,pd) basis set. In addition, the results of NBO calculations to obtain the localization of molecular orbital involved in the ionization have been included in this table. Figure S1 demonstrates the shape of the molecular orbitals of vitamins D2 and D3. Figure 2 and 3 demonstrate the calculated photoelectron spectra of conformers of vitamin D2 and D3 and their BWP spectra and compare them with the experimental photoelectron spectra[5].

Novak et al. reported the first He-I photoelectron spectrum of vitamin D_2 and D_3, separately[5]. They also performed semi-empirical AM1 calculations to obtain the ionization and molecular orbital energies of vitamins D2 and D3. It should be mentioned that they did not performed conformational analysis on these vitamins to determine their populated conformers in the gas phase and determine the ionization energies of each conformer. Therefore, the ionization energies of these vitamins have been calculated by considering only one geometrical structure for each vitamin in the Novak et al.'s work. In addition, the molecular structures, used for calculating the ionization energies in their work, have been optimized using molecular mechanic (MM) method and the observed features in the recorded photoelectron spectra were assigned based on the Koopmans' approximation. Considering the above explanations, it was decided to calculate and assign the photoelectron spectra of vitamins D2 and D3 using a theoretical method which considers the electron correlations in this work.

Figure 2 shows there are five ionization bands for two conformers of vitamin D2 below 10 eV, while Novak et al. predicted four ionization bands in this region based on the Koopmans' approximation. In addition, it is seen that the relative energies and intensities of the calculated ionization bands of conformer 1 and 2 are different. To obtain the calculated photoelectron spectrum of vitamin D2, the sum of the Boltzmman-weighted of the individual calculated

spectrum of conformer 1 and 2 was considered (indicated by "BWP" in Figure 2). As seen, there is an excellent agreement between the BWP spectrum and the experimental spectrum of vitamin D2 in Figure 2. It is important to notice that the experimental photoelectron spectrum of vitamin D2 is very similar to the calculated spectrum of conformer II. This observation is in agreement with the population ratios of conformers of vitamin D2 obtained in this work (25.6% conformer 1; 74.3% conformer 2). Therefore, the assignment of the experimental photoelectron spectrum of D2 is explained based on the SAC-CI and NBO results of conformer 2.

Feature *A* of the experimental spectrum is mainly related to the first ionization band of conformer 1 and 2. The wavefunction of the first ionic state of D2 is a single HF ionized determinant related to high occupied molecular orbital (HOMO) which is a π molecular orbital due to π(C9- C15), π(C17-C19) and π(C23-C29) of triene system (Table S1 and Table 1). The calculated first ionization energy of conformer 2 obtained using direct SAC-CI and HF methods are 5.945 and 7.75 eV, respectively. The position of feature *A* in the experimental spectrum of vitamin D2 is about 7.528 eV. The first ionization energy of vitamin D2 calculated by Novak et al. is about 8.72 eV. It is seen that considering the electron correlations for vitamin D2 decreases the ionization energy. Therefore, the BWP spectrum of vitamin D2 (Figure 2) was shifted by 1.58 eV to the higher binding energy to match the position of the first peak of the BWP spectrum with the position of feature *A* in the experimental spectrum. The main reason of the difference between the calculated and experimental first ionization energy of vitamin D2 can be attributed to the intrinsic errors which is present in the direct SAC-CI SD-R method. The average error of direct SAC-CI method is about 0.5 eV in small molecules due to the cutoff approximation in the unlinked terms and increases with the size of molecule[32]. However, comparison of the BWP spectrum with the experimental spectrum shows that the direct SAC-CI SD-R method with D95

(df,pd) basis set can predict relative energies and intensities of the photoelectron lines quite accurately. The numbers in parenthesis in Table 1 indicate the calculated ionization energies of conformers of vitamin D considering the value of energy shift.

The second ionization band of conformer 1 and 2 corresponds to feature B of the experimental spectrum. The second ionization band of vitamin D2 should occur from HOMO-1 based on the Koopmans' approximation but, the SAC-CI result shows that this ionization can also be originated from HOMO-3 as well as HOMO-1 because of the presence of electron correlations. HOMO-1 is a π molecular oribital mostly localized on C14=C16 bond of the side chain of molecule. The assignment of the first and second ionization bands of vitamin D2 are in agreement with the assignment performed by Novak et al[5]. It is notable that the third ionization band of vitamin D2 originates mostly from HOMO-4 unlike the Koopmans' approximation (Table 1). HOMO-4 is a π molecular orbital related only to π(C9-C15) and π(C 17-C19) of triene system (Table S1). This assignment is different to what has been reported by Novak et al[5]. The wave function of the fourth ionization band is a linear combination of four single HF ionized determinants including HOMO-1, HOMO-2, HOMO-3 and HOMO-4 which shows that the amount of electron correlations have been increased in this ionic state (see Table 1). One of the most important points related to vitamin D2 is that its ionization from HOMO-2 and the lone electron pairs of OH group of molecule do not occur below 10 eV.

There are three conformers for vitamin D3 in the gas phase (Figure 1). The difference between vitamin D2 and D3 is mainly related to the side chain (there is no C=C bond in the side chain). Figure 3 shows the calculated photoelectron spectra of conformers of vitamin D3 along with their BWP spectrum. In addition, the experimental spectrum of vitamin D3 recorded by Novak et al[5] has also been included in this figure. The calculate spectra shifted by 1.6 eV to

higher binding energy for matching with the experimental spectrum. The experimental photoelectron spectrum of D3 is similar to D2 but, the first peak in the spectrum of D3 is broader than that in the spectrum of D2[5]. The reason for this has been attributed to more varied conformer population in the gas phase for vitamin D3 than D2[5] which is in agreement with the thermochemistry results obtained in this work that the number of gas phase populated conformers of D3 is higher than D2. Comparison of theory with experiment shows that feature A of the experimental spectrum of vitamin D3 has been composed of only the first ionization band of conformers. Figure 3 shows that the ionization energies of conformer 1 are higher than the other two conformers. For example, the energy order of the first ionization energies of the conformers of vitamin D3 are conformer 1> conformer3> conformer 2. The difference among the first ionization energies of conformers of vitamin D3 causes the broadening the feature A in the spectrum of vitamin D3 compared to that in the spectrum of vitamin D2.

Similar to vitamin D2, the first ionization band of vitamin D3 is related to the ionization from HOMO, which is a π molecular orbital related to triene system in molecule (Table 1 and Table S1). Table S1 reports that the HOMO of conformers 2 and 3 of vitamin D3 is mostly localized on π(C15=C9) and π(C18=C20). There is a small feature in the experimental spectrum of vitamin D3 (assigned with asterisk in Figure 3) and can be assumed as the second ionization band of vitamin D3 at the first glance while, the calculated BWP spectrum presented in this work does not show and confirm this feature. Feature B of the experimental spectrum is only related to the second ionization band of conformer 2 and 3. Therefore, it can be possible to follow the change in the total population of conformers 2 and 3 relative to conformer 1 with the temperature using the change in the intensity of this feature by photoelectron spectroscopy technique. The wavefunction of the second ionization band of conformer 2 is mainly related to HOMO-1 while

it is related to HOMO-1 and HOMO-2 (most contribution) for conformer 3. It can be seen that the Koopmans' approximation is not valid for conformer 3 unlike conformer 2. HOMO-1 of conformer 2 and 1 has mostly composed of π(C24=C28) and π(C9=C15), respectively and HOMO-2 has σ character. The third ionization band of conformer 2 is related to HOMO-2 while it is related to HOMO-1 in conformer 3 but, there is a little contribution from HOMO-3 and HOMO-2 in the main configuration of this ionic state for conformer 2 and 3, respectively. The wavefunction of the fourth ionization band of conformer 2 is a linear combination of HOMO-4 and HOMO-3 while it is related to HOMO-3 and HOMO-5 for conformer 3 with nearly the same contribution. HOMO-3 is a π molecular orbital related to C18=C20 and C9=C15. The shapes of the molecular orbitals of two conformers of vitamin D3 have been demonstrated in Figure S1.

Vitamin K

Vitamin K is a group of vitamins which have similar structures and acts as post-transational modification of certain proteins for blood coagulation and metabolic pathways in bone and other tissue[33]. There are several subtypes of vitamin K2 which differ in isoprenoid chain length. These homologues are called menaquinones, and are characterized by the number of isoprenoid residues in their side chains and abbreviated MK-2, where M stands for menaquinones, the K stands for vitamin K and the n represent the number of isoprenoid side chain residues. In this work, the photoelectron spectrum of MK-1 was calculated and assigned. There are twelve conformers for MK-1[34] and the frequency calculations show that only one of them is populated in the gas phase. The structure of this conformer has been demonstrated in Figure 1 and its calculated photoelectron spectrum has been shown in Figure 4. It should be mentioned that the energy shift about 1.5 eV is also expected for vitamin K because of using direct SAC-CI method for calculation. There is no theoretical and experimental report on the gas

phase ionization energies of vitamin K2 and its gas photoelectron spectrum in literature. There is only one report on the atmospheric pressure ionization and atmospheric pressure chemical ionization of menaquinones in the literature[35].

The first ionization band of MK-1 is related to the ionization from HOMO, HOMO-3 and HOMO-4 which the contribution of HOMO and HOMO-4 in the wavefunction is higher than HOMO-3 (Table 1). This means that the Koopmans' approximation is not valid for this vitamin. HOMO is a π molecular orbital and mostly localized on C14=C10 bond of the side chain of molecule and HOMO-4 is a nonbonding orbital related to the lone electron pairs of oxygen atoms of menaquinones (Table S1 and Figure S3) based on the NBO calculations. Therefore, the ionization of MK-1 occurs from two different places in the molecule with the nearly same probability. Another interesting point is that the first ionization of this vitamin does not occur from the π electron of aromatic ring. The wavefunction of the second ionization band is a linear combination of three ionized HF determinants including HOMO-1 (the most contribution), HOMO-2 and HOMO-3. HOMO-1 is a π molecular orbital localized on the aromatic ring (π(C13=C16); π(C12=C15); π*(C6=C7); see Figure S3) which the ionization probability from π(C13=C16) and π(C12=C15) is higher than π*(C6=C7) . The third ionization band is related to HOMO-2 (more contribution), HOMO-3 and HOMO-4 with different probability. HOMO-2 is a π molecular orbital related to the π system of aromatic ring and C3=C4. HOMO-3 is a π molecular orbital mostly related to the C3=C4 of menaquinones and mostly localized on this bond (Figure S3). The assignment of the fifth ionization band is similar to the first ionization band because the wavefunction of this ionic state is a linear combination of two ionized determinants related to HOMO and HOMO-4. Finally, it is important to notice that the first

ionization of vitamin K does not take place form the aromatic ring and occurs from the unsaturated C14=C10 bond of side chain and the oxygen atoms of menaquinones.

Vitamin E

Vitamin E is a group of vitamins, which include tocopherol and tocotrienol[36]. In this work, the ionization energies of the tocopherol group are calculated. There are four tocopherol form of vitamin E including α-, *β*-, γ- and δ - tocopherol. The most biologically active form of vitamin E is α- tocopherol[37]. Figure 5 shows the molecular structures of four forms of vitamin E. The only reported experimental photoelectron spectrum of vitamin E in literature is related to the work of Nagaoka et al15. They recorded the He-I photoelectron spectra of α-, *β*-, γ- and δ - tocopherol in the range of 8 to 21 eV. Figure 6 and 7 show the calculated photoelectron spectra of different forms of vitamin E and compare them with their corresponding experimental photoelectron spectra recorded by Nagaoka et al[15]. As seen, there is a very good agreement between the calculated and experimental spectra. It should be mentioned that the calculated spectra of α- tocopherol, β- tocopherol and tocol have been shifted to higher binding energy by 1.6 eV in Figure 6. Similarly, the calculated spectra of δ- tocopherol and γ-tocopherol have been shifted by 1.5 and 1.7 eV to higher binding energy, respectively. As seen in Figure 6 and 7, the calculated five ionization bands produce three visible features in the calculated photoelectron spectra except for α-tocopherol. The increasing order of the first ionization energy for vitamins E, based on the calculations, as follows α- tocopherol<β- tocopherol< γ- tocopherol< δ- tocopherol < tocol (Table 2).

The first ionization bands of all forms of vitamin E are related to the ionization from HOMO. This molecular orbital is mostly localized on the aromatic ring (Figures S2 and S3) and

related to two $\pi_{C=C}$ and one $\pi^*_{C=C}$ of the ring (Table S2). Table S2 also shows that there is a small probability for the ionization of vitamin E from the lone electron pairs of oxygen atom. Nagaoka et al[15] has assigned the first ionization band of vitamin E to only the ionization of lone electron pairs of oxygen atoms based on the calculation using HF/STO-3G method while, this ionization band has been mostly attributed to $\pi_{C=C}$ and $\pi^*_{C=C}$ of the aromatic ring based on the SAC-CI calculation in this work. The second ionization band of all forms of vitamin E is mainly related to the ionization of HOMO-1 which has been localized on the phenyl ring. HOMO-1 is a π molecular orbital related to $\pi_{C=C}$ of aromatic ring. The shapes of HOMO and HOMO-1 of all form of vitamin E have been demonstrated in Figures S2 and S3. Based on the above assignment, the first and second ionization of vitamin E originates from the π electrons of the aromatic ring. The calculated spectra in Figure 6 and 7 shows that the energy difference between the first and second ionization band decreases in the α-tocopherol, β- tocopherol, γ- tocopherol and δ-tocopherol compared to tocol. The third ionization band in the calculated spectrum of α-tocopherol is seen as a resolved feature and has been identified with asterisk in Figure 6. The third ionization band is related to HOMO-2 which is an σ orbital. The other molecular orbitals of all forms of vitamin E have σ character. The most important point about the ionization of vitamin E is that its ionization from the lone electron pairs of oxygen atom does not take place below 10.5 eV and this conclusion is against the assignment of Nagaoka et al[15].

Vitamin A

Vitamin A and its derivatives are very sensitive to light and heat because of the polyene skeleton present in their structures. Katsumata et al[20] studied the electronic structure of vitamin A and its derivatives using gas phase photoelectron spectroscopy for understanding their

biological activity. They recorded the gas phase He-I photoelectron spectrum of vitamin A (all-*trans*-retinol and its two derivatives (13-*cis*-retinoic acid and all-*trans*-retinoic acid). In addition, they performed *ab* initio calculations at the HF/6-311G level of theory to calculate the ionization energy and molecular orbitals of each compound without considering the electron correlations. It should be mentioned that they assigned the photoelectron spectra considering the Koopmans' approximation. There is no *ab* initio calculation on the ionization and photoelectron spectra of vitamin A and its derivatives considering the electron correlations in literature.

There are thirty, thirty seven and twenty two conformers for vitamin A, 13-*cis*-retinoic acid and all-*trans*-retinoic acid, respectively. Thermochemistry calculations, performed in this work, showed that only two conformers are populated in the gas phase for vitamin A and all-*trans*-retinoic acid while only one conformer is populated for 13-*cis*-retinoic acid in the gas phase. The molecular structures of conformers have been demonstrated in Figure 8. Figure 9 shows the calculated photoelectron spectra of conformers of vitamin A and their BWP spectrum and compares them with the experimental photoelectron spectrum of vitamin A[20]. In addition, the calculated spectrum of 13-*cis*-retinoic acid and its experimental spectrum have been included in this figure. Figure 10 shows the calculated photoelectron spectra of conformers of all-*trans*-retinoic acid and its BMP spectrum and compares them with its experimental spectrum[20].

The calculated photoelectron spectra of two conformers of vitamin A are very similar (Figure 9). The calculated BWP spectrum of vitamin A describes its photoelectron spectrum[20] very well. Unfortunately, the resolution of the experimental spectrum[20] is not good enough but, the features can be seen in it. The calculated photoelectron spectra of conformers of all-*trans*-retinoic acid (Figure 10) and 13-*cis*-retinoic acid are very similar to vitamin A. This means that the calculated ionization bands originate from the region of molecule, which is the same in three

compounds. The calculated BWP spectra of vitamin A (1.5 eV) and all-*trans*-retinoic acid (1.3 eV) and the spectrum of 13-*cis*-retinoic acid (1.25 eV) were shifted to higher binding energy to have the best agreement with the experiment. The main configuration of ionic wave functions of vitamin A, all-*trans*-retinoic acid and 13-*cis*-retinoic acid, obtained from SAC-CI calculations and reported in Table 3, shows that the electronic correlations are not negligible in the calculation of ionization energies in the considered energy region. Because the wave function of some ionic states are a linear combination of two or more single HF ionized determinants. To see the effect of the correlation energy on the relative energy position of ionization bands, typically the calculated ionization energies of the conformers of vitamin A, relative to the energy of the first ionization band, have been plotted versus the number of ionization band in Figure 11. As seen, there is a considerable difference between the plot obtained using HF theory (without electron correlation) and that obtained using SAC-CI theory. In addition, the plot, obtained using the calculated ionization energies of Katsumata et al[20], has been included in this figure. It is seen that the electronic correlations are absent in the calculations of Katsumata et al. because their plot is very close to the plots obtained in this work using HF/D95(df,pd) method. Comparison of theory with experiment in Figures 9 and 10 again confirms that although the calculated photoelectron spectra shifted to higher binding energy but the direct SAC-CI method can predict the relative energy of ionization bands very well.

The first and second ionization bands of vitamin A, all-*trans*-retinoic acid and 13-*cis*-retinoic acid corresponds to HOMO and HOMO-1, respectively (Table 3). HOMO is a π molecular orbital related to five conjugate $\pi_{C=C}$ but, mostly localized on three C=C bonds (identified with black asterisk in Figure 8). Similarly HOMO-1 is a π molecular orbital but it has been mostly concentrated only on one C=C bond (identified with blue asterisk in Figure 8; see

also Table S3). The shape of the molecular orbitals of vitamin A, all-*trans*-retinoic acid and 13-*cis*-retinoic acid have been shown in Figure S4 and S5. The wave function of the third ionization band of conformers of vitamin A, 13-*cis*-retinoic acid and conformer 1 of all-*trans*-retinoic acid is a linear combination of two single HF ionized determinants including HOMO-2 (major contribution) and HOMO-3. The ionic wave function of Conformer 2 of all-*trans*-retinoic acid is mainly originated from HOMO-2. The third feature in the experimental spectrum of these compounds has been composed from the third ionization band of each conformer. HOMO-2 is a π molecular orbital mostly concentrated on one C=C bond (Table S3). For example, this C=C bond, for the conformer 1 of vitamin A, is C18=C20 which its π contribution in HOMO-2 is about 30.3%. Katsumata et al[20] proposed that the fourth feature of the experimental photoelectron spectra of vitamin A and its derivatives have been composed of the fourth and fifth ionization bands based on the assignment using Koopmans' approximation. The SAC-CI calculations showed that the fourth feature in the experimental spectrum has been composed of only the fourth ionization band. The reason for this difference is related to the absence of electron correlations in the calculations of Katsumata et al[20]. The wavefunction of the fourth ionic state of vitamin A is a linear combination of three single ionized HF determinants including HOMO-3 and HOMO-4 (major contribution) (Table 3). The main configuration of the fourth ionic state of all-*trans*-retinoic acid and 13-*cis*-retinoic acid is a linear combination of HOMO-3 and HOMO-6. It is seen that the assignment of the fourth ionization band of vitamin A is different from all-*trans*-retinoic acid and 13-*cis*-retinoic acid. HOMO-3 is related to the chain of five $\pi_{C=C}$ for all compounds and HOMO-4 is related to σ_{C-C} of cyclohexene ring. The position of the fifth ionization band of vitamin A, identified by Katsumata et al[20] in their experimental spectra (see Figures 8 and 9), is not confirmed with the calculated spectra in this work. For

example, our theoretical calculations show that the fifth ionization band of all-*trans*-retinoic is around 10.2 eV while Katsumata et al[20] considered the feature around 10.8 eV containing three ionization bands including the fifth, sixth and seventh. Finally, the theoretical calculations show that the ionization of vitamin A and its derivatives from the lone electron pairs of oxygen atoms does not take place below 11 eV.

Conclusion

The ionization energy and valence photoelectron spectra of different vitamins including A, K, E and D were calculated using direct SAC-CI method. The present calculations finely simulated the shape of the experimental spectra and provided the detailed assignment of the spectra. As mentioned before, there was an energy shift for matching the calculated spectra with the experimental spectra. This energy shift was mainly attributed to the intrinsic error present in the direct SAC-CI method, which increases with size of basis set and partly due to the incompleteness of basis set. Such energy shift can be seen in the calculation of the near edge X-ray photo absorption spectra calculations of guanine by Plekan et al. using algebraic-diagrammatic construction approximation (ADC) and the 6-31G basis set[38,39]. However, we showed that the present direct SAC-CI SD-R method in combination with the D95(df,pd) basis set can predict the relative energies and intensities of the photoelectron lines of the compounds considered in this work quite accurately.

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Figure Captions

Fig. 1. The molecular structures of the conformers of vitamins D2, D3 and K. The atoms of each structure have been numbered, sequentially. The numbers below the structures show the percentage of population of conformers in the gas phase.

Fig. 2. Comparison of the calculated photoelectron spectra of the conformers of vitamin D2 and their BWP spectrum with the experimental photoelectron spectrum of this vitamin[5]. Vertical lines show the calculated position and intensity of ionization bands.

Fig. 3. Comparison of the calculated photoelectron spectra of the conformers of vitamin D3 and their BWP spectrum with the experimental photoelectron spectrum of this vitamin[5].Vertical lines show the calculated position and intensity of ionization bands.

Fig. 4. Calculated photoelectron spectrum of vitamin K (MK-1). Vertical lines show the calculated position and intensity of ionization bands.

Fig. 5. The molecular structure of different forms of vitamin E including (*a*) α-tocopherol (*b*) *β*-tocopherol (*c*) γ- tocopherol (*d*) δ - tocopherol and (e) tocopherol.

Fig. 6. Comparison of the calculated photoelectron spectrum of Tocopherol, α- Tocopherol and β-Tocopherol with their experimental spectra[15].Vertical lines show the calculated position and intensity of ionization bands.

Fig. 7. Comparison of the calculated photoelectron spectrum of γ- Tocopherol and δ-Tocopherol with their experimental spectra[15].Vertical lines show the calculated position and intensity of ionization bands.

Fig. 8. The molecular structures of conformers of vitamin A and its derivatives including 13-*cis*-retinoic acid and all-*trans*-retinoic. The atoms have been sequentially numbered. The numbers aside the structures show the percentage of the population of conformers in the gas phase.

Fig. 9. Comparison of the calculated photoelectron spectra of conformers of vitamin A, their BWP spectrum and the calculated spectrum of 13-*cis*-retinoic acid with the experimental photoelectron spectrum of vitamin A[20]and 13-*cis*-retinoic acid[20].The numbers above the experimental spectrum shows the visible features identified by Katsumata et al[20].

Fig. 10. Comparison of the calculated photoelectron spectra of conformers of all-*trans*-retinoic acid and its BWP spectrum with the experimental photoelectron spectrum of all-*trans*-retinoic acid[20].

Fig. 11. Variation of the energy positions of the ionization bands of the conformers of vitamin A relative to their first ionization bands versus the ionization band number.

Table Captions

Table 1. Calculated ionization energies and the main electronic configurations of the ionic states of most populated conformers of vitamin D2 and D3 obtained using Direct SAC-C-CI theory. The numbers in parenthesis are the calculated ionization energies considering the energy shift (1.58 and 1.6 eV for vitamin D2 and D3, respectively).

Table 2. Calculated ionization energies and the main electronic configurations of the ionic states of the different forms of vitamin E obtained using Direct SAC-C-CI theory. The numbers in parenthesis are the calculated ionization energies considering the energy shift (1.6 eV for α- tocopherol, β- tocopherol and tocopherol. 1.5 and 1.7 eV for δ- tocopherol and γ- tocopherol, respectively).

Table 3. Calculated ionization energies and the main electronic configurations of the ionic states of vitamin A and its derivatives obtained using Direct SAC-C-CI theory. The numbers in parenthesis are the calculated ionization energies considering the energy shift (1.5 eV for vitamin A, 1.3 eV for all-*trans*-retinoic acid and 1.25 eV for 13-*cis*-retinoic acid).

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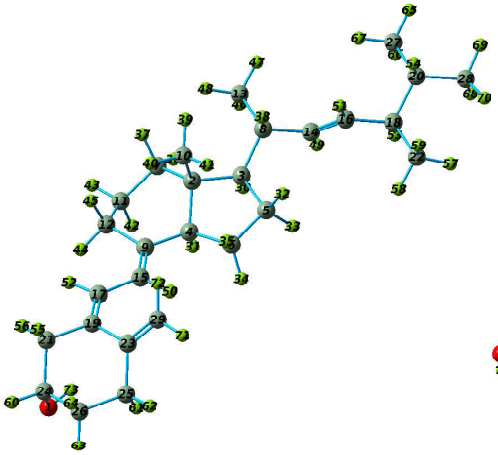
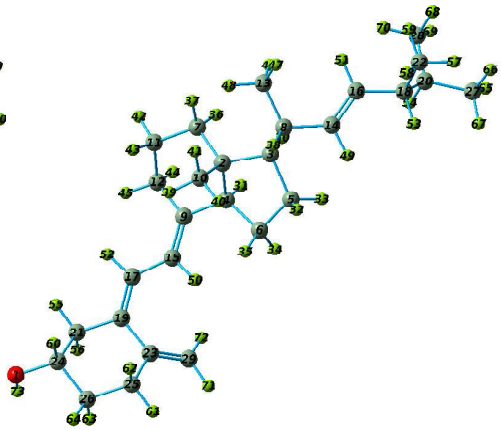
Figure 1



D2; conformer I
25.6%



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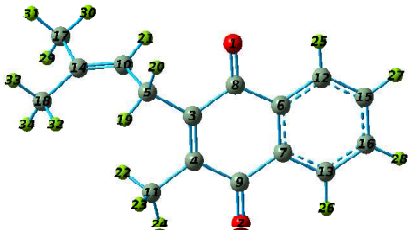
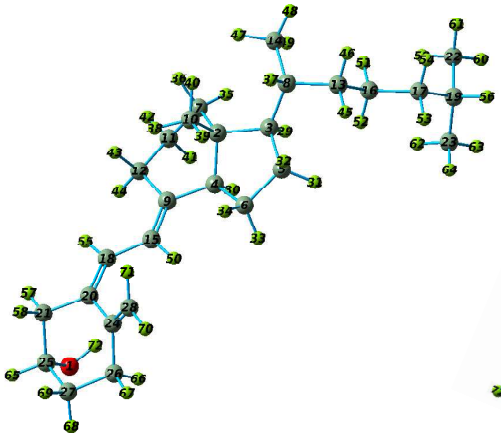


K; MK-1



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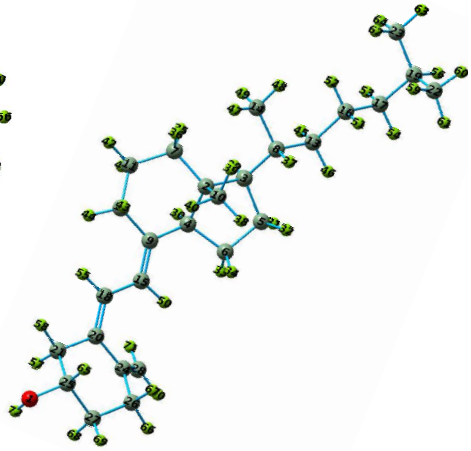
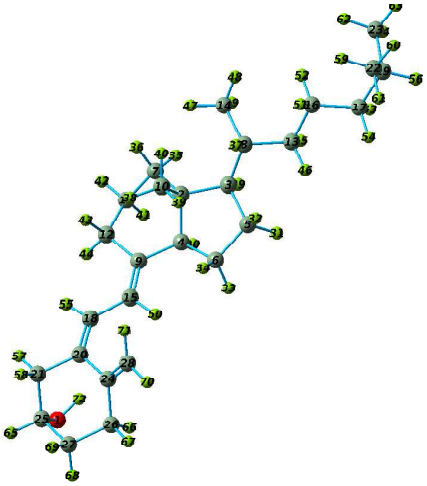
11.5%



D3; conformer II
39.5%



D3; conformer III
41.7%

Figure 2

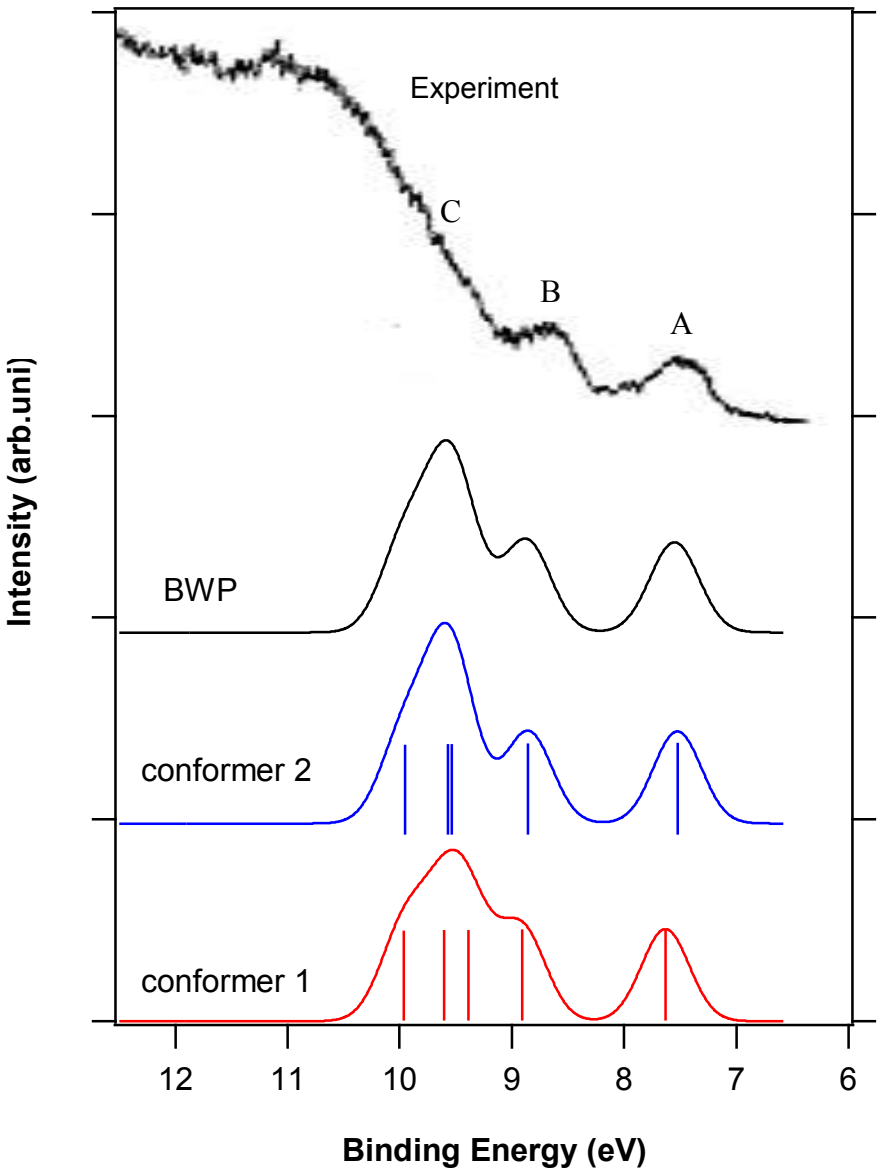
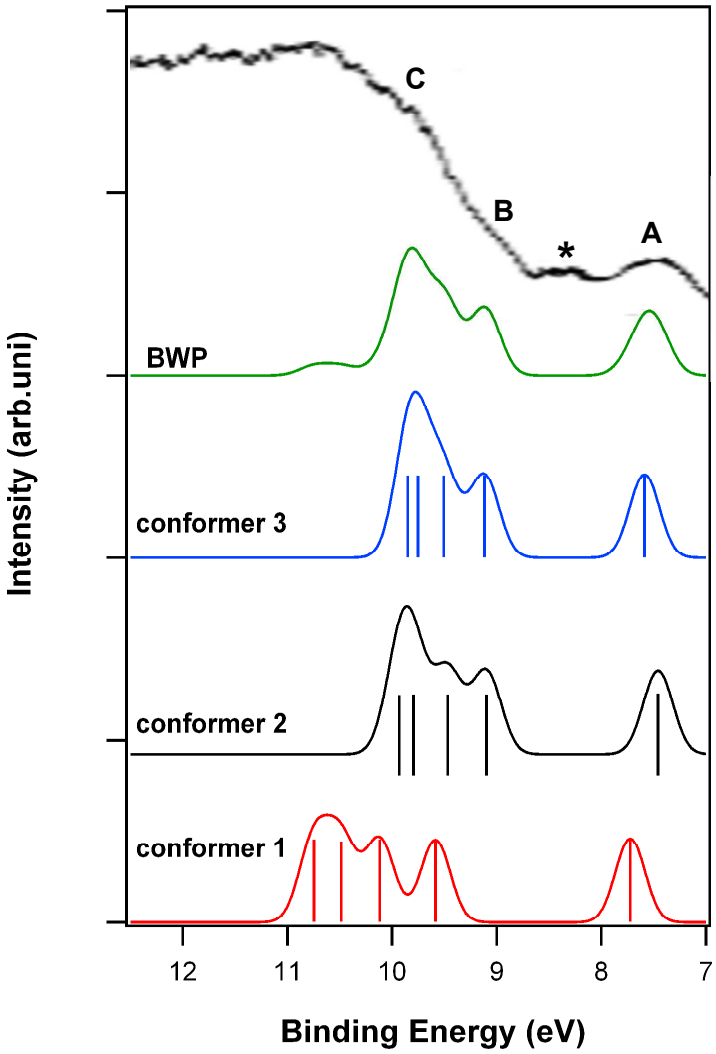


Figure 3



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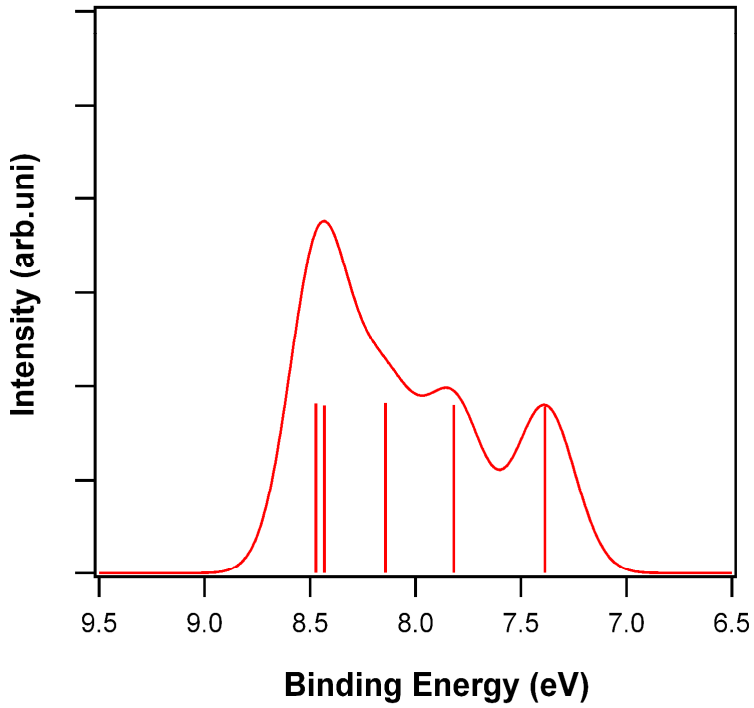

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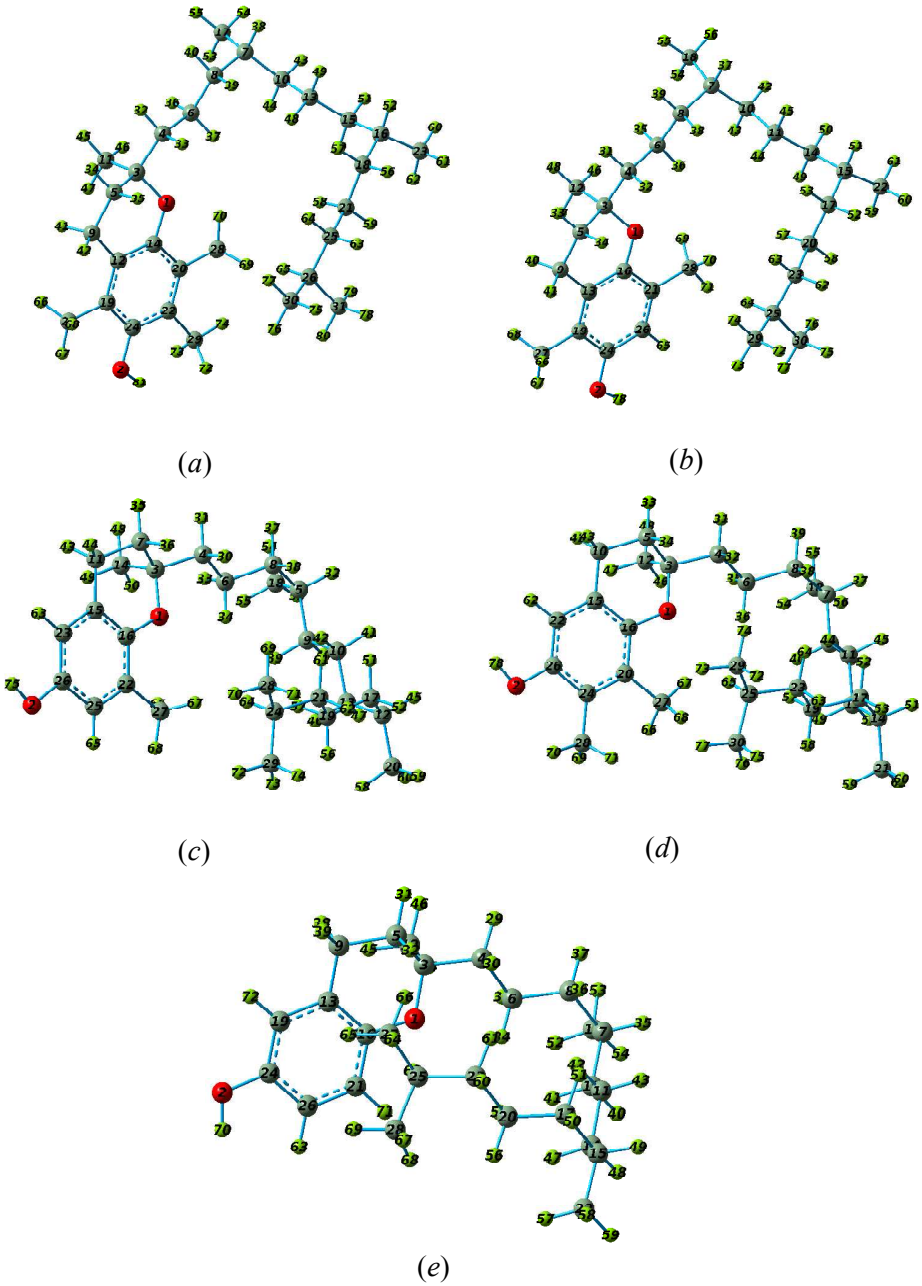


(*a*) (*b*) (*c*) (*d*) (*e*)

Figure 6

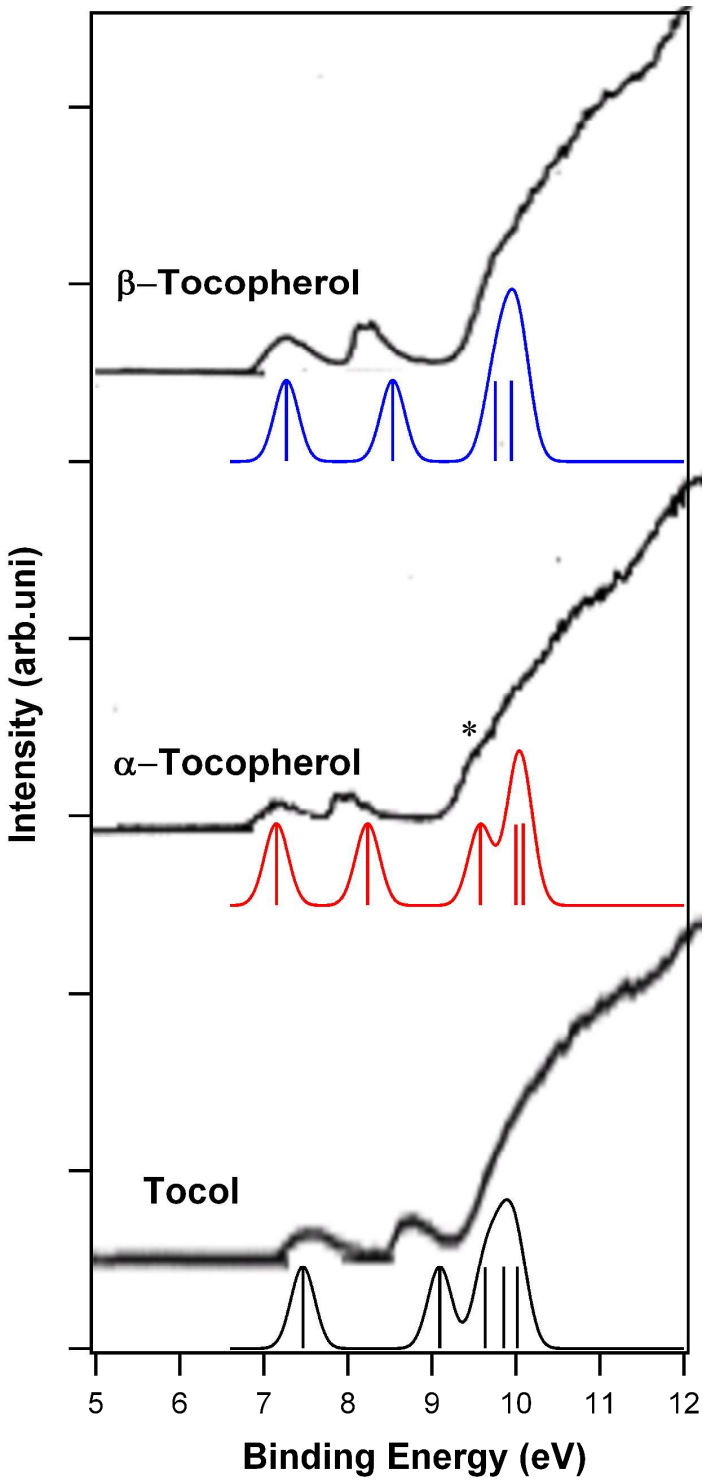


Figure 7

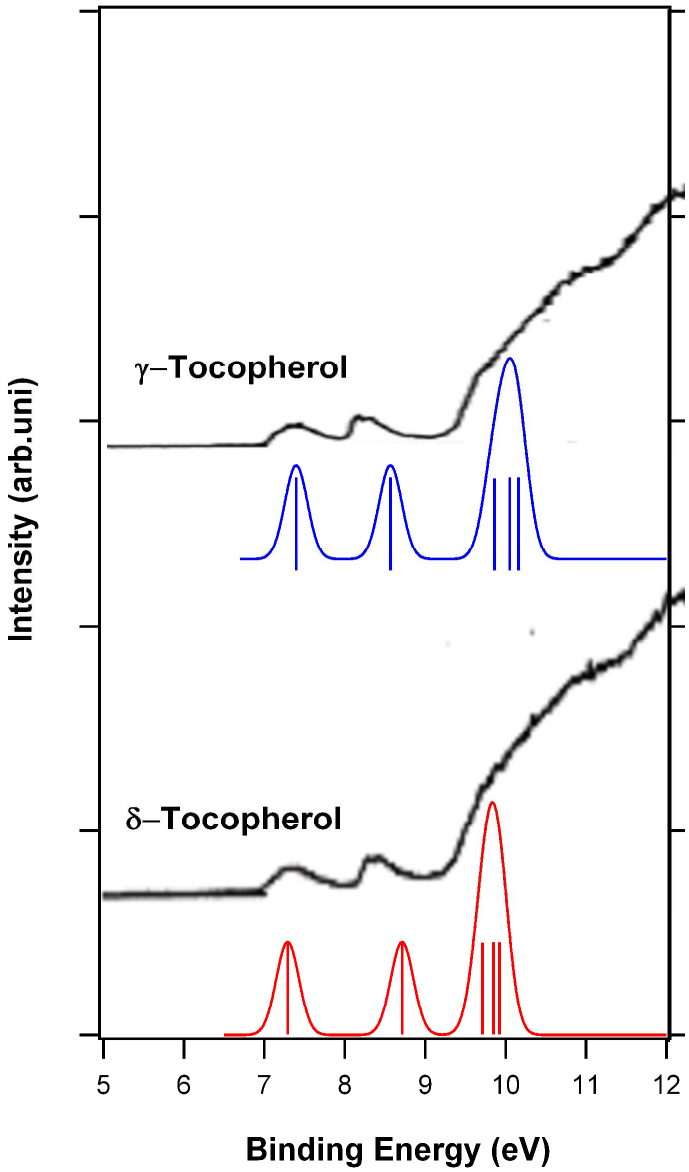
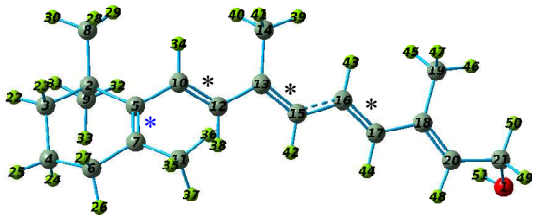


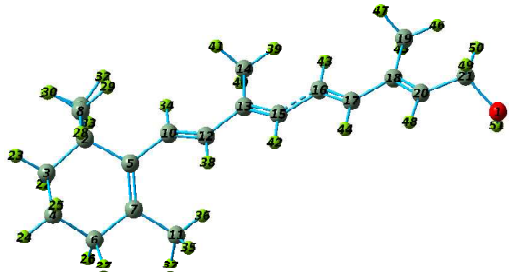
Figure 8

59%



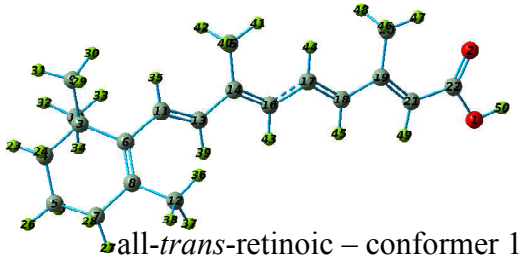
Vitamin A– conformer 1

40.3%



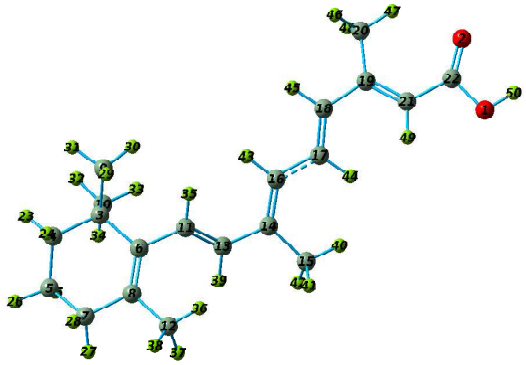
Vitamin A– conformer 2

49.75%

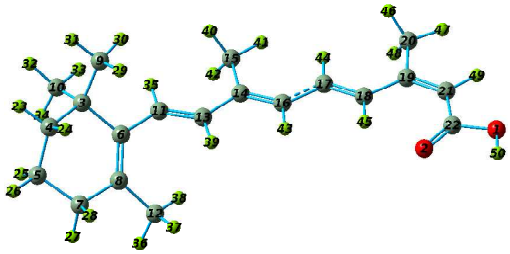


all-*trans*-retinoic – conformer 1

50.25%



all-*trans*-retinoic – conformer 2



13-*cis*-retinoic acid

Figure 9

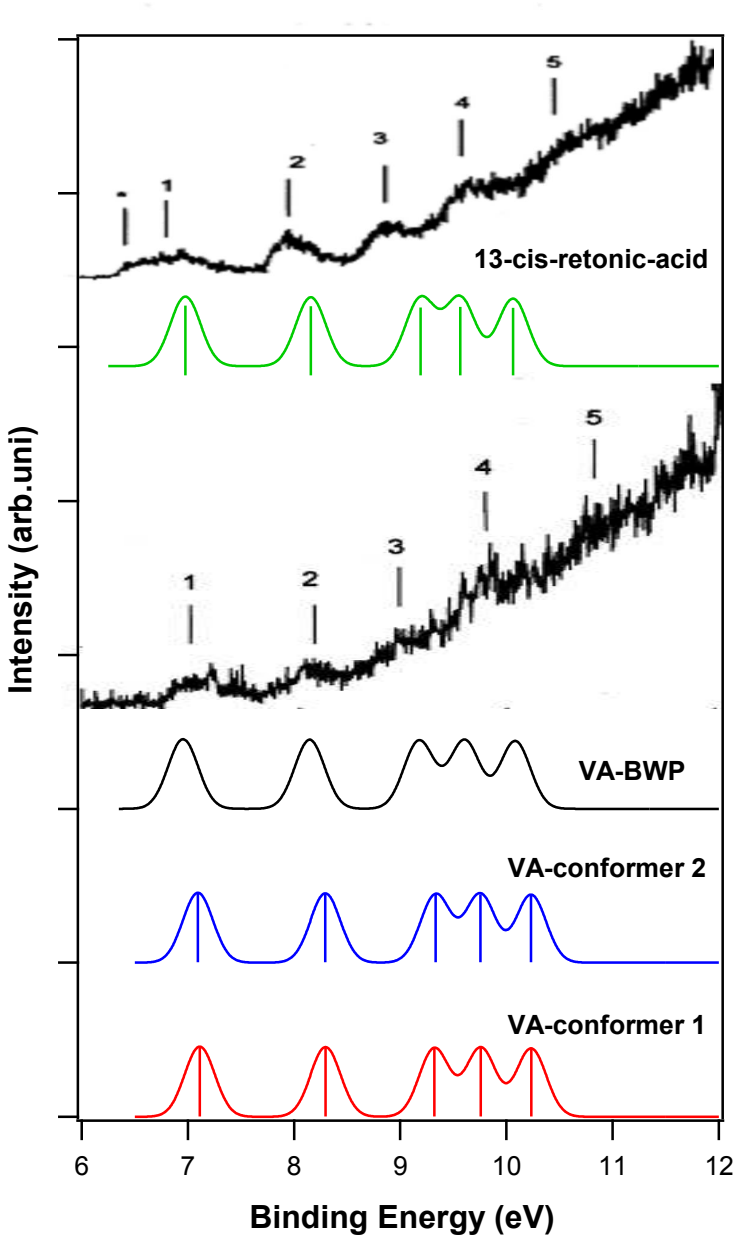


Figure 10

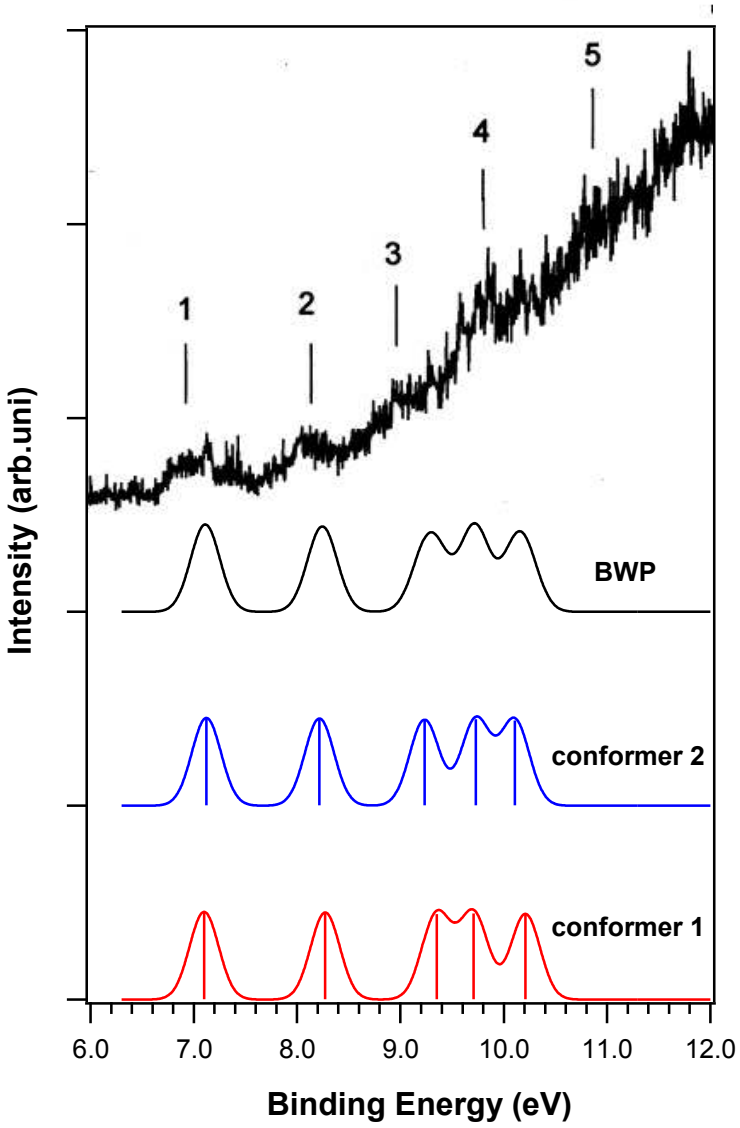


Figure 11

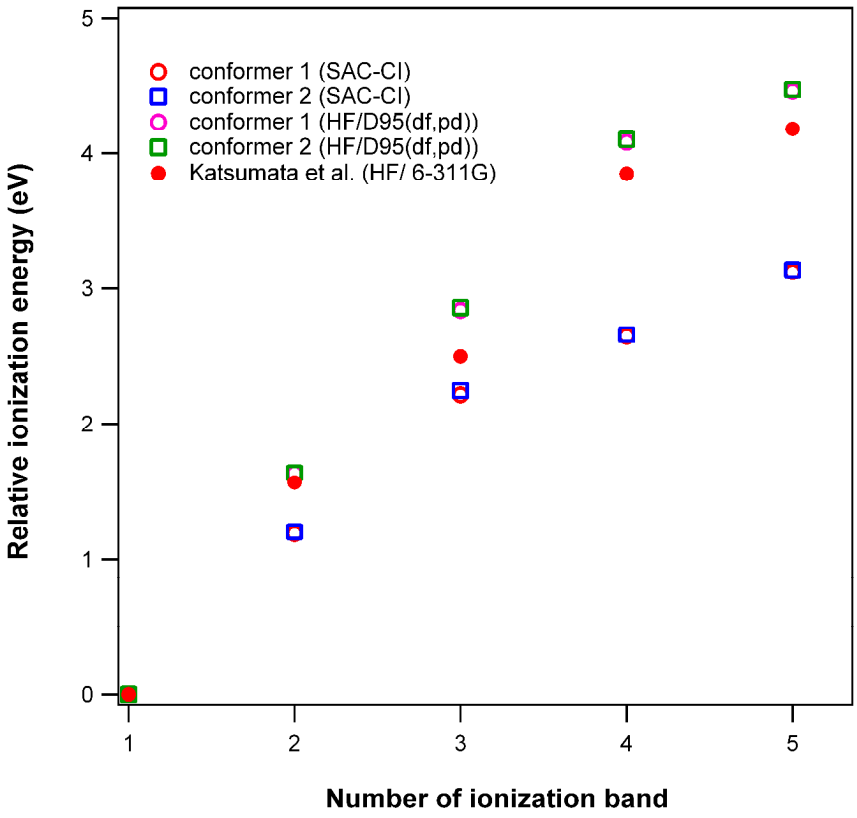


Table 1

		State (^2A)	Main electronic configuration	Ionization energy (eV)	Intensity
Vitamin D2	**Conformer 2**	1	0.94(HOMO)	5.945 (7.528)	0.914
		2	-0.89(HOMO-1)+0.24 (HOMO-3)	7.274 (8.854)	0.913
		3	-0.9(HOMO-4)+ 0.21(HOMO-3)	7.957 (9.537)	0.904
		4	-0.20 (HOMO-2)-0.69 (HOMO-3)-0.51 (HOMO-4)-0.30(HOMO-1)	7.990 (9.57)	0.904
		5	-0.49 (HOMO-3)+0.72(HOMO-4)	8.373 (9.953)	0.900
Vitamin D3	**Conformer 2**	1	0.94(HOMO)	5.858 (7.458)	0.914
		2	0.92 (HOMO-1)	7.498 (9.098)	0.902
		3	-0.87 (HOMO-2)+0.30 (HOMO-3)	7.868 (9.468)	0.903
		4	0. 53 (HOMO-4)-0.64 (HOMO-3)	8.196 (9.796)	8.196
		5	0.52 (HOMO-3)+ 0.72 (HOMO-4)	8.332 (9.932)	0.898
	Conformer 3	1	0.94(HOMO)	5.987 (7.587)	0.914
		2	0.39 (HOMO-1)-0.84 (HOMO-2)	7.518 (9.118)	0.902
		3	0.38 (HOMO-2)+0.84 (HOMO-1)	7.906 (9.506)	0.905
		4	0.21 (HOMO-2)+0.70 (HOMO-3)-0.23 (HOMO-4)-0.48 (HOMO-5)	8.153 (9.753)	0.901
		5	-0.88 (HOMO-3)-0.21 (HOMO-4)	8.250 (9.85)	0.903
Vitamin K (MK-1)		1	-0.67 (HOMO)+0.57(HOMO-4)+0.24(HOMO-3)	7.386	0.899
		2	-0.87 (HOMO-1)-0.26 (HOMO-3) -0.24(HOMO-2)	7.819	0.907
		3	0.75(HOMO-2)+0.47(HOMO-3)-0.25 (HOMO-4)	8.142	0.909
		4	0.67 (HOMO-3) +0.41(HOMO-2)+0.35(HOMO-1)+0.33(HOMO-5)	8.432	0.897
		5	0.67(HOMO-4)-0.65(HOMO)	8.472	0.891

Table 2

	State (^2A)	Main electronic configuration	Ionization energy (eV)	Intensity
Tocopherol	1	-0.93 (HOMO)	5.865(7.465)	0.912
	2	0.95(HOMO-1)	7.494(9.094)	0.910
	3	-0.91(HOMO-2)	8.035(9.635)	0.907
	4	0.93(HOMO-3)	8.256(9.856)	0.909
	5	0.94(HOMO-4)	8.416(10.016)	0.911
α -Tocopherol	1	-0.94 (HOMO)	5.550(7.15)	0.910
	2	0.95(HOMO-1)	6.636(8.236)	0.911
	3	-0.89(HOMO-2)	7.978(9.578)	0.895
	4	-0.8(HOMO-3)-0.20(HOMO-4)+ 0.44 (HOMO-5)	8.399(9.999)	0.901
	5	-0.95(HOMO-4)	8.486(10.086)	0.911
β-Tocopherol	1	0.93(HOMO)	5.669(7.269)	0.912
	2	0.94(HOMO-1)	6.934(8.534)	0.911
	3	-0.77(HOMO-2)+0.40 (HOMO-4)	8.154(9.754)	0.902
	4	-0.91 (HOMO-2)-0.20 (HOMO-3)	8.347(9.947)	0.910
	5	-0.81 (HOMO-4)-0.460(HOMO-2)	8.457(10.057)	0.912
γ- Tocopherol	1	0.94(HOMO)	5.696(7.396)	0.911
	2	-0.95(HOMO-1)	6.868(8.568)	0.912
	3	0.94(HOMO-2)	8.163(9.863)	0.902
	4	-0.72(HOMO-3)+ 0.59 (HOMO-4)	8.350(10.05)	0.910
	5	0.76(HOMO-4)+ 0.59 (HOMO-3	8.459(10.159)	0.912
δ- Tocopherol	1	-0.94(HOMO)	5.79(7.29)	0.912
	2	0.95(HOMO-1)	7.213(8.713)	0.911
	3	0.92(HOMO-2)	8.213(9.713)	0.912
	4	0.8(HOMO-3)-0.45 (HOMO-4)	8.348(9.848)	0.909
	5	-0.20(HOMO-6)+ 0.77(HOMO-4)+ 0.45(HOMO-3)	8.423(9.923)	0.904

Table 3

		State (^2A)	Main electronic configuration	Ionization energy (eV)	Intensity
Vitamin A	**Conformer I**	1	-0.94(HOMO)	5.611(7.111)	0.91
		2	-0.92(HOMO-1)	6.798(8.298)	0.904
		3	-0.87(HOMO-2)-0.25 (HOMO-3)	7.823(9.323)	0.889
		4	-0.72(HOMO-3)-0.43(HOMO-4)	8.260(9.76)	0.893
		5	0.22(HOMO-2)-0.38 (HOMO-3) -0. 81(HOMO-4)	8.734(10.234)	0.884
	Conformer II	1	-0.94(HOMO)	5.594(7.094)	0.910
		2	0.92(HOMO-1)	6.796(8.296)	0.903
		3	0.88(HOMO-2)+ 0.24 (HOMO-3)	7.835(9.335)	0.888
		4	-0.72(HOMO-3)+ 0.44(HOMO-4)	8.255(9.755)	0.894
		5	-0.20(HOMO-2)-0.39 (HOMO-3)+ 0. 81(HOMO-4)	8.733(10.233)	0.883
all-trans-retinoic acid	**Conformer I**	1	-0.93(HOMO)	5.800(7.1)	0.905
		2	-0.92(HOMO-1)	6.973(8.273)	0.898
		3	0.85(HOMO-2)+ 0.31 (HOMO-3)	8.049(9.349)	0.882
		4	-0.64(HOMO-3)- 0.45(HOMO-6)	8.407(9.707)	0.890
		5	-0.28(HOMO-2) -0.38 (HOMO-3) -0. 79(HOMO-4)	8.909(10.209)	0.884
	Conformer II	1	0.94(HOMO)	5.822(7.122)	0.90662
		2	0.93(HOMO-1)	6.917(8.217)	0.90185
		3	-0.90(HOMO-2)	7.933(9.233)	0.88685
		4	-0.82(HOMO-3)+ 0.30(HOMO-6)	8.428(9.728)	0.89329
		5	-0.89(HOMO-4)-0.21(HOMO-3)	8.806(10.106)	0.88183
13-cis -retinoic		1	0.93(HOMO)	5.726(6.976)	0.906
		2	0.92(HOMO-1)	6.908(8.158)	0.899
		3	-0.83(HOMO-2)- 0.32 (HOMO-3)	7.943(9.193)	0.882
		4	0.68(HOMO-3) - 0.49(HOMO-6)	8.316(9.566)	0.889
		5	0.33(HOMO-2)-0.41 (HOMO-3) -0. 76(HOMO-4)	8.8139(10.063)	0.878