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DFT AND TD-DFT INVESTIGATIONON: PHOTOSTABILITY OF THE AVOBENZONE IN DIFFERENT SOLVENTS

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Abstract. In this work, a detailed study of the structural, energetic and electronic properties of the avobenzone tautomers was carried out using the DFT method and its approach dependent on time (TDDFT). The B3LYP functional and 6-311G+ basis sets are used in our calculations. We have selected solvents employed in the cosmetic industry such as fatty acid (hexanoic acid), fatty alcohol (1-hexanol) and cyclohexane. They differ in terms of polarity and proticity. The objective of this study is to examine, from a theoretical point view, the effect and the influence of these solvents on the stability of avobenzone. We have demonstrated that the stability and the absorbance of avobenzone are solvent-dependent. The TDDFT study shows that the absorption spectrum of the 1.3 diketoavobenzone forms (1.3, D.K.A) is shifted down to the UVC region in hexanoic acid.

Keywords: Avobenzone, Keto-enolic, equilibrium, Photostability, DFT, TDDFT.

1 Introduction

The scientific world has recently paid a lot of attention to studies on the UV-absorbing properties of the UV filters. Many experimental and theoretical investigations have been carried out in this context, in order to explain the process involved.

Avobenzone is one of the most common UVA filters [1]. Its forms have a wavelength of maximum absorption (λ_{max}) ranging from 350 to 365 nm depending on the solvent used [2,3], but it has been reported to partially decompose after irradiation. This issue has motivated a number of studies on its photochemical and photophysical properties. The avobenzone photostability has been shown to be very sensitive to the properties of the solvent environment. However, the photochemistry of the avobenzone is complex and difficult to understand due to the presence of tautomers that exhibit different properties.

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In fact, this molecule has a diketo function which can be converted to the enol one by a keto-enolic equilibrium [4]. It exists in three tautomeric forms:1.3 diketoavobenzone (1.3, D.K.A), methyl-enolavobenzone (M.E.A) and Tert-butyle-enolavobenzone (T.E.A) as shown in Figure1. The keto-tautomer exists only in one geometric form. As for the enol-tautomer, we need to precise that it occurs in two forms,due to its asymmetry character.

In 2009, Cecilia P and her team have shown that the diketo form is responsible for the photodegradation [5]. In 2015, a theoretical study describing the photophysical characteristics of the tautomer's of avobenzone was published [6,7]. Mturi and Martincigh have proved in their study that the photostability of avobenzone is strongly dependent on solvents [8]. These authors have studied experimentally the photostability of avobenzone in four solvents of different polarity and proticity and have concluded that avobenzone is photostable in polar protic solvents, such as methanol, but unstable in DMSO, which is a polar aprotic solvent. UV-filters are mixed with multiple ingredients to make the cream practical to use, resistant to water and perfumed. The fatty acids are to be found among these ingredients [9]. We have selected solvents employed in the cosmetic industry and differ in polarity and proticity such as a fatty acid (hexanoic acid), a fatty alcohol (1-hexanol) and cyclohexane.

The present work uses DFT and TDDFT in order to study the effect and the influence of these solvents on the stability of avobenzone. Firstly, we have examined the structure and the energetic properties of the three avobenzone tautomers (1.3, D.K.A, M.E.A and T.E.A) (Figure 1), in both gas phase and in the presence of the solvents mentioned above. Secondly, we have analyzed the electronic properties and the photophysical profile of avobenzone. Finally, the UV spectral profile of avobenzone was also simulated.

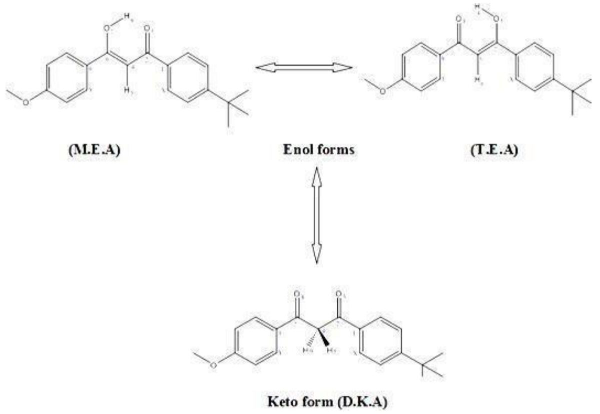


Fig. 1. Schematic drawing of the Forms Included in the Tautomerization Process studied in this work.

2 Results and discussion

2.1 Structural study

The structures of the three tautomeric forms of avobenzone were optimized by the DFT / B3LYP / 6-311 + G level of theory, in the gas phase and in several solvents. The optimized geometries are shown in Figure 2.

The result of this first analysis shows that the tautomer 1.3 D.K.A does not have a plane conformation, unlike the M.E.A and the T.E.A (which have a plane structure). This is quite supported by the presence of two adjacent carbonyl groups in the keto form (1.3 D.K.A) increase its angular torsion and prevent the plane structure of 1.3 D.K.A form. However, the formation of an intra-molecularsix-chain ring, due to the hydrogen bonding, implies a plane conformation to the two enol forms.

This observation is confirmed by two data: first, the measured values of the two dihedral angles between the two cycles of the system (methoxybenzene and t-butylbenzene), with d1 -78.16 ° and d2 180 ° for 1.3 DCA and d1 d2 180 ° for the MEA and the TEA (See Tables 1), second, the value of the plane angles (A1=120) for DCA and (A1=106) for TEA and DKA, which corresponds to the carbons SP2 and SP respectively.

It's very important to indicate that the calculations carried out in various solvents give very similar or even identical structural values. Therefore, according to this result, it can be said that the change of environment (solvents used) does not influence the geometric parameters.

		Dihedral angles			
		Gas phase	**Cyclohexane**	**Hexanoic Acid**	**1-Hexanol**
D.K.A	**C_1-C_2-C_4.C_7**	77	76	178	176
	C_2-C_4-C_7.C_9	76	180	180	180
T.E.A	**C_1-C_2-C_4.C_6**	180	180	180	180
	C_2-C_4-C_6 -C_9	180	180	180	180
M.E.A	**C_1-C_2-C_4.C_6**	180	180	180	180
	C_2-C_4-C_6.C_9	180	76	178	176
		Angles A_1 (°)			
D.K.A	**C_2-C_4-C_7**	106	106	106	106
T.E.A	**C_2-C_5-C_7**	120	120	120	120
M.E.A	**C_2-C_4-C_6**	120	120	120	120

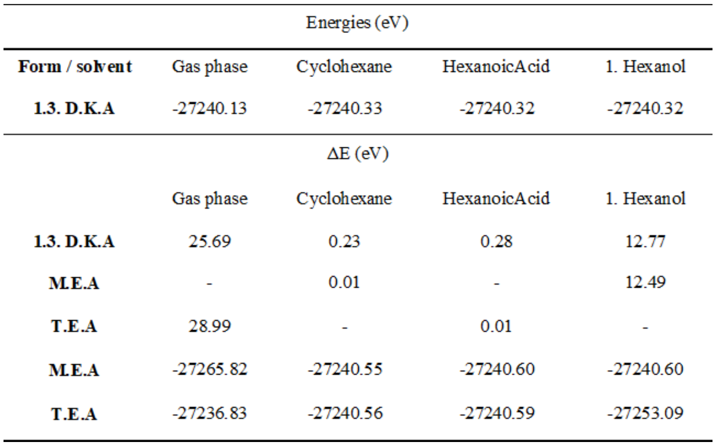
Table 1: Main structural parameters computed for the tautomer geometries D.K.A, M.E.A and T.E.A

3 Computational details

All the calculations have been carried out at the DFT level using the GAUSSIAN 09 program package [10-12]. The popular B3LYP (Becke, three-parameter, Lee-Yang-Parr) exchange-correlation functional has been used throughout our analysis with specifies the 6-311G+ basis for first-row atoms, include the diffuse functions. All the structures have been defined throughout a vibrational analysis in the harmonic approximation, with no imaginary frequency for stable states. We have used the time-dependent density functional theory (TD-DFT) calculations to generate UV-vis spectra in the gas phase and in solvents of different polarity and proticity, namely, hexanoic acid, 1-hexanol and cyclohexane. The solvent effect was introduced by the CPCM model [13-19].

3.1 Energy analysis

The avobenzone is involved in a keto-enol equilibrium, which is influenced by the UV radiation, the temperature, the solvent and the concentration. Our calculations generally suggest that the enol tautomers of avobenzone are more stable than its keto form. The energy differences, shown in Table 2, are almost insignificant, particularly in cyclohexane and hexanoic acids.



		Energies (eV)		
Form / solvent	Gas phase	Cyclohexane	HexanoicAcid	1. Hexanol
1.3. D.K.A	-27240.13	-27240.33	-27240.32	-27240.32
		ΔE (eV)		
	Gas phase	Cyclohexane	HexanoicAcid	1. Hexanol
1.3. D.K.A	25.69	0.23	0.28	12.77
M.E.A	-	0.01	-	12.49
T.E.A	28.99	-	0.01	-
M.E.A	-27265.82	-27240.55	-27240.60	-27240.60
T.E.A	-27236.83	-27240.56	-27240.59	-27253.09

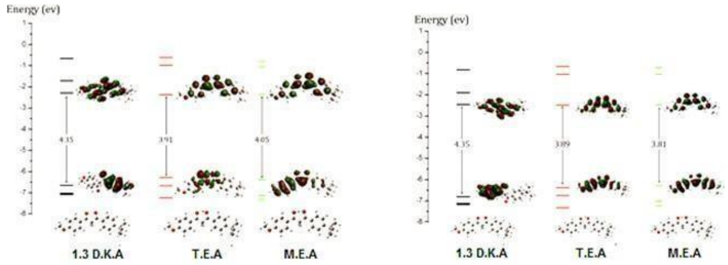
Table 2: Total energy calculated for the three forms of avobenzone (eV)

3.2 Orbital description

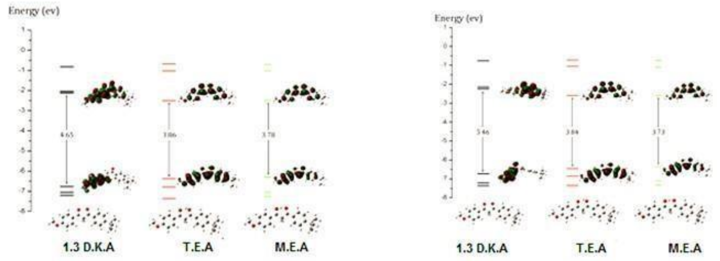
The orbital diagrams, in Figure 3, show that all the atoms of the molecule, for the T.E.A and the M.E.A tautomers, except for those of the t-butyl group, contribute to the two molecular frontier orbitals: the Highest Occupied (HOMO) and the Lowest Unoccupied (LUMO). This proves a strong resonance in the enol forms, which explains the difference in absorption as compared to the keto form.

The HOMO of the1.3 D.K.A is located only on the -t-butylbenzene moiety in the gaseous state. However, this localization is completely reversed in various solvents (located on the methoxybenzene moiety). This is explained by the presence of the oxygen atom which increases the solute-solvent interactions. It should be noted that in the solvents used, the HOMO-1 molecular orbital is located on the t-butylbenzene fragment.

Generally, the energy gap (ELUMO - EHOMO) is larger in the keto form than the two enol forms. The calculated value in gas phase (4.35 eV) is identical to the one obtained in the cyclohexane. This value increases in hexanoic acid (4.65 eV) and also in 1-hexanol (5.46 eV). This observation is in accordance with the literature data (the ketone function is stabilized in protic polar solvent.



(a) Gaz phase (b) Cyclohexane



(c) Hexanoic acid (d) 1-Hexanol

Fig. 2. Orbital energy level diagrams of the molecular orbitals calculated in different environments throughout the DFT/ B3LYP/6-311+G level of theory.

3.3 TD-DFT Investigation

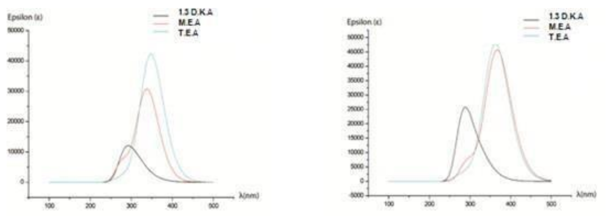
Absorption spectra We have calculated the absorption of three tautomers using TD-DFT method in order to understand the effect of the solvent on the UV spectra profile and the electronic transitions corresponding to the λ_{max}. Figure 4.

The comparison of the results obtained from the TDDFT calculations to the experimental values of avobenzone recorded in cyclohexane shows a good similarity. The absorption of avobenzone in 1-hexanol and cyclohexane is identical (λ_{max} 290 nm) but it has a different profile in hexanoic acid (λ_{max} = 230 nm).

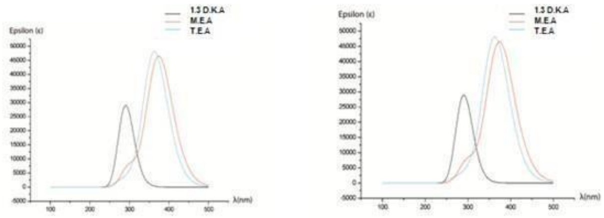
The hypsochromic shift observed for hexanoic acid is more significant than that one of cyclohexane and 1-hexanole.

The maximum wavelengths as well as the intensity of absorption of the enol and the keto forms are different according to their respective energy gaps. The absorption of the keto form is shifted towards the UVB region which is logical considering that its gap is the largest.

All the results obtained show that the absorption of the two enol forms is almost identical in the gas phase as well as in the three studied solvents.



(a) Gaz phase (b) Cyclohexane



(c) Hexanoic acid (d) 1-Hexanol

Fig. 3. Computed absorption spectra of the compounds 1.3 D.K.A, M.E.A and T.E.A recorded in different environments.

Energies and types of electronic transitions From Table 3 and 4, it appears, on one hand that the electron transitions corresponding to the max always occur between the molecular orbitals HOMO and LUMO for the two enol forms with an energy excitation of about 350 nm. On the other hand, in the keto form, electrons are promoted between different orbital levels. For example the electron transition corresponding to the λmax in cyclohexane is occurred between HOMO and LUMO + 1.

Furthermore, the plane conformations observed for the two enol forms promote the electron resonance across the molecule, which could be responsible for the difference in the electron excitations between the enol and the keto forms.

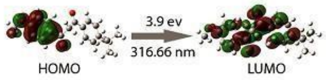
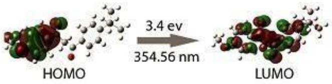
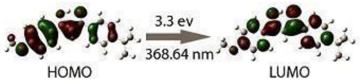
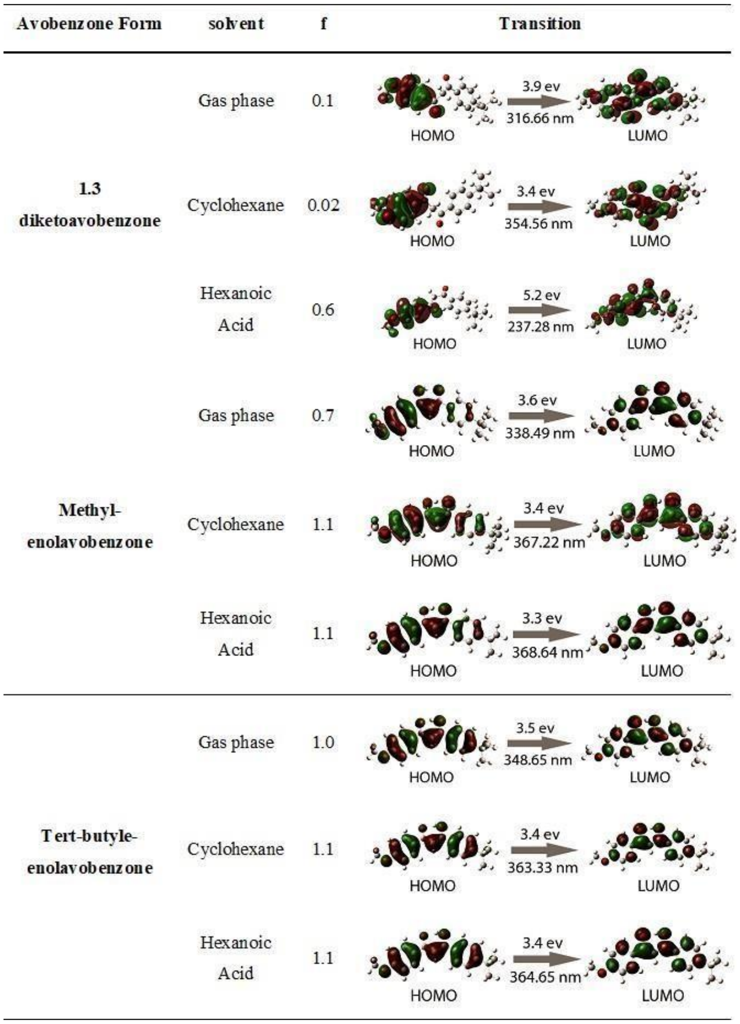
Avobenzone Form	solvent	f	Transition
1.3 diketoavobenzone	Gas phase	0.1	
	Cyclohexane	0.02	
	Hexanoic Acid	0.6	
Methyl-enolavobenzone	Gas phase	0.7	
	Cyclohexane	1.1	
	Hexanoic Acid	1.1	
Tert-butyle-enolavobenzone	Gas phase	1.0	
	Cyclohexane	1.1	
	Hexanoic Acid	1.1	

Table 3: Orbital energy level diagrams of the molecular orbitals involved in the HOMO-LUMO transitions for the avobenzone tautomers calculated throughout the TD-DFT/B3LYP/6311+G level of theory



Avobenzone Form	solvent	f	Transition
1.3 diketoavobenzone	Gas phase	0.1	HOMO 3.9 ev 316.66 nm LUMO
	Cyclohexane	0.02	HOMO 3.4 ev 354.56 nm LUMO
	Hexanoic Acid	0.6	HOMO 5.2 ev 237.28 nm LUMO
Methyl-enolavobenzone	Gas phase	0.7	HOMO 3.6 ev 338.49 nm LUMO
	Cyclohexane	1.1	HOMO 3.4 ev 367.22 nm LUMO
	Hexanoic Acid	1.1	HOMO 3.3 ev 368.64 nm LUMO
Tert-butyle-enolavobenzone	Gas phase	1.0	HOMO 3.5 ev 348.65 nm LUMO
	Cyclohexane	1.1	HOMO 3.4 ev 363.33 nm LUMO
	Hexanoic Acid	1.1	HOMO 3.4 ev 364.65 nm LUMO

Table 4. Orbital energy level diagrams of the molecular orbitals involved in the excitation transitions corresponding to max for the avobenzone tautomers calculated throughout the TD-DFT/B3LYP/6311+G level of theory

4 Conclusion

A theoretical study was carried out on avobenzone in order to analyze the solvent effect on its photostability and UV-visible profile.

This study is based on a structural, energetic, orbital and electronic analysis of avobenzone in different environments (gas phase, cyclohexane, 1-hexanol and hexanoic acid). We have demonstrated that the enol forms of avobenzone (M.E.A and T.E.A) are more stable than the keton form (1.3, D.K.A). The three studied tautomers have showed different UV absorption profiles which can be explained by the difference in their conformations: planar for both enol forms and non-planar for the keton form. Indeed, the planar conformation of the enol form makes easy the resonance throughout the molecule. It is also demonstrated that the stability and the absorbance of avobenzone are solvent-dependent. The keto tautomer absorbs in the UVB region essentially in cyclohexane and 1-exanole, and its absorption is shifted to the UVC region in the case of hexanoic acid ($\lambda_{\mathrm{m}}ax$ = 237.28 nm).

All in all, the quantum computing can play a valuable role in interpreting and why not in predicting new UV absorbers.

References

1. Lu´ıs P d S, Paulo J O F, Dar´ıo J R D, Margarida S M, Joaquim C G EdS. Structural, Energetic, and UV–Vis Spectral Analysis of UVA Filter 4-tert-Butyl-4-methoxydibenzoylmethane. J. Phys.Chem., 2014, 118(8), 1511–1518.
2. Minoru Y, Mayumi K. Photothermal Tautomerization of a UV Sunscreen (4-tert-Butyl-4-methoxydibenzoylmethane) in Acetonitrile Studied by Steady-State and Laser Flash Photolysis. J. Phys. Chem. A.,2013, 117(9), 1946–1951
3. Halliday G M, Agar N S, Barnetson R St C, Ananthaswamy H N, Jones A M. UV-A Fingerprint Mutations in Human Skin Cancer. Photochem.Photobiol., 2005, 81, 3-8
4. Venditti E, Spadoni T, Tiano L, Astolfi P, Greci L, Littarru G P, Damiani E. Invitro photostability and photoprotection studies of a novel 'multi-active' UV-absorber. Free Radical Bio Med., 2008, 45(3), 345-354.
5. Paris C, Lhiaubet-Vallet V, Jimenez O, Trullas C, Miranda M A.A Blocked Diketo Form of Avobenzone: Photostability, Photosensitizing Properties and Triplet Quenching by a Triazine-derived UVB-filter. Photochem.Photobiol., 2009, 85, 178-184.
6. Lu´ıs P dS, Paulo JOF, Margarida S M,Joaquim C G EdS. A theoretical study of the UV absorption of 4-methylbenzylidene camphor: from the UVB to the UVA regionPhotochem. Photobiol. Sci.,2015, 14, 465-472.
7. Gustavo H G T, Vinicius G. M, Ricardo D G, Claudinéia A S O P, Maria V R V, Kathia M H, André R B.Theoretical study of tautomers and photoisomers of avobenzone by DFT methods. J. MolModel.,2015, 21(12), 319.
8. Georges J M, Bice S M. J.Photostability of the sunscreening agent 4-tert-butyl-4-methoxydibenzoylmethane (avobenzone) in solvents of different polarity and proticityPhotochem. Photobiol A., 2008, 200(2-3), 410-420.
9. Zoe D D M D. Hair, sun, regulation, and beauty. J. Cosmet. Dermatol., 2014, 13, 1-2.

10. Frisch M. J. et al (2010) Gaussian 09, Revision A.02, Gaussian, Inc., Wallingford CT.
11. Adamo C, Barone V.Toward reliable density functional methods without adjustable parameters: The PBE0 model. J.Chem. Phys., 1999,110, 6158.
12. Becke A D.Density-functional thermochemistry. III. The role of exact exchange. J. Chem. Phys., 1993, 98, 5648–5652
13. Zhao Y, Truhlar D G.The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements: two new functionals and systematic testing of four M06-class functionals and 12 other functionals. Theor. Chem. Acc., 2008, 120, 215–241.
14. Yanai T, Tew D, Handy N.A new hybrid exchange–correlation functional using the Coulomb-attenuating method (CAM-B3LYP). Chem. Phys. Lett., 2004, 393, 51–57.
15. Hehre W J, Ditchfield R, Pople J A.Self—Consistent Molecular Orbital Methods. XII. Further Extensions of Gaussian—Type Basis Sets for Use in Molecular Orbital Studies of Organic Molecules. J. Chem. Phys., 1972, 56, 2257–2261.
16. Bader R F W, Essén H.The characterization of atomic interactions.J. Chem. Phys., 1983, 80 :1943–1960.
17. Bone R G A, Bader R F W.Identifying and Analyzing Intermolecular Bonding Interactions in van der Waals Molecules. J. Phys. Chem., 1996, 100, 10892–10911.
18. M.F. Bobrov, G.V. Popova, V.G. Tsirelson. A topological analysis of electron density and chemical bonding in cyclophosphazenes PnNnX2n (X = H, F, Cl; n = 2, 3, 4). Russ. J. Phys. Chem., 2006, 80(4), 584–590.
19. Tomasi J, Mennucci B, Cammi R. Quantum Mechanical Continuum Solvation Models Chem. Rev., 2005, 105, 2999-3094.