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Computational Study of the Visible Spectrum of Curcumin's Protonation States

Peter Braegelmann

Joseph D. Alia
University of Minnesota - Morris, aliaj@morris.umn.edu

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Computational Study of the Visible Spectrum of Curcumin's Protonation States

Peter Braegelmann and Joseph Alia

Division of Science and Mathematics, University of Minnesota, Morris

Abstract: Curcumin, the main dye in the important Indian spice turmeric, has received much attention recently for its potential anti-cancer and anti-Alzheimer properties.[1] Our study computes the thermodynamics and spectroscopic properties of curcumin's various protonation states using several methods and compares the results to experiment. M06/3-21G* gave the best thermodynamic results, while M06 with 3-21G* and 6-31G* gave good spectroscopic results for the neutral and dianionic forms of curcumin. However, applying diffuse functions appears to be necessary for the trianionic form. Interestingly, M06 and B3LYP with 6-31+G* gave good spectroscopic results for the singly anionic form.

Background and Introduction

Curcumin, the main pigment of the spice turmeric, is believed to be responsible (along with other curcuminoids) for the spice's beneficial health properties, acting as an antioxidant and anti-inflammatory agent.[2] The polyprotic molecule, which displays tautomerization as seen in ***Figure 1***, has enjoyed attention recently in the scientific literature with focus devoted to exploring its stability,[2] solubility,[2] bioavailability, chelation with metals,[3] radical activity, degradation, use as an anti-cancer and anti-Alzheimer's drug,[1] and more. Curcumin has also been commonly used for years in the spectrophotometric quantification of boron.

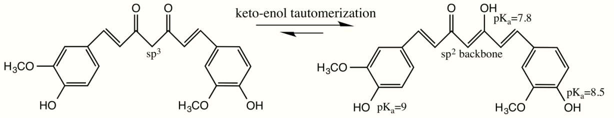

Figure 1: keto and enol forms. Lit. pK_a values for the 3 acidic protons shown.[4] Curcumin can also exist as H_4Curc^+ in very acidic media.

The focus in the present research was to computationally study curcumin's theoretical thermodynamics and UV-visible light absorptions in its various protonation states to find methods that agree with experiment. Comparison of these theoretical results with experimental results is relevant because the keto, enol, and different protonation states of curcumin at different pH values are expected to absorb light at different wavelengths. Several popular density functionals were used with small basis sets and time-dependent (TD) approximations to see which gave best agreement with experimental visible absorption spectra of curcumin at different pH's.

Future Work & Acknowledgements

- In-depth study of conformers, degradation, and solvent effects
- Study of H-atom abstraction
- Free radicals and their mechanistic pathways
- Develop undergrad labs/experiments for study abroad program
- TD B3LYP calculations on further protonation states

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Methods

All computations were done using the Gaussian 09 package. H_3Curc (enol), H_3Curc (keto), and H_2Curc^- (enolate) were optimized with HF, B3LYP, M06, M06-HF, and M06-2X using 3-21G* and the SMD solvent model with water as the solvent. Next, ΔG° for enol-keto tautomerization was calculated using thermodynamic data gathered from Gaussian. Since M06/3-21G* gave results that best agree with literature (i.e. enol form more stable then keto form), higher basis sets with this level of theory were employed for computations on further conformers and protonation states of curcumin. Time-dependent (TD) HF, B3LYP, M06, M06-2X, and M06-HF calculations were carried out from the optimized geometries on each respective level. Visible light absorptions were gathered from these calculations and compared to experiment. Lastly, the same optimization and TD calculations were performed on various H-bonded conformers of curcumin dimers and trimers.

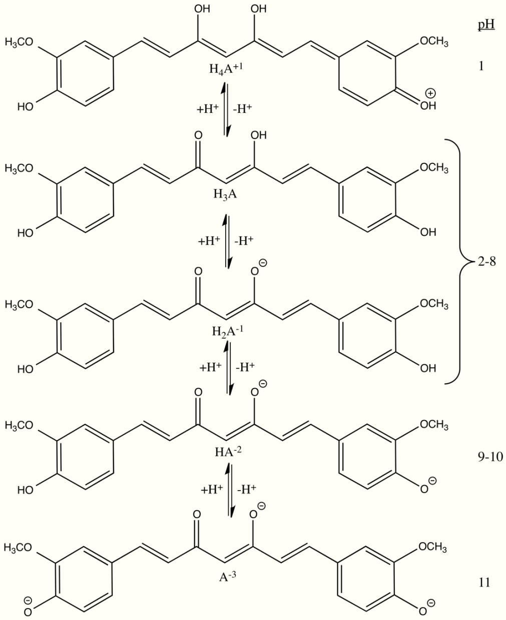


Figure 2: The various protonation states of curcumin and the pHs corresponding to those states.[5]

Results

Thermodynamics

Computed Values	M06/ 3-21G*	M06/ 6-31G*	M06/ 6-31+G*	M06-2X/ 6-31G*	M06-HF/ 6-31G*	HF/ 3-21G*	HF /6-31G*	B3LYP/ 6-31G*
ΔG° (G° enol – G° keto)	-33.302	-0.02363	5.8680	-13.655	-17.859	29.356	42.331	38.702

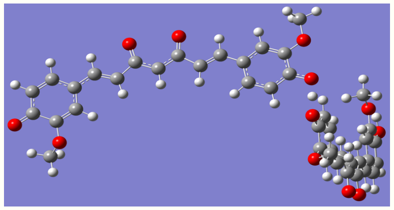
Table 1: Difference in Gibbs free energy between enol and keto forms. A lower negative value indicates that the enol form is favored in enol-keto tautomerization

Spectroscopy

λ_{max} (nm)	M06/ 3-21G*	M06/ 6-31G*	M06/ 6-31+G*	M06-2X/ 6-31G*	M06-HF/ 6-31G*	HF/ 6-31G*	B3LYP/ 3-21G*	B3LYP/ 6-31G*	Experimental[6]	Experimental Literature[5]
H_4A^{+1}	528	529	537	--	--	--	--	--	~555	555
H_3A (enol)	434	438	452	375	327	300	436	450	430	420-430
H_3A (keto)	352	356	368	306	274	268	328	362	--	--
H_2A^{-1}	392	401	417	356	326	288	381	419	??	420-430
HA^{-2}	459	457	471	--	--	--	--	--	~450	430 & 520
A^{-3}	443	455	482	--	--	--	--	--	470	480

Table 2: Theoretical UV-vis absorptions compared to experimental and literature values. Highlighted values are in good agreement with experiment/literature. M06/3-21G* accurately describes absorption, but the diffuse function of M06/6-31+G* appears to be necessary to describe the trianionic form. The computed values have relatively good agreement with experimental values.[5]

Image 1: Bent dimer of two dianionic curcumin molecules showing unusually short H-bonds (1.18-1.26 Å). Without solvation, the dimer optimized as a planar species.



Conclusions

M06/3-21G* gives best thermodynamic results for enol-keto tautomerization, and only M06/6-31+G* gave pKa values close to literature: 9.554, 12.03, and 11.25 for pK_{a1}, pK_{a2}, and pK_{a3} respectively. M06/3-21G* accurately describes the absorptions of the neutral and dianionic forms, but the diffuse function of M06/6-31+G* is needed for the trianionic form. It appears that SMD should be used with M06 for best results. The formation of H-bonded dimers and trimers (as Möbius bands) is supported theoretically and experimentally.[6] Lastly, some unusually short H-bonding was observed in dimers and trimers.

References

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