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Pseudo-Jahn-Teller Effect and Photoprotective Potential of Curcumin

Does nature favor symmetry?

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ABSTRACT

This work presents theoretical investigation of curcumin, organic dye produced by *Curcuma longa* species. Molecular and electronic structures of its keto–keto, enol–keto and enolate forms were analyzed. High-symmetric tautomers in gas-phase together with their deprotonated forms in various symmetric groups were identified using density functional theory and hybrid functional. Lower-symmetric unstable geometries were clarified by Pseudo-Jahn-Teller (PTE) effect, applying PTE vibronic interactions between the ground electron state and selected excited states. Theoretical results indicate significance of PTE effect which may alter aforementioned levels of photodynamic processes producing stable enol and keto curcumin structures. PTE may play an essential role and opens new opportunities for understanding photoprotection and bioactivity of natural dyes.

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INTRODUCTION

Nature seems to like symmetry. However, there are only few types of biomolecules in plants and fungi that are symmetric. Concept of molecular symmetry in chemistry and biology explains various properties of compounds such as their toxicity. It is a well-known fact that high-symmetric xenobiotics may perform a negative role in living systems.[1] If an aromatic entity is necessary in some biochemical processes, the symmetry is usually lowered by substituting side chains using, e.g., an alkyl, hydroxyl, or acetate group. Curcumin (diferuloylmethane) has an interesting position among symmetric organic molecules in plants. This yellow pigment of turmeric (*Curcuma longa*) has been recently examined and shown the protective effects against skin carcinogenesis caused by chronic UV irradiation.[2,3] This mechanism of photoprotective effect of curcumin is still unclear. In principle, it can be based on fluorescence, phosphorescence, and/or nonradiative transitions. Upon the absorption of a high energy dose, a low-energy photon may be generated due to the luminescence. Alternatively, the excited state curcumin can interact with the highly reactive singlet oxygen molecule with the subsequent formation of the less reactive triplet oxygen molecule.[4] Such processes demand the appropriate setting of energy levels of electronic and vibration states. From a theoretical point of view, the (Pseudo)-Jahn-Teller effect (PJTE) can particularly modulate these energy levels of symmetric compounds.

METHODS AND MATERIALS

Gaussian16 software was used for all quantum-chemical calculations.[5] Geometries of various forms of curcumin in singlet ground or excited states were optimized within C_{2v}, C_2, C_s or C_1 symmetries using the M06-2X hybrid functional[6] with standard cc-pVDZ basis sets for all atoms from the Gaussian library. The Time-dependent DFT (TD-DFT) treatment[7] for up to 30 vertical electronic states was used for excited state calculations. For comparison, optical transitions were also calculated using the 3-parameter hybrid B3LYP functional.

Table 1. Relative DFT energies (in kJ/mol) and imaginary vibrations of optimized molecules for different electronic states.

Model	Form	C=O vs. OCH3 conf.	Symmetry	State	DFT energy	Imagin. vibration
Ia	keto-keto	*anti, anti*	C_{2v}	X^1A_1	–1263.18213	a_2
			$\mathbf{C_2}$	$\mathbf{X^1A}$	–1263.18970	-
Ib	keto-keto	*syn, syn*	C_{2v}	X^1A_1	–1263.18222	a_2
			$\mathbf{C_2}$	$\mathbf{X^1A}$	–1263.19285	-
IIa	enol-keto	*anti, anti*	C_{2v}	X^1A_1	–1263.19665	b_1
			$\mathbf{C_s}$	$\mathbf{X^1A'}$	–1263.20488	-
			C_s	$1^1A''$	–1263.19234	a”
			$\mathbf{C_1}$	$\mathbf{X^1A}$	–1263.19946	-
IIb	enol-keto	*syn, syn*	C_{2v}	X^1A_1	–1263.19614	b_1
			$\mathbf{C_s}$	$\mathbf{X^1A'}$	–1263.20438	-
			C_s	$1^1A''$	–1263.19183	a”
			$\mathbf{C_1}$	$\mathbf{X^1A}$	–1263.20048	-
IIIa	enolate	*anti, anti*	$\mathbf{C_{2v}}$	$\mathbf{X^1A_1}$	–1262.63429	-
IIIb	enolate	*syn, syn*	$\mathbf{C_{2v}}$	$\mathbf{X^1A_1}$	–1262.63305	-

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RESULTS

Curcumin symmetric neutral keto-keto (I models) and enol-keto (II models) forms as well as anionic enolate (III models) forms were studied (Figure 1.). Geometry optimizations of these systems started in the highest identified C_{2v} symmetry groups followed by re-optimization within its C_2, C_s, and C_1 subgroups:

a. Keto-keto forms (Ia, Ib)
  - Unstable geometries: C_{2v} symmetry with a single imaginary a_2 vibration
  - Stable geometries: C_2 symmetry ($K(C_{2v}, a_2)$ kernel subgroup)
  - The pseudo-JT vibronic interaction between the X^1A_1 and the 1^1A_2 in C_{2v} symmetry corresponds to the 1^1A in C_2 symmetry

b. Enol forms (IIa, IIb)
  - Unstable geometries: C_{2v} symmetry with a single imaginary b_1 vibration
  - Stable geometries: C_s symmetry with the preserved σ_v mirror plane ($K(C_{2v}, b_1)$ kernel group)
  - The pseudo-JT vibronic interaction between the X^1A_1 and the 1^1B_1 in C_{2v} symmetry corresponds to the $1^1A'$ in C_s symmetry
  - Stable geometries: C_1 symmetry ($K(C_s, a'')$ kernel subgroup)
  - The pseudo-JT interaction between the excited electron states of the C_s symmetry structures (hidden JT effect)
  - The pseudo-JT interaction between $1^1A''$ and near A’ excited electron states within the C_s symmetry group

c. Enolate structures (IIIa, IIIb)
  - Only C_{2v} symmetry with no imaginary frequency – weak pseudo-JT effect in the systems

Table 2. Symmetry group / electronic ground state (GS), excitation energies E_{exc} in eV and oscillator strengths *(f)* in atomic units for the corresponding electron transitions of the excited states for the optimized structures in relevant electron states.

Model	Group/ GS	Exc. el. state	E_{exc}	f	Group/ GS	Exc. el. state	E_{exc}	f
Ia	C_{2v}/X^1A_1	1^1B_1	3.443	0.00	C_2/X^1A	1^1B	3.616	0.00
		$\mathbf{1^1A_2}$	**3.621**	0.00		1^1A	3.688	0.01
		1^1B_2	4.191	1.38		2^1B	4.154	1.39
		1^1A_1	4.378	0.13		2^1A	4.340	0.10
		2^1B_2	4.900	0.08		3^1B	4.714	0.00
Ib	C_{2v}/X^1A_1	1^1B_1	3.441	0.00	C_2/X^1A	1^1B	3.484	0.02
		$\mathbf{1^1A_2}$	**3.621**	0.00		1^1A	3.699	0.00
		1^1B_2	4.171	1.34		2^1B	3.960	0.91
		1^1A_1	4.353	0.13		2^1A	4.190	0.32
		2^1B_2	4.867	0.02		3^1B	4.813	0.01
IIa	C_{2v}/X^1A_1	$\mathbf{1^1B_1}$	**3.388**	1.75	$C_s(\sigma_v)/X^1A'$	$1^1A'$	3.475	1.81
		1^1B_2	4.048	0.00		$\mathbf{1^1A''}$	**3.850**	0.00
		1^1A_1	4.164	0.07		$2^1A'$	4.159	0.08
		$\mathbf{2^1B_1}$	**4.472**	0.07		$3^1A'$	4.610	0.02
		2^1A_1	4.770	0.00		$4^1A'$	4.792	0.00
IIa	$C_s/1^1A''$	$1^1A'$	3.371	1.77	C_1/X^1A	1^1A	3.446	1.40
		$\mathbf{1^1A''}$	**3.217**	0.00		2^1A	3.884	0.00
		$2^1A'$	3.957	0.13		3^1A	4.177	0.19
		$3^1A'$	4.551	0.02		4^1A	4.583	0.05
		$4^1A'$	4.687	0.01		5^1A	4.797	0.00
IIb	C_{2v}/X^1A_1	$\mathbf{1^1B_1}$	**3.372**	1.78	$C_s(\sigma_v)/X^1A'$	$1^1A'$	3.459	1.83
		1^1B_2	4.044	0.00		$\mathbf{1^1A''}$	**3.848**	0.00
		1^1A_1	4.120	0.07		$2^1A'$	4.118	0.07
		$\mathbf{2^1B_1}$	**4.441**	0.04		$3^1A'$	4.593	0.01
		2^1A_1	4.790	0.00		$4^1A'$	4.800	0.01
IIb	$C_s/1^1A''$	$1^1A'$	3.352	1.80	C_1/X^1A	1^1A	3.424	1.48
		$\mathbf{1^1A''}$	**3.216**	0.00		2^1A	3.892	0.00
		$2^1A'$	3.916	0.11		3^1A	4.149	0.17
		$3^1A'$	4.536	0.02		4^1A	4.573	0.05
		$4^1A'$	4.695	0.02		5^1A	4.810	0.00
IIIa	C_{2v}/X^1A_1	1^1B_2	2.952	0.00				
		1^1B_1	3.045	0.72				
		1^1A_2	3.612	0.00				
		1^1A_1	3.637	0.01				
		2^1B_1	4.404	0.00				
IIIb	C_{2v}/X^1A_1	1^1B_2	2.955	0.00				
		1^1B_1	3.056	0.79				
		1^1A_2	3.621	0.00				
		1^1A_1	3.680	0.00				
		2^1B_1	4.373	0.02				

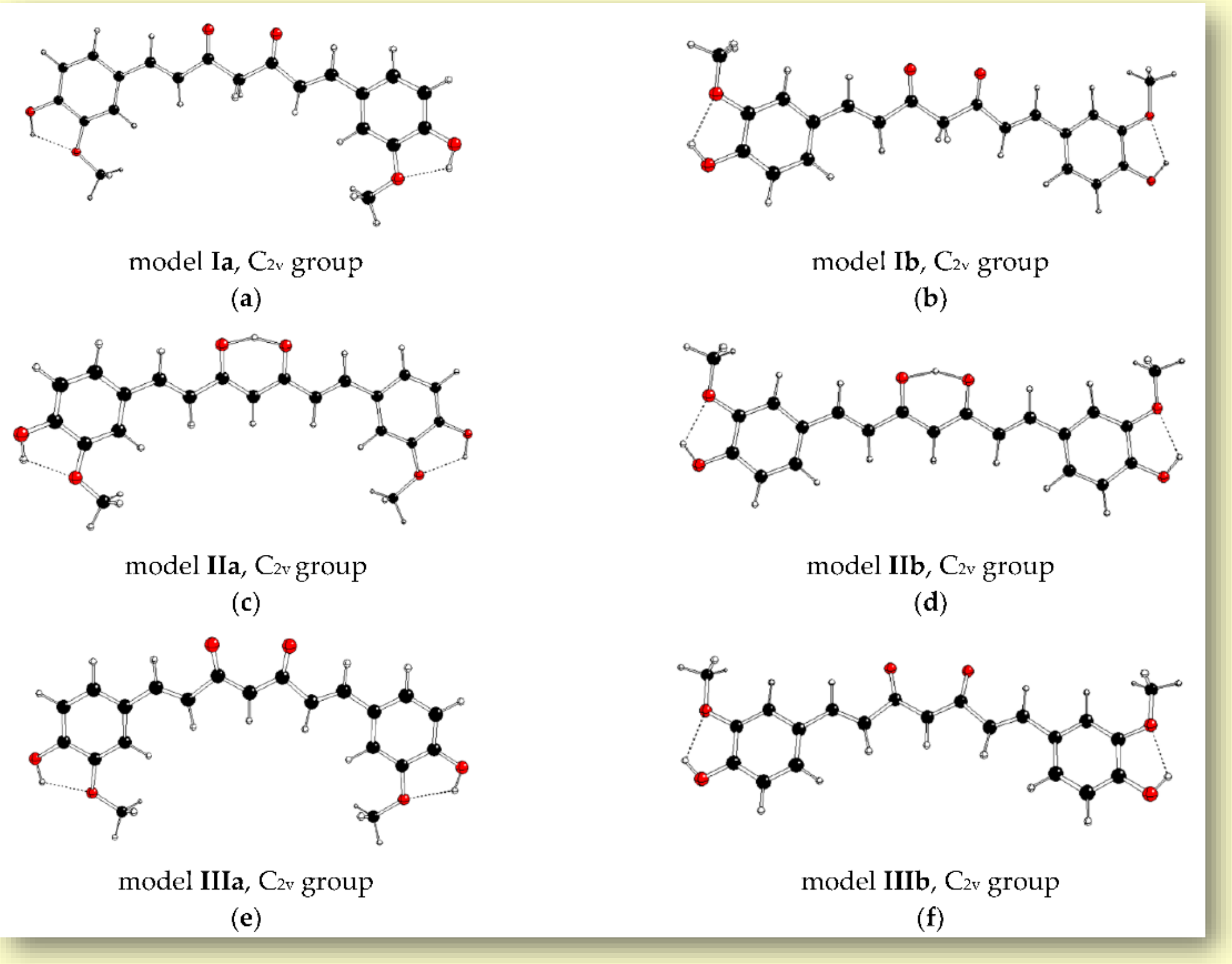

Figure 1. M06-2X/cc-pVDZ optimized curcumin structures of C_{2v} symmetry of the neutral keto-keto (a, b) and enol (c, d) forms and anionic enolate forms (e, f)

Table 3. PJT stabilization energies E_{JT} for the relevant electronic states of the stable optimized structures of JT subgroups related to their parent groups and electron states

Model	Parent group			Subgroup		EJT
	Symmetry	Electronic state		Symmetry	Electronic state	/ eV
Ia	C_{2v}	X^1A_1		C_2	X^1A	0.206
Ib	C_{2v}	X^1A_1		C_2	X^1A	0.289
IIa	C_{2v}	X^1A_1		$C_s(\sigma_v)$	X^1A'	0.224
	C_s	$1^1A''$		C_1	X^1A	0.194
IIb	C_{2v}	X^1A_1		$C_s(\sigma_v)$	X^1A'	0.224
	C_s	$1^1A''$		C_1	X^1A	0.235

CONCLUSIONS

The theoretical study of curcumin tautomers in C_s, C_{2v}, C_2 and C_1 symmetry point groups showed:

1. Based on the normal mode analysis, unstable geometries with corresponding symmetries were determined. The indicated symmetry descent was ascribed to the PJT vibronic interaction between the ground electron state and the selected excited states.
2. The PJT effect may modulate the setting of electronic and vibration energy levels upon photodynamic processes. This fact may play the essential role in photoprotection action and activity of symmetric naturally occurring dyes.
3. Our findings open new ways on the study and understanding of photodynamic processes for (quasi)symmetric organic molecules in plants and fungi.

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