

Ultraviolet Absorption Spectrum of Malonaldehyde in Water Is Dominated by Solvent-Stabilized Conformations

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S Supporting Information

ABSTRACT: Free energy calculations for eight enol isomers of malonaldehyde (MA) and simulation of the ultraviolet (UV) absorption spectrum in both the gas phase and water (pH = 3, where the molecule exists in neutral undeprotonated form) show that in water the two *s-trans* nonchelated enol conformers of MA become thermodynamically more stable than the internally hydrogen-bonded (“chelated enol”) conformer (CE). The pure CE conformer in water has a slightly red-shifted UV spectrum with respect to that in the gas phase, but the blue-shifted spectrum observed in water at pH 3 is dominated by solvent-stabilized conformations that have negligible populations in the gas phase. Density functional calculations with the solvation model based on density (SMD) and an ensemble-averaged vertical excitation model explain the experimental observations in detail.

As the simplest and smallest β -diketone, malonaldehyde (MA) is a good model molecule to study the roles of β -diketones in a variety of applications, e.g., applications as chelating agents of transition metals¹ and as ultraviolet filters.² In the gas phase, MA exists mainly as a chelated enol (CE) conformer, which is favored compared to other conformers (keto and nonchelated enol (NCE) conformers) by an intramolecular hydrogen bond. The conformational equilibrium of MA in solution is greatly influenced by the nature of the solvent (e.g., its polarity and proticity) and by the pH value in aqueous solution.³

Experimentally, the ultraviolet (UV) absorption,^{4,5} nuclear magnetic resonance (NMR),^{6,7} and infrared spectra⁸ have been used to assign the dominant conformer of MA in diverse solvents. Since the 1960s, MA has been believed to exist in aqueous solution with pH \leq 3 as the CE conformer with a strong UV absorption band peaked at \sim 245 nm; for pH $>$ 7, MA is completely deprotonated to the *s-trans* enolate anion, which absorbs at 267 nm.^{4,5} In a recent ultrafast photoisomerization study⁹ of intramolecularly H-bonded symmetric β -diketones, the UV-induced photoisomerization of MA in water at pH = 3 was analyzed as a process of converting CE to NCE conformers.

In 1968, Kwon et al.⁵ assigned the absorption band of MA in chloroform, which has maximum at 271 nm (corresponding to an excitation energy of 4.59 eV), to *s-trans* enol (nonchelated enol, which is TTT or TTC in Figure 1) based on the NMR study of Bothner-By and Harris,⁷ who concluded that the enol form of MA in chloroform is predominantly in *s-trans* conformations. However, in the same year, George and Mansel⁶ reported that

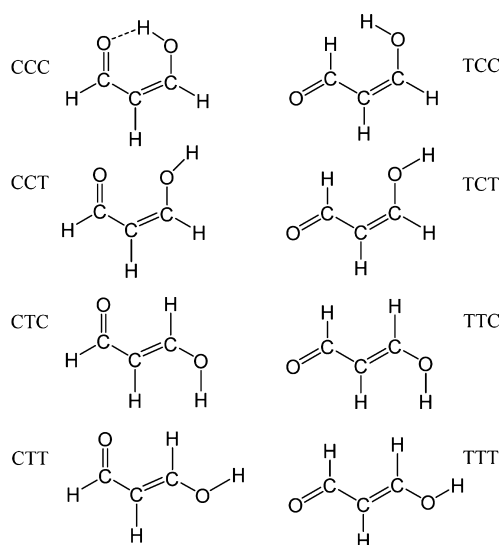


Figure 1. Schematic picture of the enol isomers of MA. C and T stand for the *cis* and *trans* character of C–C, C=C, and C–O bonds. CCC is the chelated enol (CE) conformer. The other seven isomers are nonchelated enol (NCE) conformers.

MA should be present as an *s-cis* enol (in particular, the CE conformer) in chloroform based on their NMR study, and they pointed out that Bothner-By and Harris were misled by polar impurities in the solution (the solution contained ethanol, water, hydrochloric acid, and the original acetal). Therefore, the 271 nm absorption of MA in chloroform should be due to the CE conformer instead of the *s-trans* conformers assigned by Kwon et al.⁵ This finding motivated us to study the effect of solvent on conformational populations and spectra of MA by computations. In this work, we choose water as solvent and a pH value of 3 where the molecule exists in neutral undeprotonated form.

Our calculations on the spectrum of MA have two steps. In the first step we calculate the conformational populations in the ground electronic state prior to photon absorption. In the second step we calculate the excitation probabilities for each conformation and weight them according to the ground-state population. All our calculations are for 300 K, and we use a standard state of a 1 M ideal solution for aqueous solution.

We use two levels of theory for ground-electronic-state conformational equilibria: (i) Kohn–Sham density functional

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theory with the M06 exchange-correlation functional¹⁰ and the def2-TZVP basis set,¹¹ a combination denoted as M06, and (ii) the CCSD(T) coupled cluster method¹² with the jun-cc-pVTZ one-electron basis set¹³ and the F12a method¹⁴ to include explicitly correlated basis functions, a combination denoted CC. Density functional calculations were performed using *Gaussian 09*;¹⁵ the CC calculations were performed using *Molpro*.¹⁶

We optimized the geometries of all enol isomers of MA in the gas phase and in water by M06, using the solvation model based on density (SMD)¹⁷ to introduce the solvation effects (electrostatics, cavitation, dispersion, and solvent structure, including hydrogen bonding) in water. The M06 standard-state free energy of conformation n in the gas phase is denoted $G^\circ(n, g, \text{M06})$ and is calculated by the quasiharmonic approximation for vibrations with a frequency scaling factor of 0.982.¹⁸ The CC standard-state free energy of conformation n in the gas phase is estimated by

$$G^\circ(n, g, \text{CC}) = G^\circ(n, g, \text{M06}) + E(n, g, \text{CC}) - E(n, g, \text{M06}) \quad (1a)$$

where E is electronic energy including nuclear repulsion, and all quantities in eq 1a are computed at the M06 optimized geometry. Note that this is a standard way to combine two levels, and it would be denoted CC//M06 in the single-point energy notation of Pople. The M06 standard-state free energy of conformation n in the aqueous phase is given by

$$G^\circ(n, \text{aq}, \text{M06}) = G^\circ(n, g // \text{aq}, \text{M06}) + G_s^\circ(n) \quad (1b)$$

where $G^\circ(n, g // \text{aq}, \text{M06})$ is a gas-phase free energy computed by M06 at the optimized aqueous geometry with aqueous frequencies, and $G_s^\circ(n)$ is the free energy of solvation calculated by SMD/M06. This is then improved as in eq 1a to obtain $G^\circ(n, \text{aq}, \text{CC})$.

The enol isomers, shown in Figure 1, include one CE conformer, also labeled as CCC for consistency with other isomers, and seven NCE isomers (CCT, CTC, CTT, TCC, TCT, TTC, and TTT), where C and T stand for the *cis* and *trans* characters of C–C, C=C, and C–O bonds in that order. The keto conformer may have a larger equilibrium population in polar protic solutions than in the gas phase, but since it has a much weaker absorption in the region of interest and since we are concerned with the spectral shape (not its absolute intensity) and on assignment of the strong absorption band of MA in water at pH = 3, we need not consider the keto tautomer; therefore, all our populations refer to relative conformational populations of only the enol conformers.

Table 1 supports the accepted assignment of the chelated enol (CCC) as the most stable conformer in the gas phase, and we find it is more stable than any other enol conformer by 6–11 kcal/mol in free energy as a result of the intramolecular hydrogen bond. However, in water, the effect of the intramolecular hydrogen bond is weaker due to the formation of intermolecular hydrogen bonds with water molecules. For this reason and because the CE conformer is less polar than the other conformers, we find that the polar water stabilizes the seven NCE conformers more, so much so that the two *s-trans* NCE conformers (TTC and TTT) have lower free energies than the CCC one in water. The population of conformer n in aqueous solution is given by

$$P_n = \frac{\exp[-\beta G^\circ(n, \text{aq}, \text{CC})]}{\sum_{n'} \exp[-\beta G^\circ(n', \text{aq}, \text{CC})]} \quad (2)$$

Table 1. Relative Free Energies (kcal/mol), Populations, and Calculated Vertical Excitation Energies^a (VEE, eV) of the $\pi\pi^*$ State in Water

n	in the gas phase		in water		
	$G^\circ(n, g, \text{CC})$	P_n	$G^\circ(n, \text{aq}, \text{CC})$	P_n	VEE ^a
CCC	0.00	100%	0.43	20%	5.07
CCT	11.38	0% ^b	3.87	0%	5.19
CTC	7.44	0%	2.83	0%	5.16
CTT	7.88	0%	2.75	0%	5.14
TCC	8.54	0%	3.19	0%	5.25
TCT	8.36	0%	1.90	2%	5.24
TTC	5.73	0%	0.06	37%	5.70
TTT	6.82	0%	0.00	41%	5.68

^aCalculated with VEM/M06. ^bFor all rows, 0% denotes <0.007% in the gas phase and $\leq 0.4\%$ in water.

where β is $1/RT$ where R is the gas constant and T is temperature. Based on this formula, we predict that in water, MA exists mainly as a mixture of the three isomers (TTT, TTC, and CCC), with CCC constituting only 20% of the population, as seen in Table 1.

Excitation energies of the first ten excited states are calculated by using linear-response time-dependent density functional theory¹⁹ with the M06 functional and the minimally augmented def2-TZVP basis set (ma-TZVP²⁰) and are denoted TDM06. The simplest approach to modeling the spectrum for a given electronic state is to calculate the vertical excitation energy (VEE) from the ground electronic state to the excited state using the ground-state equilibrium geometry according to the Franck–Condon principle and to compare this to the position of the band maximum in an experimental absorption spectrum. With this simple approximation, TDM06 yields a VEE of 3.96 eV (313 nm) for the first excited state S_1 of the CE conformer in the gas phase, which is an $\pi\pi^*$ state with a very small calculated oscillator strength f of 0.0009. The second excited-state S_2 is a $\pi\pi^*$ state that has the largest calculated f of 0.2, and it has a calculated VEE of 5.12 eV (242 nm), which is 0.41 eV higher than the energy of 4.71 eV that corresponds to the experimental band maximum (263 nm).²¹ In the ten excited states we calculated, the state that has the second largest f (in particular 0.02) is an $n\sigma^*$ state with Rydberg character and its VEE is 6.53 eV (190 nm). This $n\sigma^*$ state should be mainly responsible for the second intense absorption band maximum (190 nm) in the experiment.²¹

Next we consider aqueous solution. A state-specific vertical excitation model (VEM)²² is used to calculate the $\pi\pi^*$ excitation energies of all eight enol conformers in water. The model, denoted VEM/M06, accounts for the bulk-electrostatic contribution to solvatochromic shifts by solving the nonhomogeneous-dielectric Poisson equation by an integral equation formalism using the relaxed electronic state density matrix from TDM06 calculations based on two-time-scale solvent response. The vertical excitation energies obtained this way are in Table 1.

The VEE (5.07 eV: 244.5 nm) of the $\pi\pi^*$ state of the CE conformer in water agrees well with the experimental absorption maximum (245 nm: 5.06 eV) in water at pH = 3; however, we will show below that this good agreement is fortuitous. The TTT and TTC isomers, which are thermodynamically more stable than CE conformer in water, have higher VEEs (~ 5.7 eV: 218 nm), and the other isomers have VEEs in the region of 5.14–5.25 eV range (236–241 nm). All the NCE conformers have larger oscillator strengths than CE in water, and the f values of TTT ($f = 0.45$) and TTC ($f = 0.47$) are about twice that of CE ($f = 0.23$).

Next we include conformational and vibrational broadening as follows. For each conformation, we average the vertical excitation energy of one or more states over a set of molecular configurations (for gas-phase spectra) or MA–water cluster configurations (for aqueous spectra). The configurations are sampled from a molecular dynamics (MD) trajectory simulation (details are in Supporting Information) carried out by *NAMD*.²³ Then we take a weighted average of these spectra by weighting each conformation with the aqueous P_n . This includes the thermal conformational and ground-state vibrational broadening, and a critical aspect is that it includes the variation of oscillator strength with geometry. Then we use the computer code *Multiwfn*²⁴ to broaden each line by a Gaussian function with a half width at half-maximum (HWHM) of 0.25 eV;²⁵ this accounts for missing effects such as lifetime broadening, thermally excited vibrations, and rotations (whose effect is not included in the molecular dynamics runs, which are based on ground-state classical harmonic vibrational motions), anharmonic broadening, quantum effects, and instrumental resolution. The broadening width is large enough to produce a smooth profile of electronic spectrum.

In the gas phase, the calculated populations shown in Table 1 imply that absorption is dominated 100% by the CE conformer. So we used the TDM06 excitation energies of the $\pi\pi^*$ states for 200 MD snapshots of CE in the simulation of UV spectrum. As shown in Figure 2, our simulated $\pi\pi^*$ absorption maximum is at

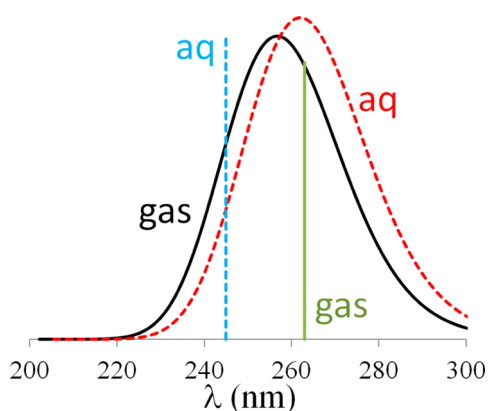


Figure 2. Simulated $\pi\pi^*$ absorption spectrum of the chelated enol (CE) conformer of MA. The vertical lines mark the positions of the band maxima observed in experiments.

256 nm (4.84 eV), and it agrees reasonably well with the strongest peak in the experiments,²¹ which is at 263 nm (4.71 eV). We see that the ensemble averaging and broadening of the spectrum due to a single conformation shifted the simulated maximum of $\pi\pi^*$ absorption by 0.28 eV compared to a simple VEE calculation, which indicates that the usual practice of interpreting spectra with the unaveraged VEE method is very dangerous.

As a check, presented in the SI, we repeated the calculation including 10 low-lying excited states for each of the 200 MD snapshots; this leads to two intense bands. There is hardly any change in the simulated spectrum for wavelengths greater than 235 nm, so the first maximum remains at 256 nm. This confirms that the strongest absorption is due to the $\pi\pi^*$ state. The simulated second strong absorption peaks at 193 nm and is also in good agreement with the experimental observation (190 nm: 6.53 eV).

In water, based on the experimental assignment, we first simulated the $\pi\pi^*$ absorption by only including CE conformer; this is also shown in Figure 2. We calculated the ensemble average of the $\pi\pi^*$ VEE obtained with VEM/TDM06 for the 200 CE–water clusters sampled from MD simulations. (With 200 samples, the results in Figure 2 are well converged with respect to the number of samples.) Each cluster contains the four water molecules closest to the two oxygen atoms to explicitly include hydrogen bonding and first-solvation-shell-specific complexation; each cluster is surrounded by SMD continuum solvent. Figure 2 shows that the simulated $\pi\pi^*$ absorption maximum of the CE conformer in water is slightly red-shifted to 262 nm (4.73 eV) with respect to that in the gas phase, in contrast to the distinct blue-shift observed⁹ in experiments. The absorption maximum is far from the experimental observation of 245 nm (5.06 eV) in water at pH = 3, and in fact, it is located in the absorption range of 255–271 nm (4.86–4.58 eV) of the photoisomerization product of MA in Verma et al.'s study.⁹ This raises the question: is the discrepancy due to inadequacies of the theory or have the experiments on this prototype molecule been misinterpreted? The conclusion of this letter will be that the latter answer is the correct one.

Next, we considered the effect of conformational populations on the spectrum in water. We renormalized the populations of the conformers in water in Table 1 by neglecting those with P_n smaller than 3%, so we only consider three conformers with renormalized populations of 42%, 38%, and 20% for TTT, TTC, and CCC, respectively. We first simulated the $\pi\pi^*$ absorption spectra of pure TTT and pure TTC in the same way as we did for the CE conformer; this is in Figure 3. Then we weighted these spectra using the renormalized populations; this is shown in Figure 4.

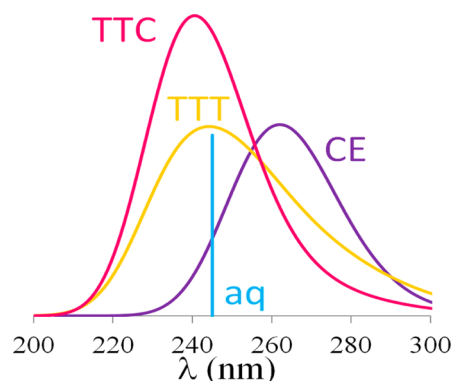


Figure 3. Simulated $\pi\pi^*$ absorption spectrum in water at pH = 3 by including only one conformer for three choices of the conformer: the chelated enol (CE) or the TTT or TTC nonchelated enol. The vertical line marks the strongest experimental peak.

As Figure 4 shows, the $\pi\pi^*$ absorption band of MA simulated in water by considering three conformers has a maximum (243 nm: 5.10 eV), very close to the experimental value (245 nm: 5.06 eV). Thus, the simulations reproduce the blue shift of the spectrum of MA upon dissolution in water mainly by accounting for the solvent-stabilized TTT and TTC conformers, which Figure 3 shows to contribute much more intensity than is provided by the chelated conformer. A key point is that gas-phase conformer is red-shifted by solvent, but the solvent-stabilized conformers account for the experimental blue shift. Clearly, the

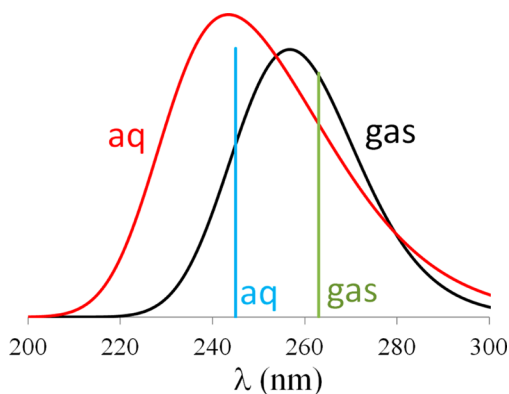


Figure 4. Simulated $\pi\pi^*$ absorption spectrum of MA in water at pH = 3, as a mixture of three enol isomers (nonchelated enols TTT (42%) and TTC (38%), and chelated enol CE (20%)), as compared to the gas phase absorption. The vertical lines mark the strongest peak values observed in experiments.

previous assignment of the enol conformer in water at pH = 3 has to be corrected.

The present findings imply changes in the interpretation of the ultrafast photoisomerization of MA in water at pH = 3. First, the main reactants are probably the TTT and TTC isomers due to their large equilibrium populations and dominant contributions to the spectra. Whereas the previous interpretations of possible photochemical or other nonradiative processes^{9,26,27} were in terms of an intramolecular hydrogen (proton) transfer process of the CE excited state conformer followed by dynamical rotamerizations, the present study shows that one must also consider initial NCE conformers that do not have a hydrogen transfer path. Second, the experimentally observed⁹ growing photoproduct absorption ranging from 255 to 271 nm after ~200 ps can be attributed to any of the enol conformers including CE, except for TTT and TTC, because as shown in Table 1 the other six conformers all have at least 0.43 eV lower VEEs than TTT and TTC in water, and they all could be responsible for the red-shifted absorption band of the product(s).

In summary, the UV absorption spectrum of MA in water is dominated by two solvent-stabilized conformations. The present study has several more general implications: (1) It is not sufficient to consider only electrostatic, polarization, and dispersion contributions to solvatochromic shifts, which has been standard for many years; one must also consider solvent-induced shifts in conformational equilibria, which can change the interpretation not just quantitatively but even qualitatively. (2) Even for a single conformer, ensemble averaging of excitation energies and oscillator strengths can have a significant effect on the location of the band maxima,²⁸ with a shift of 0.28 eV being observed here. (3) Quantum chemical analysis has reached a stage where conformational details that are often impossible to glean from experiment, can be calculated semiquantitatively and provide essential information necessary for a proper interpretation of experimental data.

■ ASSOCIATED CONTENT

📄 Supporting Information

Computational details of the MD simulations, optimized geometries and energetics of isomers of MA in the gas phase and in water, and complete refs 15 and 16. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b04845.

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Notes

The authors declare no competing financial interest.

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