Preface

The 4th International Conference on Functional Materials Science 2018 (ICFMS 2018) was international conference for promoting collaborative research program on physical and chemical studies of functional materials under the collaboration between Indonesian researchers and some researchers from institutions/universities in Asia and Europe, held in Bali, Indonesia, November 13-15, 2018. It was jointly organized by Institut Teknologi Bandung, Universitas Padjadjaran, Institut Teknologi Sepuluh November, Universitas Gadjah Mada, Universitas Indonesia, and RIKEN Nishina Center, Japan.

Our first conference held in Bali on April 27-28, 2011, successfully gathered researchers from 14 universities in Indonesia and 10 institutions/universities in Asia and Europe. Our second conference held in Lombok on November 12-13, 2014, also successfully gathered researchers from more universities and institutions in Asia and Europe. The third conference held in Bali on October 19-20, 2016, also successfully gathered researchers from more universities and institutions in Asia and Europe.

For the 4th ICFMS 2018, more than 120 papers were presented in both oral and poster presentation in various scopes including (1) Advanced and Functional Materials, (2) Materials and Devices, (3) New Materials for Energy and Energy Conversion (4) Biomaterials, (5) Theoretical/Modeling/Computer Simulations of Functional Materials, (6) Spectroscopy for Advanced Materials, (7) Hybrid and Composite Materials, and (8) Magnetic Materials. Each published paper was peer-reviewed by two reviewers for quality ensuring.

In conjunction with 4th ICFMS 2018, we also hosted the 2nd RIKEN Symposium, which was a continuation of the successfully previous 1st event in the frame of "International Workshop on Organic Molecule Systems" held in Penang, Malaysia, 2017, in collaboration between RIKEN Nishina Center and Universiti Sains Malaysia (USM). This symposium was intended to provide a platform for the exchange of research knowledge on organic molecular systems achieved by using muons as well as expanding the RIKEN's worldwide networks and linkages in collaborative research endeavors. Additionally, this activity also aims to encourage young students and researchers to work in the muon field in the future.

As an additional activity preceding the 4th ICFMS 2018, the organizing committee also offered a paper writing clinics for participants, especially for young scientists and students.

We believed great participation from all participants, organizing committees, and all reviewers made our conference successful.

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Solvent Effect on Bond Dissociation Enthalpy (BDE) of Tetrahydrocurcumin: A Theoretical Study

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Abstract. Solvent effect on bond dissociation enthalpy (BDE) of different functional groups of tetrahydrocurcumin is investigated. This is to evaluate how the polarity of a medium affect BDE and to clarify which functional groups hold the key role in its antioxidant activity through hydrogen transfer. We occupy density functional theory to calculate BDE through geometrical optimization and frequency calculation at six sites of tetrahydrocurcumin in water, methanol and chloroform solvents. The solvents represent polar and non-polar medium. Our result shows that BDE is lower in non-polar medium and hydrogen transfer is favored in this medium. A phenolic group is responsible for the antioxidant activity of tetrahydrocurcumin.

Introduction

Tetrahydrocurcumin ($C_{21}H_{24}O_6$), a polyphenol, is a derivative of curcumin that possesses antioxidant activity. This molecule is produced through hydrogenation of curcumin [1], which is extracted from the root of turmeric (*Curcuma longa*) [2]. In Indonesia, turmeric is commonly used as a spice. One latest research revealed that tetrahydrocurcumin has a significant protective effect against lipid peroxidation. This protective effect is due to the antioxidant activity of tetrahydrocurcumin [3].

Antioxidant activity of an antioxidant molecule, as well as tetrahydrocurcumin, is correlated to its ability to transfer a hydrogen atom toward free radical hence preventing it to promote lipid peroxidation [4]. Bond dissociation enthalpy (BDE) is one criterion to measure antioxidant activity. Low X-H BDE marks an easy dissociation, thus a fast hydrogen atom transfer from antioxidant molecule toward free radical can be achieved.

Evaluation of the antioxidant activity of tetrahyrocurcumin has a long history. In 1995, Osawa et.al evaluates antioxidant activity of curcuminoids and their derivatives by using linoleic acid and concludes that tetrahydrocurcumin has the highest protective effect [5]. By performing an assay using an organic radical in methanol solution, Portes et.al shows that tetrahydrocurcumin is more efficient in scavenging the organic radical as compared to curcumin. They attribute this efficiency to the presence of benzylic hydrogen in tetrahydrocurcumin [6]. Morales et.al agrees with their result but attribute

the efficiency to the presence of phenolic and enolic groups in tetrahydrocurcumin [1], see Fig 1. The disagreement on which functional groups of tetrahydrocurcumin holds the key role to its antioxidant activity has triggered us to evaluate BDE to clarify this problem.

We aim our research to evaluate the BDE of tetrahydrocurcumin in various solvents that represent polar and non-polar medium and to formulate how solvents affect the BDE by occupying density functional theory (DFT). In one previous study which uses DFT to evaluate BDE of resveratrol (a molecule with one phenolic group), it is concluded that BDE is lower in the gas phase and non-polar medium. Thus, we would expect that dissociation of an X-H bond of tetrahydrocurcumin is affected by the polarity of the medium [7]. Three solvents are chosen to represent polar and non-polar medium, which are water (we assume that biological system contains mostly water), methane (antioxidant assay is mostly done in methanol environment [6]), and chloroform. Water and Methanol represent a polar medium while chloroform represents a non-polar medium.

Computational Details

We conduct our research by using a DFT scheme. DFT solves Kohn-Sham equation numerically to generate electronic energy of many-electron system. To do so, two approximations which are exchange-correlation (XC) functionals and basis set (BS) are needed. In this research, tetrahydrocurcumin which consists of carbon, hydrogen and oxygen atoms is chosen as the many-electron system. We also choose M05-2X functional and 6-31++G(d,p) BS as our approximations for two reasons. First, the developer of M05-2X functional suggests it for bond dissociation energies calculation [8]. Second, 6-31++G(d,p) adds polarization and diffuse functions on hydrogen atoms.

All calculation is performed using a Gaussian 09 program package [9]. We do our calculation in two ways, (1) full geometry optimization and frequency calculation using M05-2X//6-31++G(d,p) directly, and (2) full geometry optimization and frequency calculation using M05-2X//6-31G then continue to single-point energy (SPE) and frequency calculations using M05-2X//6-31++G(d,p). Full geometry optimization predicts the most stable geometry of tetrahydrocurcumin as well as calculating its electronic energy. SPE calculation calculates the electronic energy of certain geometries. Meanwhile, frequency calculation will ensure that the calculated geometries are located at the lowest point of a potential well. We conduct our research in three stages as follow.

Stage 1: Geometry calculation at the ground state. First, we vary the orientation of -OH and -OCH3 groups at the phenolic group of tetrahydrocurcumin in three different combinations. Then we calculate
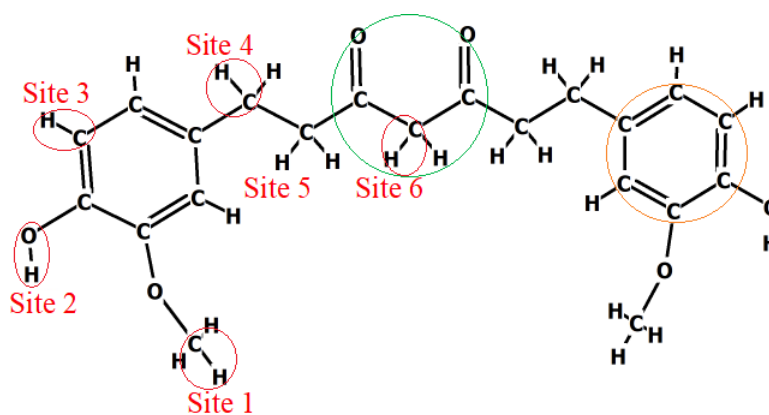
Fig. 1: Kekule structure of tetrahydrocurcumin. There are two information presents through this figure. (1) Functional groups of tetrahydrocurcumin which are marked by green and orange circles. The green circle marks beta-diketone group (this group can be arranged in either diketo or enol tautomer) and orange circle marks benzene group. When -OH group is included in the benzene group, it is called a phenolic group. (2) Six chosen sites of tetrahydrocurcumin marked by site 1 until site 6.

the electronic energy of each combination. The aim of this stage is to determine which combination is the molecular geometry of tetrahydrocurcumin at the ground state. The molecular geometry is used to verify that XC functional and BS chose are appropriate to study tetrahydrocurcumin system.

Stage 2: Tetrahydrocurcumin in solvents. Second, we continue to calculate the electronic energy of tetrahydrocurcumin and tetrahydrocurcumin radical in various solvents environment. The solvent effect is built with the polarized continuum model (PCM) method [10], where the solvent is modeled as a cavity with certain dielectric constant.

Tetrahydrocurcumin radical is formed when dissociation occurs, which is in this research is performed through one hydrogen atom abstraction from site 1 to 6 (see Fig 1). Site 1, site 2 and site 3 represent C-H and O-H bonds at a phenolic group. Site 4 and site 5 represent C-H bonds at the carbon chain. Meanwhile, site 6 represents C-H bond at the beta-diketone group. Abstraction sites are only chosen from one part of the molecule due to the symmetrical geometry of the tetrahydrocurcumin molecule. The radicals generated are called rad 1 to rad 6 based on the abstraction sites.

Stage 3: Bond Dissociation Enthalpy. Third, we calculate the BDE of tetrahydrocurcumin in three different solvents. Frequency calculation provides thermal correction to electronic energy yielding enthalpy (H) at 298.15 K. BDE of an O-H or C-H bond in tetrahydrocurcumin can be calculated according to Eq. 1. H(THC-H), H(THC·) and H(H·) represent enthalpy of tetrahydrocurcumin molecule that possesses complete hydrogen atoms, enthalpy of tetrahydrocurcumin molecule without one hydrogen atom (or also called tetrahydrocurcumin radical), and enthalpy of a hydrogen atom.

$$BDE = H(THC·) + H(H·) − H(THC − H) \qquad (1)$$

Results and Disscusion

Molecular Geometry of Tetrahydrocurcumin at the Ground State. Figure 2 displays optimized molecular geometry of tetrahydrocurcumin with three different combinations of -OH and -OCH3 groups orientation. Among the combinations, the electronic energy of geometry (a) is 0.31 eV and 0.40 eV lower than electronic energy of geometry (b) and (c), respectively. From frequency calculation, we confirm that geometry (a) is located at the lowest point of potential well since there is no imaginary frequency is generated. In this geometry, the orientation of -OH group bends toward -OCH3 group. This formation supports hydrogen bonding to form between H4 and O5 atoms, thus stabilizes this geometry. From this result, we suggest that geometry (a) represents the molecular geometry of tetrahydrocurcumin at the ground state.
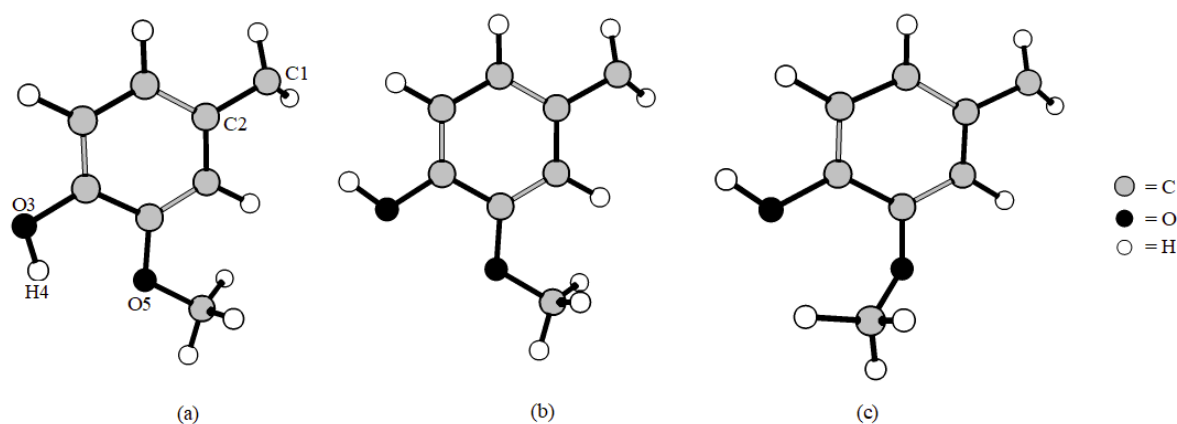
Fig. 2: Geometry (a), (b) and (c) present three different combinations of -OH and -OCH3 groups at a phenolic group to form molecular geometry of tetrahydrocurcumin. Only one phenolic group of the molecule is presented to emphasize the combinations made. The atomic numbering in geometry (a) is presented to briefly explain this molecular structure according to Table 1.

Table 1 presents some calculated and experimental parameters of molecular geometry of tetrahydrocurcumin at the ground state. The atomic numbering used here is referring to Fig 2. We compare our calculated parameters to two previous experimental parameters, which are crystal structure of tetrahydrocurcumin [2] and phenol molecule at gas phase [11]. The difference between the calculated and experimental values of H4 and O5 distance is rather big. However, this distance is still in the range where a hydrogen bonding could form [2]. For C-C and O-H bonds, XC and BS chosen has managed to predict their bond length almost accurately. This verified that M05-2X and 6-31++G(d,p) are appropriate to study tetrahydrocurcumin molecule.

Table 1: Selected parameter of molecular geometry of tetrahydrocurcumin

Parameter ()	Calculated	Experiment	Δ
C1-C2	1.51	1.52[a]	0.01
O3-H4	0.98	0.82[a],0.96[b]	0.02
H4$\cdots$O5	2.10	2.23[a]	0.13

[a] is taken from [2]

[b] is taken from [11]

Tetrahydrocurcumin in solvents. Three different solvents, represent polar and non-polar medium, are selected in this research. They are water, methanol, and chloroform. In our simulation, the solvents are treated as a cavity with different dielectric constant. For the polar medium, which is water and methanol, the dielectric constants are 78.36 and 32.61. Meanwhile, for a non-polar medium, which is chloroform, the dielectric constant is 4.71.

Tetrahydrocurcumin can maintain its geometry as placed in a different solvents environment. In water and methanol solvents, C-C, O-H, and H$\cdots$O values do not change (The values are 1.51, 0.97, and 2.10 Å, respectively). In chloroform solvent, the bond length of O-H increases by 0.01 Å. This slight elongation certainly will affect hydrogen bonding [12] that formed between H4 and O5 atoms.

As a good antioxidant candidate, tetrahydrocurcumin is expected to be very unreactive after transferring a hydrogen atom toward free radical. The unreactivity should be achieved to prevent the tetrahydrocurcumin radical re-abstracting a hydrogen atom from free radical [4]. One way to measure this unreactivity is from its electronic energy.

The relative electronic energy of tetrahydrocurcumin radicals in water, methanol and chloroform solvents is reported in Table 2. In water and methanol solvents, the electronic energy is increasing in the following order : Rad 2 < Rad 4 < Rad 6 < Rad 5 < Rad 1 < Rad 3. Low electronic energy in Rad 2 can be explained from the largest reduction of bond length near the abstraction site as a compensation to the loss of hydrogen - the reduction is 0.12 Å. Compare to Rad 2, bond lengths near site 3 experience the least reduction among all - the reduction is only 0.01-0.02 Å. Thus, Rad 3 becomes the most unreactive. In chloroform solvent, the electronic energy of tetrahydrocurcumin radicals decreases by an average of 0.23 eV as compared to two previous solvents. The presence of this solvent stabilizes tetrahydrocurcumin radicals and greatly affects Rad 4, 5 and 6 by maintaining the changing of bond length near the abstraction sites in a moderate reduction - the reduction is in the average of 0.08 Å.

Bond Dissociation Enthalpy. As initial evaluation of tetrahydrocurcumin's antioxidant ability, it is necessary to consider BDE value. Low BDE value marks good antioxidant ability of tetrahydrocurcumin since it facilitates a hydrogen atom transfer toward free radical.

Table 3 reports the calculated BDE value of tetrahydrocurcumin in three different solvents. Site 2 has the lowest BDE value in all solvents studied, so it represents the first site that can transfer a hydrogen atom. This result has no conflict to previous results by Morales et.al [1] and Murakami et.al [13]. The use of XC functional that can treat non-covalent interaction like hydrogen bonding and BS that adds polarization and diffuse functions on hydrogen atoms in this research have lowered BDE value by 1.92 Kcal/mol as compared to the result reported by Murakami et.al. Beside Site 2, Site 4, 5 and

Table 2: Relative electronic energy of tetrahydrocurcumin radical at various solvents.

Rad	Water E[eV]	Methanol E[eV]	Chloroform E[eV]
Rad 1	0.71	0.70	0.49
Rad 2	0.00	0.00	0.00
Rad 3	1.40	1.39	1.20
Rad 4	0.33	0.33	0.13
Rad 5	0.41	0.41	0.08
Rad 6	0.35	0.35	0.16

Table 3: Calculated Bond Dissociation Enthalphy in Various Solvents at 298.15 K.

Abstraction Site (Bond)	BDE [kcal/mol]			
	Water	Methanol	Chloroform	Gas Phase
Site 1 (C-H)	97.42	97.42	95.61	
Site 2 (O-H)	81.82	82.31	80.95	$86.28(88.20^c)$
Site 3 (C-H)	114.04	114.07	112.60	
Site 4 (C-H)	87.77	87.79	86.16	
Site 5 (C-H)	90.34	90.35	86.81	
Site 6 (C-H)	89.74	89.81	88.49	

^{c} is taken from [13]

6, which are C-H bonds, should also be considered as a transfer site especially in chloroform solvent. The importance of C-H bonds of polyphenols in antioxidant activity has been stated previously by Hassanzadeh et.al [14]. We also observe a peculiar trend in Site 5 in the chloroform solvent. Table 2 reports that Rad 5 has lower electronic energy as compared to Rad 4. But increasing temperature to 298.15 K (when frequency calculation is performed) probably affects translation, rotation and vibrational motion of Rad 5 almost as much as Rad 4, thus contributes to their similar enthalpy values. Site 1 and 3 are the least to expect to involve in antioxidant activity of tetrahydrocurcumin. Dissociation at these C-H bonds in a phenolic group will promote the lowest electron delocalization in phenyl ring [15].

Conclusion

We have evaluated bond dissociation enthalpy of tetrahydrocurcumin in three different solvents represent polar and non-polar medium using density functional theory. Our results suggest that polarity of medium affects the BDE of tetrahydrocurcumin. Non-polar medium lowers BDE value, thus hydrogen transfer is favorable in this medium. Meanwhile, in a polar medium, hydrogen transfer is less favored. In our future work, we plan to check the antioxidant activity of tetrahydrocurcumin in a polar medium through electron transfer. Our calculation predicts O-H bond in a phenolic group that holds the key role to tetrahydrocurcumin antioxidant activity regardless of the medium. We also suggest C-H bond in the carbon chain as well as in beta-diketone group to be considered as hydrogen transfer sites.

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