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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Table of Contents

Chapter 2: Bio- and Food Technologies, Materials in Biomedicine

Chapter 3: Investigation of Magnetic and Superconducting Properties

Chapter 4: Materials for Technologies of Energy Storage and Conversion

Chapter 5: Modeling, Computational Procedures and Devices in Research of Functional Materials

Materials Science Forum
ISSN: 1662-9752, Vol. 966, pp 229-233
doi:10.4028/www.scientific.net/MSF.966.229

Submitted: 2018-12-04
Revised: 2019-05-16
Accepted: 2019-05-16
Online: 2019-08-06

Predicting Notable Radical Scavenging Sites of Gnetin C Using Density Functional Theory

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Keywords: bond dissociation energy, density functional theory, gnetin C, radical scavenging activity.

Abstract. We have been investigating the scavenging activity of gnetin C theoretically in the molecular level. In this work, we perform density functional based calculations to predict the possible site of gnetin C for free radical scavenging activity. The water solvent effect is considered as polarizable continuum model. All possible scavenging sites have been evaluated by obtaining the bond dissociation enthalpy (BDE) for one hydrogen atom abstraction. The results demonstrate that O-H bonds generally have lower BDE relative to C-H bonds of gnetin C. We also find that C-H bonds in 5-membered heterocyclic ring have exceptionally lower BDE. This could be additional possible sites for gnetin C to scavenge more free radicals in addition to hydroxyl groups.

Introduction

The unbalance numbers of reactive oxygen species (ROS) in the body can cause a disturbance called oxidative stress. The oxidative stress causes three main oxidative damages namely protein oxidation, lipid peroxidation, and oxidative damage to DNA. The combination of these three oxidative damages contributes to aging process [1-3] and development of several chronic diseases such as cancer, diabetes, and neurological disease [4].

To overcome the oxidative stress, a substance which has an ability to inhibit, prevent, or eliminate the oxidative damage to the target molecule is needed. This substance is known as antioxidant [5]. A class of phenolic compounds is a type of antioxidant which could stabilize free radicals by transferring electrons, so electrons in an outermost orbital of free radical are paired [6]. Moreover, phenolic compounds can also be a radical scavenger by donating a hydrogen atom to radicals [7].

Resveratrol has been extensively studied for its role as an antioxidant in the biological system [8-13]. Numerous studies also show that resveratrol is a potential drug candidate for multi-purpose treatment because of its potent antioxidant properties [14]. Due to its promising application, we extend the study of antioxidant activity to its dimer, gnetin C. An experimental study shows that dimer resveratrol from melinjo has a good activity to scavenge 2,2-diphenyl-1-picryl-hydrazyl (DPPH) [15]. However, the theoretical study of antioxidant activity of dimer resveratrol is still limited.

This work is an initial study to understand the antioxidant behavior of dimer resveratrol in water environment using density functional theory (DFT). Therefore, in this study, we examine the possible site of gnetin C to interact with radical as the first step. The possible site is evaluated by determining

bond dissociation enthalpy (BDE) of hydrogen abstraction. This work will be the base for further study of the reaction between radical and gnetin C.

Computational Detail

The hydrogen donation process is simplified into a reaction model as shown in Eq. 1.

$$\mathrm{Res}_{(\mathrm{H})} \rightarrow \mathrm{Res}^{\bullet} + \mathrm{H} \tag{1}$$

$\mathrm{Res}_{(\mathrm{H})}$ represents gnetin C as a neutral molecule. Gnetin C radical ($\mathrm{Res}^{\bullet}$) is modeled by eliminating one hydrogen atom (H) from each different sites, including O-H and C-H sites.

All electronic calculations are performed based on DFT as implemented in Gaussian 09 software package [16]. In the calculations, we employ B3LYP as exchange correlation and 6-31++G(d,p) as basis set. We choose B3LYP because it gives a good prediction in our previous molecular study [17, 18]. We consider aqueous solvation using polarizable continuum model (PCM). The ground state geometry of gnetin C is performed by full geometry optimization. All of possible radical structures are optimized using unrestricted calculation. Frequency calculation is also carried out to ensure that ground state structure has no imaginary frequency, and to give thermal correction at 298.15 K. Finally, bond dissociation enthalpy (BDE) is obtained by the following equation:

$$\mathrm{BDE} = (\mathrm{H}_{\mathrm{Res}} + \mathrm{H}_{\mathrm{H}}) - \mathrm{H}_{\mathrm{Res}\bullet} \tag{2}$$

$\mathrm{H}_{\mathrm{Res}}$, $\mathrm{H}_{\mathrm{Res}\bullet}$, and H_{H} denote the enthalpies of gnetin C, gnetin C radical, and a hydrogen atom, respectively.

Results and Discussions

The optimized structure of gnetin C and site numbering of hydrogen abstraction are shown in Fig. 1. The ground state of gnetin C is found to have a singlet spin multiplicity, while the gnetin C radical is in a doublet spin multiplicity. The geometric structure of gnetin C does not change when it becomes radical after donating a hydrogen atom. O-H bond length is predicted to be around 0.970 Å, and the C-H bonds vary from 1.086 to 1.090 Å.

Bond dissociation enthalpy (BDE) is an important parameter that has been used to evaluate the antioxidant activity of polyphenols [19]. BDE describes the stability of hydroxyl bond. The lower the values of BDE, the more stable phenoxy radical formed after donating a hydrogen atom to free radical. Based on BDE value, we evaluate the possible sites of gnetin C to react with free radical. However, in this study, we do not limit the determination of BDE for hydroxyl bond only but also consider the possibility of C-H as hydrogen atom donor.

All the 22 sites of gnetin C has been examined. The 22 sites consist of five O-H bonds and 17 C-H bonds. The details of BDE value are listed in Table 1. In most of the cases, BDE values of O-H bonds are less than that of C-H bonds. It ranges from 74.85 to 82.71 kcal/mol. The experimental BDE for gnetin C has not been reported yet. However, the reported experimental BDE for structurally related to resveratrol is within this range, 78.9 kcal/mol [20]. These BDE values are also close to the average values for experimental BDE of polyphenols [21]. These point out that most of the antioxidant activities of gnetin C are mainly related to its hydroxyl groups.

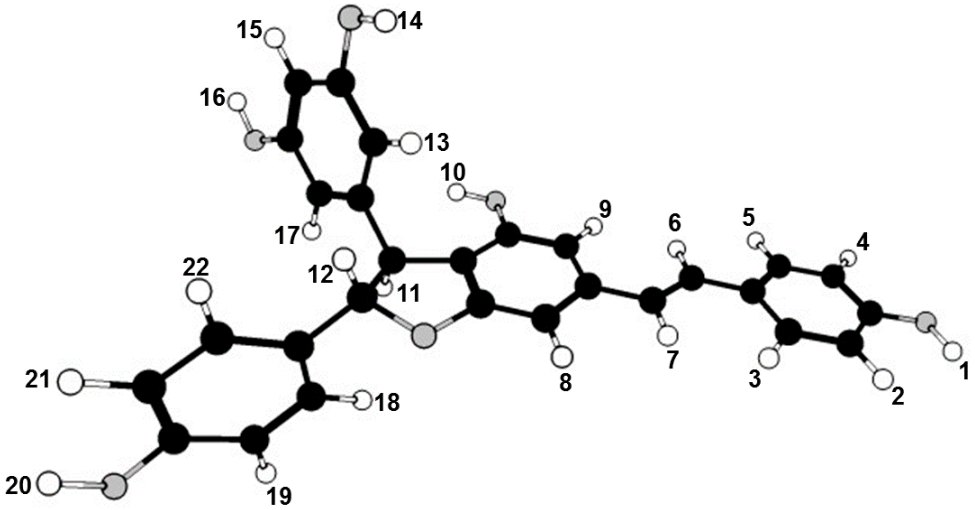

Fig. 1: The geometric structure of Gnetin C. The black, grey, and white atoms represent C, O, and H atoms.

Table 1: Bond dissociation enthalpies of O-H and C-H bond in gnetin C, at T=298.15 K.

Site number	BDE (Kcal/mol)	Site number	BDE (Kcal/mol)
1-OH	74.85	8-CH	113.81
10-OH	81.90	9-CH	112.13
14-OH	82.71	11-CH	75.74
16-OH	82.44	12-CH	79.68
20-OH	81.54	13-CH	112.59
2-CH	113.81	15-CH	110.34
3-CH	109.70	17-CH	113.58
4-CH	112.41	18-CH	110.34
5-CH	110.71	19-CH	112.36
6-CH	100.33	21-CH	111.84
7-CH	100.76	22-CH	110.78

In contrast to most of C-H bond sites, the C-H bonds which located in the conjugation chain connecting two phenyl rings have lower BDE. Site 11 and 12 even have a low BDE as O-H site does. The absence of double bond in this conjugation chain significantly lessens BDE of C-H bond. This exception may contribute to the antioxidant activity of dimer resveratrol in addition to hydroxyl group. Therefore, these sites are also important to be considered for scavenging site.

Conclusion

Bond dissociation enthalpies of gnetin C to donate one hydrogen atom have been determined. Our results suggest that O-H sites are important sites for scavenging free radical. As dimer resveratrol, the C-H bond in conjugation chain between two phenyl rings in its dimer may also be considered as additional scavenging sites. Nevertheless, the BDE value is not enough to explain the antioxidant activity of dimer resveratrol since the reactivity also depends on the type of radical. The thermodynamic and kinetic study of the reaction between gnetin C and hydroperoxyl radical should be performed. At this point, unnecessary interacting site for further study has been eliminated. The further study is underway and will be reported in somewhere else.

Acknowledgment

We thank to Institut Teknologi Bandung (ITB) and Research Center for Nanosciences and Nanotechnology (RCNN) for computer facilities support. VK also thanks to Lembaga Pengelola Dana Pendidikan (LPDP) for the doctoral scholarship. We also thank ”Hibah Mandat grant 2018 of Airlangga University” that has funded this research.

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