Molecular Understanding of Solvents and Glycitein Interaction during Extraction

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Supporting Information

ABSTRACT: Hydrogen bonding interaction plays a crucial role in liquid systems. Methanol, ethanol, and acetone are the most commonly used solvents to extract isoflavones from soybeans. The structural and electronic properties of the molecular clusters of naturally occurring glycitein with solvents were investigated using the density functional method employing the B3LYP-D3/cc-pVTZ approach. The influence of the solvent was carried out by using the polarized continuum model (PCM). The geometry optimization, vibrational frequencies, and topological parameters have been assessed at the same level of theory. From the molecular structure and thermodynamic point of view, the most stable structures are formed by the interaction between the carbonyl group of glycitein and MeOH or EtOH. For acetone–glycitein, the strongest interaction is formed by the interaction of the hydroxyl group of glycitein with the carbonyl group of acetone. All the hydrogen bonds in the MeOH/EtOH/acetone–glycitein complexes are closed-shell interactions. This study can help increase the efficiency of extraction.

1. INTRODUCTION

Soybeans contain a wide range of isoflavones, such as daidzein, glycitein, genistein, and so forth. Soy isoflavones are naturally occurring polyphenol compounds and structurally similar to estradiol. Soybeans contain 3 mg g\(^{-1}\) (dry weight) of isoflavones.\(^1\) Meanwhile, isoflavones are similar to the antioxidant flavonoids that are found in other vegetables, plants, and flowers. Among all the soy isoflavones, genistein and daidzein are the major portions of isoflavones in soybeans. Daidzein and genistein from soybeans are a source of phytoestrogens for humans. On the other hand, most of the natural estrogenic substances show weak activities. As a result, they have been widely investigated for their important health-enhancing properties such as prevention of sex hormone-dependent cancer, improvement of bone health, and so forth.\(^2\)

For instance, genistein has many health benefits as an antioxidant, inhibitor to regulate cell divisions and cells survival, antiangiogenetic agent, and so forth.\(^3,4\) Their estrogenic activities have been demonstrated to bind to estrogen receptors from different animals, such as mice, rats, sheep, and so forth.\(^5\)

Meanwhile, glycitein (C\(_{16}\)H\(_{12}\)O\(_{5}\), 7,4′-dihydroxy-6-methoxyisoflavone) is about 5–10% of the total soy isoflavones.\(^6\) Thus, it is essential to assess the chemical and physical activity of glycitein. One of the studies showed that glycitein is much weaker in estrogenic activity than other soy isoflavones.\(^7\) In contrast, glycitein actually has a stronger estrogenic response on an equal amount basis in the mice uterine enlargement assay.\(^7\) However, there are a variety of impurities in soy which can influence the quality of the isoflavones during production. Therefore, removal of the impurities below the acceptable level is required. One of the commonly employed separation method is extraction, and isoflavones are normally extracted from foods with methanol, ethanol, acetonitrile, and so forth.\(^8–10\) The extraction can be carried out either at room temperature or above.\(^11\) Meanwhile, hydrogen bonding interactions between solute and polar organic solvents play a crucial role in the extraction reaction.\(^12\) However, few studies have been focused on the extraction mechanism. Density functional theory (DFT) calculations are one of the effective methods to obtain the conformation, electronic structures, and inter/intramolecular interactions of isoflavones, such as daidzein, genistein, and so forth.\(^13,14\) On the other hand, the intermolecular interaction in solvents, namely, hydrogen bonding interaction, has a great influence on the extraction process.\(^15\) The main aim of this study is to calculate the hydrogen bonding interaction between glycitein and methanol (MeOH), ethanol (EtOH), or acetone in the extraction reaction from a theoretical point of view.

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2. RESULTS AND DISCUSSION

2.1. Conformational Analysis. The framework and atom numbering of glycitein are presented in Figure 1. There are two phenyl rings (I and III) and one heterocyclic ring (II) in glycitein. They contain several functional groups: −OCH₃, −OH, and −C═O. The optimization of the glycitein monomer at the B3LYP-D3 DFT functional level converged to eight different conformers when one rotates the −OₐHₐ, −OₐHₐ, or −OₑHₑ functional groups (Figure 2). Then, it can be noticed that all the eight conformers have nonplanar structures, and they can be divided into two groups: OₐHₐ, −OₐHₐ, −OₑHₑ, and −OₑHₑ intramolecular hydrogen bonded structures (Figure 2, A and B) and non-hydrogen-bonded structures (Figure 2, C−H). Meanwhile, there is a torsion angle between the II and III rings as seen in Figure 1. In a previous study, the conformational absolute minimum of glycitein by rotating the II and III rings was found with a torsion angle of 40° (B3LYP/6-311G(d,p)).¹⁶ In this study, the torsion angles were calculated to be 40.9°−41.9° for all eight conformers. As a result, the coplanarity between the II and III rings is lost, whereas the coplanarity remains between the I and II rings. In the most stable conformers [glycitein (A) and glycitein (B), Figure 2], the hydroxyl group OₐHₐ interacts with the Oₐ carbonyl atom to form an intramolecular hydrogen bond. This makes the glycitein (A) and glycitein (B) conformers at least ∼19 kJ mol⁻¹ more stable than the non-hydrogen-bonded conformers. Meanwhile, the geometric difference between glycitein (A) and glycitein (B) is the orientation of the −OₑHₑ group. Glycitein (A) is only slightly about 0.8 kJ mol⁻¹ more stable than glycitein (B). In contrast, the rotational barrier between the two conformers is much higher about 14.3 kJ mol⁻¹. However, different orientations of the −OₑHₑ group are unlikely to affect the relative stability of the molecular interaction between glycitein and various solvents in this work, and the strongest interaction is the one between carbonyl oxygen and solvents. Meanwhile, the EtOH monomer has two conformers: a trans-conformer and a gauche-conformer.¹⁷ The gauche-conformer is about 0.3 kJ mol⁻¹ [B3LYP-D3/cc-pVTZ, corrected with zero-point vibrational energy (ZPVE)] more stable than the trans-conformer. Thus, the only most stable glycitein (A) and the gauche-EtOH conformer will be used to study the molecular interaction in this study. The notations “glycitein” and “EtOH” in the following text will refer to glycitein (A) and gauche-EtOH, respectively.

Glycitein interacts with solvents (such as MeOH, EtOH, and acetone) during extraction as either a hydrogen bond acceptor or a hydrogen bond donor. When it acts as a hydrogen bond acceptor, there are five different docking sites for the hydrogen atom of MeOH, that is, Oₐ, Oₐ, Oₐ, Oₐ, and Oₐ (Figure 1). The labels of hydrogen, carbon, and oxygen atoms are in white, gray, and red colors, respectively. The Oₐ atom together with the Oₐ atom belongs to the hydroxyl groups of the glycitein molecule. The Oₐ and Oₐ atoms, on the other hand, belong to an ether group while Oₐ is derived from a carbonyl group. As a
hydrogen bond donor, the two hydroxyl groups, −O\(_2\)H\(_2\) and −O\(_3\)H\(_3\), can donate their hydrogen atoms to a hydrogen bond acceptor, such as acetone. The most stable structures of the MeOH–glycitein complexes at the B3LYP-D3/cc-pVTZ level are presented in Figure 3. The MeOH molecule acts as a hydrogen bond donor and acceptor in MeOH–glycitein (A). MeOH is the hydrogen bond donor approaching to glycitein in MeOH–glycitein (B–E), while MeOH is the hydrogen bond acceptor in MeOH–glycitein (F). The binding energy (BE) is one of the most effective indicators to reveal the relative stability of a structure. BE of a stable interacted complex is often negative. The lower BE means a stronger molecular interaction. Meanwhile, ZPVEs are quite large about 4.6–6.6 kJ mol\(^{-1}\) for the studied systems, and basis set superposition errors (BSSEs) vary from 6.8 to 9.9 kJ mol\(^{-1}\) (Table S1, Supporting Information). The binding energies in Figure 3 were calculated at ambient conditions (298.15 K and 1 atm) at the B3LYP-D3/cc-pVTZ level and corrected with ZPVE and BSSE. Based on the binding energies, the strength as a hydrogen bond acceptor can be sorted as Oc > O\(_b\) > O\(_e\) > O\(_a\) > Od. This indicates that the carbonyl oxygen is the best hydrogen bond donor, and this is in line with previous studies: (i) the O–H···O=C (carbonyl oxygen) hydrogen bonding interactions are about 9.6–11.0 kJ mol\(^{-1}\) (B3LYP/6-31+G(d)) more favorable than the O–H···O (ester oxygen) hydrogen bonding interaction in the MeOH–α-hydroxyster systems, where α-hydroxyster is methyl glycolate, methyl lactate, or methyl α-hydroxyisobutyrate;\(^{(16)}\) (ii) the O–H···O=C (carbonyl oxygen) hydrogen bonding interaction is about 9.7 kJ mol\(^{-1}\) also more stable than the corresponding O–H···O (ester oxygen) hydrogen bonding interaction in the MeOH–methyl lactate system.\(^{(19)}\) All these imply that the most favorite docking site for the incoming MeOH is the carbonyl group oxygen O\(_c\).

Meanwhile, the strength as a hydrogen bond donor is sorted as O\(_2\)H\(_2\) > O\(_3\)H\(_3\). Thus, for the EtOH–glycitein and acetone–glycitein systems, only the most stable structures formed between EtOH/acetone and the O\(_2\) or O\(_3\)H\(_3\) group of glycitein were studied. The most stable structures of the EtOH–glycitein and acetone–glycitein complexes at the B3LYP-D3/cc-pVTZ level are presented in Figure 4. This demonstrates that the driving force for extracting glycitein is the hydrogen bonding interaction between the solvent (a hydrogen bond donor, such as MeOH and EtOH) and carbonyl oxygen O\(_c\) of glycitein, or between the solvent (a hydrogen bond acceptor, such as acetone) and the hydroxyl group O\(_2\)H\(_2\) of glycitein.

### 2.2. Solvent Effects and Their Influence on the Hydrogen Bond

In order to study the effects of solvents on the electronic energies, geometrical parameters, and IR frequencies of the glycitein-containing complexes, the most stable conformers of the MeOH–glycitein, EtOH–glycitein, and acetone–glycitein structures were fully optimized within the polarizable continuum model (PCM) at the B3LYP-D3/cc-pVTZ level of theory. The calculated geometrical parameters and interaction energies of the most stable conformers of MeOH–glycitein, EtOH–glycitein, and acetone–glycitein in different solvents are present in Table 1. The relative permittivity (ε) values of acetone, ethanol, and methanol are 20.493, 24.852, and 32.613, respectively.\(^{(20)}\) The structure is stabilized in the solvent, and it is due to immersion in the solvent. The stabilized energy (Δ\(E_S\)) can be calculated as follows

\[
ΔE_S = E_{\text{solute}}(\text{solvent}) - E_{\text{gas}}(\text{solvent})
\]

where \(E_{\text{solute}}(\text{solvent})\) is the electronic energy in the solvent, and \(E_{\text{gas}}(\text{solvent})\) is the electronic energy in the gas phase. Meanwhile, the major components of the hydrogen bonding interaction energy are electrostatic and charge-transfer; thus, the effect of the solvent polarity on the hydrogen bond is expected.\(^{(21)}\) In this study, the polarity of the solvent plays an important role in extraction, and this is due to the hydroxyl groups of glycitein. MeOH–glycitein is stabilized by 38.2 kJ mol\(^{-1}\) (in the MeOH solvent), 37.5 kJ mol\(^{-1}\) (in the EtOH solvent), and 36.8 kJ mol\(^{-1}\) (in the acetone solvent) as compared with the electronic energy in the gas phase, whereas the EtOH–glycitein complex is stabilized by 37.4–38.8 kJ mol\(^{-1}\) in the three solvents. In contrast, the acetone–glycitein complex is favored by 44.2–45.7 kJ mol\(^{-1}\) in the three solvents. It should be mentioned that the dipole moments of the three complexes were found to be 1.86, 2.87, and 5.96 D for MeOH–glycitein, EtOH–glycitein, and acetone–glycitein, respectively, at the B3LYP-D3/cc-pVTZ level of theory (gas phase). To summarize, the PCM model indicates that acetone–glycitein is stabilized more than EtOH–glycitein and MeOH–glycitein. This is due to the higher dipole moment of the former when the solvent affects MeOH, EtOH, and acetone solvents were taken into account. For the glycitein-containing complexes, BEs were obtained at −39.1 to −36.2 kJ mol\(^{-1}\) in the gas phase. This is much more stable than some MeOH-containing hydrogen bonded systems (gas phase), where MeOH–dimethylamine (DMA), MeOH–trimethylamine (TMA), and MeOH–dimethylether (DME) were obtained to be about −21.2 to −19.7 kJ mol\(^{-1}\) (B3LYP/aug-cc-pVTZ).\(^{(22,23)}\) Meanwhile, BEs were calculated to be −34.6 to −32.7 kJ mol\(^{-1}\) in the three solvents. This means that the monomers in the three solvents bind to each other slightly less favored than the monomers in the gas phase bond to each other.

The OH-stretching vibrational frequencies of MeOH, EtOH, and glycitein monomers are red-shifted \(Δv = v_{\text{monomer}} - v_{\text{dimer}}\) by about 11–20 cm\(^{-1}\) in the three solvents when compared with the values in the gas phase. The corresponding OH bond lengths are increased by 0.001–0.002 Å in the three solvents. Meanwhile, the C=O stretching vibrational frequencies of acetone and glycitein are also red-shifted by 36–56 cm\(^{-1}\) in the solvent, and the C=O bond distances are

![Figure 4. Most stable EtOH–glycitein and acetone–glycitein molecular clusters optimized at the B3LYP-D3/cc-pVTZ level. Binding energies (corrected with ZPVE and BSSE) are given in brackets. Hydrogen bonds between EtOH/acetone and glycitein are represented by dashed lines.](image-url)
The simulated 200−270 nm wavelength of MeOH−glycitein only increased by 0.003 Å during complexation. However, the NH bond lengths in the O−H···N hydrogen bond complexes (gas phase) were 0.012 to 0.020 Å. These are similar with the hydrogen-bonded complexes (gas phase): MeOH−glycitein containing complexes (gas phase): MeOH−glycitein, acetone−glycitein, and EtOH−glycitein. The corresponding red shifts are significantly increased to 282−428 cm−1 in the three solvents. This is because the strength of the hydrogen bond dramatically increases in the three solvents. Upon complexation, the changes of the OH bond length of the glycitein-containing complexes vary from 0.012 to 0.020 Å. These are similar with the previous studies in the O−H···N hydrogen bonded system. In the study of the MeOH−DMA and MeOH−TMA complexes (gas phase), the OH bond lengths in the O−H···N hydrogen bonds were calculated to be elongated by 0.016−0.018 Å during complexation. However, the NH bond distances in the N−H···N hydrogen bonds (gas phase) were only increased by 0.003−0.004 Å (QCISD/aug-cc-pVTZ) in DMA−DMA and 0.005 Å [CCSD(T)−F12a/VQZ−F12] in DMA−TMA upon hydrogen bond formation. Consequently, comparable red shifts were also found in MeOH-containing complexes (gas phase): MeOH−TMA (333 cm−1, local mode model), MeOH−DME (234 cm−1, B3LYP-D3/aug-cc-pVTZ), and MeOH−DMA (301 cm−1, local mode model).

The most stable conformers of glycitein and MeOH−glycitein in both the gas phase and the MeOH solvent were used to simulate the ultraviolet−visible (UV−vis) absorption spectra. The first 200 singlet−singlet spin-allowed excited states were calculated, and the max absorption wavelengths \( \lambda_{\text{max}} \) of the electronic excitation energies, and the oscillator strengths \( f \) were obtained using time-dependent (TD)-DFT at the B3LYP-D3/cc-pVTZ level. The simulated 200−350 nm UV−vis spectra are displayed in Figure 5. The simulated spectra were formed because of the electronic transitions from the highest occupied molecular orbitals (HOMOs) to the lowest unoccupied molecular orbitals (LUMOs). The five important frontier molecular orbitals of glycitein (in the MeOH solvent): HOMO − 2, HOMO − 1, HOMO, LUMO, and LUMO + 1, are illustrated in Figure 6. It is clear that the five frontier molecular orbitals are the \( \pi \) and \( \pi^* \) molecular orbitals locating at the \( I, II, \) and \( III \) rings of glycitein (in the MeOH solvent). One can notice that it is the \( \pi \rightarrow \pi^* \) transitions taking place in the UV−vis region with high extinction coefficients. The max absorption wavelengths \( \lambda_{\text{max}} \) of glycitein were calculated to be 271.63 nm (gas phase) and 270.49 nm (in the MeOH solvent). The max absorption wavelengths \( \lambda_{\text{max}} \) of MeOH−glycitein were calculated to be 271.62 nm (gas phase) and 273.54 nm (in the MeOH solvent). Moreover, the experimental UV−vis spectral data for glycitein were \( \lambda_{\text{max}} \) of 257 nm (in the MeOH solvent). Our calculated \( \lambda_{\text{max}} \) is slightly larger than the experimental value, and this may be due to the DFT method used which overestimates the UV−vis spectra. Moreover, our calculations show that the max absorption is mainly formed by three excitations: +0.66 (HOMO → LUMO + 1), +0.14 (HOMO − 1 → LUMO + 1), and 0.15 (HOMO − 1 → LUMO). The interacting site in MeOH−glycitein is the carbonyl group of glycitein. The interaction only has a slight effect on the \( \pi \) and \( \pi^* \) molecular orbitals located at the \( I, II, \) and \( III \) rings of glycitein. Thus, the max absorption wavelength is only marginally influenced by the hydrogen bonding interaction.

| conformer solvent | BE (eV) | \( \Delta v \) (cm−1) | \( \Delta r_{\text{OH}} \) (Å) | \( \Delta E(H) \) (eV) | \( \rho \) (BCP) | V(\( \rho \)) (BCP) | dipole moment |
|------------------|---------|-----------------|-----------------|-----------------|--------------|----------------|--------------|
| MeOH−glycitein   | −37.2   | 255             | 0.014           | 0.041           | 0.024        | 0.145          | 1.86         |
| acetone−glycitein| −25.2   | 294             | 0.015           | 0.050           | 0.027        | 0.166          | 2.80         |
| MeOH−glycitein   | −25.1   | 312             | 0.015           | 0.050           | 0.027        | 0.166          | 2.89         |
| EtOH−glycitein   | −24.9   | 311             | 0.015           | 0.050           | 0.027        | 0.166          | 2.84         |
| acetone−glycitein| −39.1   | 227             | 0.012           | 0.045           | 0.024        | 0.137          | 2.87         |
| acetone−glycitein| −27.8   | 282             | 0.013           | 0.047           | 0.026        | 0.153          | 3.40         |
| MeOH−glycitein   | −27.7   | 284             | 0.013           | 0.047           | 0.026        | 0.153          | 3.49         |
| EtOH−glycitein   | −27.6   | 283             | 0.013           | 0.047           | 0.026        | 0.153          | 3.44         |
| acetone−glycitein| −36.2   | 298             | 0.015           | 0.051           | 0.025        | 0.143          | 5.96         |
| MeOH−glycitein   | −28.2   | 426             | 0.020           | 0.061           | 0.028        | 0.177          | 5.87         |
| EtOH−glycitein   | −28.1   | 428             | 0.020           | 0.061           | 0.028        | 0.177          | 5.88         |

*BEEs are given in kJ mol−1. \( \Delta v = \nu_{\text{monomer}} − \nu_{\text{dimer}} \) (in cm−1). \( \Delta r_{\text{OH}} = r_{\text{dimer}} − r_{\text{monomer}} \) (in Å), is the change in the OH bond length upon complexation. QTAIM parameters [\( \Delta E(H) \), \( \rho(BCP) \), \( V(\rho(BCP)) \)] are given in au. Dipole moment is given in debye.
bond, such as, bond critical points (BCPs), ring critical points (RCPs), and Laplacian \( \nabla^2 \rho(r) \) at BCPs, and atomic charge \( \Delta q(H) \) and atomic energy \( [\Delta E(H)] \) of the hydrogen bond donor atom, were calculated with the AIM2000 program package. The QTAIM topological plots of the most stable MeOH—glycitein, EtOH—glycitein, and acetone—glycitein conformers with BCPs, RCPs, and electron density paths are displayed in Figure 7. The corresponding parameters in the gas phase and the solvents are listed in Table 1. Moreover, the strengths of the studied hydrogen bonds increase in solvents. However, the dielectric constants of the three solvents are very close to each other, so the increase in the strength of the hydrogen bond seems very close in the three solvents as well.

For a hydrogen bond, the electron density \( \rho(BCP) \) and the Laplacian of charge density \( \nabla^2 \rho(BCP) \) at BCPs should be in the range 0.002–0.040 au and 0.014–0.139 au, respectively.28,29 For the studied systems in Table 1, \( \rho(BCP) \) and \( \nabla^2 \rho(BCP) \) were calculated to be in the ranges 0.024–0.028 and 0.137–0.177 au, respectively. However, the \( \nabla^2 \rho(BCP) \) values are higher than the upper range of the Laplacian criteria for a hydrogen bond.28,29 The \( \nabla^2 \rho(BCP) \) values for the interactions between benzoic acid/cis-pinonic acid—sulfuric acid were also calculated to be exceeding the upper range of hydrogen bond criteria.30 This is due to the formation of strong hydrogen bonds. On the other hand, there is also a charge transfer (CT) when a hydrogen-bonded complex is formed, leading to a decreased charge on the hydrogen atom.31 The quantity of CT reveals a part of the stabilization energy of the hydrogen bonded system, and it determines the electron delocalization interaction between the two interacted systems.32 This means that the more electron transfer it does, the more stable the system is. In this study, there are about 0.09–0.11 electrons from the hydrogen bond acceptor to the donor. The results of \( \Delta q(H) \) demonstrate that the hydrogen bond strengths in the gas phase are greater than the ones in the solvent.

### 3. CONCLUDING REMARK

In the present study, DFT has been used to investigate the naturally occurring isoflavonoid compound, glycitein. The hydrogen bonds were analyzed using the B3LYP-D3 level of theory at the cc-pVTZ basis set. The effects of various solvents (methanol, ethanol, and acetone) on the hydrogen bond between glycitein and various solvents were investigated. This study aimed to determine the electronic energies, geometric parameters, solvent effects, and so forth of the molecules in question. The results obtained from DFT and the topological parameters suggest that the most stable clusters are found to be stabilized by hydrogen bonds formed with the hydroxyl group

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**Figure 6.** Molecular orbital surfaces and energy levels at the B3LYP-D3/cc-pVTZ level for the HOMO – 2, HOMO – 1, HOMO, LUMO, and LUMO + 1. Isosurface value is ±0.02 au.

**Figure 7.** QTAIM topological plots of the most stable MeOH—glycitein, EtOH—glycitein, and acetone—glycitein conformers (gas phase) obtained at the B3LYP-D3/cc-pVTZ level. The BCPs, RCPs, and CCP are represented by the red, yellow, and green balls, respectively.
of glycitein and the carbonyl group of acetone or with the carbonyl group of glycitein and MeOH/EtOH. The UV–vis adsorption spectra were calculated with TD-DFT to investigate the electronic properties. The analysis of the solvent effect demonstrated that the polar solvent stabilizes the complexes. The changes of the OH bond lengths are larger in the three solvents because of the polar environments.

4. METHODOLOGY
All the computations have been performed using the Gaussian 09 Revision E.01 software package. Because of the excellent computational time and electronic properties (such as electronic structures, vibrational frequencies, and so forth), the DFT method has been used. The B3LYP-D3 approach was carried out. This approach is a hybrid functional of the DFT method, and it contains the Becke’s three-parameter nonlocal exchange functional with the correlation functional of the Lee–Yang–Parr (B3LYP) method and the Grimme’s D3 dispersion correction. Previous studies on small hydrogen-bonded molecular clusters were found to offer very accurate electronic energetics, vibrational frequencies, structural information, and so forth. Moreover, the Dunning’s correlation consistent triple-zeta basis set (cc-pVTZ) was used throughout the computational process. Vibrational frequencies of the optimized structures were computed at the same level of theory to confirm the nature of stationary points. The corresponding ZPVE correction and thermodynamic corrections were added to electronic energies. Meanwhile, BSSE was added to BEs by using the typical counterpoise method. For UV–vis calculations, the electronic maximum absorption wavelengths \( \lambda_{max} \) of glycitein and MeOH–glycitein in the MeOH solvent were computed using the TD-DFT method at the B3LYP-D3/cc-pVTZ level.

Several different solutions (methanol, ethanol, and acetone) to investigate the influence of the solvent on hydrogen bonds were used, and the corresponding effects were compared with those in the gas phase. The solvation effects were calculated considering the cavity of series of spheres by the aid of the cavity integral equation formalism variant model. The analysis of the electronic charge density \( \rho \), its Laplacian \( V^2 \rho \) at BCPs, changes in atomic charge \( \Delta Q(H) \), and changes of atomic energy \( \Delta E(H) \) at the H atom was performed by making use of the theory of molecular structure to investigate the nature of hydrogen bonds. The topological QTAIM was performed using the “output = WFN” option for the AIM keyword as implemented in Gaussian 09 Revision E.01 and AIM2000 software.

ASSOCIATED CONTENT
2 Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.9b02464.

Calculated BE, ZPVE, BSSE, enthalpy of formation \( \Delta H_{298}^{\text{cal}} \), and Gibbs free energy of formation \( \Delta G_{298}^{\text{cal}} \) of MeOH–glycitein at the B3LYP-D3/cc-pVTZ level (PDF)

ASSOCIATED CONTENT

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Notes

The authors declare no competing financial interest.

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