Theoretical Study on Ionization of Boric Acid in Aqueous Solution by Ab Initio and DFT Methods at T=298.15 K

T=298,15 K’da Ab İnitio ve DFT Yöntemleri ile Borik Asidin Sulu Çözeltisinin İyonlaştırılması Üzerine Teorik Bir Çalışma

ABSTRACT

Objectives: The aim of this research work was to theoretically calculate the pK$_a$ value of boric acid in aqueous solution by theoretical methods at T=298.15 K.

Materials and Methods: Boric acid has antifungal and antiviral properties. It is used in various prescription pharmaceutical products. The ab initio and density functional theory (DFT) methods were used in this research work.

Results: To explain the determined acidic dissociation constant, the various molecular conformations and solute-solvent interactions of the species of boric acid were considered. The basis set at the B3LYP/6-31+G (d) level of theory was selected for DFT calculations. We analyzed the formation of intermolecular hydrogen bonds between several species of boric acid and water molecules through Tomasi’s method.

Conclusion: The result showed that there was comparable agreement between the experimentally and theoretically determined pK$_a$ values for boric acid.

Key words: Boric acid, acidic dissociation constant, DFT, ab initio

ÖZ

Amaç: Bu araştırmının amacı, boric asidin sulu çözeltisinin pK$_a$ değerini teorik olarak T=298,15 K’da hesaplamaktır.

Gereç ve Yöntemler: Borik asit antifungal ve antiviral özelliklere sahiptir. Çeşitli reçeteli farmasötik ürünlerde kullanılır. Bu araştırma çalışmalarında ab initio ve yoğunluk fonksiyonel teorisi (DFT) yöntemleri kullanılmıştır.

Bulgular: Belirlenen asid disosiyasyon sabitini açıklamak için, borik asit türlerinin çeşitli moleküller konforlarsı ve çözünlen-cözülmen etkileşimleri göz önünde bulunduruldu. B3LYP / 6-31 + G (d) teori düzeyindeki temel set DFT hesaplamaları için seçilmiştir. Tomasi metodu ile çeşitli borik asit türleri ve su molekülleri arasında intermoleküller hidrojen bağlarının oluşumu analiz edildi.

Sonuç: Çalışmanın sonucu, borik asit için deneysel ve teorik olarak belirlenen pK$_a$ değerleri arasında karşılaştırılabilir bir uyum olduğunu göstermiştir.

Anahtar kelimeler: Borik asit, asid disosiyasyon sabiti, DFT, ab initio
INTRODUCTION

Boric acid is a weak acid that forms a white and water-soluble powder. It can be naturally found in seawater, many plants, and most fruits. Boric acid has been used as a mild antiseptic or bacteriostat in eyewashes and mouthwashes. Aqueous solutions of boric acid are topically used for ophthalmic irritation to cleanse, refresh, and soothe irritated eyes and used for removal of loose foreign material, air pollutants, or chlorinated water.

Boric acid is predominantly eliminated unchanged through the kidney; small amounts are also excreted in sweat, salvia, and feces. Boric acid is concentrated in the brain and liver. Boric acid and its derivatives have been shown to promote riboflavinuria in both animals and humans. Metabolism of inorganic borates by biological systems is not feasible because excessive energy is required to break the boron-oxygen bond. Inorganic borates, in low concentrations, convert to boric acid at physiological pH in the aqeous layer overlying mucosal surfaces prior to absorption.

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Equilibrium constants for ionization reactions are usually called ionization constants or acidic dissociation constants (pK_a). pK_a is an important physico-chemical parameter in drug absorption. Many drug compounds include at least one acid and/or basic group, and the ionization state of these groups plays an important role in determining the physico-chemical properties of compounds. Information about the pK_a value of compounds plays a major role in the expansion of drug formulations.

Reliable and accurate methods for calculating relative and absolute pK_a values are important for understanding of the effective pK_a values in molecules. Some studies detailing the acid-base properties of compounds in aqueous solutions and in the gas phase are also available. Different experimental procedures are frequently used for the determination of acidity constants. These methods are high-pressure liquid chromatography, liquid-liquid partitioning chromatography, and methods that involve potentiometric titrations or chromatography, liquid-liquid partitioning chromatography, and gas chromatography.

RESULTS AND DISCUSSION

The trend of a molecule to lose its H⁺ is quantified as pK_a. Boric acid is a weak acid and it has three acid groups. A proton can separate from the hydroxyl group to give an ionized species (Figure 1). This concept of microscopic ionization constant is shown in Equation 1:

\[
k = \frac{[\text{H}^+][\text{B(OH)}_2\text{O}^-]}{[\text{B(OH)}_3^-]}
\]  
Equation (1)
The total free energies (in Hartree and kJ.mol$^{-1}$) for the single and solvated species of boric acid, in water, were calculated at the B3LYP/6-31+G(d) level of the theory, using Tomasi’s method, at $T=298.15$ K and the results are shown in Table 1. This table shows that the total free energy for various species of boric acid increases with increasing number of water molecules. It shows that the solvation process causes an increase in the total free energy for various species of boric acid. In other words, solvation of the boric acid is an endothermic process. The values of total free energy for various species of boric acid (Table 1) were applied to calculate the $pK_a$ value of boric acid. In addition, these data help us to suggest an appropriate reaction regarding the deprotonation process of boric acid.

Various reactions including the neutral and anion species of boric acid were considered in the program Excel and some of these reactions were not considered further because their equilibrium constants were not comparable with the experimental ones. The selected equation for the deprotonation process of boric acid as well as the experimentally determined and theoretically calculated $pK_a$ is shown in Table 2.

### Ionization constant of boric acid

In aqueous solutions, the molecule of boric acid can undergo the below reaction:

$$H_3L(H_2O)_4 + OH^- \rightarrow H_2L^- (H_2O)_3 + 2H_2O$$

$K_a=1.008 \times 10^{-14}$

Equation (3)

The very low amount of $K_w$ shows that a few water molecules are ionized in pure liquid water.

The reaction of Equation 3 can be obtained by combining Equations 2 and 3:

$$H_3L(H_2O)_4 + OH^- \rightarrow H_2L^- (H_2O)_3 + 2H_2O$$

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The reaction of Equation 4 can be obtained by combining Equations 2 and 3:

$$H_3L(H_2O)_4 \rightarrow H_2L^- (H_2O)_3 + H_3O^+$$

$K_a=1.008 \times 10^{-14}$

Equation (4)

It is clear that the value of $K_a$ can be calculated using $K_c$ and $K_w$ as below:

$$K_a=K_c \times K_w$$

Equation (5)

Equation 5 was applied to calculate the values of the ionization constant of boric acid, $K_a$, in water at $T=298.15$ K. The theoretically calculated value of $pK_a$ for boric acid at $T=298.15$ K is shown in Table 2. As can be seen in this table, there is a good agreement between the experimentally determined ($pK_a=9.237$) and theoretically calculated $pK_a$ values of boric acid at this temperature.

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Table 1. The calculated total free energy ($G_{sol}^{\text{cal}}$) using Tomasi’s method at the B3LYP/6-31+G(d) level of theory for neutral and cationic species of boric acid at 298.15 K

| No | Species            | $G_{sol}^{\text{cal}}$ (Hartree) | $G_{sol/molecule}$ (kJ.mol$^{-1}$) |
|----|--------------------|----------------------------------|-----------------------------------|
| 0  | H$_3$L             | -252.913276                      | -664023.7424                     |
| 1  | H$_2$L$^-$ (H$_2$O) | -328.959459                      | -431841.4884                     |
| 2  | H$_2$L$^-$ (H$_2$O)$_2$ | -405.824119                | -355163.7074                     |
| 3  | H$_2$L$^-$ (H$_2$O)$_3$ | -482.272605                | -316551.6507                     |
| 4  | H$_2$L$^-$ (H$_2$O)$_4$ | -558.723888                | -293385.8854                     |
| 0  | H$_3$O$^+$         | -76.862                          | -201801.1616                     |
| 0  | H$_2$O             | -76.434                          | -200677.4477                     |
| 0  | OH$^-$             | -75.952                          | -199411.9569                     |

Table 2. The value of $pK_a$ for the deprotonation of boric acid obtained using the Tomasi’s method at the B3LYP/6-31+G(d) level of theory, at 298.15 K

| Species | Selected equations | $pK_a$ (calculated) | $pK_a$ (experimental) |
|---------|--------------------|---------------------|----------------------|
| Boric acid | $H_3L(H_2O)_4 \rightarrow H_2L^- (H_2O)_3 + H_3O^+$ | 9.36436             | 9.237                |
Study on H-bonding between selected species of boric acid and water

The structural properties of a species, solved in water, can help us to understand the interaction between this species and water (H-bonding). One of the most important of these structural properties is the bond length between the indicated atoms from solute and solvent (water) molecules (in Å). These data, for neutral and cation species of boric acid, are listed in Table 3. The power of hydrogen bonds can be classified as strong (bond length is between 1.2 Å and 2.2 Å and the angle is between 175° and 180°), moderate (bond length is between 1.5 Å and 2.2 Å and the angle is between 130° and 180°), and weak (bond length is between 2.2 Å and 3.2 Å and the angle is between 90° and 150°). As can be seen in Table 3, for H2L(H2O)4, the bond length between atom H6, from boric acid, and O9, from water, is 2.124582 (dH6O9=2.124582). In addition, for H2L-(H2O)3, the bond length between atom O 2, from boric acid, and H 19, from water, is 2.098563 (dH19O2=2.098563). These data show that for boric acid the power of H-bonding between H2L(H2O)4 and water and also between H2L-(H2O)3 and water are classified as moderate.

It must be noted that IHBs data can be used in the design of benefit and help us to predict nano drugs.

CONCLUSION

In this research work, we showed the feasibility of a theoretical method, DFT and ab initio, to calculate the ionization constants of boric acid at T=298.15 K. As a result, we selected various acid-base reactions that include the solvation of the hydrogen, hydroxyl ions, and other anions or neutral molecules in protic solvents such as water, which possess a high hydrogen-bond-donor capability. The calculations performed at the B3LYP/6-31+G (d) level of theory at 298.15 K.

Conflicts of interest: No conflict of interest was declared by the authors. The authors alone are responsible for the content and writing of the paper.
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