HNUE JOURNAL OF SCIENCE DOI: 10.18173/2354-1059.2022-0027
Natural Sciences 2022, Volume 67, Issue 2, pp. 103-109
This paper is available online at http://stdb.hnue.edu.vn

DETERMINING THE THERMODYNAMIC DISSOCIATION CONSTANTS OF 5-BROMO-6,7-DIHYDROXY-*N*-METHYL-3-SULFOQUINOLINE IN AQUEOUS SOLUTION AT 25 ^{O}C BY POTENTIOMETRIC METHOD

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Abstract. In this report, the thermodynamic dissociation constants of 5-bromo-6,7-dihydroxy-*N*-methyl-3-sulfoquinoline (signed H_2BDMS) acid were firstly determined in the aqueous solution using potentiometric titration at (25.0 ± 0.1) ºC in the ionic medium of 0.10 M KCl solution. This new acid is a compound containing the quinoline ring that may be applied in many branches of chemistry, biology, and medicine. The pK_a values of H_2BDMS acid which were determined by the potentiometric method are pK_{a1} = 2.79 ± 0.02 and pK_{a2} = 7.80 ± 0.06. To increase the precision and accuracy of the results, the pK_a values were calculated at various concentration levels. The structure of the new acid and data of potentiometric titration were analyzed in detail before calculating and assigning the pK_a values to suitable functional groups. These results will be applied to our further studies of this compound.

Keywords: dissociation constants, potentiometric titration, 5-bromo-6,7-dihydroxy-*N*-methyl-3-sulfoquinoline.

1. Introduction

The thermodynamic dissociation constant of acid-base is one of the most important parameters for chemistry and other fields [1], thus it is necessary to determine this parameter for a new acid for its further studies. To determine the p*K*a values, a lot of methods can be chosen but the potentiometric titration method has some outstanding advantages such as simple procedure, saving time, giving fast results as well as still ensuring precision and accuracy [1, 2]. This method has been verified and confirmed by many previous studies [3, 4, 5].

In this report, a new acid named 5-bromo-6,7-dihydroxy-*N*-methyl-3-sulfoquinoline (signed H_2BDMS) acid - molecular formula: $C_{10}H_8O_5NSBr$ is a derivative of quinoline that was synthesized from eugenol [6, 7] (see Figure 1). This compound that contains the quinoline skeleton has been known to be applied for synthesizing organic chemistry and manufacturing medicines. Moreover, these acids can also be used as ligands for determining

Received May 27, 2022. Revised June 10, 2022. Accepted June 18, 2022.
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metallic ions in analytical chemistry because they have a lot of functional groups that can form stable complexes with metallic ions [6, 7]. These acids' fluorescence properties will also be studied to apply in many branches of chemistry [8]. In the laboratory of the Faculty of Chemistry, Hanoi National University of Education, H_2BDMS was synthesized as the diagram in Figure 1 [6, 7]. The structure of H_2BDMS acid was studied in detail by spectra such as IR, H^1NMR, D^2NMR, and MS [7, 8]. It has been determined that in the aqueous solution, H_2BDMS is a new diprotic acid and the dissociation constants of these acids have not been found in any literature. Therefore, it is necessary to determine pK_a values for further research about their properties and applications.

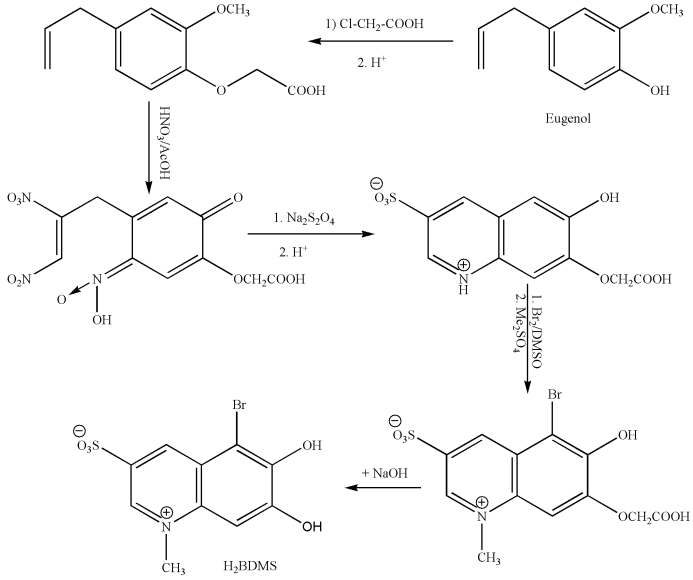

Figure 1. The synthesized diagram of 5-bromo-6,7-dihydroxy-N-methyl-3-sulfoquinoline

2. Content

2.1. Theory and experiment

2.1.1. Theory for calculating the dissociation constant of acid

For a potentiometric titration, V_0 mL of a diprotic acid solution (H_2A, C_0 mol.L^{-1}) was titrated with V mL of KOH standard solution (C mol.L^{-1}) at a given ionic strength (I) which was maintained by KCl solution. At all times during the titration process, we always have

$$[H^+] + [K^+] = [OH^-] + [HA^-] + 2[A^{2-}] \quad (1)$$

Rearranging Eq. (1) and using the φ term as a reverse form of activity coefficient, we obtain

$$\left(h - \frac{K_w}{h}\right)\varphi_1 \frac{V + V_0}{C_0 V_0} + \frac{CV}{C_0 V_0} = \frac{h\varphi_1 K_{a1} + 2\varphi_2 K_{a1} K_{a2}}{h^2 + h\varphi_1 K_{a1} + \varphi_2 K_{a1} K_{a2}} \quad (2)$$

where $[H^+]$ and $h = (H^+)$ are equilibrium concentration and activity of H^+ ion, respectively. φ_1, φ_2,..., φ_m are the inverse forms of activity coefficients which were estimated by the Davies equation [9].

$$\lg \varphi_i = 0.5115 \times Z_i^2 \times \left(\frac{\sqrt{I}}{1+\sqrt{I}} - 0.2 \times I \right) \quad (3)$$

where I is ionic strength and Z_i is the ionic charge.

The left-hand of Eq. (2) was defined as

$$Q = \left(h - \frac{K_w}{h} \right) \varphi_1 \frac{V + V_0}{C_0 V_0} + \frac{CV}{C_0 V_0} \quad (4)$$

Therefore, Eq. (2) is

$$Q = \frac{h\varphi_1 \times K_{a1} + 2\varphi_2 \times K_{a1}K_{a2}}{h^2 + h\varphi_1 \times K_{a1} + \varphi_2 \times K_{a1}K_{a2}} \quad (5)$$

When rearranged, Eq. (5) becomes

$$h^2Q = h\varphi_1(1-Q) \times K_{a1} + \varphi_2(2-Q) \times K_{a1}K_{a2}. \quad (6a)$$

The Eq. (6) likes a linear equation

$$Y = a_1X_1 + a_2X_2 \quad (6b)$$

where Y, X_1, X_2, and a_1, a_2 were defined as

$$\begin{cases} Y = h^2Q \\ X_1 = h\varphi_1(1-Q) \\ X_2 = \varphi_2(2-Q) \end{cases} \text{ and } \begin{cases} a_1 = K_{a1} \\ a_2 = K_{a1}K_{a2} \end{cases} \quad (6c)$$

The values of Q, Y, X_1, and X_2 will be obtained from data of potentiometric titration such as h, C_0, C, V_0, V, and φ. A linear least-square method will be done for n experimental points ($n > m$) and the pK_a values will be obtained from a_1, and a_2.

2.1.2. Chemicals and apparatus

Acid H_2BDMS was synthesized, re-crystallized in a strong acid medium, and dried [6, 7, 8]. Its purity was confirmed by H^1NMR and thermal analysis. Chemicals that are used without further purification include potassium hydroxide (KOH, Merck, > 85%), potassium chloride (KCl, Merck, > 99.5%), and oxalic acid ($H_2C_2O_4.2H_2O$, Merck, > 99.5%). All titrations were carried out by a pH meter (SI Analytics, Lab 850, Germany) with a combined glass electrode. The electrode system was standardized by standard buffer solutions (pH = 4.01; 7.01 and 10.01).

2.1.3. Sample preparation and procedure

Three studied solutions of H_2BDMS acid and 4.798×10^{-3} M KOH standard solution were prepared in a 0.10 M KCl solution that will maintain a given ionic strength (I = 0.10 M). The KOH standard solution was prepared from solid KOH in deionized water with N_2 aeration to reduce the amount of dissolved CO_2. This solution then is standardized by the $H_2C_2O_4$ primary standard solution. The studied concentration of H_2BDMS solutions are to include $C_{01} = 7.893\times10^{-4}$ M (*Sol. 1*), $C_{02} = 8.540\times10^{-4}$ M (*Sol. 2*), $C_{03} = 9.812\times10^{-4}$ M (*Sol. 3*) and these solutions were prepared from solid H_2BDMS that was synthesized, re-crystallized in the strong acid medium.

Pipette V_0 = 20.00 mL of each acid solution into a 100-mL beaker. Add a given volume of KOH standard solution ($C = 4.798\times10^{-3}$ M) to the studied solution, mix well until the solution reaches equilibrium, and record the pH values. All titrations were carried out in an aqueous solution of constant ionic strength (maintained by 0.1 M of KCl solution)

under an N_2 atmosphere at (25 ± 0.1) ^oC. Each studied solution was titrated 3 times to get an average value of pH.

2.2. Results and discussion

The titrated results of the solutions were shown in Table 1 and the titration curves were shown in Figure 2.

Table 1. The potentiometric titration results of H_2BDMS solutions with KOH standard solution

V_{KOH} (mL)	pH_1	pH_2	pH_3	V_{KOH} (mL)	pH_1	pH_2	pH_3
0.00	3.302	3.307	3.234	5.20	8.218	7.380	7.023
0.20	3.343	3.341	3.266	5.40	8.471	7.494	7.154
0.40	3.387	3.381	-	5.60	8.753	7.605	7.281
0.60	3.433	3.421	3.337	5.80	9.009	7.717	7.382
0.80	3.485	3.465	-	6.00	9.235	7.833	7.479
1.00	3.541	3.514	3.416	6.20	9.411	7.956	7.580
1.20	3.603	3.563	-	6.40	9.497	8.084	7.690
1.40	3.699	3.618	3.503	6.60	9.623	8.214	7.804
1.60	3.744	3.677	-	6.80	9.730	8.345	7.923
1.80	3.830	3.742	3.608	7.00	9.823	8.479	8.041
2.00	3.929	3.813	3.665	7.20	9.903	8.606	8.160
2.20	4.048	3.895	3.729	7.40	9.978	8.709	8.287
2.40	4.195	3.988	3.798	7.60	10.038	8.812	8.435
2.60	4.388	4.095	3.876	7.80	10.096	8.915	8.602
2.80	4.662	4.226	3.964	8.00	10.148	9.003	8.771
3.00	5.141	4.394	4.064	8.20	-	9.078	8.926
3.20	5.844	4.620	4.188	8.40	-	9.150	9.019
3.40	6.335	4.963	4.327	8.60	-	9.213	9.118
3.60	6.681	5.534	4.523	8.80	-	9.272	9.217
3.80	6.937	6.050	4.781	9.00	-	9.318	9.316
4.00	7.143	6.390	5.212	9.20	-	-	9.405
4.20	7.325	6.638	5.763	9.40	-	-	9.484
4.40	7.489	6.835	6.174	9.60	-	-	9.556
4.60	7.652	6.998	6.462	9.80	-	-	9.620
4.80	7.820	7.137	6.682	10.00	-	-	9.676
5.00	8.008	7.265	6.865				

(-) The pH of these points has not been measured

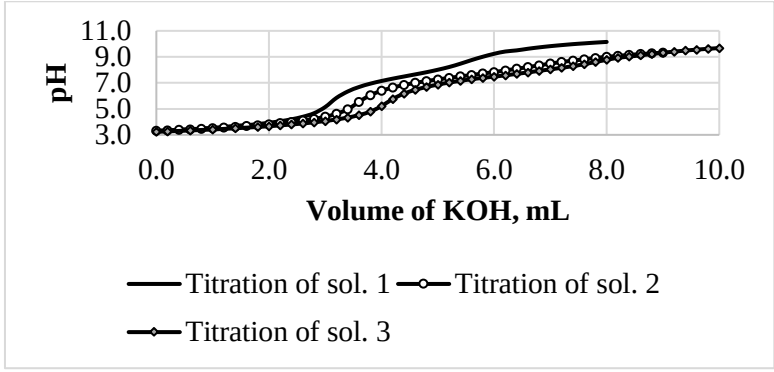

Figure 2. The titration curves of H_2BDMS solutions with KOH standard solution

On these titration curves, only one titration jump was observed in which the estimated pH range of titration jumps of H_2BDMS is about from 4.3 to 6.4. Based on the titration data, we have estimated the equivalent volume (V_E, mL) of KOH for each titration. Then, the titration ratio of KOH and each acid at the equivalent point was calculated for all studied solutions. The V_E values for the H_2BDMS solutions C_{01}, C_{02} and C_{03} M are V_{E1} = 3.29 mL, V_{E2} = 3.56 mL and V_{E3} = 4.09 mL, respectively. So, the mole numbers of the reactants are calculated and their ratio at the equivalent point (EP) is estimated. The results of this calculation are shown in Table 2.

Table 2. The mole numbers of the reactants and the reacted ratio (KOH and H_2BDMS) at the EP

Solution of H_2BDMS (M)	**Mole of H_2BDMS (mmol)**	**Mole of KOH (mmol)**	**The reacted ratio**
$C_{01} = 7.893.10^{-4}$	$20 \times 7.893.10^{-4}$	$3.29 \times 4.798.10^{-3}$	1 : 1
$C_{02} = 8.540.10^{-4}$	$20 \times 8.540.10^{-4}$	$3.56 \times 4.798.10^{-3}$	1 : 1
$C_{03} = 9.812.10^{-4}$	$20 \times 9.81.10^{-4}$	$4.09 \times 4.798.10^{-3}$	1 : 1

The results in Table 2 show that at the equivalent point, the titration ratio of KOH and H_2BDMS acid is 1:1. This means that in the titration process to the equivalent point, only one proton of H_2BDMS was neutralized. Based on these results, we have chosen the suitable ranges from titration data for calculations of the pK_a values of this acid. Similar to the previous research [3, 4, 5], the range of pH < 4.3 was chosen to estimate the pK_{a1}, and the range of pH > 6.4 has been used to estimate the pK_{a2} value. In these ranges, the composition of the studied solutions is the buffer. So, the calculation using the titration data of these ranges is more accurate.

By using the principle that has been mentioned above, we have calculated the values of dissociation constants of H_2BDMS acid. The results are shown in Table 3.

Table 3. The calculated pK_a values of H_2BDMS acid

C	pK_{a1}	pK_{a2}
C_{01}	2.71 ± 0.03	7.99 ± 0.14
C_{02}	2.88 ± 0.02	7.82 ± 0.07
C_{03}	2.78 ± 0.03	7.58 ± 0.07
Mean	***2.79 ± 0.02***	***7.80 ± 0.06***

The results in Table 3 indicate that the dissociation constants that have been determined have great repeatability and reliability. In the electron structure of the H_2BDMS molecule, the positive mesomeric effect (+M) of two OH groups as well as the positive charge center (CH_3N^+) in the quinoline ring will strongly sift electrons into the ring. This effect leads to a great increase in the acidic strength of two OH groups. In addition, due to the negative inductive effect of the bromine atom next to the OH group (bond to the atomic carbon C6), the acid strength of this OH group is increased strongly (see Figure 3). Therefore, the pK_{a1} = 2.79 ± 0.02 was assigned for this OH group and the pK_{a2} = 7.80 ± 0.06 was assigned for the remaining OH group (bond to the atomic carbon C7). These pK_a values are also suitable compared with some similar compounds containing the quinoline ring in the literature [10].

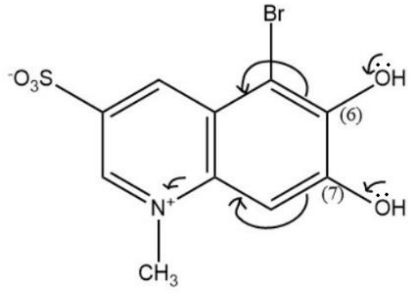

Figure 3. The structure of the H_2BDMS molecule

3. Conclusions

We have applied successfully the potentiometric titration method to determine the thermodynamic dissociation constants of new acid in the aqueous solution at 25 ^oC. This is the first time that the dissociation constants of 5-bromo-6-hydroxy-*N*-methyl-3-sulfoquinoline-7-yloxy) Acetic acid is pK_{a1} = 2.79 ± 0.02 (for the OH group bonding to carbon C6) and pK_{a2} = 7.80 ± 0.06 (for the OH group bonding to carbon C7).

By repeating the experiments with many levels of the analyte concentration, the pK_a values of H_2BDMS that were determined by the potentiometric titration method are so high in accuracy and precision that they can be used as a reference for other research on this acid.

REFERENCES

[1] Jetse R., Arno H., Antonie L., and Bram T., 2013. Development of methods for the determination of pK_a values. *Analytical Chemistry Insights*, Vol. 8, pp. 53 - 71.

[2] Bebee, P., Vrushali, T., Vandana, P., 2014. A review of various analytical methods used in the determination of constant. *International Journal of Pharmacy and Pharmaceutical Science*, Vol. 6, Issue 8, pp. 26-34.

[3] Tran The Nga, Le Thi Hong Hai, and Dao Thi Phuong Diep, 2020. Determination of dissociation constants of (5, 6-dioxo-3-sulfoquinoline-7-yloxy) acetic acid in aqueous solution at 25 ^oC by potentiometric titration. *Russian Journal of Physical Chemistry A*, Vol. 94, No. 3, pp. 576-580.

[4] Bui Thi Minh Anh, Hoang Thi Thu Hong, Nguyen Thu Hien, Nguyen Thi Lien, Dao Thi Phuong Diep, Tran The Nga, 2018. Determination of the dissociation constant of ethyl ammonium and 2-furoic acid in aqueous solution at 298.15 K. *HNUE Journal of Science*, Vol. 63, Issue 11, pp. 117-126.

[5] Tran The Nga, Dao Thi Phuong Diep, 2019. Determination of equilibrium constants of citric acid from the pH values of the potentiometric titration. *Vietnam Journal of Chemistry*, Vol. 57, No. 2E, pp. 311-315.

[6] Thi Hong Hai Le, Thi Ngoc Vinh Nguyen, Tuan Cuong Ngo, Van Co Le, Thi Yen Hang Bui, Thi Da Tran, Huu Dinh Nguyen, and Luc Van Meervelt, 2020. Synthesis, Crystal Structures, Fluorescence and Quantum Chemical Investigations of some Multi-Substituted Quinoline Derivatives. *Journal of Fluorescence*, Doi.org/10.1007/s10895-020-02648-2.

[7] Nguyen Huu Dinh, Le Van Co, Nguyen Manh Tuan, Le Thi Hong Hai, and Luc Van Meervelt, 2012. New route to novel Polisubstituted Quinolines Starting with Eugenol, the main constituent of Ocimum Sanctum Oil. *Heterocycles*, Vol. 85, No. 3, pp. 627-637.

[8] Nguyen Huu Dinh, Vu Thi Len, Bui Thi Yen Hang, and Le Thi Hoa, 2029. Synthesis and Reactions of a new Quinone Quinoline 7-(Carboxymethoxy)-3-sulfoquinoline-5,6-dione. *Journal of Heterocyclic Chemistry*, DOI 10.1002/jhet.3490.

[9] Ingmar, G., Federico, M., Kastriot, S., and Hans, W., 2013. *Guidelines for the extrapolation to zero ionic strength.* France: OECD Nuclear Energy Agency.

[10] John, A. D., 1999. *Lange's Handbook of Chemistry 15th*, New York: McGraw-Hill, 1999, p. 864-912.