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ТЕРМОДИНАМИЧЕСКИЕ ХАРАКТЕРИСТИКИ РЕАКЦИЙ КИСЛОТНО-ОСНОВНОГО ВЗАИМОДЕЙСТВИЯ В ВОДНОМ РАСТВОРЕ ПИРИДОКСАЛЬ-5'-ФОСФАТА

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В качестве объекта исследования нами был выбран 3-гидрокси-2-метил-5-[(фосфонокси)метил]-4-пиридинкарбоксальдегид пиридоксаль-5'-фосфат, PLP) - одно из важнейших биологически активных соединений. Прямым калориметрическим методом измерены тепловые эффекты взаимодействия раствора пиридоксаль-5' - фосфата с растворами азотной кислоты и гидроксида калия при 298,15 К и значениях ионной силы 0,5; 1,0 и 1,5 при фоновом электролите нитрате калия. Измерения проводились на калориметре с изотермической оболочкой и автоматической записью температурно-временной кривой, в реакционном сосуде объемом 60 см^3 и при Т = (293,15–308,15 К) ± 0,01 К и Р = 100,5± 0,7 кПа. Относительная погрешность измерения для теплоты растворения стандартного вещества составляла-0,1-0,3%. Близкие значения констант диссоциации пиридоксаль-5'- фосфата не позволяют выделить такую область pH, где происходил бы только один из процессов ступенчатой диссоциации, в связи с чем измерялся суммарный тепловой эффект протонирования пиридоксаль-5'-фосфата. Расчет равновесного состава системы с учетом процессов ступенчатой диссоциации пиридоксаль-5'-фосфата и диссоциации воды проводился по программе KEV. Тепловые эффекты ступенчатой диссоциации пиридоксаль-5'-фосфата рассчитаны с использованием универсальной программы HEAT. Поскольку тепловые эффекты разбавления были измерены в трех диапазонах концентраций KNO_3: 0,4-0,5; 0,9-1,0; 1,4-1,5 моль/л, количество экспериментов в каждой серии было не менее четырех. Для расчета доверительного интервала среднего значения ΔН критерий Стьюдента взяли 0,95. Были найдены стандартные тепловые эффекты ступенчатой ионизации пиридоксаль-5'-фосфата путем экстраполяции экспериментально полученных количеств пиридоксаль-5' - фосфата на нулевую ионную силу раствора.

Ключевые слова: термодинамика, калориметр, энтальпия, пиридоксаль-5'-фосфат

THERMODYNAMIC CHARACTERISTICS OF ACID-CORE REACTIONS INTERACTIONS IN THE WATER SOLUTION PIRIDOXAL-5'-PHOSPHATE

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As the object of the study, we selected 3-hydroxy-2-methyl-5-(phosphonic) methyl-4-pyridincarboxaldehyde (pyridoxal-5'-phosphate) which is one of the most important biologically active compounds. Direct calorimetric method was used to measure the thermal effects of interaction of the solution of pyridoxal-5'-phosphate with solutions of nitric acid and potassium hydroxide at 298.15K and ionic strength values of 0.5; 1.0 and 1.5 against the background of electrolyte-supporting potassium nitrate. The measurements were carried out in a calorimeter with an isothermal shell equipped with a 60 cm^3 reaction vessel and electric calibration at T = 298.15K ± 0.01 К and P = 100.5± 0.7 kPa and automatic recording of the temperature-time curve. Relative measurement error for heats of dissolution of a standard substance was -0.1-0.3%. Close values of constant sequencing of pyridosal-5'-phosphate do not allow to distinguish such an area of pH where only one of the processes of step dissociation would occur. In this regard the total thermal effect of protonation of pyridoxal-5'-phosphate would be measured. Calculation of the equilibrium composition of the system took into account processes step dissociation and water dissociation was carried out according to the KEV program. The thermal effects of stepwise dissociation of pyridoxal-5'-phosphate are calculated using the universal HEAT program. Because, the thermal effects of dilution were measured in three concentration ranges of KNO_3: 0.4-0.5;0.9-1.0; 1.4-1.5 mol /l, the number of experiments in each series was at least four. To calculate the confidence interval of the average value of DH Student's criterion was taken at a confidence interval of 0.95 The standard thermal effects of stepwise ionization of pyridoxal-5'-phosphate were found by extrapolation of experimentally obtained amounts of piridoxyxal-5'-phosphate to zero ion force of the solution.

Key words: thermodynamics, calorimeter, enthalpy, pyridoxal-5'-phosphate

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INTRODUCTION

For a long time, the name "vitamin B_6" meant a set of biologically active compounds – derivatives 3-hydroxy-2-methylpyridine. The most important of these are pyridoxin, pyridoxal, pyridoxamine, pyridoxal-5'-phosphate, pyridoxamine-5'-phosphate and pyridoxin-5'-phosphate. In enzymatic catalysis most active phosphorylase esters are pyridoxal-5'-phosphate and pyridoxamine-5'-phosphate [1-3]. We have selected 3rd-hydroxy-2-methyl as the subject of the study-5-[(phosphonoxes)Methyl]-4-pyridincarboxaldehyde (pyridosal-5'-phosphate, PLP):

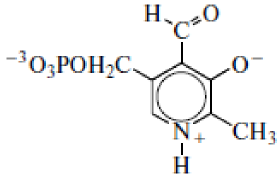

Fig. 1. Structural formula of pyridoxal-5'-phosphate molecule (pH=2.5)

Рис. 1. Структурная формула молекулы пиридоксаль-5'-фосфата

PLP is one of the most important biologically active compounds. PLP-dependent ferments play a key role in the metabolism of amino acids, fats and carbohydrates, as well as hormone biosynthesis, neurotransmitters [4-8].

In literature, there is a greater amount of data on constants of the ionization of pyridoxal-5-phosphate [9-15]. These works are performed at different ionic strength values, against the background of supporting electrolytes that differ in nature. Therefore, in order to compare and analyze literature data, it is necessary for each ionic strength values find the most probable values of the dissociation constants. In this way, the constants are extrapolated to zero ionic strength using the lowest squares method using an equation with one individual parameter [16]. The values of $pK_1^0 = 3.65 \pm 0.05$, $pK_2^0 = 6.22 \pm 0.05$ and $pK_3^0 = 8.41 \pm 0.05$ and calculated the step constants of acid ionization at fixed ionic strength values of (I = 0.5; 1.0; 1.5). These values were later used to select calorimetric measurements and calculate results.

Data on the heat of acid-basic interactions involving pyridoxal-5'-phosphate are very few. In [13], the authors gives the following values: ΔrH_1 = -18.0 kJ/mol, ΔrH_2 = 4.2 kJ/mol and ΔrH_3 = -25.1 kJ/mol at 298.15 K and an ionic strength of I = 0.1 (background electrolyte KCl). Studies were performed by calorimetric method titration at a single value of ionic strength, the effect of concentration background electrolyte on acid-base interaction processes were not considered by the authors.

The aim of this work is to study the background electrolyte concentration on the thermal effects of stepwise dissociation of pyridoxal-5'-phosphate based on the experimental determination of the ionization enthalpy of pyridoxal-5'-phosphate in an aqueous solution at 298.15 K and ionic strengths of 0.5; 1.0 and 1.5 against potassium nitrate; calculation of standard thermodynamic characteristics of stepwise dissociation of pyridoxal-5'-phosphate.

EXPERIMENTAL PART

Pyridoxal-5'-phosphate (manufactured by Sigma-Aldrich USA, $C_8H_{11}NO_6P$ M = 274.14) was used without preliminary purification. The purity of the reagents declared by the manufacturer was more than 98 wt. % The carbon-free KOH solution and the HNO_3 solution were prepared according to the usual procedure [17] from reagents of the “chemically pure” grade; concentrations were determined by the titrimetric method. The preparation of potassium nitrate qualification "chemically pure" was purified by recrystallization from bidistillate.

The measurements were carried out in a calorimeter with an isothermal shell equipped with a 60 cm^3 reaction vessel and electric calibration at T = 298.15 K ± ± 0.01 K and P = 100.5 ± 0.7 kPa and automatic recording of the temperature-time curve, which was in principal very similar to the device described several times [18-21] KMT-14 thermistor was used as a temperature sensor. Thermostatically controlled calorimetric cells were carried out in a thermostat equipped with a PID controller with an accuracy of 0.002 K. The thermostat temperature sensor was a platinum resistance thermometer. The calorimeter was calibrated by a current. The volume of the calorimetric fluid was 42.83 ml. Ampoule displacement – was 1-1.6 $см^3$, the maximum thermometric sensitivity of the calorimetric setup was $(0.5\text{-}2)\cdot10^{-2}$ J/mm chart recorder. Relative measurement error for heats of dissolution of a standard substance was -0.1-0.3%. The weights were weighed on the scales of VLR-200 with accuracy $2\cdot10^{-4}$ g. The operation of the installation was checked by the integral enthalpies of dissolution of crystalline potassium chloride in water and was considered suitable for measurement, if the value defined in it $\Delta_{sol}H_{298,15}(KCl\infty H_2O)$ differed from the standard was not more than 0.3%. The most reliable current value was used as a standard $\Delta_{sol}H_{298,15}(KCl\infty H_2O)$ = 17.234 ± 0.018 kJ/mol conforming to the standard SRM 1655NBS. The nearly identical value was obtained elsewhere [22, 23]. The thermal value of the calorimeter for water was 87 ± ± 12 J/K [24].

The processes of sequential protonation of the anion L^{3-} in an aqueous solution can be represented by the scheme:

$$L^{3-} + H^+ = HL^{2-} \qquad \Delta rH_1 \qquad (1)$$

$$HL^{2-} + H^+ = H_2L^- \qquad \Delta rH_2 \qquad (2)$$

$$H_2L^- + H^+ = H_3L \qquad \Delta rH_3 \qquad (3)$$

As it can be seen from the equilibrium diagram in an aqueous solution of pyridoxal-5'-phosphate (Fig. 2). The close values of the stepwise dissociation constants do not allow us to distinguish a region of pH where only one of the processes would proceed. Calculation of the equilibrium composition of the system took into account processes (1-3) and water dissociation was carried out according to the “KEV” program [25]. In this regard, the total thermal effect of protonation of particles L^{3-}, HL^{2-} and H_2L^- was measured. Moreover, the selection of conditions during the experiment was carried out in such a way that the proportion of processes (1), (2) and (3) changed in the series of experiments with a maximum difference in the first and last experiment of the series.

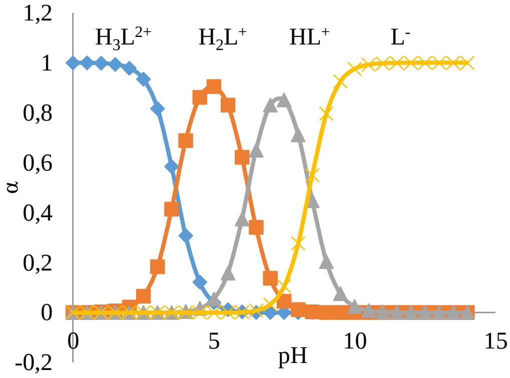

Fig. 2. Equilibrium diagrams in an aqueous solution of pyridoxal-5 - phosphate T=298.15 K

Рис. 2. Диаграммы равновесий в водном растворе пиридоксаль-5'-фосфата T=298,15K

The heat of dissociation of pyridoxal-5'-phosphate was determined by the following method. The total thermal effect of the attachment of protons to particles H_2L^-, HL^{2-} and L^{3-} was measured in several pH ranges and based on these data, the enthalpies of acid dissociation were calculated for each step. The enthalpies of the interaction of pyridoxal-5'-phosphate neutralized to pH = 9.1 with nitric acid solutions of various concentrations (from 0.00465 to 0.06198 mol/L) were measured. The solution of mineral acid was placed in a calorimetric glass, and in an ampoule an exact weighed portion of solution of pyridoxal-5'-phosphate with pH = 9.1. The pH of the solution after mixing the reagents (pH) varied from 5.9 to 3.1. The measurements were carried out at three values of ionic strength I = 0.5; 1.0; 1.5 (KNO_3) and at temperatures of 298.15 K. The thermal effects of diluting a solution of pyridoxal-5'-phosphate with a pH of 9.1 in solutions of a background electrolyte were also measured. Since the ionic strength created by pyridoxal-5'-phosphate in the glass after breaking the ampoule in the series of experiments varied from 0.01 to 0.1, a different amount of background electrolyte was added in each experiment. In this regard, the thermal effects of dilution were measured in three concentration ranges of KNO_3: 0.4-0.5; 0.9-1.0; 1.4-1.5 mol/l. The number of experiments in each series was at least four. To calculate the confidence interval of the average value of ΔH Student's criterion was taken at a confidence interval of 0.95.

RESULTS AND DISCUSSION

The total thermal effect of protonation (processes 1-3) during the calorimetric experiment was calculated per mole of pyridoxal-5'-phosphate;

$$\Delta rH = \Delta rH_{mix} - \Delta rH_{dil}$$

$$\Delta rH = \Delta[OH^-]\Delta Hw + \Delta[L^{3-}]\Delta rH_1 + \Delta[HL^{2-}] \Delta rH_2 + \Delta[H_2L^-]{*}\ \Delta rH_3/C^0\ H_3L \qquad (4)$$

Where $\Delta[OH^-]$, $\Delta[L^{3-}]$, $\Delta[HL^{2-}]$, $\Delta[H_2L^-]$ – is the difference between the final and initial equilibrium concentrations of the corresponding particles; C^0_{H3L} – is total concentration of pyridoxal-5'-phosphate, taking into account dilution to the volume of calorimetric liquid; ΔrH_1 ΔrH_2 ΔrH_3 – is molar thermal effects of particle H_2L^-, HL^2- and L^3- protonation processes respectively.

Each series of experiments included from 3 to 5 measurements. To calculate the confidence interval, the average student's criterion was taken at a confidence level of 0.95. The error was calculated by the formula: $S = t_{p,f}\times[\Sigma\Delta^2/n(n-1)]^{1/2}$, where $t_{p,f}$ is the Student criterion with a confidence level of 0.95 and the number of degrees of freedom f = 5. Based on the obtained experimental data, we searched for stepwise heats of ionization of pyridoxal-5'-phosphate, the calculation was performed according to the program «HEAT». Errors in $\Delta_{dis}H$ values are increased in comparison with those calculated using the least squares method, since the error in the operation of the setup does not allow us to give them less than ± 0.2 kJ/mol. The standard thermal effects of stepwise ionization of pyridoxal-5'-phosphate were found by extrapolating the experimentally obtained values of the heats of dissociation of pyridoxal-5'-phosphate (Table 1) to the zero ionic strength of the solution according to equation (5) [16]:

$$\Delta rH_i - \Delta Z^2\Psi(I) = \Delta rH_i^0 + b\cdot I \qquad (5)$$

where ΔrH_i, ΔrH_i^0 – is change in enthalpy at a finite value of ionic strength and at I = 0, respectively, Ψ(I) – is the theoretically calculated ionic strength function Δz^2 – is the difference between the squared charges of the reaction products and the starting components, b – is empirical coefficient. The standard enthalpies of stepwise dissociation of pyridoxal-5'-phosphate are given in Table. 2.

Table 1

Thermodynamic characteristics of step dissociation processes of pyridoxal-5 ' - phosphate at T=298.15 K and different values of ionic strength

***Таблица 1.* Термодинамические характеристики процессов ступенчатой диссоциации пиридоксаль-5'-фосфата при T=298,15К и различных значениях ионной силы**

I	pK	ΔG, kJ/mol	ΔrH, kJ/mol	-ΔS, J/mol K
T=298.15K				
$H_3L = H_2^- + H^+$				
0.5	3.26 ± 0.05	18.61 ± 0.3	-19.37 ± 0.2	127.4 ± 1.2
1.0	3.30 ± 0.05	18.84 ± 0.3	-20.11 ± 0.2	130.6 ± 1.1
1.5	3.43 ± 0.05	19.58 ± 0.3	-20.77 ± 0.2	135.3 ± 1.1
$H_2L^- =HL^{2-} + H^+$				
0.5	5.47 ± 0.05	31.22 ± 0.3	5.19 ± 0.2	87.3 ± 1.1
1.0	5.56 ± 0.05	31.74 ± 0.3	5.87 ± 0.2	86.8 ± 1.1
1.5	5.66 ± 0.05	32.31 ± 0.3	6.44 ± 0.2	86.8 ± 1.1
$HL^{2-} = L^{3-} + H^+$				
0.5	7.14 ± 0.05	40.76 ± 0.3	-26.31 ± 0.2	224.9 ± 1.1
1.0	7.29 ± 0.05	41.61 ± 0,3	-27.39 ± 0.2	231.4 ± 1.1
1.5	7.43 ± 0.05	42.41 ± 0.3	-28.49 ± 0.2	237.8 ± 1.1

Table 2

Standard thermodynamic characteristics of step dissociation processes of pyridoxal-5 ' - phosphate T=298.15 K

***Таблица 2.* Стандартные термодинамические характеристики процессов ступенчатой диссоциации пиридоксаль-5'-фосфата**

pK^0	ΔG^0, kJ/mol	ΔrH^0, kJ/mol	$-\Delta S^0$, J/mol K
$H_3L = H_2L^- + H^+$			
3.65±0,05	20.83±0.6	-18.67±0.30	132.4±0.9
$H_2L^- = HL^{2-} + H^+$			
6.22±0,05	35.50±0.6	4.52±0.30	103.9±0.9
$HL^{2-} = L^{3-} + H^+$			
8.41±0,05	48.00±0.6	-25.32±0.30	245.9±0.9

Change in enthalpy of pyridine nitrogen ionization – ΔrH_3, and phenolic group – ΔrH_1, are exothermic at all values of the ionic strength of the solution. However, the change in enthalpy for the second stage of ionization (phosphate group) – ΔrH_2 is exothermic. The change in entropy during the dissociation of pyridoxal-5'-phosphate is significant in absolute value, and an increase in the charge of the anionic particle sharply affects the value $\Delta_{dis}S$. An increase in the particle charge leads to a sharper change $\Delta_{dis}S$.

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