ASSESSMENT OF POLYFUNCTIONAL MACROCYCLIC COMPOUNDS IN SOLUTION BY CRYOSCOPIC METHOD

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Abstract. *The article considers the synthesis of meso-tetrakis(1'-methyl-pyrid-4-yl)porphyrin tetratosylate and meso-tetrakis(1'-methyl-carboxymethylpyrid-4-yl)porphyrin tetrabromide. The authors qualified the porphyrin ligands in terms of the electron and ^{1}H NMR spectroscopy. The research determines the decrease of freezing point (ΔT^{fr}) of aqueous solutions of porphyrins, as well as a model N-methyl-pyridinium salt (1-methyl-pyridinium iodide). We used the obtained experimental values of ΔT_3 to determine the isotonic coefficient. The obtained results indicate the compounds are almost completely dissociated in the indicated concentration range in dilute solutions.*

For citation:

Introduction

Porphyrins are tetrapyrrole macrocycles. Their main feature is diversity, which determined by their special molecular structure. Porphyrins include numerous macrocyclic aromatic polyamines containing a multiloop **(I),** closed-loop conjugated π-system. This system is based on a planar 16-membered macrocycle of carbon and nitrogen atoms. Not only all porphyrins, but also their nitrogen-substituted ones (azaporphyrins and phthalocyanines) are derived from porphine **(I)** by substitution of various types at 1-8 positions (*β*-positions of pyrrole cycles), and in methine bridges (*meso*-positions) [1-2]. As a result, a large set of porphyrin ligands with different properties is obtained. Their modification can vary almost infinitely.

(I)
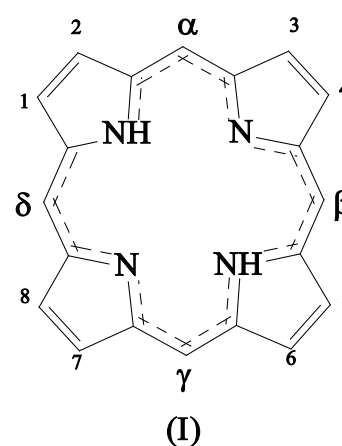
Scientists have been conducting fundamental and applied research on porphyrins for more than half a century. However, the interest of scientists for studying the properties of these unique molecules is the same [3]. The promising catalytic properties of porphyrins make it possible to use them in various fields of chemical technology [4-6], biology, and medicine, for example, in photodynamic therapy [7-9], as photosensitisers in systems for converting solar

energy into chemical and electrical energy [10-11]. Reasonably, they possess high extinction coefficients due to their extended conjugated electron system.

Most of synthetic porphyrins have low solubility in media with high polarity. At the same time, the growing interest to these compounds due to the possibility of their use in biology and medicine is associated with the need to synthesise new derivatives with solubility in aqueous media. *Ortho-*, *meta-* and *para-N*-methyl-substituted derivatives of 5,10,15,20-tetrapyridylporphyrin are well soluble in water, have a significant photocytotoxic effect, and are being actively studied for further application for the inactivation of bacteria and viruses [12-13].

Meanwhile, there are a number of peculiarities when studying water-soluble porphyrins. Firstly, water is a specific solvent, and the reaction mechanisms occurring in it differ significantly from those in other media [14]. In particular, aqueous solutions are characterised by heterolytic reactions in contrast to nonpolar organic solvents, in which homolytic processes are observed. Secondly, water is the main medium for processes occurring in living cells. Therefore, the study of the properties of porphyrins and metalloporphyrins in aqueous solutions is of great importance from the point of view of biochemistry, for example, for modelling the natural photosynthetic process.

The practical importance of water-soluble porphyrins determines the relevance of the search for their optimal structure with given properties. One of the proposed methods for assessing the state of salts of cationic *meso*-pyridylporphyrins in aqueous solution is cryoscopic. In [15], this method was also applied during the study of α-amino acids. The main purpose of the present study is to gain insight into the cryoscopic study of porphyrins differing in functional substitution at the pyridyl nitrogen atom and, based on the results obtained, calculate the number of ions formed by the porphyrin molecule in the electrolyte.

Main body

We synthesized 5,10,15,20-tetrakis(1'-methyl-pyrid-4-yl)porphyrin tetratosylate (**1**), 5,10,15,20-tetrakis(1'-carboxymethyl-pyrid-4-yl)porphyrin tetrabromide (**2**) and the pyridyl fragment model salt 1'-methyl-pyridinium iodide by the procedure described in [12, 16]. We recorded the electronic absorption spectra on a SF-56 spectrophotometer (LOMO, Russia); FT-IR spectra of porphyrins **1-2** on a VERTEX 80v spectrophotometer within the wavelength range 4000-400 cm^{-1}; 1H NMR spectra in DMSO d$_6$ on a Bruker 500 spectrophotometer. The water we used for the experiment was distilled twice. We cooled the distillate with conductivity <10^{-6} S cm-cm^{-3} at room temperature, and determined ΔT^{fr} of porphyrin and model salt solutions in the concentration range (10^{-3}-10^{-4} mol·kg^{-1}).
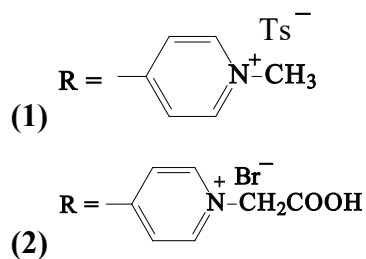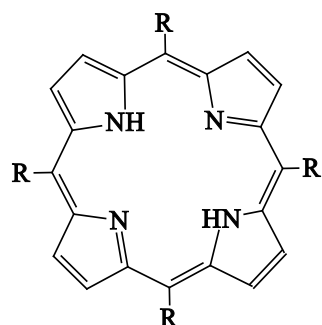
Porphyrins **1** and **2** have a structure in which the functional groups are firstly bonded to one of the ionised nitrogen atoms and secondly distant from the central secondary (=NH) and tertiary (-N=) amino groups, although they are in electronic interaction with them through a conjugated π-system.

Compounds **1** and **2** have a positive (+) charge on the pyridinium nitrogen atom $= \overset{+}{\underset{|}{N}} -$, which does not change with changing of pH. It is not a coordination centre in solutions for either cations or anions. However, pyridinium cations are strong solvation centres by ion-dipole mechanism. Pyridinium charges are polarising centres (negative induction effect, -I) for the porphyrin N-H bonds of the H_2N_4 reaction centre and for the four -COOH groups (Compound **2**) in particular. Due to the presence of numerous solvation centres, porphyrins are soluble in water, which is unusual for these hydrophobic macroheterocycles.

However, any liquid freezes at the temperature at which the saturated vapour pressure above it becomes equal to the saturated vapour pressure above the crystals. Raoul's law for extremely dilute solutions of a non-volatile solute states that the vapour pressure of the solvent over the solution is always less than that over the pure solvent. It is known that the solution always freezes at a lower temperature than the pure solvent. The cryoscopic constant does not depend on the nature of the dissolved substance and its concentration, but is determined by the properties of the pure solvent; its physical meaning is that it is numerically equal to ΔT_{fr} of a solution whose molality is 1 mol per 1 kg of solvent. For water, the most common solvent, $K_{cr}(H_2O) = 1,86$ K·mol^{-1}·kg.

The lowering of the solution freezing temperature is determined by the equation:

$$\Delta T_{fr} = T_{fr}^0 - T_{fr},$$

where ΔT_{fr} is the decrease of the solution freezing temperature compared to the pure solvent; T_{fr}^0 is the freezing temperature of the pure solvent; T_{fr} is the freezing temperature of the solution.
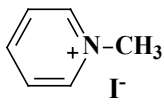
The colligative properties of solutions depend on the total number of the dissolved substance particles. The concentration of a solution is usually stated in terms of formula units (molecules). As a result of electrolytic dissociation of a dissolved substance (electrolyte), the number of its particles in solution increases. The isotonic coefficient (i) is introduced into the equations describing the colligative properties of electrolyte solutions to accommodate this factor.

$$\Delta T_{fr} = i \cdot K_{cr} \cdot C_m,$$

where T_{fr}^0 is the freezing temperature of the pure solvent; T_{fr} is the freezing temperature of the solution; C_m is the molar concentration of the solution; K_{cr} is the cryoscopic constant; i is the isotonic coefficient.

Table 1 shows the values of ΔT_{fr} and i in aqueous electrolyte for porphyrins (**1-2**) and 1-methyl-pyridinium iodide, as well as potassium chloride and carbonic acid diamide salts, for which the number of ions in solution is known. We determined the values of ΔT_{fr} experimentally.

Table 1. Values of ΔT_{fr} and i for porphyrins (**1-2**) and 1-methyl-pyridinium iodide in aqueous electrolyte

Compound	m, g	$m(H_2O)$, g	ΔT_{fr}	i	M_{calc}, g/mol
(NH₂)₂CO	0.30090	50.0078	0.190	$1.019 \approx 1$	58.9039
	0.90015	49.9897	0.560	$1.004 \approx 1$	59.8080
	3.01542	50.2878	1.840	$0.991 \approx 1$	60.6150
	3.00240	49.9871	1.850	$0.995 \approx 1$	59.7423
	3.00240	49.9871	1.860	$0.999 \approx 1$	60.0635
KCl	0.37265	50.0025	0.372	$2.001 \approx 2$	37.2631
	0.37271	50.0092	0.373	$2.005 \approx 2$	37.1642
	1.86590	65.1527	1.380	$1.931 \approx 2$	38.6002
	1.86590	50.1427	1.770	$1.906 \approx 2$	39.1039
	3.72760	49.9908	3.540	$1.902 \approx 2$	39.1785
(1)	0.05954	60.33765	0.007	$5.202 \approx 5$	262.202
	0.05954	50.56095	0.008	$4.982 \approx 5$	273.789
	0.05954	40.51995	0.01	$4.991 \approx 5$	273.308
	0.12274	50.0039	0.016	$4.780 \approx 5$	285.348
(2)	0.05379	49.7100	0.016	$9.338 \approx 9$	125.7913
	0.10630	76.0504	0.020	$9.036 \approx 9$	129.9914
	0.10630	67.7305	0.023	$9.255 \approx 9$	126.9211
	0.10630	49.9990	0.030	$8.911 \approx 9$	131.8146
⌬⁺N–CH₃ I⁻	1.10493	49.9985	0.371	$1.995 \approx 2$	110.7941
	1.10500	49.9960	0.370	$1.989 \approx 2$	111.1061
	1.90924	60.0026	0.531	$1.983 \approx 2$	111.4574
	1.90924	50.0013	0.630	$1.961 \approx 2$	112.7331
	2.93741	50.0077	0.960	$1.942 \approx 2$	113.8071

According to the experimental data (see Table 1), a weak dependence of i values on Cm can be observed. Data show the decrease of i value with increasing molality of solutions of both porphyrins and salts, indicating possible incomplete dissociation. The number of the dissolved model salt particles, 1-methyl-pyridinium iodide, is close or equal to two, as expected. For porphyrin **1**, the value of i was close to five, which indicates dissociation of the substance into four tosylate anions and a large porphyrin cation. For porphyrin **2**, the number of particles in solution is close to nine. This fact corresponds with the results of [17], in which experimental data on the pH change of solution due to ionisation of four $\geq N^{+}\text{-}CH_2COOH$ groups are presented, the true constants of step ionisation (true - since the concentrations of ions in solution are small) of porphyrin **2** are calculated, and the equivalence of all four $\geq N^{+}\text{-}CH_2COOH$ groupings of carboxymethyl-substituted porphyrin and the possibility of their cleavage of H^{+} in solution are discussed. Due to the very strong proton-acceptor properties of the pyridinium cation $=\overset{+}{N}-$, $-CH_2COOH$ correspond in strength to the acetic acid halogen derivatives $HalCH_2COOH$, $Hal_2CNCOOH$ and even $Hal_3CNCOOH$. Since the electron acceptor field $4 = N^{+}<$ extends to the H_2N_4 reaction centre of tetrapyridylporphine, a significant decrease in the basic properties of the tertiary nitrogen atoms $(=N-)$ and a strong increase in the acidic properties of the N-H groups are expected.

Conclusions and recommendations

The data obtained allow us to evaluate the state of polyfunctional macrocyclic compounds in solution. In particular, the water-soluble porphyrins studied in this paper are organic salts.

According to the results of the experiment in the specified concentration range, these salts in dilute solutions are almost completely dissociated.

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