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Interaction between creatinine and sulfonated derivatives of cobalt phthalocyanine

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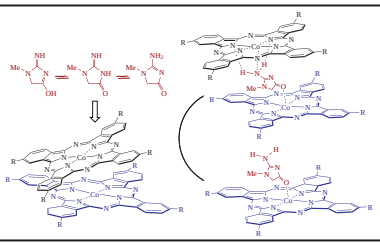
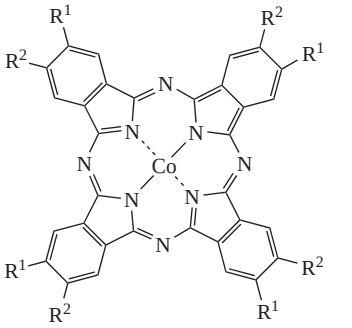
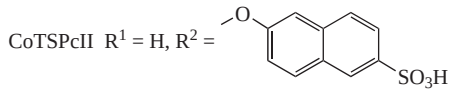
Sulfonated derivatives of cobalt phthalocyanine strongly fix the creatinine (2-amino-1-methyl-1*H*-imidazol-4-ol) thus forming ordered dimeric structures. Such bonding may be used to create materials for sorption of creatinine from the solutions and to form direct liquid-phase systems based on metal phthalocyanines.



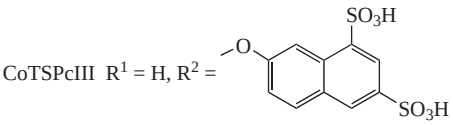
The methods of supramolecular chemistry of metallophthalocyanines (MPc) allow one to obtain liquid-phase systems possessing biological and catalytic activity.[1,2] Especially promising areas of research are the creation of transport systems[3] for the targeted delivery of medicines and purification of biological fluids from toxins[4] and molecular magnets.[5] In this context, the problems of MPc self-organization in solutions,[6] on the surface of solid-phase supports[7] and their interactions with various biomolecules[8,9] are to be solved. It is necessary to provide transparency of the metal in the composition of MPc for coordination interaction in the course of the material formation. In our opinion, one more important point is intermolecular interaction of the MPc with compounds contained in human blood and other biological fluids and organs. Such interactions can often have an unpredictable impact on the macrosystem and dramatically change its properties.



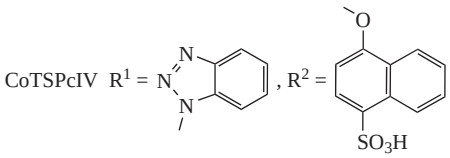
CoTSPcI R^1 = H, R^2 = $-S(=O)(=O)-OH$



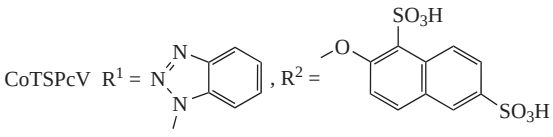
CoTSPcII R^1 = H, R^2 = O-(naphthyl)-SO_3H



CoTSPcIII R^1 = H, R^2 = O-(naphthyl)-SO_3H, SO_3H



CoTSPcIV R^1 = (imidazolyl), R^2 = O-(naphthyl)-SO_3H



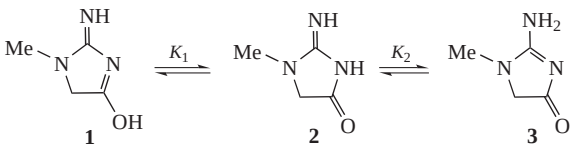
CoTSPcV R^1 = (imidazolyl), R^2 = O-(naphthyl)-SO_3H, SO_3H

Here we present the results of our study of the intermolecular interaction between creatinine (2-amino-1-methyl-1*H*-imidazol-4-ol) and cobalt complexes of sulfonated phthalocyanines in water media. Creatinine is involved in energy metabolism,[10] muscular and other tissues and is always present in human blood. The presence of anchoring groups in the macrocycle makes it possible to obtain hybrid materials based on polymeric matrix.[11,12] High degree of creatinine bonding by Co^{II} porphyrins[13] and their structural analogues combined with possibility of chemical anchoring on the polymers are promising for creating the materials for blood dialysis.

It was shown previously[14–16] that CoTSPcI–CoTSPcV† molecules in water media are associated and form H- and J-aggregates.

At the same time, introduction of polydentate ligands with equal coordination centers into the system leads to the transformation of the macrocycle dimeric structures and formation of close-packed sandwich-type dimers.[16–18] In case of ligands having different reaction centers, the variety of specified type associates with changing thermodynamic stability is increased.

Creatinine molecule may be presented as a mixture of three tautomeric forms (**1**–**3**) due to migration of the proton.



1 ⇌ (K_1) **2** ⇌ (K_2) **3**

† For synthesis and characteristics of cobalt phthalocyanines, see Online Supplementary Materials.

Table 1 Energies of the creatinine tautomeric transformations.

Calculation basis	G_1 (a.u.)	G_2 (a.u.)	G_3 (a.u.)	ΔG_{1-2} / kJ mol^{-1}	ΔG_{2-3} / kJ mol^{-1}	ΔG_{1-3} / kJ mol^{-1}	K_1	K_2	K_{1+2}
B3LYP/6-31G**	–396.0298	–396.0517	–396.0482	57.4276	9.18925	48.2383	0.9771	0.9963	0.9735
PBE0/6-31G**	–395.5879	–395.6105	–395.6066	59.1394	10.23945	48.8999	0.9764	0.9959	0.9724
B3LYP/cc-pVDZ[19]	–	–396.1524	–396.1488	–	–	–	–	–	–

Tautomeric form **2** acts as intermediate transition between acidic form **1** and basic form **3**. Quantum-chemical modeling of tautomeric forms of creatinine in B3LYP and PBE0 (basis 6-31G**) approximations allowed us to estimate the probability of the existence of creatinine conformers (Table 1). Based on the obtained results, we can make a conclusion about the equilibrium between imine **2** and amine **3** forms. Transition in tautomeric form **1** is energetically less favorable. These results are consistent with known suggestion about the creatinine tautomerization degree in solutions and crystal state.[19] The obtained ^{1}H NMR (D_2O) spectrum [δ: 2.95 (Me), 3.96 (CH_2), 4.7 (NH_2)] confirms the assumption about the predominant existence of tautomeric form **3** in the solution.

Tautomer **2** has the charge –0.153 on the imine nitrogen atom, 0.025 on the amine one, and –0.327 on the oxygen. Tautomer **3** has positive charge 0.121 on the amine type nitrogen, –0.278 on the aza-bridge, and –0.285 on the oxygen atom. These data allow us to suggest that oxygen of the creatinine acts as a donor atom during the first step of complexation. This fact is very important for formation of the ordered systems upon complexation with metal phthalocyanines because it creates geometric possibility of forming a sandwich dimer asymmetrical structure.

Coordination of creatinine by H-aggregates of CoTSPcI and CoTSPcIII is accompanied by their dissociation and formation of the monomolecular complexes in water solution at pH 7.0–7.6. Isosbestic points are detected in the electronic absorption spectrum. There is splitting of the NH_2 signal in the ^{1}H NMR spectrum of creatinine reflecting the different effects of the macrocycle ring and central cation of cobalt. Creatinine molecule coordinates parallel to the plane of the macrocycle and simultaneously stabilizes the complex by the hydrogen bond between the inner nitrogen atom of the MPc and the proton of the creatinine amine group. Note that the Q-band of the electronic absorption spectrum remains broadened under formation of the complex of CoPcI with creatinine and the relaxation effect is observed in the range of the dimer band (630 nm), which is related to the formation of the adducts of molecular complex with the solvent. It is not observed in the case of CoTSPcIII.

Removal of the ionogenic group from the conjugated macrocycle system decreases contribution of electronic effects of substituents on the state of coordination unit. Complexation of the CoTSPcII does not cause the dissociation of the dimers. Rising in the amount of associated forms is connected with transformation of aggregates formed by π–π-interaction of macrocycles affording dimers with ligand participation. Further accumulation of the ligand in the system leads to dissociation of the sandwich dimer and formation of the monoligand complexes. Stability of the CoTSPcII complex with creatinine is several times lower as compared to similar complexes for CoTSPcI and CoTSPcIII (Table 2).

Table 2 Stability constants for CoTSPc molecular complexes with creatinine in water at 298.15 K.

Macrocycle	Composition	K_s / dm^3 mol^{-1}
CoTSPcI	1 : 1	8700 ± 50
CoTSPcII	1 : 1	2100 ± 80
CoTSPcIII	1 : 1	5500 ± 20
CoTSPcIV	1 : 2	2800 ± 60
CoTSPcV	not formed	–

Modification of the phthalocyanine macrocycle by triazole fragment leads to the change of complexation process character. First of all it is due to decrease in the macrocycle solubility in water; therefore, we had to use water–alkali media. Ionization of the macrocycles and creatinine occurs in water–alkali media at pH < 10. It promotes anion–cation interaction between the ligand and macrocycle periphery. Several steps are observed in electronic absorption spectrum upon complexation of the CoTSPcIV, which indicates that the process is complex. First step is destruction of the H-aggregates without formation of CoTSPcIV monomers. Unstable equilibrium of various associates is observed until the CoTSPcIV : L reaches 1 : 0.7 molar ratio. Formation of the molecular complexes of the 1 : 2 composition occurs upon increase in the ratio. At tenfold molar excess of the ligand in solution, when additional coordination of the creatinine on central cation is impossible, a specific interaction with peripheral substituents occurs, which leads to decrease in the macrocycle solvation and results in precipitation of the light green needle crystals at 25 °C. The crystals are dissolved on raising the temperature to 30–33 °C. Modification of the peripheral substituent by additional sulfonic group in case of CoTSPcV leads to the processes similar to those for CoTSPcIV. The obtained data allow us to conclude that modification of the metal phthalocyanines by triazole fragment makes the coordination manner between creatinine and macrocycle ionic.

Our results make a definite contribution to the study of interactions between metallophthalocyanines and creatinine, which should be helpful both in managing the aggregation of metallophthalocyanines in liquid-phase systems and the creation of materials for hemodialysis.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2017.01.004.

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