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Influence of the Chemical Modification of Porphyrins on Their Coordination and Acid–Base Properties

N. Zh. Mamardashvili, Yu. B. Ivanova, V. B. Sheinin, O. A. Golubchikov, and B. D. Berezin

Institute of Solution Chemistry, Russian Academy of Sciences, Ivanovo, Russia

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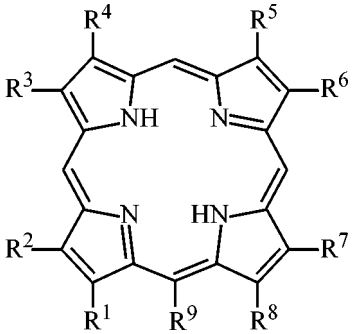
Abstract—For 3,7,13,17-tetramethyl-2,8,12,18-tetrabutylporphyrin, 5,15-diphenyl-3,7,13,17-tetramethyl-2,8,12,18-tetrabutylporphyrin, and the cyclophane dimer in which the monomeric porphyrin fragments are bound via *meta* positions of the benzene rings with two $–O(CH_2)_3O–$ bridges, the kinetics of complexation with copper(II) acetate in acetonitrile and the base ionization in the presence of perchloric acid were studied. The reactivity of these compounds in complexation with the metal cation in acetonitrile correlates with their basicity.

Chemical modification of the macroring significantly affects the physicochemical properties of porphyrins. In this work we studied the effect of *meso* substitution and chemical dimerization on the coordination and acid–base properties of octaalkylporphyrins.

According to published data [1], the rate of coordination of phylloporphyrin **I** with Cu(II) ions in ethanol is by a factor of 3 higher than that of pyrroporphyrin **II**. The *meso* ethyl substitution in octaethylporphyrin **III** increases the rate of the reaction with zinc acetate in acetonitrile by a factor of 6 (Table 1). Introduction of the hexyl group in *meso* position of hexamethyldiethylporphyrin **IV** increases the rate of coordinartion with copper or zinc acetate in propanol by approximately an order of magnitude [1, 2], i.e., with increasing length of alkyl group in the *meso* position (Alk = CH_3, C_2H_5, C_6H_{13}) the reaction rate increases by a factor from 3 to 10. Introduction of a single *meso*-phenyl substituent (**VI**) has practically the same effect as introduction of the hexyl group (**V**) [3], with the effect on the reactivity being stronger (by a factor of 2) for the reaction with Zn(II), as compared to Cu(II).



I, $R^1 = CH_2CH_2COOH$, $R^2 = R^3 = R^5 = R^7 = R^9 = CH_3$, $R^4 = R^6 = C_2H_5$, $R^8 = H$; **II**, $R^1 = CH_2CH_2COOH$, $R^2 = R^3 = R^5 = R^7 = CH_3$, $R^4 = R^6 = C_2H_5$, $R^8 = R^9 = H$; **III**, $R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = R^7 = R^8 = C_2H_5$, $R^9 = C_2H_5$; **IV**, $R^1 = R^2 = R^3 = R^6 = R^7 = R^8 = CH_3$, $R^4 = R^5 = C_2H_5$, $R^9 = C_6H_{13}$; **V**, $R^1 = R^4 = R^5 = R^8 = CH_3$, $R^2 = R^3 = R^6 = R^7 = C_2H_5$, $R^9 = C_6H_{13}$; **VI**, $R^1 = R^4 = R^5 = R^8 = CH_3$, $R^2 = R^3 = R^6 = R^7 = C_2H_5$, $R^9 = C_6H_5$.

In [4] we studied the kinetics of complexation of copper(II) acetate with porphyrin **VIII** and its derivatives containing substituents (*o*-CH_3O, *m*-CH_3O, *m*-NH_2, *m*-NO_2, and *p*-NO_2) in the phenyl fragments. We found that, owing to the absence of conjugation of the π-electron systems of the phenyl and porphyrin moieties, substituents have practically no effect on the reactivity of the tetrapyrrole macroring in ethanol, acetic acid, and pyridine. In this work we studied the

Table 1. Kinetic parameters[a] of coordination of octaalkylporphyrins **I**–**VI** with copper and zinc acetates in alcohols at 298 K [2, 3]

Comp. no.	*meso* Substituent	$C^0_{salt} \times 10^3$, M	k	E	$\Delta S^{\neq}$
I	CH_3	0.92 ($CuAc_2$)	48.50	10.0	–18.7
II	H	2.61 ($CuAc_2$)	15.50	7.0	–32.3
III	C_2H_5	1.15 ($ZnAc_2$)	25.0	35.0	–109.4
IV	C_6H_{13}	0.33 ($ZnAc_2$)	23.4	42.1	94.6
V	C_6H_{13}	0.34 ($CuAc_2$)	20.1	44.2	–81.9
V	C_6H_{13}	0.24 ($ZnAc_2$)	29.0	34.4	–111.1
VI	C_6H_5	0.37 ($CuAc_2$)	30.2	48.7	–64.9
VI	C_6H_5	0.20 ($ZnAc_2$)	45.0	38.2	–94.7

[a] The dimensions of the parameters are as follows: k, $l\,mol^{-1}\,s^{-1}$; E, $kJ\,mol^{-1}$; $\Delta S^{\neq}$, $J\,mol^{-1}\,K^{-1}$.

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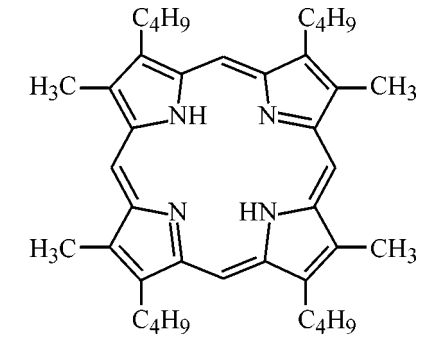
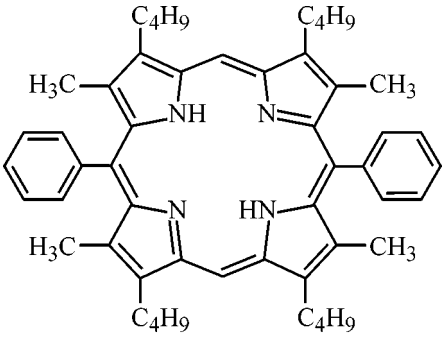
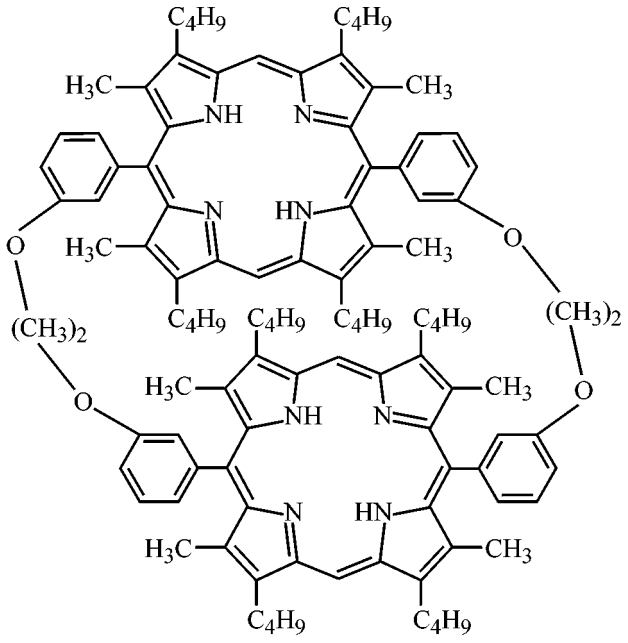


VII



VIII



IX

variation of the kinetic parameters of complexation of β-octaalkylporphyrin **VII** with copper(II) acetate in acetonitrile at *meso*-diphenyl substitution (compound **VIII**) and at chemical dimerization (compound **IX**) of the molecule.

It is known that distortion of the planar structure of porphyrin molecules at *N*-methylation sharply accelerates their complexation with transition metal salts [3]. The ^{1}H NMR and electronic spectra showed [5] that the planarity of the macroring in **VIII** is distorted owing to steric strains produced by the phenyl groups.

Table 2. Kinetic parameters[a] of complexation of porphyrins **VII**–**IX** in acetonitrile

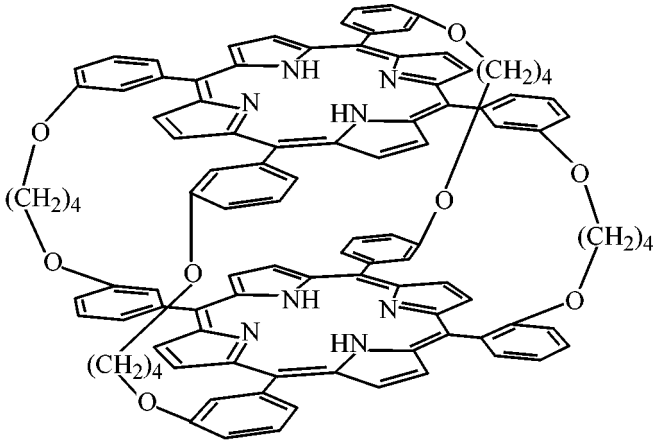
Comp. no.	*meso* Substituent	*T*, K	$k^{(1.5)} \times 10^2$	*E*	$\Delta S^{\neq}$
VII	H	288	8.41 ± 0.21		
		298	17.10 ± 0.02	46 ± 1	–113 ± 2
		308	30.60 ± 0.04		
VIII	C_6H_5	288	3.15 ± 0.11		
		298	9.23 ± 0.23	77 ± 2	87 ± 6
		308	26.8 ± 0.09		
IXa	Ar	288	10.7 ± 0.21		
		298	19.4 ± 0.06	95 ± 2	53 ± 2
		308	38.0 ± 0.42		
IXc	Ar	288	8.92 ± 0.03		
		298	18.7 ± 0.48	52 ± 4	–92 ± 1
		308	36.6 ± 0.35		

[a] The dimensions of the parameters are as follows: $k^{(1.5)}$, $l^{0.5}\ mol^{-0.5}\ s^{-1}$; *E*, kJ mol^{-1}; $\Delta S^{\neq}$, J mol^{-1} K^{-1}.

Therefore, we expected that *meso*-diphenyl-substituted octaalkylporphyrin **VIII** would be more reactive toward copper(II) acetate as compared to unsubstituted porphyrin **VII**. The negative inductive effect of the two benzene fragments, decreasing the electron density on the NH bonds in porphyrin **VIII**, should also facilitate the reaction. The decreased reactivity of **VIII** compared to **VII** is probably due to the fact that a significant contribution to the transition state energy is made by coordination interaction between the metal cation and the porphyrin nitrogen atoms (Table 2). *meso*-Phenyl substitution decreasing the electron density on the tertiary nitrogen atoms in **VIII** weakens the coordination interaction of the cation of the solvation complex with porphyrin in the transition state. As a result, the reaction rate decreases. The increase in the activation energy and entropy is probably due to a decrease in the solvation of the transition state of the salt–porphyrin system in going from *meso*-unsubstituted porphyrin **VII** to its diphenyl derivative **VIII**.

The reactivity of dimeric porphyrins in complexation with metal ions is mainly determined by the mutual influence of the porphyrin fragments, which depends on the distance between the macroring planes and on their mutual orientation. According to published data [6], in linear porphyrin dimers with one or

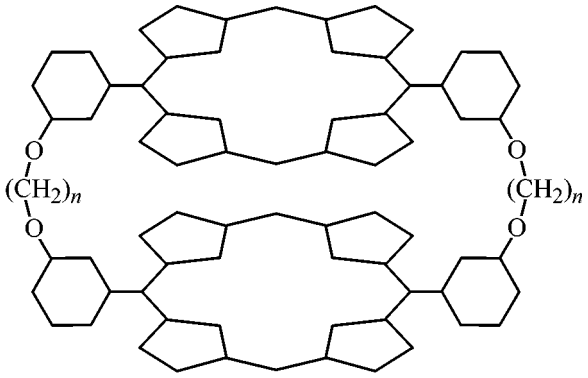
two flexible links the interaction of the macrorings is not manifested. In the sterically strained tetraphenylporphine dimer **X** with the even number of atoms in the bridges the mutual influence of the macrorings is strong. Reaction of **X** with *d*-metal salts successively yields mononuclear and then binuclear complexes, with the coordination of the second metal occurring faster than that of the first metal [6].



X

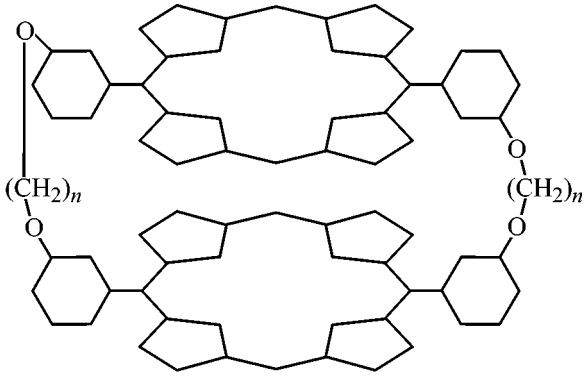
The increased reactivity of dimer **X** as compared to the monomeric analog is explained in [7] by distortion of the tetrapyrrole fragments in the cyclophane structure. In this work we studied dimeric porphyrin **IX** with two ether bridges $O(CH_2)_3O$ in the *meta* positions of the phenyl substituents. The distance between the porphyrin molecules in dimer **IX** is no less than 3.6 Å [8]. This compound exists as an equilibrium mixture of numerous conformers. Passing from one conformer to another is accompanied by insignificant changes in the strain energy.

Hence, in the reaction system there are conformational isomers differing in shape. Furthermore, compound **IX** has atropoisomers differing in the orientation of the bridging ether oxygen atoms. In reaction of any isomer with copper(II) acetate, first the mononuclear complex of the dimeric porphyrin is formed, which then transforms into the binuclear complex. After "freezing" the reaction of atropoisomer **IXc** (with the smallest distance between the macroring planes) with copper(II) acetate at 50% conversion, we separated the resulting mixture by TLC on Silufol plates and obtained three separate spots of the porphyrin fraction, belonging to the initial porphyrin and its mononuclear and binuclear complexes (R_f 0.55, 0.45, and 0.22, respectively; eluent pyridine–hexane, 1 : 4). Despite the presence of three colored species, the spectra of the system porphyrin–$Cu(Ac)_2$ exhibit clear isobestic points (Fig. 1). The electronic absorption



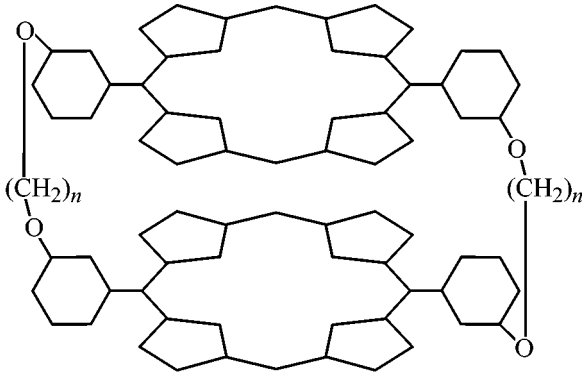
IXa

α,α,α,α atropoisomer



IXb

α,β,α,α atropoisomer



IXc

α,β,α,β atropoisomer

spectrum of the mononuclear copper complex of **IXc** is a superposition of the spectra of the initial porphyrin and its binuclear complex. This is due to the fact that even in the α,β,α,β atropoisomer the distance between the porphyrin fragments is too large for significant mutual influence.

Study of the formation of the binuclear complex from copper(II) acetate and either single atropoisomer

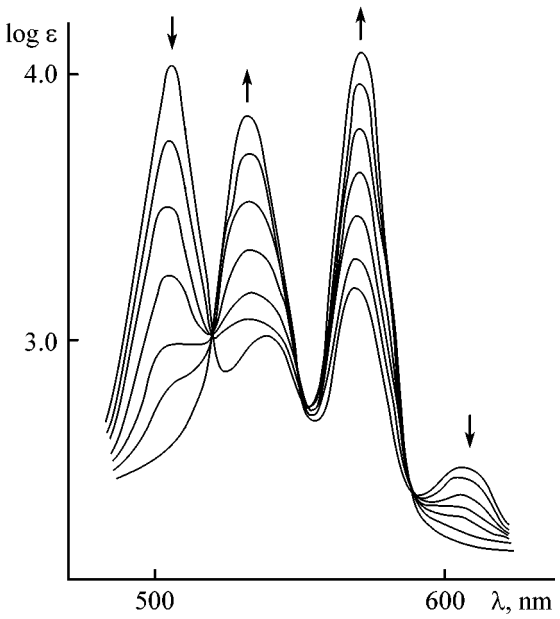
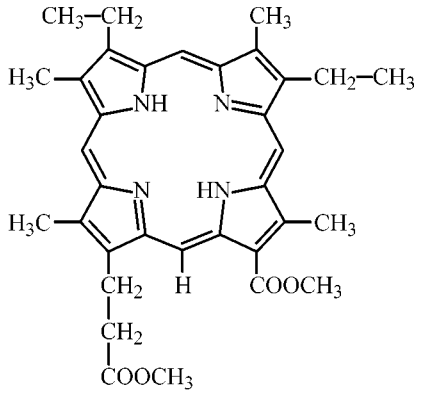


Fig. 1. Variation of the absorption spectra in the course of complexation of α,β,α,β atropoisomer of dimeric porphyrin **IX** with $Cu(Ac)_2$ in acetonitrile at 298 K. Arrows denote the directions of spectrum variation at successive recordings.

Table 3. Base ionization constants of the cationic species of porphyrins in acetonitrile at 298 K [4, 10]

Porphyrin	pK_3	pK_4
Porphine (**XII**)	9.15 ± 0.15	6.2 ± 0.15
Rhodoporphyrin (**XIII**), dimethyl ester[a]	10.22 ± 0.01	5.72 ± 0.01
Pyrroporphyrin (**II**), methyl ester	10.97 ± 0.02	6.76 ± 0.02
Phylloporphyrin (**I**), methyl ester	12.20 ± 0.01	8.86 ± 0.01
Tetraphenylporphine (**XI**)	10.35 ± 0.02	10.40 ± 0.02
Tetraphenylporphine dimer (**X**)	12.65 ± 0.25	13.77 ± 0.27

[a]



or a mixture of three atropoisomers showed that the kinetic parameters of these processes are the same within the determination error (in Table 2 are given the data for the α,β,α,β atropoisomer). Comparison of the rate constants of formation of the binuclear and mononuclear copper complexes from the dimeric ligand shows that the rates of coordination of the first and second cations are practically equal (Table 2). The fact that the mutual influence of the porphyrin fragments is not manifested in the complexation kinetics is probably due to a possible mutual shift of the macrorings.

Comparison of the reactivities of the monomeric (**VIII**) and dimeric (**IX**) porphyrins shows that the cyclophane porphyrin reacts with copper acetate in acetonitrile faster. Despite conformational flexibility of **IX**, the tetrapyrrole macrorings in **IX** are more deformed than in **VIII**. The decrease in the aromaticity of the ring, leading to localization of electrons on the nitrogen atoms of the reaction center, facilitates the coordination interaction metal–nitrogen, and the reaction rate increases (Table 2).

Of considerable interest in discussion of the coordination properties are data on the base ionization of porphyrins. In the absence of specific interactions of the protonated porphyrin species with the solvent and solution components, protonation of the two tertiary nitrogen atoms occurs in two separate stages, with addition of the second proton being naturally more difficult than addition of the first proton. Specific solvation of porphyrin cations and their association with acid anions level out the stepwise protonation to an extent increasing as the donor power of the solvent or nucleophilicity of the anion increase [9].

In the same solvent, protonation of different porphyrin molecules can occur differently. For example, it was shown in [10] that titration of natural porphyrins with perchloric acid in acetonitrile is accompanied by successive formation of the monoprotonated and diprotonated species. Two pronounced steps are seen in the titration curves. With tetraphenylporphine **XI**, the first and second protonation steps are not resolved. The dissociation constants of the cationic forms of these porphyrins, corresponding to equilibria (1) and (2), are listed in Table 3.

$$H_3P^+ \overset{k_3}{\rightleftarrows} H_2P + H^+, \quad (1)$$

$$H_4P^{2+} \overset{k_4}{\rightleftarrows} H_3P^+ + H^+. \quad (2)$$

The increased basicity of tetraphenylporphine as compared to unsubstituted porphine **XII** is explained

in [9] by distortion of the macroring due to *meso* substitution. This effect is particularly pronounced in the sterically distorted cyclophane dimer of tetraphenylporphine **X** with four linking bridges: Distortion of the planar structure of the porphyrin fragments increases the basicity by a factor of ~2500 as compared to the monomeric analog [7].

The base properties of porphyrins **VII**–**IX** were studied by spectrophotometric titration with the potentiometric monitoring of the acidity. Titration was performed with 0.2 M $HClO_4$ in acetonitrile. Under these conditions the acid is fully dissociated [9]. Titration of monomeric porphyrins **VII** and **VIII** reveals successive formation of the mono- and dicationic species. Figure 2 shows as example the titration curves of **VII** (pronounced steps, each characterized by a specific set of isobestic points, are observed). For dimer **IX**, the stepwise protonation is leveled out: The first and second protonation steps are resolved neither in the electronic spectrum not in the titration curves. Although dimeric porphyrin **IX** is a tetraacid base, the cationic species H_8P^{4+}, H_7P^{3+}, H_6P^{2+}, and H_5P^{+}, apparently, cannot be observed separately, and in equilibria (3) $pK_8 = pK_7$ and $pK_6 = pK_5$ (denoted in Table 4 as pK_4 and pK_3, respectively).

$$\begin{aligned} H_8P^{4+} &\overset{pK_8}{\rightleftarrows} H_7P^{3+} + H^+, \\ H_7P^{3+} &\overset{pK_7}{\rightleftarrows} H_6P^{2+} + H^+, \\ H_6P^{2+} &\overset{pK_6}{\rightleftarrows} H_5P^{+} + H^+, \\ H_5P^{+} &\overset{pK_5}{\rightleftarrows} H_4P + H^+. \end{aligned} \qquad (3)$$

This is due to the fact that the porphyrin macrorings of the dimer are separated by a large distance and are protonated simultaneously. Therefore, the acid–base equilibria of the cyclophane dimer of *meso*-diphenylporphyrin **IX** can be described by Eqs. (1) and (2) assuming that they characterize the behavior of one of the fragments. Table 4 shows that in going from *meso*-diphenyl-substituted porphyrin **VIII** to dimer **IX** (with increase in the steric strain in the molecule) the basicity of the porphyrin increases. This is due to the fact that the distortion of the planar structure of the macrorings makes the reaction center more accessible for protonation. Since the protonation of the porphyrin molecule is accompanied by distortion of the macroring, for the monomeric porphyrin this process requires additional energy consumption, whereas in dimer **IX** the porphyrin fragments are

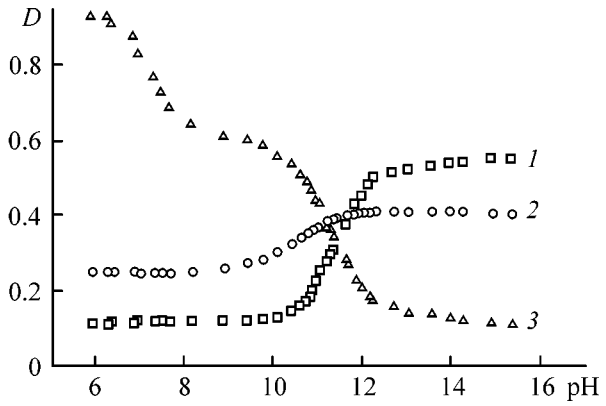


Fig. 2. Titration curves of 3,7,13,17-tetramethyl-2,8,12,18-tetrabutylporphyrin (**VII**) in acetonitrile at 298 K. Analytical wavelength, nm: (*1*) 495, (*2*) 527, and (*3*) 550.

deformed already in the initial state, and protonation is easier.

Comparison of the monomeric porphyrins **VII** and **VIII** shows that *meso*-phenyl substitution decreases the basicity of the porphyrin (Table 4). Apparently, two phenyl groups in the opposite parts of the molecule do not cause significant distortion of the macroring (in contrast to tetraphenylporphine), and the electronic effect of these substituents should be considered.

Our results show that the reactivity of **VII**–**IX** in complexation with copper(II) cation in acetonitrile correlates with their basicity. The decrease in the basicity of the *meso*-phenyl-substituted porphyrin as compared to β-octaalkylporphyrins is accompanied by a decrease in the reactivity of the macroring toward copper(II) acetate in acetonitrile. On the contrary, the increase in the basicity in going from monomer **VIII** to dimer **IX** results in the increased rate constant of formation of metal porphyrins.

EXPERIMENTAL

Porphyrins **VII**–**IX** were prepared according to [5, 8] and purified by column chromatography on alu-

Table 4. Base ionization constants of the cationic species of porphyrins **VII**–**IX** in acetonitrile, 298 K

Comp. no.	*meso* Substituent	pK_3	pK_4
VII	H	11.43 ± 0.06	7.42 ± 0.04
VIII	C_6H_5	10.57 ± 0.02	8.42 ± 0.02
IX	Ar	11.69 ± 0.02	11.62 ± 0.01

mina (eluent benzene–chloroform, 1 : 2) followed by recrystallization from methanol. Cyclophane dimer **IX** was prepared as a mixture of three atropoisomers, which were separated by TLC.

Acetonitrile was purified according to [11]; the water content, as determined by Fischer titration, was 0.01%. Kinetic experiments were performed in quartz cells with ground-glass stoppers at temperatures from 288 to 308 K. The fluctuations of temperature did not exceed ±0.1 K. The concentrations of porphyrins were monitored spectrophotometrically with a Specord M-40 device. Since in acetonitrile the order of the metal porphyrin formation reaction is 1 with respect to the ligand and 0.5 with respect to copper(II) acetate, the true rate constant for **VII**–**IX** was determined from the equation of the order 1.5 [4]. The experimental data are listed in Table 1. The base ionization of porphyrins **VII**–**IX** was studied by spectrophotometric titration with potentiometric monitoring of the solution acidity [9].

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