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Thermodynamic Study of the Interaction Between Some Recently Synthesized Benzo-Substituted Macrocyclic Diamides with Some Pyridinium Ion Derivatives in Acetonitrile Solution

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The formation of pyridinium, 2-methyl pyridinium, 2,4-dimethyl pyridinium and 2,4,6-trimethyl pyridinium complexes with the some recently synthesized benzo-substituted macrocyclic diamides was investigated conductometrically in acetonitrile solution at various temperatures. The formation constants of the resulting 1:1 complexes were determined from the computer fitting of the molar conductance-mole ratio data. In all cases studied, the stability of complexes decreases in the order Py^+ > 2m-Py^+ > 2,4dim-Py^+ > 2,4,6trim-Py^+. The enthalpy and entropy of complexation reaction were determined from the temperature dependence of the formation constants. In all cases, the complexes were enthalpy stabilized but entropy destabilized.

Key words: pyridinum ion derivatives, macrocyclic ligands, complexation, conductance, thermodynamic parameters, acetonitrile

It is well known that amine transport plays an important role in biological systems [1,2]. Amine groups are also constituents of many biologically important compounds, such as amino acids and drugs, whose transport mechanisms across membranes is largely unknown. On the other hand, organic amines are known to block either sodium or potassium ions in nerve channels and, in some cases, this results in the death of the organisms [3,4]. Thus, during the past two decades, considerable attention has been given to the interaction between different protonated amines and macrocyclic ligands, that serve as interesting model compounds for the study of the molecular effect on membrane permeability [5–7]. In the best of our knowledge, there is no report on the thermodynamic data for the complexation of benzo-substituted macrocyclic diamides and pyridinium ion derivatives.

1,13-Diaza-2,3;11,12-dibenzo-4,7,10-trioxacyclononadecane-14,19-dione (L_1), 1,13-diaza-2,3;11,12-dibenzo-4,7,10-trioxacyclopentadecane-14,15-dione (L_2), 1,15-diaza-3,4;12,13-dibenzo-5,8,11-trioxacyclononadecane-2,14-dione (L_3), and 1,15-diaza-3,4;12,13-dibenzo-5,8,11-trioxacyclouneicosanedecane-2,14-dione (L_4) were first synthesized by our research group [8]. We have recently reported the successful use of these macrocyclic diamides as neutral carriers in construction of a stron-

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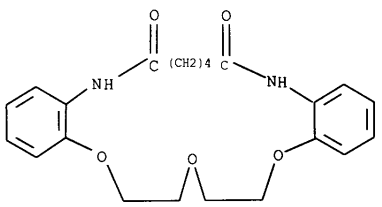
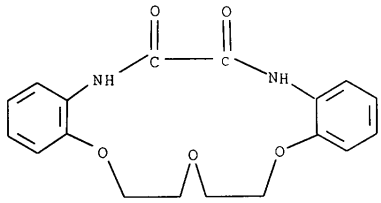
tium-PVC membrane sensor [9] and in polarographic study of mercury complexes in binary acetonitrile–water mixtures [10].

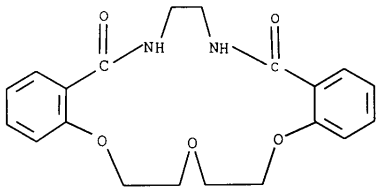
In this paper we report a conductance study of pyridinium ion derivatives and four benzo-substituted macrocyclic diamides (L_1–L_4) in acetonitrile solution at various temperatures, in order to investigate the stoichiometry, stability, selectivity and thermodynamic parameters ΔH^0 and $\Delta\ ^0$ of the resulting complexes in solution.



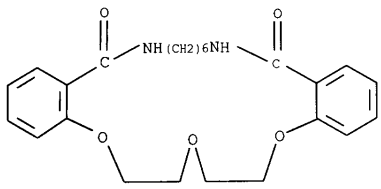
(L_1)



(L_2)



(L_3)



(L_4)

EXPERIMENTAL

All chemicals used were of the highest purity available from Merck. Perchlorate salts of pyridinium, 2-methyl pyridinium, 2,4-dimethyl pyridinium and 2,4,6-trimethyl pyridinium ions were prepared from the 1:1 interaction of perchloric acid with pyridine, 2-methyl pyridine, 2,4-dimethyl pyridine and 2,4,6-trimethyl pyridine, respectively. The resulting perchlorate salts were recrystallized three times from triply distilled deionized water and vacuum dried over P_2O_5 for 72 h. Benzo-substituted macrocylic diamides (L_1–L_4) were purified and dried by the previously reported method [8]. Reagent grade acetonitrile (AN) was purified and dried by the previously described method [11]. The conductivity of solvent was less than 1.0×10^{-7} $s^{-1}cm^{-1}$.

Conductivity measurements were carried out with a Metrohm 660 conductivity meter. A dip-type conductivity cell, made of platinum black, with a cell constant of 0.8310 cm^{-1} was thermostated at the desired temperature ±0.05°C using a phywe immersion thermostat.

In a typical run, 15 cm^3 of a pyridinium perchlorate solution (5.0×10^{-5}mole dm^{-3}) was placed in a water-jacketed cell equipped with a magnetic stirrer and connected to the thermostat circulating water at the desired temperature. In order to keep the electrolyte concentration constant during the titration, both the starting solution and the titrant had the same pyridinium ion concentration. Then, a known amount of the macrocyclic solution was added stepwise. The conductance of the solution was measured after each addition, until the desired ligand-to-cation mole ratio was achieved.

RESULTS AND DISCUSSION

In order to evaluate the influence of various benzo-substituted macrocyclic diamides on the molar conductance of the pyridinium ions used in AN solution, the conductivity at a constant pyridinium salt concentration (5×10^{-5}mol dm^{-3}) was monitored, while increasing the macrocycle diamide concentration at three different temperatures. The resulting molar conductance vs. macrocyclic diamides/cation mole ratio plots are shown in Fig. 1.

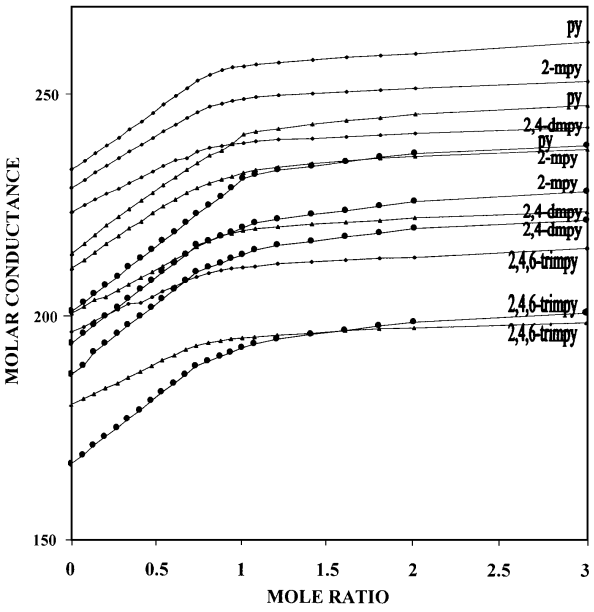


Figure 1. Molar conductance (Ω^{-1}cm^2 mol^{-1}) vs [L_4]/[pyridinium ions] curves in acetonitrile solution at (-●-) 15, (-▲-) 25, (-◆-) 35°C.

As seen from Fig. 1, in most cases, and especially at lower temperature, addition of the macrocyclic diamide to pyridinium ion causes a continuous linear increase in the molar conductance, which begins to level off at mole ratios larger than one, indicating the formation of a relatively stable 1:1 complex. This could be due to the lower mobility of the solvated cation, existance of some ion pairing in the initial salt [12] and/or the release of some high mobility protons into solution brought about upon complexation of the metal ion with the ligand [13]. However, in some cases such as pyridinium ion derivatives and at higher temperature, although the molar conductance does not show any tendency for leveling off, even at mole ratio about 3, the corresponding mole ratio plots show a considerable change in their slopes at a mole ratio of about one, emphasized the formation of some weaker 1:1 complexes in solution. The 1:1 binding of different pyridinium ions (M^+) used with four macrocyclic diamides (L), can be expressed by

$$M^+ + L \underset{}{\overset{K_f}{\rightleftharpoons}} ML^+ \quad (1)$$

The corresponding equilibrium constant, K_f, is

$$K_f = \frac{[ML^+]}{[M^+][L]} \times \frac{f(ML^+)}{f(M^+)\ f(L)} \quad (2)$$

where $[ML^+]$, $[M^+]$, [L] and f represent the equilibrium molar concentration of complexes, free cation, free ligand and the activity coefficient of the species indicated.

For the dilute solution we used the activity coefficient of the unchanged ligand, f(L) can be reasonably assumed as one [14]. The use of Debye-Hückel limiting law of 1:1 electrolytes [15] leads to the conclusion that $f(M^+) \sim f(ML^+)$, so the activity coefficient in (2) cancels out. Thus, the complex formation constant in term of the molar conductance can be expressed as [16]

$$K_f = \frac{[ML^+]}{[M^+][L]} = \frac{(\Lambda_M - \Lambda_{obs})}{(\Lambda_{obs} - \Lambda_{ML})[L]} \quad (3)$$

where

$$[L] = C_L - \frac{C_M(\Lambda_M - \Lambda_{obs})}{(\Lambda_M - \Lambda_{ML})} \quad (4)$$

Here, Λ_M is the molar conductance of the protonated amine before ligand addition, Λ_{ML} the molar conductance of the complexed amine, Λ_{obs} the molar conductance of the solution during titration, C_L the analytical concentration of the macrocycle added, and C_M the analytical concentration of the amine salt. The complex formation constant, K_f, and the molar conductance of complex, Λ_{ML}, were obtained by computer fitting of (3) and (4) to the molar conductance-mole ratio data, using a non-linear least-squares program KINFIT [17]. The assumed 1:1 stoichiometry for the resulting complexes was further supported by the fair agreement between the observed and calculated molar conductances. It should be noted that in acetonitrile as a solvent of intermediate donor number (DN = 14.1) and dielectric constant (ε = 38.0) [18], it was assumed that the association to ion pairs is negligible under the highly dilute experimental conditions used [19]. The macrocyclic diamide concentration in solution was also sufficiently low ($< 1.4 \times 10^{-4}$ mol dm^{-3}) to avoid corrections for viscosity changes [20].

All calculated formation constants are summarized in Table 1. At different total concentrations (in the range 1.0×10^{-4}–1.0×10^{-5} mole dm^{-3}), the K_f values, obtained for a given BSMD-py^+ system, are essentially the same within experimental error; once again supporting the existence of negligible ion-pairing of the pyridiniums perchlorates used in AN solution.

In order to achieve a better understanding of the thermodynamic behavior, it is useful to consider the enthalpic and entropic contributions to the complexation reac-

tions. The ΔH^0 and ΔS^0 values for these reactions were evaluated from the corresponding $\log K_f$ and temperature data by applying a linear least-squares analysis according to

$$2.303 \log K_f = -\frac{\Delta H^0}{RT} + \frac{\Delta S^0}{R}$$

The enthalpies and entropies of complexation were determined in the usual manner from the slopes and intercepts of the plots and the results are summarized in Table 2. It is noteworthy that the validity of ΔS^0 and, especially, ΔH^0 values was checked by using the modified Van't Hoff equation, suggested by Hepler [21], in which the correct calculation of ΔH^0 and ΔC_p^0 and Δ^0 from temperature dependence of equilibrium constants is presented. The ΔG^0 values, calculated from $\Delta G^0 = -RT\ln K_f$ at 20°C are also included in Table 2. The data given in Table 2 have also shown for different macrocyclic diamide-pyridinium ion systems, that there is a linear relationship between $\log K_f$ and 1000/T.

Table 1. Formation constants for different benzo-substituted macrocyclic diamides and pyridinium ion derivatives at various temperatures.

	$\log K_f$			
Temp.(K)	288	293	298	308
L_1				
py	6.25 ± 0.08	6.10 ± 0.04	5.97 ± 0.07	5.72 ± 0.06
2mpy	5.92 ± 0.07	5.82 ± 0.06	5.71 ± 0.06	5.49 ± 0.05
2,4-Dmpy	5.65 ± 0.06	5.55 ± 0.03	5.41 ± 0.06	5.18 ± 0.05
2,4,6-Trimpy	5.20 ± 0.05	5.11 ± 0.04	4.97 ± 0.05	4.76 ± 0.04
L_2				
py	5.16 ± 0.04	5.04 ± 0.05	4.92 ± 0.04	4.70 ± 0.04
2mpy	4.87 ± 0.04	4.73 ± 0.04	4.64 ± 0.03	4.43 ± 0.04
2,4-Dmpy	4.70 ± 0.04	4.61 ± 0.04	4.48 ± 0.04	4.38 ± 0.04
2,4,6-Trimpy	4.50 ± 0.03	4.41 ± 0.02	4.30 ± 0.03	4.12 ± 0.03
L_3				
py	5.59 ± 0.05	5.44 ± 0.04	5.33 ± 0.05	5.09 ± 0.05
2mpy	5.24 ± 0.04	5.09 ± 0.05	4.99 ± 0.04	4.76 ± 0.05
2,4-Dmpy	5.08 ± 0.04	4.94 ± 0.03	4.83 ± 0.04	4.63 ± 0.04
2,4,6-Trimpy	4.88 ± 0.03	4.74 ± 0.03	4.66 ± 0.03	4.45 ± 0.03
L_4				
py	6.54 ± 0.08	6.25 ± 0.06	6.17 ± 0.07	5.91 ± 0.07
2mpy	6.09 ± 0.07	5.92 ± 0.04	5.82 ± 0.07	5.57 ± 0.06
2,4-Dmpy	5.79 ± 0.06	5.63 ± 0.06	5.54 ± 0.05	5.31 ± 0.05
2,4,6-Trimpy	5.34 ± 0.06	5.19 ± 0.03	5.1 ± 0.05	4.88 ± 0.04

Table 2. Thermodynamic parameters ΔH^0, ΔS^0 and ΔG^0 for different benzo-substituted macrocyclic diamides-pyridinium ions complexes in acetonitrile solution.

ligands	py			2-mpy		
	$-\Delta H^0$(KJ/Mol)	$-\Delta S^0$(J/Mol)	$-\Delta G^0$(KJ/Mol) (from K_f at 20°C)	$-\Delta H^0$(KJ/Mol)	$-\Delta S^0$(KJ/Mol)	$-\Delta G^0$(KJ/Mol) (from K_f at 20°C)
L_1	10.83 ± 0.05	8.79 ± 0.03	33.99 ± 0.07	10.01 ± 0.02	8.40 ± 0.03	32.52 ± 0.06
L_2	9.71 ± 0.03	8.21 ± 0.04	28.02 ± 0.05	8.77 ± 0.02	8.17 ± 0.02	26.42 ± 0.05
L_3	10.21 ± 0.02	8.37 ± 0.03	30.35 ± 0.05	9.80 ± 0.04	8.21 ± 0.03	28.42 ± 0.05
L_4	11.02 ± 0.04	8.91 ± 0.04	35.14 ± 0.06	10.64 ± 0.04	8.6 ± 0.02	33.14 ± 0.05
	2,4-Dmpy			2,4,6-Trimpy		
	$-\Delta H^0$(KJ/Mol)	$-\Delta S^0$(J/Mol)	$-\Delta G^0$(KJ/Mol) (from K_f at 20°C)	$-\Delta H^0$(KJ/Mol)	$-\Delta S^0$(J/Mol)	$-\Delta G^0$(KJ/Mol) (from K_f at 20°C)
L_1	9.59 ± 0.04	7.40 ± 0.03	30.81 ± 0.07	8.99 ± 0.02	7.36 ± 0.04	28.30 ± 0.06
L_2	8.33 ± 0.03	7.29 ± 0.04	25.51 ± 0.04	7.83 ± 0.03	7.25 ± 0.05	24.48 ± 0.05
L_3	9.21 ± 0.02	7.35 ± 0.03	27.50 ± 0.05	8.74 ± 0.03	7.30 ± 0.02	26.54 ± 0.05
L_4	9.81 ± 0.03	7.49 ± 0.03	30.24 ± 0.05	9.38 ± 0.04	7.45 ± 0.03	27.79 ± 0.04

The data given in Table 1 clearly indicate, that in the case of all pyridinium ion derivatives used, the stability of the resulting 1:1 complexes decreases in the order $L_4 > L_1 > L_3 > L_2$ and selectivity pyridine can be summarized as follow $Py^+ > 2m\text{-}Py^+ > 2,4dim\text{-}Py^+ > 2,4,6trim\text{-}Py^+$.

The pyridinium ion is a planar cation, in which the positive charge is mainly localized on the -NH group [22]. Molecular model shows that this cation can partially penetrate inside the cavity of macrocyclic diamides, so that the positive nitrogen atom can presumably interact with all donating atoms of the ring. Thus, there are at least three factors, which can significantly contribute to the stability of the protonated pyridinium complexes with macrocyclic diamide ligands: (1) steric hindrance of guest groups; (2) electronic withdrawing or donating effects of guest groups and (3) the size and conformation of the ligand.

The steric bulk will be a hindrance to the host-guest complexation only in as much as it is allowed to interfere directly with the site of complexation. Consequently, the substitution of the methyl group in ortho positions of pyridinium ion is expected to largely influence the stability of the resulting macrocyclic diamide complexes. As it is seen from the observed stability sequence, increasing the number of methyl groups in the ortho position results in a loss of complex stability, while the resulting complexes do not seem to demonstrate a high degree of sensitivity to the electronic effect. A similar conclusion has been reached before [7].

As it is seen from structure of ligands, the total number of ring atoms in the macrocyclic diamide used is 15 (for ligand L_2), 17 (for ligand L_3), 19 (for ligand L_1) and 21 (for ligand L_4). The pyridinium ion derivatives with the large ionic radius pen-

etrate inside the cavity of ligands in the order 21 > 19 > 17 > 15. Comparison of the data given in Table 2 shows the variations of stability of the resulting complexes in the order $L_4(21) > L_1(19) > L_3(17) > L_2(15)$. The thermodynamic data given in Table 2 show that, in all cases, the complexes are enthalpy stabilized but entropy destabilized. It should be noted that a similar behavior was previously observed in non-aqueous solvents [23,24]. It has been reasonably assumed that the decrease in entropy upon complexation is related to a change in the conformational entropy of the macrocyclic diamides, from a rather flexible structure in the free state to a rigid conformation in the complexed form. The degree of macrocyclic diamide flexibility in the free state would vary with its size as well as the macrocycle, diamide-solvent interaction [25,26].

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