Chromo-ionophoric Properties of *para*-(5-phthalhydrazide-azo)-phenylene-*N*-aza-15-crown-5 in the Presence of Lithium and Sodium Ions

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*Investigations on the hydrophobic and ionophoric character of para-(5-phthalhydrazide-azo)-phenylene-N-aza-15-crown- (**1**) were carried out by reversed phase thin layer chromatography (RP-TLC) and spectrophotometric measurements. The study included complexes with Li⁺ and Na⁺ cations (as perchlorates in acetonitrile and as dibenzyldithiocarbamate salts in chloroform). In both cases, the stoichiometry of complexes was 1:1:1 (**1**:M⁺:anion pair). The complex stability (logK$_S$) is similar.*

Keywords: N-Phenylaza-15-crown-5 derivative with a Luminol moiety, hydrophobic/hydrophilic balance, RP-TLC, Li⁺ and Na⁺ complexes, UV-Vis, stability constants

In a previous paper, the synthesis and spectral properties (NMR, UV-Vis) of *para*-(5-phthalhydrazide-azo)-phenylene-*N*-aza-15-crown-5 (**1**) (scheme 1), obtained from N-phenylaza-15-crown-5 (**2**), and Luminol or 5-amino-2,3-dihydro-1,4-phthalazine-dione (**3**), were reported [1].

As an azo dyestuff, compound **1** has a red-brick color in crystalline state and in solutions. Compound **1** has the following properties [1]: (i) positive solvatochromy in electronic absorption spectra depending on the solvent polarity [2], (ii) in acidic medium a significant bathochromic shift (23 nm) in the visible spectrum is due to the formation of tautomeric cations **1a** or **1b**; the ¹H-NMR spectrum in TFA at different temperatures agreed with a positively charged nitrogen from the macrocycle (this was a reversible process proved by adding a base); (iii) in alkaline medium, a significant hypsochromic shift (85 nm) occurred in visible range, the anionic species **1c** and **1d** (scheme 1) depending on the aqueous (**1c**) and nonaqueous (**1d**) medium, respectively, as in the case of compound **3** [3-5]. The well-known ionophoric properties [6, 7] of N-phenylaza-15-crown-5 (**2**) for alkali metals suggest similar properties for compound **1** which have not been investigated so far. The present paper reports the hydrophobic/hydrophilic properties of compound **1** and its ionophoric character towards Li⁺ and Na⁺ alkali cations under the form of perchlorates in acetonitrile, and dibenzyldithiocarbamates in chloroform.

Experimental part
Reagents and Apparatus

The following compounds were employed throughout the experiments: compound **1** obtained by synthesis [1], compounds **2** and **3** purchased from Merck, LiClO$_4$ (Pierce Erochimie B. V), NaClO$_4$·H$_2$O (Aldrich), (C$_6$H$_5$CH$_2$)$_2$NC(S)

SLi, (C$_6$H$_5$CH$_2$)$_2$NC(S)SNa, obtained by synthesis according to literature data [8, 9]. Silica gel glass plates RP-18 F$_{254S}$ (for RP-TLC) were from Merck. UV-Vis spectra were recorded using a UV-Vis Analytik Jena SPECORD 200.

The hydrophobicity of compounds **1**–**3** was studied by RP-TLC under the conditions specified in table 1. Unlike Luminol (**3**), compound **1** presents low fluorescence. The results of studies about the possible chemiluminiscence due to the Luminol moiety (**3**) will be reported in a separate communication.

Procedure
The complexing property of compound **1** was investigated at room temperature (298 K) in the following two situations:

(i) Perchlorate complexes [L...M]⁺ClO$_4$⁻ (L= **1**, M= Li⁺ or Na⁺). In an aliquot part of compound **1** in acetonitrile (0.5 . 10⁻⁵M), the alkali (Li⁺ or Na⁺) perchlorate was added gradually in order to obtain various concentrations. The spectrum in the visible range was recorded after total solvation. The absorbance values were used to compute the complexing ratio using both Job's method [10-12] and Benesi-Hildebrand's method [13], based on eq. 3.(five determinations). The complex stability (*logK$_S$*) was estimated graphically by means of Benesi-Hildebrand's method [13] (3) for five determinations and presented in Table 2.

(ii) Dibenzyldithiocarbamate complexes [L...M]⁺ (PhCH$_2$)$_2$N–CS–S⁻ (*L*= **1**, M= *Li⁺* or *Na⁺*). The complexing ratio and the complex stability (*logK$_S$*) for this type was investigated employing a similar strategy as above, starting from the aliquot part of stock solution of compound **1** (1.84 . 10⁻⁵M) in chloroform using various concentrations of dibenzyldithiocarbamate salts. The values of *logK$_S$* are shown in table 2.

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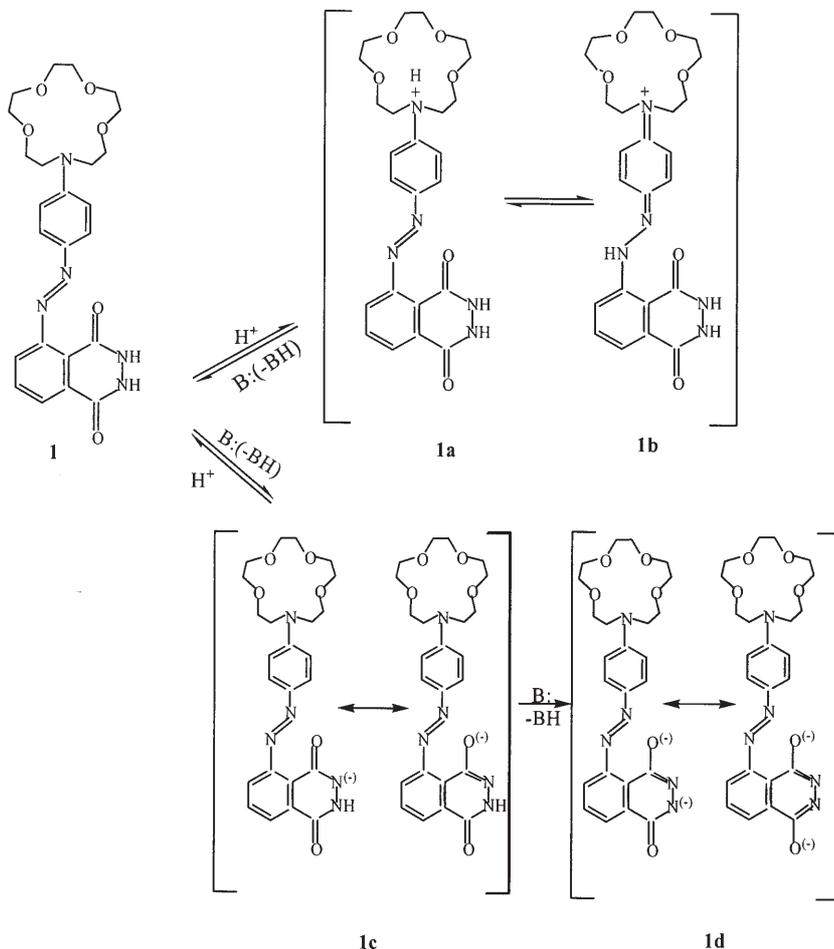
Results and Discussion

Hydrophobic/hydrophilic property of compound **1**

The hydrophobic/hydrophilic balance of a chemical species is an important property in applications, including biomedical ones. The partition coefficient in the octanol-water (*logP*) is a common parameter used in evaluating this property [14, 15]. In the case of compound **1**, the hydrophobic/hydrophilic character with respect to the medium is conditioned by the moieties forming the molecular structural assembly, that is, N-phenylaza-15-crown-5 (**2**), and Luminol (**3**), whose amino group was converted into the azo linkage by diazotization and coupling with **2**. In order to delineate the contribution of each moiety to this property, comparative investigations were carried out including compounds **2** and **3**, the starting materials for the synthesis of **1** [1]. Reversed phase thin-layer chromatography (RP-TLC) [16-18] was employed in this respect with the stationary silica gel phase having a chemically bonded hydrophobic moiety (C_{18}) and with mixtures of ethanol-water in various proportions as mobile phases (table 1).
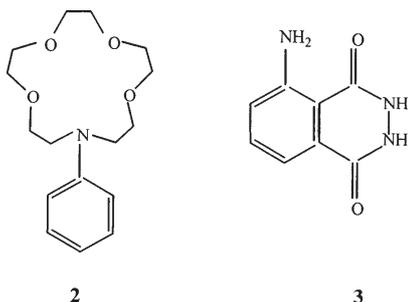
In table 1 we present the experimental results concerning the molecular hydrophobicity R_{M0} calculated from experimental chromatographic data (RP-TLC) by eqs. 1 and 2 [16-18]. Statistical analysis [19-20] involved the correlation coefficient (R), the Fisher parameter (F), and the standard deviation (SD):

$$R_M = \log(1/R_f - 1) \qquad (1)$$

$$R_M = R_{M0} + b\mathrm{K} \qquad (2)$$

The comparative experimental results on the molecular hydrophobicity R_{M0} of compounds **1**–**3** obtained from experimental data lead to the following conclusions: (i) the molecular hydrophobicity decreases in the sequence $R_{M0}\mathbf{2} > R_{M0}\mathbf{1} > R_{M0}\mathbf{3}$, meaning that the hydrophilic character increases in the reverse order; (ii) the hydrophobic character of compound **1** is decreased by attaching moiety **3** to moiety **2**, which also offers a certain hydrophilic character to compound **1**; and (iii) the accuracy of experimental results is validated by means of statistical parameter values R, F, and SD.

As expected, the experimental values of molecular hydrophobicity (R_{M0}) are fairly well correlated (R^2=0.858) with the computed hydrophobicity values (*logP*) through the fragmental method [14].

Thus compound **1** exhibits hydrophobic characteristics, solvating preferentially in non-aqueous media. However, an acidic or alkaline medium leads to solubility in aqueous media due to charged chemical species as presented in scheme 1.

*Complexing property of compound **1** towards alkali metal ions*

It is well known that compound **2** can complex alkali metal ions [6, 7], so that one may extrapolate that

Comp.	Experimental									Calcd. logP
	R_f in aqueous ethanol, conc.(v/v)				R_{M0}	b	Statistical parameters			
	A	B	C	D			R	F	SD	
1	0.812	0.718	0.468	0.457	1.453	-0.025	-0.953	19.89	0.129	1.54
2	0.625	0.371	0.375	0.243	1.567	-0.021	-0.930	12.95	0.132	0.96
3	0.875	0.857	0.837	0.812	-0.288	-0.006	-0.999	2980	0.002	-0.46

[a] Five determinations on silica gel RP-18F$_{254}$ (Merck), with percent of ethanol in mixture ethanol-water: A = 80%, B = 70%, C = 60%, D = 50%; R_{M0} = molecular hydrophobicity (eq. 2); b = change in R_M value caused by increasing the concentration (K) of the organic component in the mobile phase (eq. 1); R= correlation coefficient for parameters R_{M0} and b by eq. 2 [16-18].

compound **1** will show similar properties. Since compound **1** exhibits predominantly hydrophobic properties, its ability to form complexes with alkali metal ions was studied by visible spectral measurements employing alkali perchlorates in acetonitrile and alkali dibenzyldithiocarbamates in chloroform.

The visible spectrum (λ_{max} = 507 nm) of compound **1** in acetonitrile in the presence of perchlorates of Li$^+$ and Na$^+$ displayed hipsochromic shifts (λ_{max} = 502 nm for Li$^+$, and λ_{max} = 500 nm for Na$^+$), and slight hypochromic intensity lowering; the isosbestic points (483 nm for Li$^+$ and 486 nm for Na$^+$) validate the complexing process (scheme 2, A= ClO$_4^-$), similarly to other synthesized ligands with the same macrocyclic moiety [21].
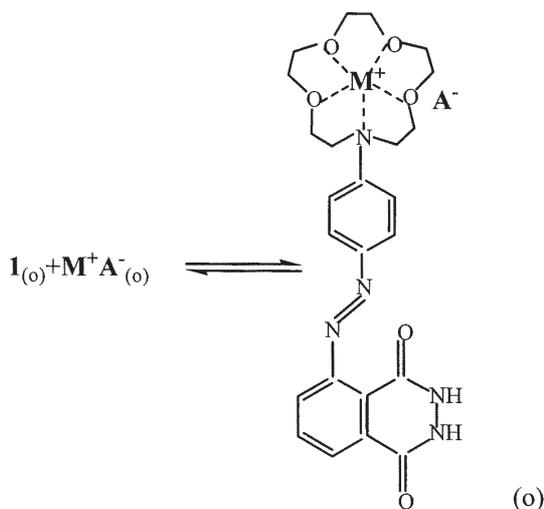
Scheme 2. Complex formation in organic solvents (o) of **1** with soluble salts **M$^+$A$^-$** where **M**= Li$^+$, Na$^+$, and **A**= ClO$_4^-$, (PhCH$_2$)$_2$N-CS-S$^-$

By applying Job's [10-12] and Benesi–Hildebrand's [13] methods (eq. 3), the complexing ratio 1:1:1 was established for Li$^+$ and Na$^+$ corresponding to supramolecular complexes of type [L...M]$^+$ClO$_4^-$ (where L= compound **1**, M= Li$^+$ or Na$^+$). The complexing ratio 1:1 (**1**: salt) of Li$^+$ ion with compound **1** is supported by the linear dependence of 1/[M$^+$] *versus* 1/(A$_0$-A') (fig. 1).

$$\frac{1}{A_0 - A} = \frac{1}{A_0 - A'}\left[\frac{1}{K_S\left[M^+\right]}+1\right] \qquad (3)$$

where:
A$_0$= initial absorbance of the ligand;
A= observed absorbance after adding the salt;
A'= absorbance of the complex,
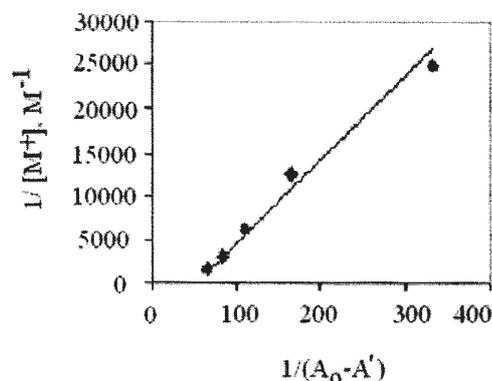
K_S= stability constant;
[M$^+$]= salt concentration.

Fig. 1. Plot of 1/[M$^+$] *versus* 1/(A$_0$-A') in acetonitrile

Table 2 contains the values of $logK_S$ for the complexes. The values show a higher stability for the Na$^+$ complex with compound **1**, which is in good agreement with data reported by literature [6], regarding the fitting between the ionic diameter and the macrocyclic cavity size (1.2-1.5Å of N-phenylaza-15-crown-5 (**2**) [6] (table 2). In the case of potassium perchlorate with larger ionic diameter for K$^+$, our investigations revealed no stable complex formation.

Continuing our study, the complex formation of compound **1** with the same alkali metal cations was investigated in chloroform by using alkali dibenzyl-dithiocarbamate salts (Li$^+$A$^-$ and Na$^+$A$^-$, A= (PhCH$_2$)$_2$N-CS-S$^-$) soluble in this solvent. Similarly to the case of acetonitrile as solvent, the spectrum of compound **1** in chloroform (λ_{max} = 505nm) displayed hipsochromic shifts in the presence of alkali dibenzyldithiocarbamate (λ_{max} = 501 nm for Li$^+$ and λ_{max} = 492 nm for Na$^+$), whereas the isosbestic points (436 nm for Li$^+$ and 437 nm for Na$^+$) validated the complexing process (fig. 2) through the mechanism presented in scheme 2. Likewise, by applying Job's [10-12] and Benesi–Hildebrand's [13] methods (3), the same complexing ratio 1:1:1 was established. The values of stability constants ($logK_S$) for the complexes were also determined graphically (table 2).

Comparatively, the values of $logK_S$ for complexes [L...M]$^+$(PhCH$_2$)$_2$N-CS-S$^-$ (L= **1**, M= Li$^+$, Na$^+$) in chloroform were relatively close to those determined for complexes [L...M]$^+$ClO$_4^-$ (L= **1**, M= Li$^+$ or Na$^+$) in acetonitrile following the same sequence of complex stability ($logK_S$Na$^+$>$logK_S$Li$^+$) correlated with the match between the ion metalic diameter (table 2) and the macrocyclic cavity size (1.2-1.5 Å) of type N-phenylaza-15-crown-5 (**2**) [6]. However, one can observe a larger
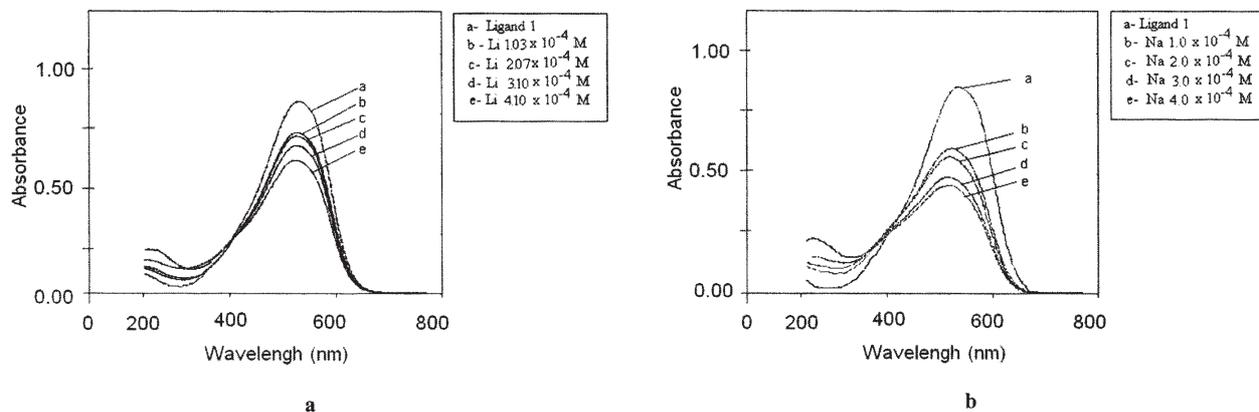
a

b

Fig. 2. Absorption spectra of compound **1** (1.84 . 10^{-5} M) in CHCl$_3$ in the presence of various concentrations of Li$^+$ (**a**) and Na$^+$ dibenzyldithiocarbamates (**b**)

Table 2

STABILITY CONSTANTS ($logK_S$) OF [L...M]$^+$A$^-$ COMPLEXES WHERE
L=**1**, M=Li$^+$ OR Na$^+$, A=CLO$_4^-$ OR A=(PHCH$_2$)$_2$N-CS-S-

M$^+$	Ionic diameter of the metal cation(Å)[10]	$logK_S$[a]	
		[L...M]$^+$ClO$_4^-$ (in CH$_3$CN)	[L...M]$^+$(PhCH$_2$)$_2$N–CS–S$^-$ (in CHCl$_3$)
Li$^+$	1.36	3.79±0.02	3.38 ± 0.01
Na$^+$	1.94	3.82±0.03	3.88 ± 0.03

[a] Five measurements

difference between $logK_S$ values in the two solvents for the Li$^+$ than for Na$^+$ salts with the two different anions.

Conclusions

The relative hydrophobic character of *para*-(5-phthalhydrazide-azo)-phenylene-*N*-aza-15-crown-5 (**1**) was measured by means of RP-TLC. The spectrophotometric investigation evidenced the ionophoric character of compound **1** due to the aza-15-crown-5 moiety, which formed complexes in acetonitrile and chloroform with perchlorate and dibenzyldithiocarbamate of Li$^+$ and Na$^+$ salts, respectively. In both cases, the stoichiometry of complexes was 1:1:1, namely [L...M]$^+$ClO$_4^-$ in acetonitrile (L= **1**, M= Li$^+$ or Na$^+$), and [L...M]$^+$ (PhCH$_2$)$_2$N–CS–S$^-$ in chloroform (L= **1**, M= Li$^+$ or Na$^+$), respectively. The stability constants of the complexes $logK_S$ were relatively close irrespective of the solvent following the sequence $logK_S$Na$^+$>$logK_S$Li$^+$, in agreement with the diameter complementarity between the cation and the intramolecular cavity of N-phenylaza-15-crown-5 (**2**).

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