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Spectroscopic Study of the Complexation of an Aza-15-Crown-5 Containing Chromofluoroionophore with Ba^{2+} and Ca^{2+} Cations

Dedicated to Prof. Dr. Karl-Heinz Drexhage on the occasion of his 60th birthday

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Abstract. The complexation of 1-[(4-benzothiazolyl)phenyl]-4,7,10,13-tetraoxa-1-aza-cyclopentadecane with Ba^{2+} and Ca^{2+} cations was investigated spectrophotometrically and spectrofluorometrically. The stability constants of the complexes formed are: for Ba^{2+} $\log K_{st} = 3.17 \pm 0.01$ (absorption) and $\log K_{st} = 2.95 \pm 0.03$ (fluorescence); for Ca^{2+} $\log K_{st} = 3.71 \pm 0.02$ (absorption) and $\log K_{st} = 3.58 \pm 0.05$ (fluorescence). Protonation of the ligand leads to fluorescence quenching. AM1 and PPP quantum chemical calculations were used to predict molecular geometry, proton affinities and the spectra of the compounds studied.

Key words: Aza-15-crown-5, chromoionophore, fluoroionophore, complex formation, alkali and alkaline earth metal ions.

1. Introduction

Chromophores and fluoroionophores containing macrocycles are often useful reagents for metal ion recognition, based on the changes in their photophysical properties upon complex formation [1, 2]. Such compounds, when able to complex with different substrates, could also serve as recognition sites in enzyme mimicking reactions [3, 4].

The changes in the absorption and emission properties depend on the reagent, the charge density of the ions and the cavity size as well as on the reaction medium [1, 5–8].

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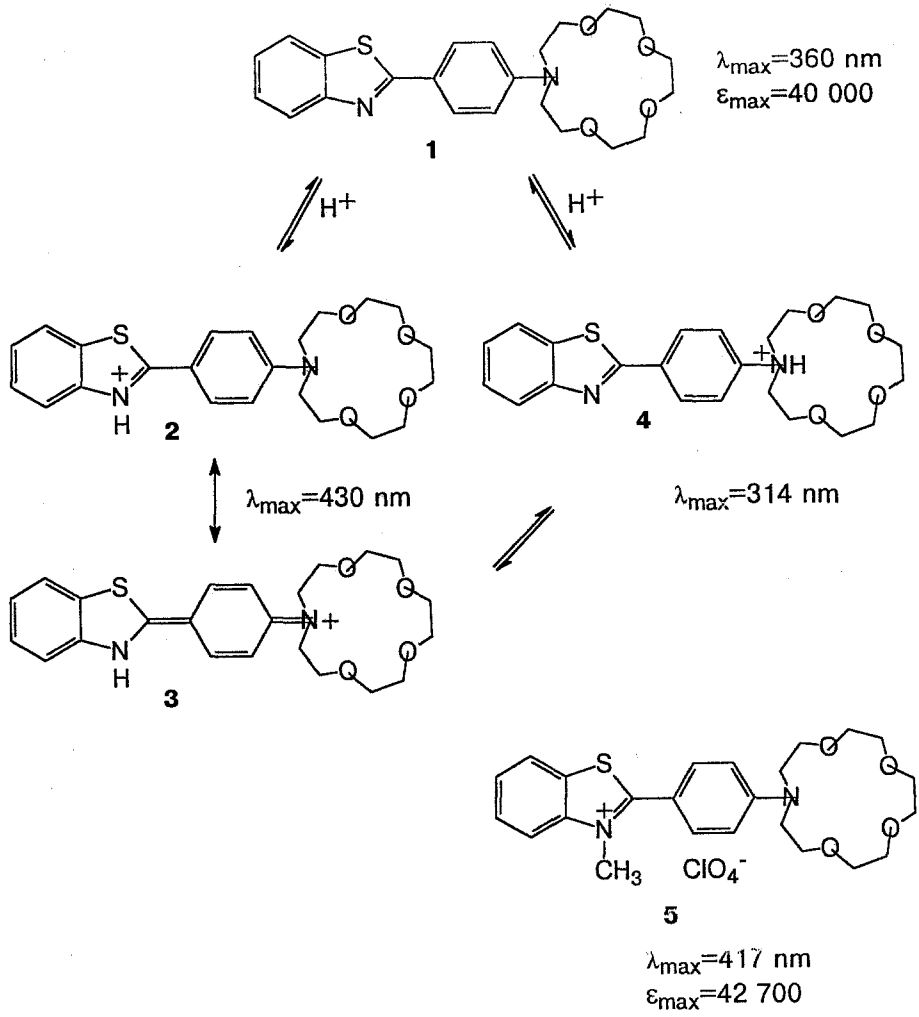

Fig. 1. Structural formulae of the neutral ligand **1**, protonated forms **3** and **4**, and quaternized compound **5**.

The aza-15-crown-5 cavity is known mainly as a complex-forming agent for alkali and alkaline earth metal ions as well as for H^+, NH_4^+ and Ag^+ [9, 10]. Several interesting reagents were obtained combining this macrocycle with some chromophores and fluorophores, and these could be used for analytical purposes [4–12].

We recently reported the synthesis of a new chromofluoroionophore **1** (Figure 1) and related compounds and their interaction with some metal ions [13]. It was shown that, among the metal ions tested, the strongest influence on the photophysical properties of **1** and **5** (Figure 1) were caused by Ba^{2+} and Ca^{2+} cations.

The present paper deals with the investigation of complex formation between Ba^{2+} and Ca^{2+} ions and compound **1**. Complexation stability constants have been calculated both spectrophotometrically and spectrofluorometrically.

2. Experimental

2.1. Materials and Methods

The ligands were synthesized as already described [13].

Acetonitrile (Uvasol) was dried by boiling with CaH_2 and was distilled before use. $Ca(ClO_4)_2$ and $Ba(ClO_4)_2$ were synthesized by using CaO and BaO, respectively and $HClO_4$, all purchased from Merck. The purity of the salts was demonstrated by gravimetric determination of Ba^{2+} and Ca^{2+} (>99%).

The solutions were used immediately after preparation, although no changes were observed on standing in daylight at room temperature. The absorption spectra were recorded after addition of different amounts of 0.01 M stock solutions of $Ca(ClO_4)_2$ and $Ba(ClO_4)_2$, respectively, to the solution of the ligand with a constant concentration of 2.42×10^{-5} M. In order to avoid extraneous salt effects the same quantity was added in the reference cell.

For the fluorimetric determinations, a ligand concentration of 4.48×10^{-6} M was chosen, at which no self quenching was observed. No peculiar salt effects were observed at the salt concentrations used. For quantum yield determination, quinine bisulfate in 1 M H_2SO_4 was chosen as a standard, for which a quantum yield of 0.546 has been reported in the literature [31].

For the spectrophotometrical determination of the stability constants, the standard procedure for a two-component mixture analysis was used [14]. A similar approach was used for the fluorimetrical calculations, which is well described in [7].

2.2. Calculations

The semiempirical quantum-chemical AM1 (Austin model 1) method [15] was chosen to study the structure of 1-[(4-benzothiazolyl)phenyl]-4,7,10,13-tetraoxa-1-aza-cyclopentadecane, **1** (Figure 1). The reliability of this method for the treatment of the structure of the similar compound 2(2′-hydroxyphenyl)benzothiazole has already been shown [16]. AM1 calculations were carried out with the MOPAC 6.0 program package [17]. The sulfur atom AM1 parameters reported by Dewar and Yuan [18] were used. The geometries of the neutral molecule **1**, the protonated forms **3** and **4**, and the quaternized compound **5** were completely optimized without any geometrical restrictions using the EF (eigenvector following) routine [19] and the keyword PRECISE. For the AM1 calculations, the molecular mechanics optimized geometry of **1** was used as the starting structure.

Molecular orbital calculations have also been performed in the π-electron approximation introduced by Pariser, Parr and Pople [20–22] (PPP method) tak-

ing account of all singly excited configurations. We used a set of parameters developed by Griffiths [23]. Only the PPP parameters for the sulfur atom were introduced by us and they are as follows: IP = 39.00 eV, $\gamma_{\mu\mu}$ = 18.50 eV and β_{c-s} = 1.67 eV. The two-center electron repulsion integrals were estimated using the Mataga–Nishimoto approximation [24, 25]. The PPP calculations were performed for the 2(4′-dimethylaminophenyl)benzothiazole fragment of the molecule **1** as well as for its protonated forms **3** and **4**. For the protonated form **3** the values IP = 18.00 and $\gamma_{\mu\mu}$ = 14.00 eV for N1 were used.

The quantity proton affinity (PA) is determined as an enthalpy of reaction for tearing off a proton in the gas phase $BH^+ \rightarrow B + H^+$ and is determined according to the formula

$$PA = \Delta H_f(B) + \Delta H_f(H^+) - \Delta H_f(BH^+)$$

The values $\Delta H_f(B)$ and $\Delta H_f(BH^+)$ are calculated by the AM1 method and the experimental values 365.7 kcal/mol (1530 kJ/mol) [26] is used for $\Delta H_f(H^+)$. It has already been shown that AM1 predicts proton affinities quite satisfactorily [27, 28].

2.3. Physical Measurements

The absorption and emission spectra were recorded on Perkin Elmer Lambda 17 and Perkin Elmer LS-5 Luminescence spectrometers, respectively.

3. Results and Discussion

The presence of a donor (amino group) and acceptor (heterocyclic nitrogen of the benzothiazole moiety) part in molecule **1** (Figure 1) leads to an intramolecular charge transfer (CT) which results in a long-wavelength, structureless absorption band at 360 nm. Figure 2 shows very good agreement between the experimental absorption curves and the corresponding calculated PPP spectra. These findings support the adequacy of our semiempirical approach. Compound **1** is highly solvatochromic (λ_{max} in CCl_4 328 nm, λ_{max} in CH_3CN 360 nm). Quaternization at the benzothiazole nitrogen atom enhances its acceptor ability so that the CT band in the absorption spectrum of **5** is red-shifted (λ_{max} 417 nm). Complex formation via the aza-15-crown-5 moiety affects the free electron pair of the amino nitrogen, thus reducing its donor character and destabilizing the first excited state, as already reported for other compounds [1, 8]. As a result, the absorption spectra of the metal ion complexes with ligands **1** and **5** are hypsochromically shifted and their molar absorption is significantly reduced. This effect is stronger with ligand **1**, whereas ligand **5** is only slightly affected. The influence on the charge transition depends on the ion's charge density and the fit into the crown ether ring, as well as on the reaction medium. The most significant changes were observed in the presence of

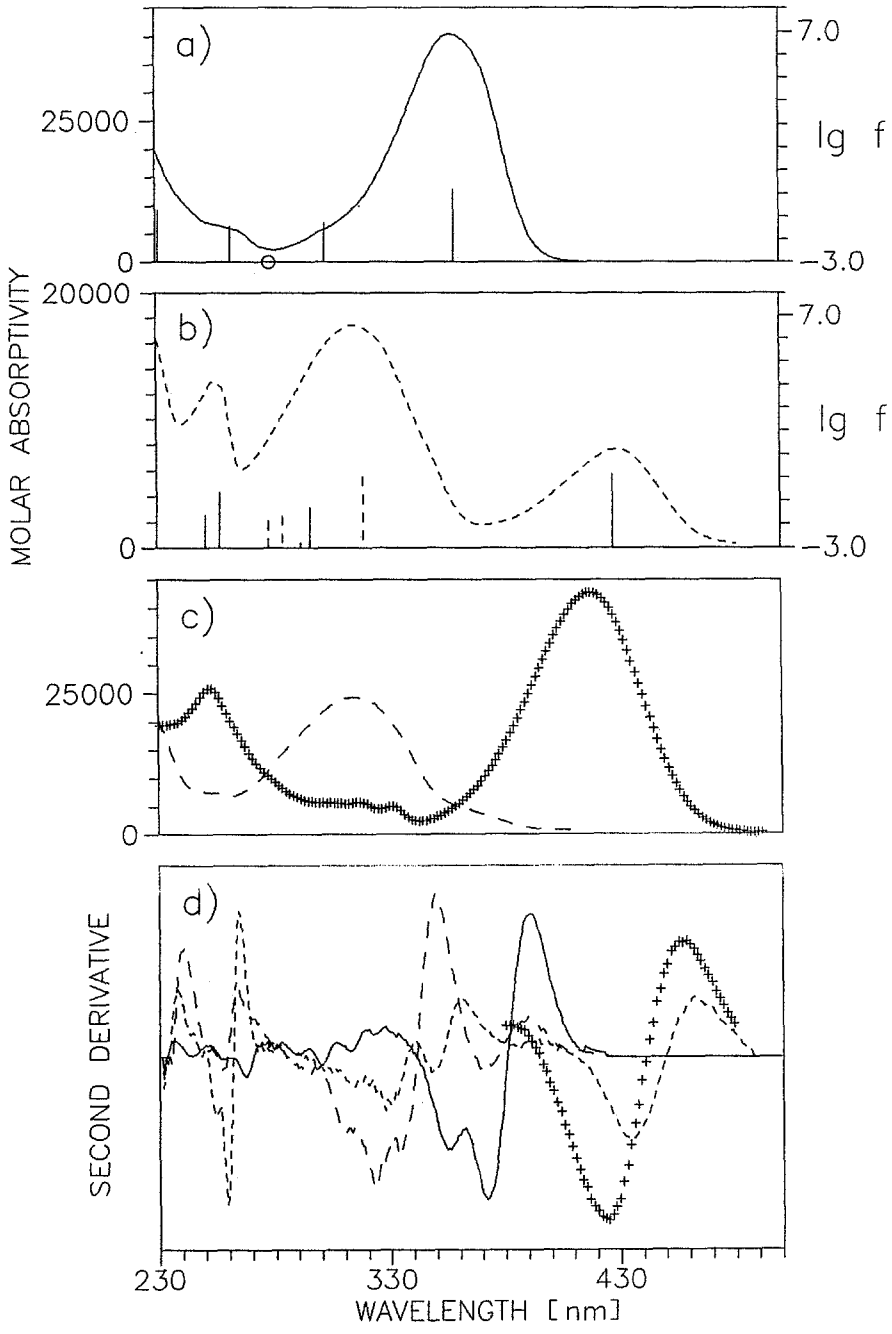

Fig. 2. (a) Absorption spectrum of **1** compared with the PPP calculated spectrum. (b) Absorption spectra of **3** and **4** compared with the PPP calculated spectra (dashed lines for **3** and solid lines for **4**). (c) Absorption spectra of complex **1** with Ca^{2+} (- - - - -) and quaternized **5** (+ + +). (d) Second derivatives of the spectra from a, b and c. The computed transitions are marked by lines; the circle marks log $f < -3$.

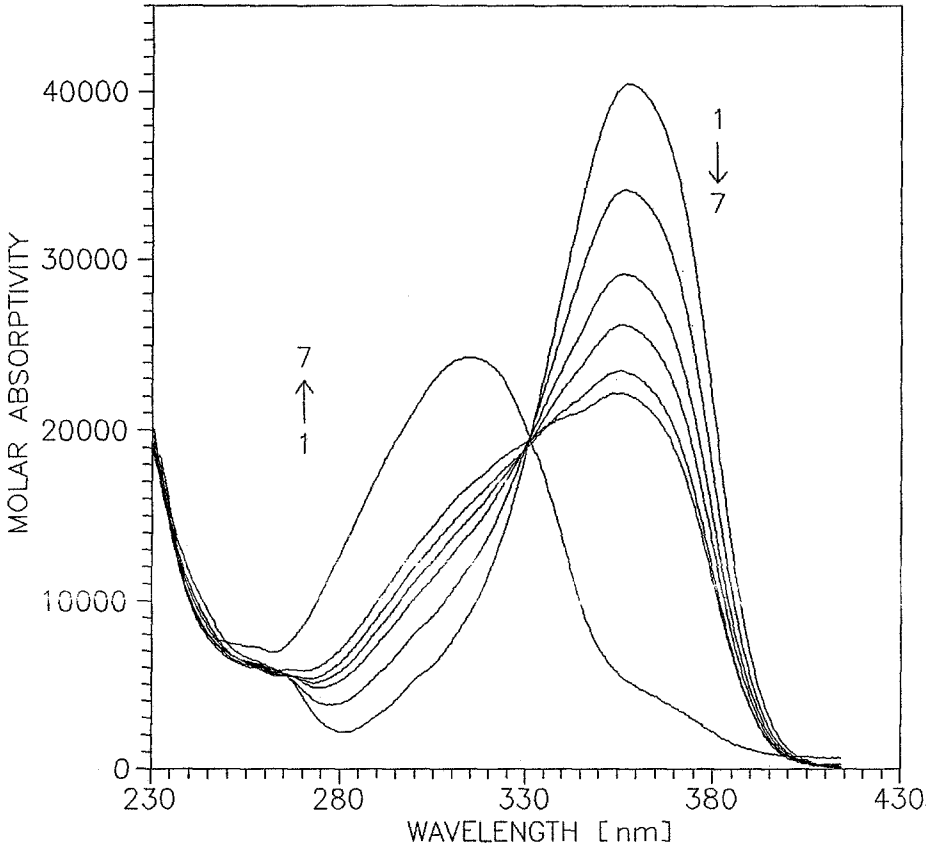

Fig. 3. Absorption spectra of ligand **1** in the presence of increasing amounts of $Ca(ClO_4)_2$.

Ba^{2+} and Ca^{2+} salts in dry acetonitrile. Complexation is highly sensitive to the presence of water which leads to complex decomposition [9].

Using spectrophotometric titration of **1** with $Ca(ClO_4)_2$ and $Ba(ClO_4)_2$ a well-defined isosbestic point was observed which was not distorted at high salt concentrations (Figure 3). At salt concentrations of 0.01 M no further changes in the absorption spectra were observed. The remaining low-intensity band at 360 nm should be assigned to the $n - \pi$ transition existing both in the ligand and the complex. The band is absent in the spectra of both protonated forms **3** and **4** and in the spectrum of the quaternized compound **5**. The stability constants obtained by least-squares regression (Table I) are comparable with those reported for other aza-15-crown-5 compounds [7–11]. The complexes formed with Ca^{2+} ions are more stable than these with Ba^{2+} ions because of the better fit between the ionic diameters of the ion and the macrocyclic cavity.

The addition of a few drops of concentrated HCl to the solution of the ligand **1** leads to complete disappearance of the absorption band at 360 nm, whereas two new absorption bands appear at 430 nm and at 314 nm owing to both protonated

TABLE I. Stability constants and quantum yields for ligand **1** and the complexes.

Compound	ϕ_c	log K_{st} (absorption)	log K_{st} (fluorescence)
11	0.87 ± 0.05		
11 + $Ba(ClO_4)_2$	0.18 ± 0.07	3.17 ± 0.01	2.95 ± 0.03
11 + $Ca(ClO_4)_2$	0.10 ± 0.08	3.71 ± 0.02	3.58 ± 0.05

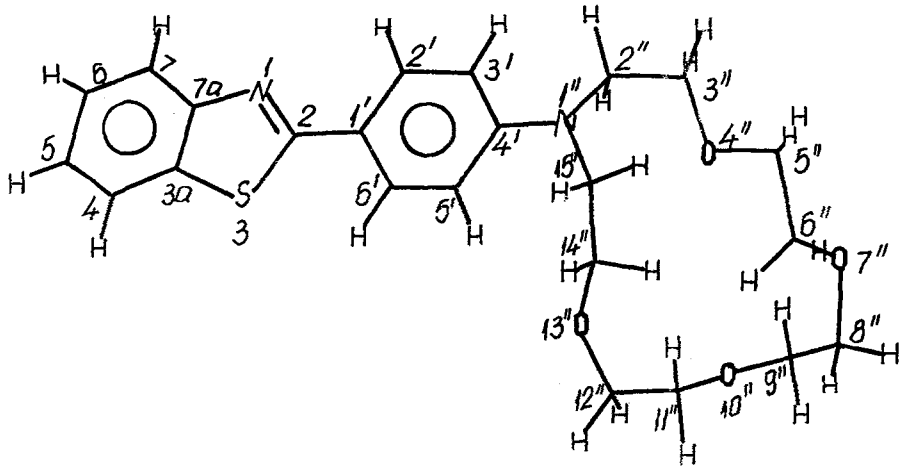

Fig. 4. AM1-calculated structure of **1**.

forms **3** and **4**. Protonated **5** absorbs at 297 nm (ϵ = 1640). After protonation at N1″ its free electron pair does not participate in the conjugated system. For this reason the PPP calculations were performed on the 2-phenylbenzothiazole fragment only. Its geometry was taken from the AM1 results (Figure 4, Table II).

Solutions of ligand **1** in many solvents (methanol, ethanol, acetonitrile) are fluorescent. Quaternization leads to fluorescence quenching so that **5** is non-fluorescent. The broad emission band maximum of **1** in acetonitrile (370–550 nm) is at 420 nm (λ_{ex} 360 nm). The excitation spectrum of **1** is a broad, structureless band which coincides very well with the absorption spectrum. Obviously the fluorescence arises from the first excited state which, in this case, results from the charge transfer. Complex formation when the CT transition is restricted was observed to lead to fluorescence quenching of the emission at 420 nm, whereas no changes in the band shape and position occur. Similar phenomena were discussed by Valeur *et al.* [7, 8, 32] as well as by Rettig [33]. Some explanations of the lack of changes in the emission band position upon complex formation were given in terms of the 'locally excited' (LE) and 'relaxed intramolecular charge transfer' (RICT) [8]. We have spectrofluorometrically estimated the stability constants of the complex formation, recording the emission at 420 nm (λ_{ex} 320 nm) by the addition of different salt

TABLE II. Calculated bond lengths (Å) for the neutral ligand **1** and protonated species **3** and **4**. Experimental data are taken from Refs. 29 and 30

Bond	Experimental	AM1-data		
		1	**3**	**4**
N(1)—C(2)	1.280[29]	1.326	1.368	1.331
C(2)—S(3)	1.749[29]	1.753	1.706	1.738
S(3)—C(3a)	1.757[29]	1.698	1.694	1.685
N(1)—C(7a)	1.404[29]	1.402	1.407	1.396
C(3a)—C(7a)		1.436	1.428	1.438
C(3a)—C(6)	1.399[29]	1.396	1.395	1.397
C(7a)—C(7)	1.369[29]	1.410	1.404	1.413
C(4)—C(5)	1.386[29]	1.386	1.390	1.386
C(5)—C(6)	1.365[29]	1.405	1.403	1.407
C(6)—C(7)	1.377[29]	1.385	1.390	1.383
C(2)—C(1′)	1.475[30]	1.452	1.423	1.455
C(1′)—C(2′)	1.402[30]	1.400	1.414	1.406
C(1′)—C(6′)	1.390[30]	1.403	1.420	1.402
C(2′)—C(3′)	1.378[30]	1.389	1.375	1.388
C(3′)—C(4′)	1.407[30]	1.417	1.434	1.411
C(4′)—C(5′)	1.413[30]	1.419	1.437	1.403
C(5′)—C(6′)	1.382[30]	1.386	1.371	1.393
C(4′)—N(1″)	1.377[30]	1.410	1.370	1.473
N(1″)—C(2″)	1.462[30]	1.452		
N(1″)—C(15″)	1.455[30]	1.444		
C(2″)—C(3″)	1.503[30]	1.531		
C(3″)—O(4″)	1.423[30]	1.423		
O(4″)—C(5″)	1.431[30]	1.422		
C(5″)—C(6″)	1.469[30]	1.527		
C(6″)—O(7″)	1.410[30]	1.427		
O(7″)—C(8″)	1.434[30]	1.420		
C(8″)—C(9″)	1.48[30]	1.525		
C(9″)—O(10″)	1.469[30]	1.426		
O(10″)—C(11″)	1.436[30]	1.427		
C(11″)—C(12″)	1.505[30]	1.525		
C(12″)—O(13″)	1.413[30]	1.419		
O(13″)—C(14″)	1.410[30]	1.429		
C(14″)—C(15″)	1.521[30]	1.539		

concentrations (Figure 5). At salt concentrations of 0.01 M no more changes in the fluorescence spectra were observed. The remaining fluorescence is due to the complex formed, and it depends on the degree of interaction between the ligand and the metal ion. Protonation at the amino and benzothiazole nitrogen leads to the structures **3** and **4** and to full fluorescence quenching.

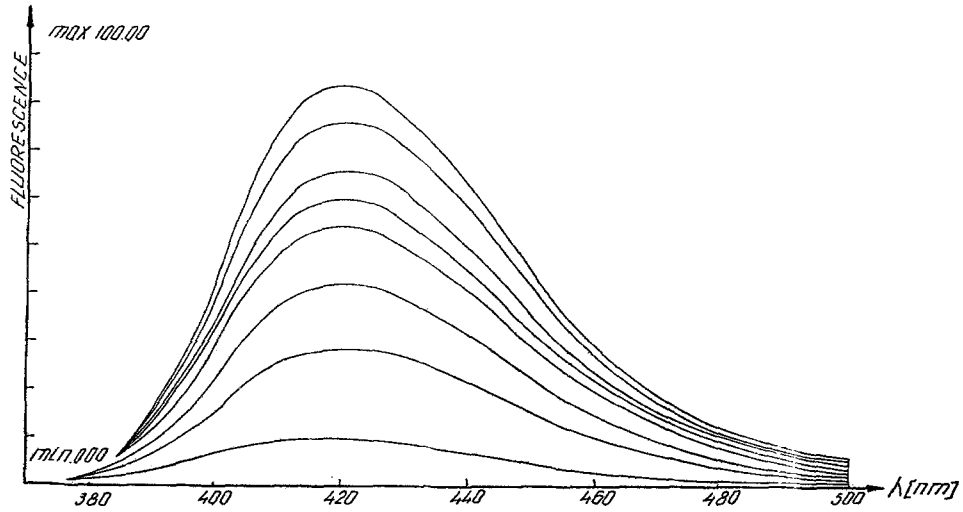

Fig. 5. Spectrofluorimetric titration of the ligand **1** with acetonitrile solutions of $Ca(ClO_4)_2$.

Since no crystals appropriate for X-ray structure determination could be isolated, the structures of the investigated compounds were estimated using a semiempirical AM1 quantum chemical method. Table II lists the calculated bond lengths for **1** as well as for the protonted forms **3** and **4**. The results obtained show very good agreement with the experimental data published previously for related compounds [29, 30]. Since the protonation does not affect the molecular geometry of the macrocycle the corresponding data are not shown in the table. Protonation at the macrocyclic nitrogen atom leads to elongation of the C(4′)—N(1″) bond, whereas the other bonds are not affected. Protonation at the benzothiazole nitrogen atom leads to shortening of C(2)—C(1′) and C(4′)—N(1″) bonds and elongation of C(1′)—C(2′) and C(1′)—C(6′) bonds. It was established that the torsion angles between the benzothiazole and phenyl moieties of **1** and **4** are the same (Table III). Protonation of the benzothiazole nitrogen results in a planar geometry of molecule **3**. The presence of an *N*-methyl group in **5** leads to significant enhancement of the torsion angle between the benzothiazole and phenyl moieties probably because of steric hindrance (Table III).

The AM1 method also predicts the proton affinity quite satisfactorily (e.g. compared with the experimental results for guanine and cytosine [28]). The proton affinities thus obtained are comparable with the values for related compounds published in Ref. [34] where the PM3 semiempirical MO method was used. From the data in Table III it can be seen that the AM1 method predicts the macrocyclic nitrogen atom to be the favorable protonation site.

TABLE III. AM1-calculated torsion angles Θ (in degrees), between the benzothiazole and phenyl moieties for compounds **1–5**; net atomic charges at nitrogen atoms N1 and N1″ (e^-) (see Figure 4); heats of formation ΔH_f and proton affinities PA (in kJ/mol).

Compound	Θ	q_{N1}	$q_{N1''}$	ΔH_f	PA
1	12.6	−0.111	−0.246	378.1	
3	1.0	−0.166	−0.216	172.9	979.1
4	12.5	−0.067	0.064	228.2	923.9
5	−32.7	−0.096	−0.227	180.6	

4. Conclusions

Some photophysical and complexation properties of a new chromofluoroionophore **1** have been investigated spectrophotometrically and spectrofluorometrically. Complex formation also leads to the observation of a hypsochromic shift of the absorption band combined with a hypochromic effect. Complexation leads to fluorescence quenching but the position of the emission maximum remains unchanged. Stability constants of the complexes have been determined, showing that this compound can be used for the determination of barium and calcium ions in acetonitrile-containing media. Protonation at both nitrogen atoms as well as quaternization at the benzothiazole nitrogen are connected with some structural changes leading to fluorescence quenching. The complexation ability of the quaternized compound **5** is lower than that of the non-quaternized compound **1**.

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