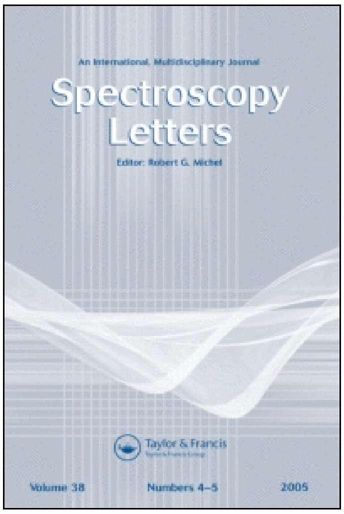

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Tautocrowns: Aza-15-Crown Moiety Conjugated to a Tautomeric Schiff Base

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Tautocrowns: Aza-15-Crown Moiety Conjugated to a Tautomeric Schiff Base

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ABSTRACT The spectral properties of a tautomeric Schiff base containing aza-15-crown-5 moiety, namely N-((4-methylnaphthalen-1-yl)methylene)-4-(1,4,7,10-tetraoxa-13-azacyclopentadecan-13-yl)aniline on addition of alkali and alkaline earth metal ions were investigated. The newly synthesized ligand exhibited very interesting color changes in presence of metal ions: from yellow (free ligand) via colorlessness (enol tautomer complex) to yellow–orange (keto tautomer complex). These changes result from 2 stepwise processes: complex formation and shift of the tautomeric equilibrium between the tautomers after addition of the metal ions.

KEYWORDS alkali and alkaline earth metal ions, aza-15-crown-5, Schiff bases, tautomerism

INTRODUCTION

Tautomerism is a process of exchange of a proton between two (or more) forms, leading to redistribution of the electronic density in the whole molecule[1] and changing substantially its spectral and photophysical properties. In the case of the tautomeric azonaphthols and related Schiff bases **1**–**6** (shown in Scheme 1), the effects of the temperature, solvents, and substituents have been clarified,[2,3] potentially creating tools to shift the tautomeric equilibrium toward the enol (**E**) or keto (**K**) form.

Almost the same can be stated for the complexation of azacrowns conjugated to a chromophore: It leads to electronic redistribution in the ligand molecule.[4] The process influences the spectral and photophysical properties of the whole molecule. The stability of the complex obtained depends on temperature, solvent, and mainly the electronic structure of the ligand. This means that by changing one of these factors, one can change the complex stability and its spectral properties.

Linking an azacrown ether to a tautomeric dye could lead to a double effect of control. On the one hand, the shift in the position of the tautomeric equilibrium will lead to electronic rearrangement in the molecule and consequently to a change of its complexation abilities. On the other hand, the process of complexation might lead to shift of the tautomeric equilibrium toward a particular tautomer. In fact, these two competitive processes can provide additional tools for design of switch on–off sensor molecules. In our best knowledge, there is limited number of systems where the crown

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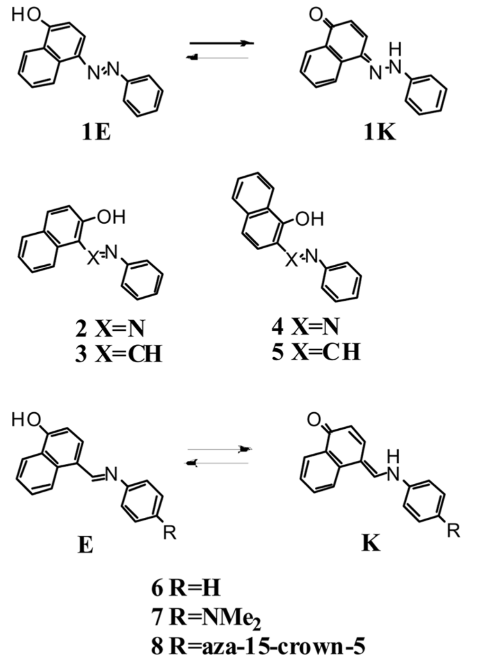


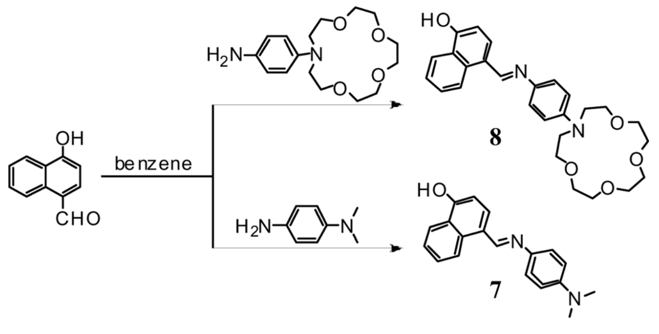
SCHEME 1 Keto–enol tautomerism in compounds 1–8.

ether is linked in a way that can influence the tautomeric equilibrium, but the changes have never been discussed in depth from this viewpoint.[5]

Previously we have synthesized a series of aza-15-crown-5 (A15C5) moiety containing Schiff bases and have shown the importance of position of crown on the complexation abilities of the ligands.[6,7] In the current article, we report the synthesis and the tautomeric changes upon complexation in a Schiff base, where the A15C5 is conjugated to the tautomeric system (compound **8**). The properties of the new ligand are discussed in comparison with the model compound **7**, where no complexation is possible.

MATERIALS AND METHODS

The synthesis of compounds **8** and **7** (the model compound of **8** in respect to the free ligand tautomerism) is summarized in Scheme 2.



SCHEME 2 Synthesis of 7 and 8.

N-((4-methylnaphthalen-1-yl)methylene)-4-(1,4,7,10-tetraoxa-13-azacyclopentadecan-13-yl)aniline (8)

From 4-hydroxy-1-naphthadehyde (0.086 g, 0.5 mmol) and 4-(1,4,7,10-tetraoxa-13-azacyclopentadecan-13-yl)aniline[6] (0.171 g, 0.55 mmol), benzene 0.216-g (93%) crystals of **1** are obtained using the above procedure: mp 159–161°C.

IR (nujol): 3550–2500 (broad, OH), 1630 (C=N), 1120 (C−O−C) cm^{-1}. ^{1}H NMR δ (CDCl$_3$): 3.52–3.73 (16H, m, OCH$_2$), 3.73–3.85 (4H, m, NCH$_2$), 5.30 (1H, s, OH), 6.70 (2H, d, Ar, J = 9.1 Hz), 6.79 (1H, d, Ar, J = 8.3 Hz), 7.23 (2H, d, Ar, J = 9.0 Hz), 7.49 (1H, ddd, Ar, J = 1.2 Hz, J = 6.9 Hz, J = 8.1 Hz), 7.60 (1H, ddd, Ar, J = 1.5 Hz, J = 6.9 Hz, J = 8.4 Hz), 7.87 (1H, d, Ar, J = 8.4 Hz), 8.34 (1H, dd, Ar, J = 1.1 Hz, J = 8.3 Hz), 8.70 (1H, d, Ar, J = 8.3 Hz), 8.78 (1H, s, CH). Anal. Calcd. for $C_{27}H_{32}N_2O_5$: C 69.81%, H 6.94%, N 6.03%; found C 69.44%, H 7.15%, N 6.61%.

4-((4-(Dimethylamino)-phenylimino)methyl)naphthalen-1-ol (7)

Solution of 4-hydroxy-1-naphthadehyde (0.086 g, 0.5 mmol) and N^1,N^1-dimethylbenzene-1,4-diamine (0.068 g, 0.5 mmol) in benzene (25 ml) is refluxed using Dean-Stark trap for 5 hr. After the completion of the reaction, benzene is evaporated under reduced pressure. The corresponding oil crystallized from acetonitrile/toluene, thus yielding 0.075-g (52%) crystals of **2**: mp 187–189°C.

IR (nujol): 3550–2500 (broad, OH), 1630 (C=N) cm^{-1} · ^{1}H NMR δ (CDCl$_3$): 2.73 (6H, s, NCH$_3$), 6.53 (2H, d, Ar, J = 9.0 Hz), 6.69 (1H, d, Ar, J = 8.0 Hz), 7.01 (2H, d, Ar, J = 9.0 Hz), 7.22 (1H, ddd, Ar, J = 1.1, 6.8, 8.0 Hz), 7.34 (1H, ddd, Ar, J = 1.5, 6.8, 8.5 Hz), 7.64 (1H, d, Ar, J = 8.1 Hz), 8.07 (1H, dd, Ar, J = 1.4, 8.2 Hz), 8.69 (1H, s, Ar), 8.85 (1H, br. s, Ar). Anal. Calcd. for $C_{19}H_{18}N_2O$: C 78.59%, H 6.25%, N 9.65%; found C 78.63%, H 5.92%, N 9.94%.

Melting points were taken on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Specord 75 instrument (Jena, Germany). ^1H NMR spectra (250.13 MHz) were obtained on a Bruker Avance DRX-250 spectrometer (Bruker Optics; Germany). The chemical shifts are given in parts per million (δ) relative to tetramethylsilane as internal standard. Microanalyses were performed on VarioEL *III* CHNS/O (Elementar Analysensysteme GmbH; Germany).

The UV-Vis spectral measurements were performed on JASCO V-570 UV-Vis-NIR spectrophotometer (JASCO, Japan), equipped with a Julabo ED5 thermostat (precision 1°C) at 20°C, in spectral-grade solvents. The complexation was studied in dry acetonitrile.[8] AR grade $LiClO_4$ (Fluka), $NaClO_4 \cdot H_2O$ (Fluka), $Mg(ClO_4)_2$ (Fluka), $Ca(ClO_4)_2 \cdot 4H_2O$ (Aldrich), $Sr(ClO_4)_2$ (Aldrich), $Ba(ClO_4)_2 \cdot aq$ (Fluka), and $BeSO_4 \cdot 2H_2O$ (Merck) were vacuum dried at 60°C from 3 to 5 days depending on the case. Spectral-grade acetonitrile (AcN) was dried with P_2O_5, distilled on CaH_2, and kept with molecular sieve.[8]

RESULTS AND DISCUSSION

Not surprisingly, the spectral properties of **8** as free ligand are identical with those of **7**. As seen in Fig. 1, in acetone, only the enol (**E**) tautomer (Scheme 1) exists, exhibiting a strong band c. 400 nm.[9] In proton donor and/or polar solvents, a low intensive band c. 500 nm, belonging to the keto (**K**) tautomer, is observed. In general, the content of the keto tautomer is low as it is in the related azonaphthols (**1**) with electron donative substituent in the phenyl ring.[2]

Herzfeld and Nagy[10] showed that the addition of $CaCl_2$ in absolute ethanol leads to change in the position of the tautomeric equilibrium in some Schiff bases. Similar, weaker effects are observed upon addition of various alkali and alkaline earth salts. As seen from Fig. 2, the addition of $NaClO_4$, $Mg(ClO_4)_2$, or $Sr(ClO_4)_2$ to solution of **7** causes changes in the intensities of the **E** (decrease) and **K** (increase) maxima. The tautomeric equilibrium is most sensitive to addition of Mg^{2+} in dry AcN. In chloroform, such changes are observed only in presence of $Mg(ClO_4)_2$. In addition, the shift in the tautomeric equilibrium is not instantaneous: The system reaches equilibrium in the frame of days. Up to now, the effect of the alkali and alkaline earth metal ions on the tautomeric equilibrium has

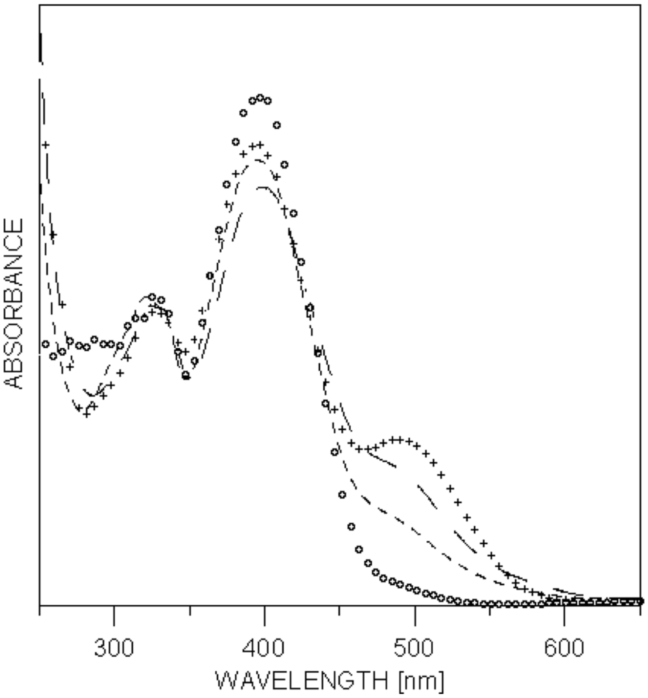


FIGURE 1 Absorption spectra of 7 (C=$1.90 \cdot 10^{-5}$ mol/l) in ethanol (+ + +), $CHCl_3$ (— — —), CH_3COCH_3 (o o o), and AcN (·······).

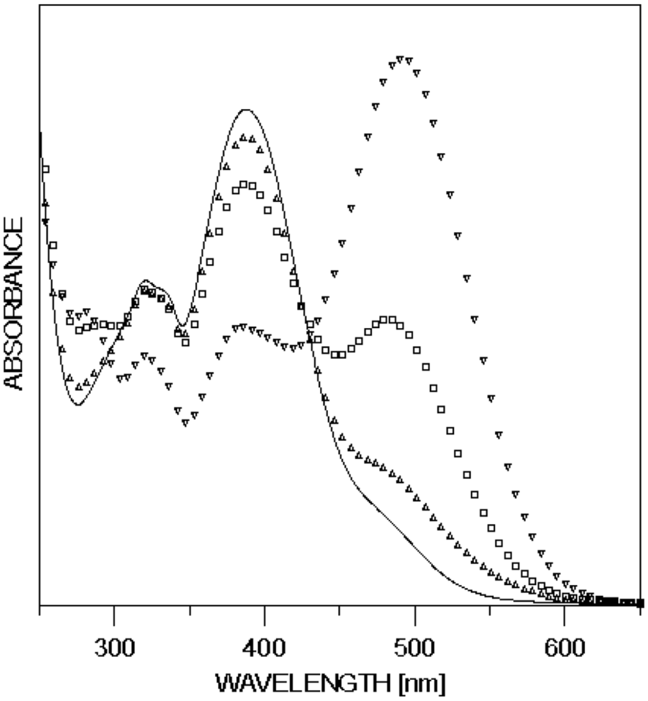


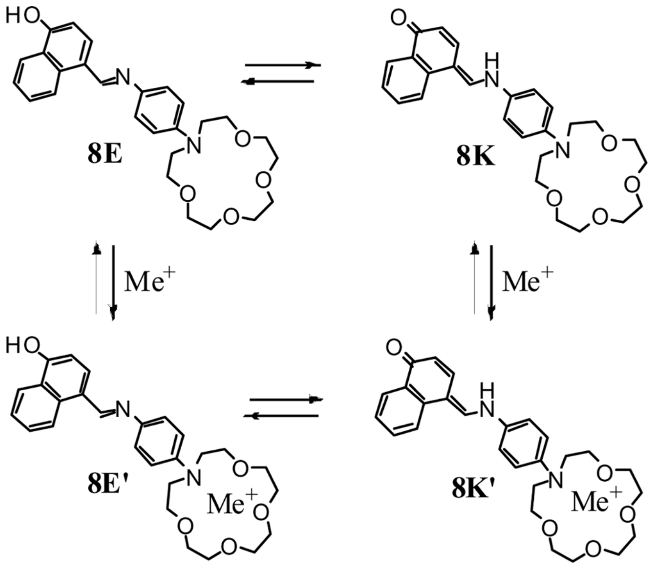
FIGURE 2 Absorption spectra of 7 in dry AcN (——, c = $6.90 \cdot 10^{-5}$ mol/l) with addition of $Mg(ClO_4)_2$ (▽▽▽, c = $2.15 \cdot 10^{-6}$ mol/l), $Sr(ClO_4)_2$ (□□□, c = $8.50 \cdot 10^{-5}$ mol/l), and $NaClO_4$ (△△△, c = $3.13 \cdot 10^{-5}$ mol/l).

remained unexplained[10,11] and has had to be taken into account in the study of the complexation of **8**.

Consequently, in the case of **8**, two competitive processes could be expected with addition of metal perchlorate: complex formation, involving the A15C5 moiety, and shift in the tautomeric equilibrium toward the **K** form as result of the metal-salt addition. According to the spectral changes caused upon addition, the alkali and alkaline earth ions can be divided (see Scheme 3 for overall description of the processes):

4. no spectral changes at all: Be^{2+};
5. appearance and simultaneous rise of intensive absorption maximum at 360 nm and low intensive band at 460 nm (Fig. 3): Li^{+} and Na^{+};
6. initial appearance of aforementioned maxima followed by a decrease of intensity of the band at 360 nm and raise of the band at 460 nm with further addition of the salt (Figs. 3 and 4): Ca^{2+}, Sr^{2+} and Ba^{2+};
7. increase of intensity of already existing maximum of the keto form at 500 nm, that is, no complexation (compare Figs. 2 and 4): Mg^{2+}.

Initially the spectral changes in all metal ions, except Mg^{2+}, are equivalent (Fig. 3): appearance of new bands at 360 nm and 460 nm and rise of their intensity upon salt addition. Simultaneously there is decrease of the existing bands at 400 and 500 nm as seen in second derivative spectra of **8** (Fig. 5).



SCHEME 3 Complexation and tautomerism in 8.

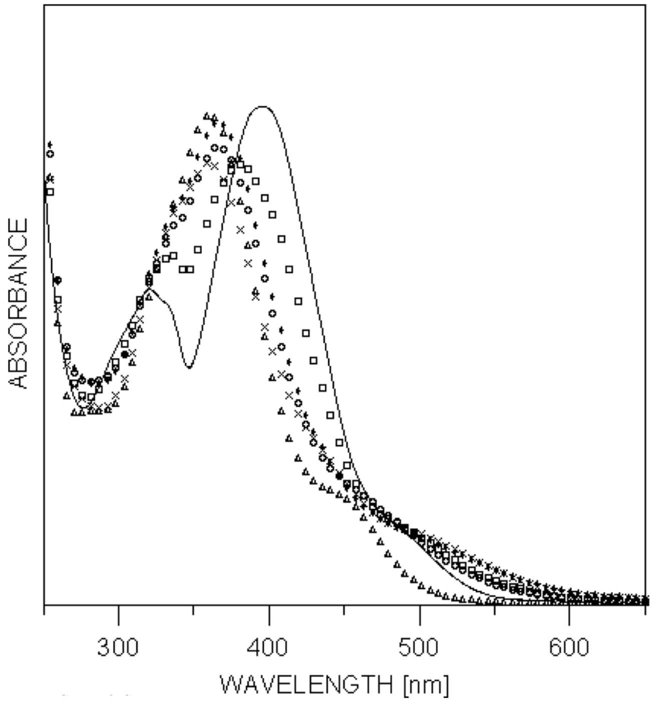


FIGURE 3 Complex formation according to Scheme 3: Absorption spectra of 8 in dry AcN (——, $c = 1.72 \cdot 10^{-5}$ mol/l) with addition of $LiClO_4$ (ººº, $c = 1.85 \cdot 10^{-4}$ mol/l), $NaClO_4$ (△△△, $c = 9.80 \cdot 10^{-4}$ mol/l), $Ba(ClO_4)_2$ (◆◆◆, $c = 2.30 \cdot 10^{-5}$ mol/l), $Ca(ClO_4)_2$ (×××, $c = 3.06 \cdot 10^{-6}$ mol/l), and $Sr(ClO_4)_2$ (□□□, $c = 4.10 \cdot 10^{-6}$ mol/l).

Upon further addition of the perchlorate in the case of Ca^{2+}, Sr^{2+} and Ba^{2+}, the intensity of the band at 360 nm reaches maximum and begins to decrease. At the same time, an elevation of the band at 460 nm is observed (Fig. 4).

The observed spectral changes suggest that the complexation and the change in the tautomeric equilibrium proceed consecutively (Scheme 3). Initially, upon addition of the metal salt, both tautomers of **8** individually bind the metal ions without a change in the position of the tautomeric equilibrium. In the complex, the nitrogen atom from A15C5 is involved,[7] effectively leading to its switch-off from the chromophore tautomeric system. Hence, the absorption spectra of the complexes of the tautomers should be the same as in **6**, where there is no substituent in the phenyl ring. Actually it is observed in Fig. 6: The absorption maxima of **6** in dry AcN are at 360 nm (**E** form) and 460 nm (**K** form), and with addition of $Sr(ClO_4)_2$ the content of the keto tautomer increases. After **8** has been fully consumed as a free ligand, the excess of the metal salt leads to shift of the tautomeric equilibrium toward the keto tautomer complex (**8K′**). In the frame of such a scheme,

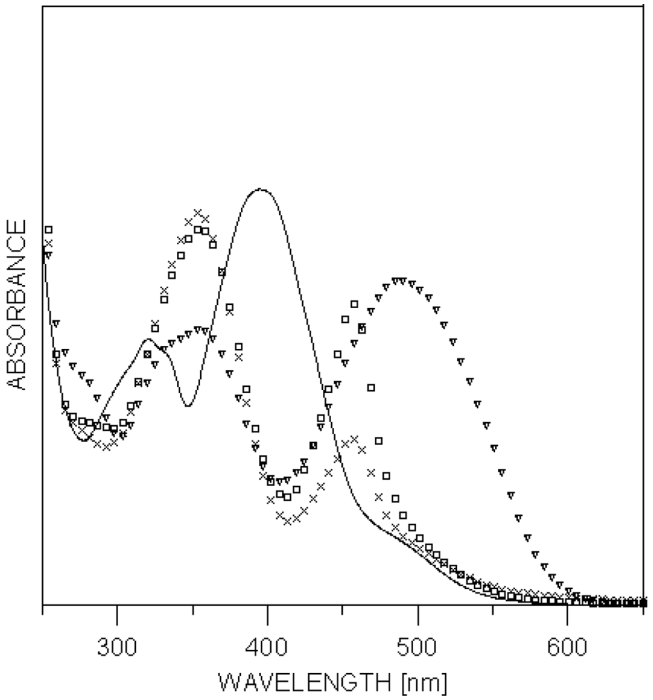


FIGURE 4 Change in the position of the tautomeric equilibrium between 8E′ and 8K′ (Scheme 3): Absorption spectra of 8 in dry AcN (——, $c = 2.60 \cdot 10^{-5}$ mol/l) with further addition of $Mg(ClO_4)_2$ (▽▽▽, $c = 9.90 \cdot 10^{-5}$ mol/l), $Ca(ClO_4)_2$ (×××, $c = 3.06 \cdot 10^{-5}$ mol/l), and $Sr(ClO_4)_2$ (□□□, $c = 4.00 \cdot 10^{-5}$ mol/l).

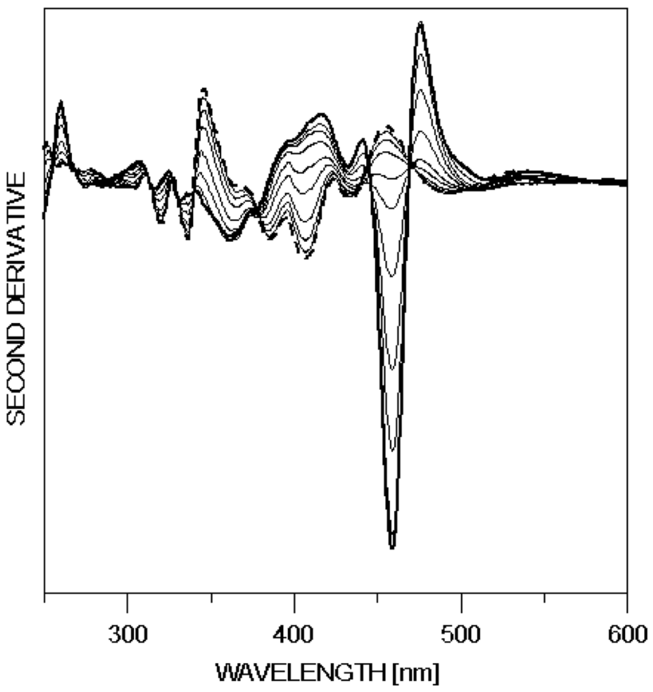


FIGURE 5 Second derivative spectra of 8 (- - - , $c = 3.20 .10^{-5}$ mol/l) with stepwise addition of $Sr(ClO_4)_2$ $c = 2.00 \cdot 10^{-7}$ mol/l, $c = 4.00 \cdot 10^{-7}$ mol/l, $c = 8.00 \cdot 10^{-7}$ mol/l, $2.00 \cdot 10^{-6}$ mol/l, $4.10 \cdot 10^{-6}$ mol/l, $8.10 \cdot 10^{-6}$ mol/l, $2.43 \cdot 10^{-5}$ mol/l, $4.00 \cdot 10^{-5}$ mol/l, $8.10 \cdot 10^{-5}$ mol/l, $c = 1.62 \cdot 10^{-4}$ mol/l (—).

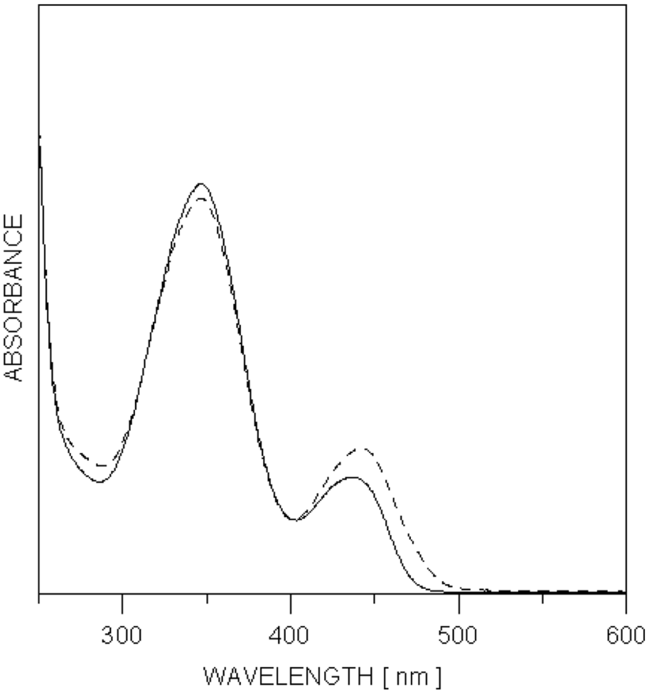


FIGURE 6 Absorption spectra of 6 in dry AcN (—, $c = 4.50 \cdot 10^{-4}$ mol/l) with addition of $Sr(ClO_4)_2$ (- - - , $c = 6.68 \cdot 10^{-5}$ mol/l).

the interaction with Li^+ and Na^+ is limited in the process of complexation due to their weaker binding ability with A15C5.[4] In the case of Ca^{2+}, Sr^{2+}, and Ba^{2+}, whose sizes correspond to A15C5 cavity, the effective complexation leads to full consumption of the free ligand, and the further salt addition changes the equilibrium between the tautomeric complexes **8E′** and **8K′**.

The complexity of the processes in solution and the lack of instantaneous shift of the equilibria do not allow us to estimate the corresponding equilibrium constants with acceptable precision. In general, we can conclude that the complexation ability of the new ligand **8** toward alkaline earth metal ions is larger than that toward alkali ions. However, the curves on Fig. 3, showing the maximal changes achieved under addition of the metal salt and attributed to the complex formation, could be used as indication of the binding ability of the ligand toward the metal ions. Taking into account the concentrations of the metal salts, which lead to final complex formation (no further changes related to complexation), we can conclude the following order of increase of the stability constants of the complexes between ligand **8** and the metal ions: $Na^+ < Li^+ < Ba^{2+} < Sr^{2+} \approx Ca^{2+}$, in accordance with the previously reported best complexation ability of A15C5 toward Ca^{2+}.[4,12]

CONCLUSIONS

The spectral changes upon addition of alkali and alkaline earth metal ions in a newly synthesized ligand where the A15C5 moiety is conjugated to a tautomeric system were investigated. In the case of alkali ions, a process of complexation was observed, causing hypsochromic shift in the positions of the tautomeric bands. The addition of Ca^{2+}, Sr^{2+}, and Ba^{2+} initially leads to complex formation, but after the free ligand has been fully consumed, a shift of the tautomeric equilibrium toward keto tautomer complex with the metal ion was observed with addition of excess of metal salt. The lack of instantaneous shift of the equilibria does not allow one to estimate the corresponding equilibrium constants with acceptable precision, but in general we can state that the complexation ability of the new ligand toward alkaline earth metal ions is larger than that toward alkali ions. This is the first discussion of the effect of the metal-salt addition on the tautomeric equilibrium in crown ether containing tautomeric Schiff bases.

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