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Letter to the Editors

Synthesis and spectroscopic properties of new Schiff bases containing the *N*-phenylaza-15-crown-5 moiety

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Abstract

A series of two Schiff bases, **1** and **2**, containing the *N*-phenylaza-15-crown-5 moiety was prepared by condensation of the formyl- and amino derivatives of *N*-phenylaza-15-crown-5 (**3**) with *p*-substituted anilines and benzaldehydes respectively. The starting macrocycle **3** was synthesized via a new modified procedure. UV- and ^{1}H-NMR spectral data of **1** and **2** are given. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Schiff bases; *N*-Phenylaza-15-crown-5; Spectroscopic properties; Chromoionophores; Complexation

1. Introduction

The recent increase in interest in the synthesis of crown ether derivatives incorporating different chromo- and fluoroionophores is due to their application as alkaline and alkaline-earth ion sensors in biochemical analysis and medical diagnostics [1–3]. Recent work has concerned the binding of various dyes to the *N*-phenylaza-15-crown-5 and their spectroscopic and complexation properties [3–12]. This letter concerns the synthesis of two new series of Schiff bases bound to the macrocycle **3**—compounds **1** and **2**.

2. Results and discussion

Schiff bases of type **1** were obtained by condensation of the known [4] 4-(1,4,7,10-tetraoxa-13-azacyclopentadecyl)benzaldehyde (**4**) with *p*-substituted anilines according to Scheme 1.

The second type of Schiff base **2** was obtained by condensation of 13- (4-aminophenyl)-1,4,7,10-tetraoxa-13-azacyclopentadecane (**5**) [4] with substituted benzaldehydes according to Scheme 2.

N-Phenylaza-15-crown-5 (**3**) was synthesized for the purposes of this investigation via a modification of the procedure of Dix and Vögtle [4]. Thus, *N*-phenyldiethanolamine was reacted with triethyleneglycol ditosylate in dilute THF solution under NaH treatment, in a manner analogous to the method used for the *N*-alkylaza-15-crown-5 [13]. The desired azacrown ether **3** was isolated from the accompanying side products as the sodium

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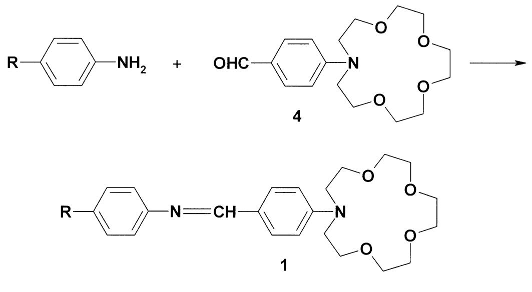
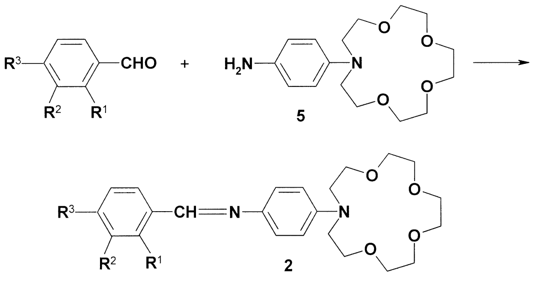


	R
a	H
b	$N(CH_3)_2$
c	OCH_3
d	OC_2H_5
e	F
f	Cl
g	Br
h	I

Scheme 1.



	R^1	R^2	R^3
a	H	H	H
b	H	H	$N(CH_3)_2$
c	H	H	NO_2
d	H	OCH_3	OCH_3
e	OH	H	H
f	H	H	OCH_3

Scheme 2.

perchlorate complex, which was destroyed by aqueous treatment [4]. The average yield (ca. 50%) was higher than that reported previously [4]. The condensation of 4-(1,4,7,10-tetraoxa-13-azacyclopentadecyl)benzaldehyde [4]) with *p*-substituted anilines, as well as of 13- (4-aminophenyl)-1,4,7,10-tetraoxa-13-azacyclopentadecane [4] with benzaldehydes was carried out after azeotropic removal of the water formed. The Schiff bases **1** and **2** obtained were characterized using elemental analysis, mp, IR-, ^{1}H-NMR- and UV–vis spectra (Table 1).

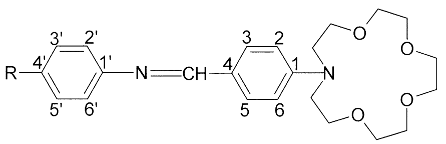
Compounds **1** and **2** exhibited in their IR spectra, bands typical of $\nu_{C=N}$ in the region 1600–1630 cm^{-1} and C–O–C in the region 1120–1130 cm^{-1}. ^{1}H-NMR spectral data are presented in Tables 2 and 3. The signals of the crown ether moiety for both series were in the range of ca. 3.6–3.7 δ ppm as multiplets for 16H and at 3.78–3.79 δ ppm as triplets for 4H (CH_2NCH_2). The singlets of the

Table 1
Preparative and elemental analysis data of compounds **1** and **2**

	General formula	Mol. mass	Yield (%)	M.p. (°C)	Solvent[a]	Calcd C%	Found C%	Calcd H%	Found H%
1a	$C_{23}H_{30}N_2O_4$	398.5	32	100–102	EtOAc	69.32	69.52	7.59	7.75
1b	$C_{25}H_{35}N_3O_4$	441.6	55	132–134	Hexane	68.00	67.58	7.99	7.90
1c	$C_{24}H_{23}N_2O_5$	428.5	71	142–143	EtOAc	67.28	67.52	7.53	7.78
1d	$C_{25}H_{34}N_2O_5$	442.5	82	115–117	EtOAc	67.85	68.24	7.74	7.90
1e	$C_{23}H_{29}N_2O_4F$	416.5	70	91–92	EtOH	66.33	66.40	7.02	7.29
1f	$C_{23}H_{29}N_2O_4Cl$	432.9	86	122–124	MeOH	63.80	63.68	6.75	7.05
1g	$C_{23}H_{29}N_2O_4Br$	477.4	28	130–132	Hexane	57.86	57.71	6.12	6.00
1h	$C_{23}H_{29}N_2O_4I$	524.4	63	128–130	EtOH	52.68	52.89	5.57	5.87
2a	$C_{23}H_{30}N_2O_4$	398.5	38	84.5–86	Hexane	69.32	69.60	7.59	7.36
2b	$C_{25}H_{35}N_3O_4$	441.6	56	148–150	EtOAc	68.00	67.58	7.99	7.95
2c	$C_{23}H_{29}N_3O_6$	443.0	44	143–144	EtOAc	62.29	62.43	6.59	6.66
2d	$C_{25}H_{34}N_2O_6$	458.5	78	118–119	EtOAc	66.67	66.97	7.25	7.31
2e	$C_{23}H_{30}N_2O_5$	414.5	20	102–103	Hexane	65.48	65.56	7.47	7.20
2f	$C_{24}H_{32}N_2O_5$	428.5	42	124–126	Hexane	67.3	67.27	7.48	7.48

[a] Solvent for recrystallization.

Table 2
^{1}H-NMR spectral data of compound **1**



	R	NCH_2	OCH_2	2-**H** 6-**H**	3-**H** 5-**H**	2′-**H** 6′-**H**	3′-**H** 5′-**H**	CH=N
a		3.79 (4H, *t*)	3.61–3.67 (16H, *m*)	6.70 (*d*, 2H, $J=8.9$)	7.74 (*d*, 2H, $J=8.0$)	7.18 (*t*, 3H)	7.36 (*t*, 2H)	8.30 (*s*, 1H)
b	2.95 (6H, *s*, N $(CH_3)_2$)	3.78 (4H, t)	3.61-3.66 (16H, *m*)	6.70 (d, 2H, $J=8.9$)	7.72 (d, 2H, $J=8.6$)	7.20 (d, 2H, $J=8.9$)	6.75 (d, 2H, $J=8.9$)	8.34 (s, 1H)
c	3.81 (3H, *s*, OCH_3)	3.79 (4H, *t*)	3.64–3.67 (16H, *m*)	6.70 (*d*, 2H, $J=8.8$)	7.73 (*d*, 2H, $J=8.4$)	7.19 (*d*, 2H, $J=8.9$)	6.91 (*d*, 2H, $J=8.9$)	8.31 (*s*, 1H)
d	1.41 (2H, *t*, OCH_2CH_3) 4.04 (3H, *q*, OCH_2CH_3)	3.78 (4H, *t*)	3.63–3.66 (16H, *m*)	6.70 (*d*, 2H, $J=8.9$)	7.73 (*d*, 2H, $J=7.8$)	7.17 (*d*, 2H, $J=8.7$)	6.89 (*d*, 2H, $J=8.9$)	8.31 (*s*, 1H)
e		3.79 (4H, *t*)	3.62–3.69 (16H, *m*)	6.71 (*d*, 2H, $J=9.0$)	7.75 (*d*, 2H, $J=5.3$)	7.17 (*d*, 2H, $J=7.8$)	7.04 (*d*, 2H, $J=8.7$)	8.26 (*s*, 1H)
f		3.79 (4H, *t*)	3.63–3.69 (16H, *m*)	6.72 (*d*, 2H, $J=8.4$)	7.71 (*d*, 2H, $J=8.4$)	7.11 (*d*, 2H, $J=8.9$)	7.31 (*d*, 2H, $J=8.9$)	8.25 (*s*, 1H)
g		3.79 (4H, *t*)	3.63–3.69 (16H, *m*)	6.71 (*d*, 2H, $J=8.6$)	7.72 (*d*, 2H, $J=9.5$)	7.08 (*m*, 2H)	7.46 (*d*, 2H, $J=8.6$)	8.25 (*s*, 1H)
h		3.79 (4H, *t*)	3.640-3.68 (16H, *m*)	6.70 (*d*, 2H, $J=9.3$)	7.73 (*d*, 2H, $J=8.9$)	7.65 (*d*, 2H, $J=8.8$)	6.94 (*d*, 2H, $J=8.4$)	8.25 (*s*, 1H)

azomethine protons were in the region of 8.25–8.60 δ ppm. In most cases, the signals of the aromatic H appeared as doublets with *J*-constants in the range of 9±1 Hz.

Investigations of the molecular structure of these compounds both in the solid state and in solution (using quantum chemical calculations, ^{1}H-, ^{13}C-NMR (solution) and ^{13}C CP MAS (solid state)) have been published elsewhere [14].

All newly synthesized Schiff bases displayed intense bands in the 350–450 nm region characterized with rather high molar absorptivities ($\varepsilon \sim 2.2–4.7\times10^4$) (Table 4). The latter characteristic is most likely due to the presence of a donor–acceptor (D–A) system in the molecules, the lone electron pair of the macrocyclic N being the donor component and the CH=N group the acceptor giving rise to charge transfer (CT) [15] within the molecule.

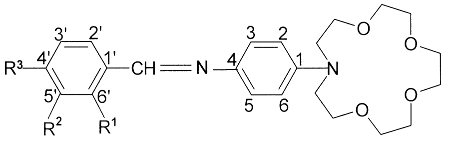
This assumption is strongly supported by the fact that metal ion coordination in the macrocyclic cavity significantly affects the spectrum, causing bathochromic and hypochromic effects [15] so long as the donor group (lone pair of the macrocyclic N) is engaged in coordination. Typical changes in the UV–vis spectrum upon complexation with Ca^{2+} are shown on Fig. 1.

The complexation properties of some of the new compounds towards alkaline, alkaline-earth, Mg^{2+} and Be^{2+} ions have been studied in detail spectrophotometrically [15]. It should be noted that some compounds formed relatively stable complexes which, in some cases, was comparable and even higher than that of the parent ligand *N*-phenylaza-15-crown-5 (**3**).

3. Experimental

Melting points were recorded using a microhot stage Boetius PHMK 05 and were uncorrected. The IR and ^{1}H-NMR spectra were recorded on Specord IR-75 (Nujol mulls) (Carl-Zeiss, Jena) and Bruker WM 250 MHz (solvent $CDCl_3$, TMS as internal standard), with chemical shifts in δ

Table 3
^{1}H NMR spectral data of compound **2**



	R^1, R^2, R^3	NCH$_2$	OCH$_2$	2-**H** 6-**H**	3-**H** 5-**H**	2′-**H** 6′-**H**	3′-**H** 5′-**H**	CH=N
a		3.78 (*t*, 4H)	3.62–3.67 (*m*, 16H)	6.69 (*d*, 2H, J=9.0)	7.23 (*d*, 2H, J=9.0)	7.87 (*m*, 2H)	7.43[a] (*m*, 3H)	8.51 (*s*, 1H)
b	3.04 (*s*, 6H, N(CH$_3$)$_2$)	3.77 (*t*, 4H)	3.61–3.69 (*m*, 16H)	6.67 (*d*, 2H, J=9.1)	7.21 (*d*, 2H, J=8.8)	7.77 (*d*, 2H, J=8.0)	6.73 (*d*, 2H, J=9.1)	8.35 (*s*, 1H)
c		3.78 (*t*, 4H)	3.62–3.69 (*m*, 16H)	6.70 (*d*, 2H, J=9.1)	7.30 (*d*, 2H, J=9.0)	8.01 (*d*, 2H, J=8.9)	8.28 (*d*, 2H, J=8.8)	8.58 (*s*, 1H)
d	3.48 (*s*, 6H, OCH$_3$)	3.78 (*t*, 4H)	3.61–3.67 (*m*, 16H)	6.68 (*d*, 2H, J=9.0)	7.22 (*d*, 2H, J=9.0)	7.60 (*s*, 6′H) 7.25–7.29 (*m*, 2′H)	6.91 (*d*, 3′H, J=8.3)	8.41 (*s*, 1H)
e		3.78 (*t*, 4H)	3.60–3.69 (*m*, 16H)	6.69 (*d*, 2H, J=9.1)	7.26 (*d*, 2H, J=9.0)	6.99 (*dd*, 1H, J=8.2)	6.91 (*td*, 3′H, J=7.5) 7.26 (d, 5′H, J=8.4) 7.33 (*td*, 4′H, J=7.6)	8.60 (*s*, 1H)
f	3.86 (*s*, 3H, OCH$_3$)	3.78 (*t*, 4H)	3.61–3.69 (*m*, 16H)	6.68 (*d*, 2H, J=9.0)	7.22 (*d*, 2H, J=9.0)	7.82 (*d*, 2H, J=8.7)	6.96 (*d*, 2H, J=8.7)	8.43 (*s*, 1H)

[a] Overlapped with the signal of 4′-H.

Table 4
UV-spectrophotometric data of ligands in acetonitrile

	$\lambda_{\max}$ (nm)	ε
1a	352	38,000
1b	379	33,000
1c	359	38,000
1d	361	39,000
1e	355	29,500
1f	361	42,000
1g	362	47,000
1h	363	36,000
2a	381	20,000
2b	386	29,000
2c	452	28,000
2d	379	26,000
2e	389	27,000
2f	376	22,000

ppm and spin–spin coupling constants J in Hz. The absorption spectra were obtained on a Perkin-Elmer Lambda 17 UV–vis spectrophotometer using dry acetonitrile as solvent.

3.1. Preparation of N-phenylaza-15-crown-5 (**3**)

Solutions of 0.181 g (1 mmol) *N*-phenyldiethanolamine and 0.459 g (1 mmol) triethyleneglycol ditosylate, each in 60 mL dry THF were added simultaneously dropwise to a stirred and boiled mixture of 0.087 g (3.63 mmol) NaH (50% suspension in parafinoil) in 90 mL dry THF within 2 h. Afterwards the reaction mixture was refluxed 2 h more, cooled and filtered. The filtrate was concentrated under reduced pressure and the dry residue dissolved in methanol; to this solution, was added a solution of 0.136 g (0.001 mmol) sodium perchlorate in methanol. The mixture was refluxed for 5 min after which, the mixture was concentrated to a small volume followed by the addition of ethylacetate. The mixture was evaporated and the residue recrystallized from ethylacetate, to give 0.21 g (50%) of the sodium complex, mp 156–159 °C. The complex was decomposed by treatment with a mixture of CH$_2$Cl$_2$:H$_2$O (1:1), the organic layer

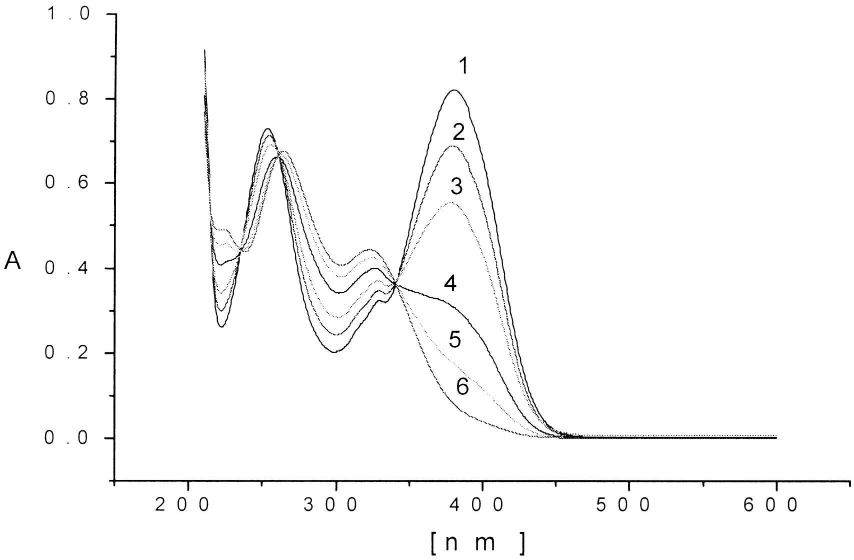


Fig. 1. Complexation of ligand **2a** with $Ca(ClO_4)_2$: 1: ligand; 2–6: increasing concentration of metal salt; *A*: absorbance.

separated, dried and evaporated to give 0.148 g of **3** (50%), mp 44–45 °C. Acc. to lit. [4], mp of **3** is 44–45 °C. The product thus prepared is sufficiently pure for further reactions.

3.2. Preparation of Schiff bases 1 and 2 (general procedure)

One millimole of 4-(1,4,7,10-tetraoxa-13-aza-cyclopentadecyl)benzaldehyde (**4**) and 1 mmol of *p*-substituted anilines or respectively 1 mmol of 13-(4-aminophenyl)-1,4,7,10-tetraoxa-13-azacyclopentadecane (**5**) and *p*-; *m*-; *o*-substituted benzaldehydes were dissolved in 40 mL dry benzene (Schemes 1 and 2). The resulting mixtures were refluxed for 4 h with azeotropic distillation of the water formed. After cooling to room temperature, benzene was evaporated under reduced pressure and the residues obtained were recrystallized from appropriate solvent (Table 1).

Acknowledgements

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References

[1] Vögtle F. Supramolekulare Chemie, vol. 1. Stuttgard: Teubner, 1989.

[2] Takagi M, Ueno K. Crown compounds as alkaline earth metal ion selective chromogenic reagents. Topics Curr Chem 1984;121:39–65.

[3] Mateeva N, Deligeorgiev T, Mitewa M, Simova S. Styryl dyes containing an aza-15-crown-5 macroheterocyclic moiety. Dyes and Pigments 1992;20(4):271–8.

[4] Dix J, Vögtle F. Ligandstruktur und Komplexierung, L. lonenselektive Farbstoffkronenether. Chem Ber 1980; 113(2):457–70.

[5] Fery-Forgues S, Le Bris M, Guette J, Valeur B. Ion-responsive fluorescent compounds. 1. Effect of cation binding on photophysical properties of benzoxazinone derivatives linked to monoaza-15-crown-5. J Phys Chem 1988;92(22):6233–7.

[6] Bourson J, Valeur B. Ion-responsive fluorescent compounds 2. Cation-steered intramolecular charge transfer in a crowned merocyanine. J Phys Chem 1989;93(9):3871–6.

[7] Mateeva N, Enchev V, Antonov L, Deligeorgiev T, Mitewa M. Spectroscopic study of the complexation of an aza-15-crown-5 containing chromofluoroionophore with Ba^{2+} and Ca^{2+} cations. J Incl Phenom Mol Recog Chem 1995;20(4):323–33.

[8] Mitewa M, Mateeva N, Antonov L. Spectrophotometric investigation on the complexation between chromo- and fluoroionophores containing aza-15-crown-5 moiety and alkaline and alkaline earth metal ions. Quim Anal (Barcelona) 1997;16(Suppl. 1):S153–0S162.

[9] Alfimov MV, Churakov AV, Fedorov YV, Fedorova OA, Gromov SP, Hester RE, et al. Structure and ion-complexing

properties of an aza-15-crown-5 ether dye: synthesis, crystallography, NMR spectroscopy, spectrophotometry and potentiometry. J Chem Soc Perkin Trans 2 1997;11:2249–56.

[10] Boila-Göckel A, Fabian WMF, Junek H. Synthesis with nitriles, XCVIII. Synthesis and characterization of (aminocyanomethylene)indandione and-pyrazolone chromoionophores as extractants for alkali metal ions. Liebigs Ann Chem 1996;3:397–402.

[11] Boila-Göckel A, Junek H. Spacer-chromoionophores-polymethine dye substituted aza-crown ethers with increased complexation ability. J Prakt Chem 1999;341(1):20–8.

[12] Kovtun JP, Shandura NP, Tolmachev AI. Ionochromic styryl dye bases. Russ J Org Chem 1997;33(11):1669–73.

[13] Schultz RA, White BD, Dishong DM, Arnold KA, Gokel GM. 12-, 15-, and 18-membered ring nitrogen pivot lariat ethers-syntheses, properties, and sodium and ammonium cation binding properties. J Am Chem Soc 1985;107(13): 6659–68.

[14] Kowalska V, Maciejewska D, Wawer I, Angelowa M, Stanoeva E, Mitewa M, et al. In: Proceedings of the 8th Bi-annual International Conference on Dyes and Pigments COLORCHEM 2000. Pardubice: Research Institute for Organic Synthesis, 2000. p. 20.

[15] Antonov L, Vladimirova M, Stanoeva E, Fabian WMF, Ballester L, Mitewa M. Complexation properties of Schiff Bases containing *N*-phenylaza-15-crown-5 moiety. J Incl Phenom (in press).