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# Synthesis and Characterization of Benzo-15-Crown-5 Ethers with Appended N<sub>2</sub>O Schiff Bases

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**Abstract**: New derivatives of benzo-15-crown-5 with flexible appended  $N_2O$  unsymmetrical Schiff bases were prepared by a two step procedure which involves: (i) preparation of  $N_2O$  Schiff bases by condensation of hydrazine with salicylaldehyde, 3-methoxysalicylaldehyde or 2-hydroxy-1-naphtaldehyde and (ii) reaction of the resulting  $NH_2$  functionalized compounds with 4'-formyl-benzo-15-crown-5.

**Keywords:** Schiff base ligands, crown ethers, hetero-binucleating ligands, hydrazine, salicylaldehyde.

## Introduction

The rapidly emerging field of hetero-binucleating ligands and the coordination chemistry of the heteronuclear complexes derived from such ligands [1-4], have prompted an extension of our work on the synthesis and redox chemistry of nickel and copper Schiff base complexes [5-10] towards complexes functionalized with crown ether derivatives. As these latter groups have a large affinity for alkaline, alkaline earth and lanthanides ions [11-14], the redox and electronic properties of the transition metal center can be modulated by the size and charge of the hard metal ions bound to the crown ether moiety. On the other hand, the extent of the interaction of hard cations with transition metal centers, mediated by hetero-binucleating ligands, can be studied by monitoring the redox and

electronic properties of the transition metal ions, and these complexes can ultimately be used as sensors (electrochemical and electronic) for alkaline, alkaline earth and lanthanide metal ions [2-4].

We have already grafted dibenzo18-crown-6-ether and benzo-15-crown-5-ether onto four-dentate  $N_2O_2$  Schiff base ligands [15,16]. These ligands were prepared by Schiff condensation of an aldehyde with a tetra-amine derivative of dibenzo-18-crown-6-ether or with a diamine derivative of benzo-15-crown-5-ether, and have the crown ether moiety grafted rigidly to the Schiff base [15,16]. We are now pursuing the synthesis of Schiff base ligands functionalized with crown ethers, but including a flexible spacer between the two subunits, and in this work we report the synthesis of benzo-15-crown-5 derivatives with appended  $N_2O$  unsymmetrical Schiff bases derived from salicylaldehydes and naphthaldehyde.

#### **Results and Discussion**

The Schiff base ligands with appended benzo-15-crown-5 were prepared in two steps as depicted in Scheme 1.



Scheme 1.

In the first step, we have prepared the new unsymmetrical  $N_2O$  ligands functionalized with  $NH_2$  groups by Schiff condensation of hydrazine with an aldehyde: salicylaldehyde, 3-methoxy-salicylaldehyde or 2-hydroxy-1-naphtaldehyde and the resulting adducts are designated by (Hsh) (I), (Hmsh) (II) and (Hnh) (III), respectively.

In the second step, the NH<sub>2</sub>-functionalized compounds were made to react with 4'-formyl-benzo-15-crown-5 and the products resulting from the second Schiff condensation are the original ligands with an appended crown ether: Hsh-b-15-c-5 (**V**), Hmsh-b-15-c-5 (**VI**) or Hnh-b-15-c-5 (**VII**). The key step in the reactions depicted in Scheme 1 is the preparation of unsymmetrical N<sub>2</sub>O Schiff bases by condensation of the aldehydes with hydrazine, due to the need to prevent formation of the symmetrical ligands (azines). The applied methodology was based on that of the preparation of unsymmetrical Schiff base derived from propylenediamine [17,18], in which the aldehyde is add to a large excess of the diamine to prevent formation of symmetrical ligands. However, the yield of N-(aminoformimidoyl)-6-methoxyphenol (**II**) using this procedure (40.6%) is much smaller than that obtained by adding hydrazine to a solution of 3-methoxysalicylaldehyde (66.2 %). The unsymmetrical compounds precipitate readily from cold solutions, and after being collected by filtration were found to be stable when kept in a dry atmosphere.

In the mass spectra of the unsymmetrical Schiff bases **I**, **II** and **III**, the peak of the molecular ion  $[M^+]$  is the most intense, what confirms the proposed structures. The IR spectra of these compounds show the C=N bond stretching vibration in the region 1623-1617 cm<sup>-1</sup> and a strong and sharp absorption due to free NH<sub>2</sub> at 3420-3380 cm<sup>-1</sup>. The electronic spectra were recorded in N,N'-dimethyl-formamide (DMF) and in the region from 330 to 550 nm, and those of **I** and **II** show one broad band at 355 nm and 358 nm, respectively, which can be deconvoluted into two bands: for **I** the bands appear at 350 nm ( $\varepsilon \approx 445 \text{ dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ ) and 364 nm ( $\varepsilon \approx 90 \text{ dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ ). On the other hand, in the spectrum of **III** four bands can be observed: two very intense ones at 348 and 361 nm ( $\varepsilon \approx 9400 \text{ dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ ) and two less intense ones at 410 and 430 nm ( $\varepsilon \approx 2000 \text{ dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ ).

For compound **V**, the mass spectrum (EI) reveals also the presence of intense peak corresponding to the molecular ion  $[M^+]$ , whereas for those of **VI** and **VII** (FAB), the  $[MH^+]$  peak was observed. With regards to the IR spectra of **V-VII**, it must be stressed that: (a) the band due to the C=N bond stretching does not shift significantly relative to those of the parent compounds; (b) no bands due to NH<sub>2</sub> stretching are present; and (c) new absorptions can be found at values characteristic of aromatic and aliphatic ether groups of crown-ethers: v(Ar-O-C)= 1268-1266 cm<sup>-1</sup> and v(C-O-C)= 1131-1125 cm<sup>-1</sup> [19]. These observations indicate that benzo-15-crown-5 have reacted with the NH<sub>2</sub> functionalized Schiff bases. The electronic spectrum of compound **V** shows one band at 349 nm. That of **VII** exhibits four bands at 371, 387, 404 and 438 nm.

The bands in the electronic spectra of compounds I-III and V-VII are assigned to  $\pi^* \leftarrow n$  and to  $\pi^* \leftarrow \pi$  transitions of the aromatic moieties, as crown ethers do not absorb above 330 nm. The observation that compounds derived from naphthaldehyde exhibit two more bands in the spectral range

used, is a consequence of the more extensive  $\pi$  delocalisation in the naphthaldehyde moiety that lowers the energy of the  $\pi$  orbitals.

## Conclusions

Our motivation behind the synthesis of this type of ligands, formed by condensation of salicylaldehyde (or derived) and NH<sub>2</sub>-functionalized crown ether was is to obtain the respective transition metal (Ni(II) and Cu(II)) complexes. Applications can be envisaged in cation recognition processes, using the spectroscopic and redox properties of transition metal complexes bound to the Schiff base.

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### Experimental

#### General

All solvents were from Merck and all other reagents from Aldrich; all were used as received. Solvents for syntheses were reagent grade and those for UV/Vis studies of analytical grade. Elemental analysis (C, H, N) were performed at the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa (Portugal), and EI and FAB mass spectra at the Facultad de Química, Universidad de Santiago de Compostela (Spain), using 3-nitrobenzylalcohol (NBA) as matrix (FAB). <sup>1</sup>H-NMR spectra were recorded on a Bruker AC 200 at 200 MHz (298 K). Chemical shifts are reported in ppm relative to TMS, used as internal standard. IR spectra in the 400-4000 cm<sup>-1</sup> region were recorded on a Biorad FTS 155, using KBr pellets. UV/Vis spectra were recorded in the 600-330 nm range on a Unicam UV-2, at room temperature, using quartz cells with a 1 cm optical path.

#### Syntheses

#### *N-(aminoformimidoyl)phenol* (Hsh, **I**).

An ethanolic solution of salicylaldehyde (0.99 g, 8.2 mmol) was added dropwise, at room temperature and with stirring, over 1 hour to hydrazine hydrate (98 %) (2.06 g, 40.3 mmol). After the addition was complete, the mixture was stirred for 10 min, and upon cooling in ice, a whitish solid appeared, which was collected by filtration, washed with diethyl ether and dried under vacuum. Yield 0.83 g (79.8 %). Anal. Calcd. for  $C_7H_8ON_2$ : C, 61.75; H, 6.09; N, 20.58. Found: C, 62.08; H, 6.11; N,

20.62. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): & 11.07 (s, 1H, -OH), 7.87 (s, 1H, -CHN), 7.22-7.18 (m, 1H, arom H), 7.12-7.09 (m, 1H, arom H), 6.96-6.93 (m, 1H, arom H), 6.89-6.86 (m, 1H, arom H), 5.43 (s, 2H, -NH<sub>2</sub>). MS (EI) m/z (%): 136 (M<sup>+</sup>, 100). IR (KBr) v/cm<sup>-1</sup>: 3383, 3280, 1617, 1572, 1491, 1465, 1405, 1271, 1198, 1097, 940, 898, 784, 749, 705, 642, 558. UV/Vis (DMF)  $\lambda_{max}/nm$  ( $\epsilon/dm^{3}mol^{-1}cm^{-1}$ ): 355 (504).

## *N-(aminoformimidoyl)-6-methoxyphenol* (Hmsh, II).

A hydrazine hydrate solution (80 %) (2.80 g, 44.7 mmol) was added dropwise, at room temperature and with stirring, over 5 min to an ethanolic solution of 3-methoxysalicylaldehyde (4.82 g, 31.7 mmol). The resulting light yellow coloured solid was washed with diethyl ether and dried under vacuum. Yield 3.52 g (66.2 %). Anal. Calcd. for  $C_8H_{10}O_2N_2$ : C, 57.82; H, 6.07; N, 16.86. Found: C, 57.97; H, 5.95; N, 16.93. <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  11.20 (s, 1H, -OH), 7.86 (s, 1H, -CHN), 6.85-6.72 (m, 3H, arom H), 5.48 (s, 2H, -NH<sub>2</sub>), 3.90 (s, 3H, -OCH<sub>3</sub>). MS (EI) m/z (%): 166 (M<sup>+</sup>, 100). IR (KBr) v/cm<sup>-1</sup>: 3416, 3369, 1623, 1573, 1468, 1411, 1320, 1257, 1247, 1089, 1072, 965, 928, 838, 813, 777, 731, 620. UV/Vis (DMF)  $\lambda_{max}$ /nm ( $\epsilon$ /dm<sup>3</sup>mol<sup>-1</sup>cm<sup>-1</sup>): 358 (856).

## *N-(aminoformimidoyl)naphthol* (Hnh, III).

This compound was prepared following the procedure described for **I**, but adding a methanolic solution of 2-hydroxy-1-naphtlaldehyde (0.87 g, 5.1 mmol) to hydrazine hydrate (98 %) (1.29 g, 25.3 mmol). After the addition was complete, the yellow-golden solid was collected by filtration, washed with diethyl ether and dried under vacuum. Yield 0.62 g (65.9 %). Anal. Calcd for  $C_{11}H_{10}ON_2$ : C, 70.95; H, 5.41; N, 15.04. Found: C, 70.53; H, 5.65; N, 15.22. <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  12.33 (s, 1H, -OH), 8.80 (s, 1H, -CHN), 8.00-7.97 (d, 1H, arom H), 7.78-7.71 (m, 2H, arom H), 7.51-7.46 (m, 1H, arom H), 736-7.31 (t, 1H, arom H), 7.21-7.18 (d, 1H, arom H), 5.54 (s, 2H, -NH<sub>2</sub>). MS (EI) m/z (%): 186 (M<sup>+</sup>, 100). IR (KBr) v/cm<sup>-1</sup>: 3390, 3375, 1621, 1603, 1579, 1466, 1417, 1315, 1281, 1241, 1181, 1082, 794, 747. UV/Vis (DMF)  $\lambda_{max}$ /nm ( $\epsilon$ /dm<sup>3</sup>mol<sup>-1</sup>cm<sup>-1</sup>): 348 (9415), 361 (9353), 410 (2383), 430 (1908).

## 4'-Formylbenzo-15-crown-5 (IV).

This compound [20] was prepared from the reaction of 1,11-dichloro-3,6,9-trioxaundecane (53.3 g, 180.0 mmol) with 3,4-dihydroxybenzaldehyde (25.0 g, 181.0 mmol) and NaOH (15.1 g, 377.5 mmol) in water/*n*-butanol. After recrystallization from hot *n*-heptane and activated charcoal, a white crystalline solid was obtained (12.44 g). Yield 23.3 %. <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  9.83 (s, 1H, -CHO), 7.46-7.38 (m, 2H, arom H), 6.96-6.92 (d, 1H, arom H), 4.23-4.17 (m, 4H, -CH<sub>2</sub>), 3.96-3.90 (m, 4H, -CH<sub>2</sub>), 3.80-3.75 (m, 8H, -CH<sub>2</sub>). MS (EI) m/z (%): 416 (M<sup>+</sup>, 100).

#### *N-(formimidoyl-benzo-15-crown-5)-N'-(formimidoyl)phenol* (Hsh-b-15-c-5, V).

To an ethanolic solution of **IV** (0.88 g, 3.0 mmol) was added a solution of **I** (0.34 g, 2.5 mmol) in ethanol. The mixture was refluxed for 3 h. The resulting light yellow compound was washed with ethanol. The compound was recrystallized from methanol and dried under vacuum. Yield 0.69 g (66.6 %). Anal. Calcd for  $C_{22}H_{26}O_6N_2$ : C, 63.76; H, 6.32; N, 6.76. Found: C, 64.34; H, 6.70; N, 6.58. <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  11.85 (s, 1H, -OH), 8.75-8.73 (d, 1H, -CHN), 8.56-8.53 (d, 1H, -CHN), 7.50-7.22 (m, 4H, arom H), 7.04-6.66 (m, 3H, arom H), 4.26-4.18 (m, 4H, -CH<sub>2</sub>), 3.97-3.92 (m, 4H, -CH<sub>2</sub>), 3.71-3.68 (m, 8H, -CH<sub>2</sub>). MS (EI) m/z (%): 414 (M<sup>+</sup>, 100). IR (KBr) v/cm<sup>-1</sup>: 2932, 2867, 1622, 1598, 1567, 1508, 1449, 1428, 1411, 1344, 1306, 1268, 1226, 1174, 1125, 1055, 1017, 986, 968, 941, 844, 813, 746. UV/Vis (DMF)  $\lambda_{max}/nm$  ( $\epsilon/dm^{3}mol^{-1}cm^{-1}$ ): 344 (26137), 356 (26698).

#### *N-(formimidoyl-benzo-15-crown-5)-N'-(formimidoyl)-6-methoxyphenol* (Hmsh-b-15-c-5 VI).

This compound was prepared by the procedure described for **V**, but using **II** (0.17 g, 1.0 mmol) and **IV** (0.37 g, 1.2 mmol). The resulting light yellow solid was washed with diethyl ether. The compound was recrystallized from methanol and dried under vacuum. Yield 0.37 g (81.6 %). Anal. Calcd for C<sub>23</sub>H<sub>28</sub>O<sub>7</sub>N<sub>2</sub>: C, 62.15; H, 6.35; N, 6.30. Found: C, 61.63; H, 6.40; N, 6.42. <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  11.81 (s, 1H, -OH), 8.75-8.71 (d, 1H, -CHN), 8.56-8.52 (d, 1H, -CHN), 7.49 (s, 1H, arom H), 7.29-7.26 (m, 1H, arom H), 7.00-6.87 (m, 4H, arom H), 4.26-4.18 (m, 4H, -CH<sub>2</sub>), 3.94-3.92 (m, 7H, -CH<sub>2</sub>, -OCH<sub>3</sub>), 3.78-3.75 (m, 8H, -CH<sub>2</sub>). MS (FAB) m/z (%): 445 ([M+H]<sup>+</sup>, 15). IR (KBr) v/cm<sup>-1</sup>: 2930, 2874, 1623, 1601, 1577, 1511, 1464, 1436, 1310, 1266, 1131, 1095, 1078, 1052, 966, 736. UV/Vis (DMF)  $\lambda_{max}/nm$  ( $\epsilon/dm^{3}mol^{-1}cm^{-1}$ ): 340 (39706), 349 (38578).

### N-(formimidoyl-benzo-15-crown-5)-N'-(formimidoyl)-naphthol (Hnh-b-15-c-5 VII).

This compound was prepared by a modification of the procedure described for **V**. To a methanolic solution of **IV** (0.20 g; 0. 7 mmol) was added a solution of **III** (0.10 g; 0.5 mmol) in methanol. The mixture was refluxed for 4.5 h. The resulting yellow solid was washed with diethyl ether, recrystallized from ethanol and dried under vacuum. Yield 0.09 g (35.9 %). Anal. Calcd for  $C_{23}H_{28}O_7N_2 \cdot 1/2$   $C_3H_5O$ : C, 66.51; H, 6.41; N, 5.70. Found: C, 66.73; H, 6.15; N, 5.68. <sup>1</sup>H-NMR ((CD<sub>3</sub>)<sub>2</sub>SO):  $\delta$  13.02 (s; 1H, -OH), 9.87 (d; 1H, -CHN), 8.78 (d; 1H, -CHN), 8.67-8.49 (m; 1H, arom H), 8.06-7.88 (m; 2H, arom H), 7.62-7.42 (m; 6H, arom H), 4.13-4.11 (m; 4H, -CH<sub>2</sub>), 3.81-3.80 (m; 4H, -CH<sub>2</sub>), 3.68-3.67 (m; 8H, -CH<sub>2</sub>). MS (FAB) m/z (%): 464 ([M+H]<sup>+</sup>, 84). IR (KBr) v/cm<sup>-1</sup>: 3445, 3408, 2931, 2876, 1720, 1623, 1580, 1544, 1512, 1436, 1419, 1405, 1278, 1239, 1183, 1137, 1052, 721, 501. UV/Vis (DMF)  $\lambda_{max}/nm$  ( $\epsilon/dm^3mol^{-1}cm^{-1}$ ): 339 (27858), 371 (30539), 387 (33496), 404 (27812), 438 (4165).

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