

## Synthesis and Spectral Investigation of Some New Crown Ether Ligands

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The new crown ether ligands (5–6) were synthesized by condensation of 4'-formyl-5'-hydroxybenzo-15-crown-5 (4) with 2-chloroaniline and 3-bromoaniline. The structure of these compounds have been elucidated on the basis of elemental analyses, IR,  $^1\text{H}$ ,  $^{13}\text{C}$  NMR, and UV-Vis spectroscopic techniques. The UV-V is spectra of the ligands (5–6) were studied in polar and non-polar solvents, as well as in acidic and basic media. The results indicate that the tautomeric equilibria (phenol-imine  $\text{O}-\text{H}\cdots\text{N}$  and keto-amine  $\text{O}\cdots\text{H}-\text{N}$  forms) are present only in the EtOH solution. But in other solvents (DMSO,  $\text{CHCl}_3$ , *n*-hexane), acidic and basic media only the phenol-imino form is dominant.

**Key Words:** Crown ether, Schiff base, Tautomerism, UV-Vis spectroscopy.

### INTRODUCTION

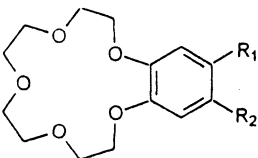
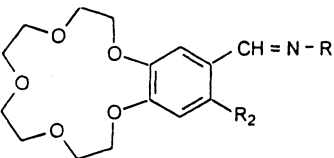
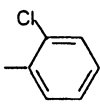
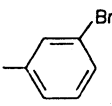
After the first report<sup>1</sup> on the synthesis of crown ethers, there has been a large amount of research on crown ethers and their reactions<sup>2–6</sup>. The number of new macrocyclic ligand molecules designed and synthesized has increased significantly and their structures have become much more complex. The incorporation of ionophoric groups in bioactive compounds to modify the corresponding pharmacokinetic properties have been adjusted in drug design. Among the possible ionophoric groups to be considered crown ethers have deserved a special attention<sup>7</sup>. Based on crown ether chemistry, new substitute crown ethers have been designed. Diverse substitute benzocrown ethers have been synthesized by either electrophilic substitution to benzocrown ethers or crown ring forming cyclization of substituted catechols<sup>8</sup>. For example, hydroxyformyl substitute benzocrown ethers are considered to be interesting starting materials for the synthesis of new molecules and utility of the reactive groups on the aromatic ring<sup>9</sup>. Crown ether Schiff base ligands are important molecules extensively studied with respect to their high affinity to interact with alkali and transition metal ions<sup>9–12</sup>. Schiff bases formed by the condensation of aromatic amines with aromatic aldehydes that contain an *ortho* hydroxy group can exist in two tautomers, namely a phenol-imine form and keto-amine form<sup>13–15</sup>. The proton

transfer from the phenolic oxygen atom to the imine nitrogen atom requires a small amount of energy (obtained by temperature or light changes), but causes remarkable structural changes within the molecule, especially in the  $\pi$ -electron distribution. Such changes are closely connected with the colour change of the substance known as thermochromism and photochromism<sup>17</sup>.

In this paper, we report the synthesis and characterization of new crown ether Schiff base ligands (**5** and **6**). Furthermore, we examine the keto-amine and phenol-imine forms of the ligands by the UV-Vis spectrophotometric method.

## RESULTS AND DISCUSSION

**Synthesis:** The structures of the compounds studied are given in **Scheme-1**. The condensation of equivalent amounts of 4'-formyl-5'-hydroxybenzo-15-crown-5 (**4**) and the appropriate amine, 2-chloroaniline or 3-bromoaniline in dry solvents, gave the respective Schiff base products (**5** and **6**). The new compounds gave spectroscopic and analytical data in accordance with the proposed structure.

	R <sub>1</sub>	R <sub>2</sub>	Compound
	H	H	<b>1</b>
	CHO	H	<b>2</b>
	H	OH	<b>3</b>
	CHO	OH	<b>4</b>
		OH	<b>5</b>
		OH	<b>6</b>

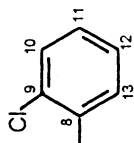
**Scheme-1**

In the IR spectra of compounds (**5** and **6**), no band is observed in the region 3650–3590  $\text{cm}^{-1}$  attributable to the stretching vibration of the free phenolic hydroxy group<sup>18</sup>, indicating the formation of a ring by the intramolecular hydrogen bond. An intramolecular hydrogen bond exists between the hydroxyl oxygen atom and the imine nitrogen atom, as determined from the X-ray structural results<sup>19, 20</sup>. A relatively strong band attributable to  $\nu(\text{C}=\text{N})$  is detected at 1627 in (**5**) and at 1619  $\text{cm}^{-1}$  in (**6**). The alkyl and aryl ether stretching bands are observed at 1054–1130 and 1270–1286  $\text{cm}^{-1}$ , respectively.

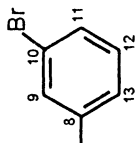
The <sup>1</sup>H NMR data of the crown ethers (**5** and **6**) are listed in Table-1. In the

Numbering of the crown ether carbons and protons.

**R** \_\_\_\_\_ **Comp.** \_\_\_\_\_



**5**



**6**

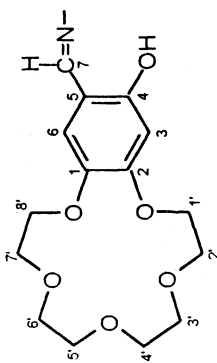


TABLE-1  
<sup>1</sup>H NMR SPECTRAL DATA. CHEMICAL SHIFTS

Compd.	OCH <sub>2</sub> CH <sub>2</sub> O	ArH(3)	ArH(6)	HC≡N	ArH(9)	ArH(10)	ArH(11)	ArH(12)	ArH(13)	OH
<b>5</b>	3.75-4.21 (m, 16H)	6.94 (s, 1H)	6.68 (s, 1H)	8.55 (s, 1H)	—	7.49 (d, 1H; j = 7.8 Hz)	7.35 (d <sup>a</sup> , 1H)	7.35 (d <sup>a</sup> , 1H)	7.23 (m, 1H)	13.40 (bs, 1H)
<b>6</b>	3.75-4.20 (m, 16H)	6.89 (s, 1H)	6.63 (s, 1H)	8.46 (s, 1H)	b	—	b	b	b	13.10 (bs, 1H)

δ [in ppm] (S: singlet, D: doublet, M: multiplet, BS: broad singlet)

<sup>a</sup>Ar—H<sub>11</sub> overlapping with Ar—H<sub>12</sub> peaks.

<sup>b</sup>The peaks are observed as multiplets between 7.44-7.22 ppm.

$^1\text{H}$  NMR spectra of the ligands (**5** and **6**) the OH protons give a broad singlet at 13.40 and 13.10 ppm, respectively. The characteristic azomethine peaks are observed as singlets at 8.55 and 8.46 ppm for the ligands (**5** and **6**), showing that these ligands are dominantly phenol-imine form in  $\text{CDCl}_3$ . The crown ether protons ( $\text{OCH}_2\text{C}(\text{H}_2\text{O})$ ) appear as multiplets between 3.75–4.21 ppm, respectively.

The  $^{13}\text{C}$  NMR data for the ligands (**5** and **6**) are summarized in Table-2. In the  $^{13}\text{C}$  decoupled NMR spectra of the compounds, eight crown ether carbons ( $\text{C}_1$ – $\text{C}_8$ ) are observed between 67.83–71.50 ppm, for the other aromatic ring carbon ( $\text{C}_1$ – $\text{C}_{13}$ ) signals are between 101.83–166.09 ppm.

TABLE-2  
SELECTED  $^{13}\text{C}$  NMR SPECTRAL DATA ( $\delta$ , [ppm])  
(For the numbering scheme see Table-1)

Compd.	$\text{C}_1$ – $8$	$\text{C}_1$ – $13$
<b>5</b>	68.73; 69.15; 69.33; 69.85 69.96; 70.83; 70.90; 71.50	102.16; 113.10; 117.06; 119.14
		125.30; 129.76; 140.93; 149.66
		152.65; 159.69; 160.07; 163.14
		166.09
<b>6</b>	67.83; 68.22; 68.58; 69.07 69.42; 69.68; 69.92; 70.11	101.83; 112.67; 116.88; 118.14
		124.76; 127.43; 139.66; 142.98
		145.10; 151.62; 157.18; 160.27
		164.13

The tautomeric equilibrium has been systematically studied by UV-Vis absorption spectra. The UV-Vis spectra of the crown ethers (**5** and **6**) were studied in polar, nonpolar, acidic ( $\text{CF}_3\text{COOH}$ ) and basic ( $\text{NEt}_3$ ) media. The calculated ratio of the keto-amine tautomers are listed in Table-3. Figs. 1 and 2 show the corresponding UV-Vis spectra of compounds (**5** and **6**) in different solvents. In solutions the tautomerism depends on the solvent polarity<sup>21–23</sup> and the ability of the solvents to form hydrogen bonds. In previous papers<sup>22, 23</sup>, in polar solvents, a new band arises at approximately 400 nm and has been logically linked to the shift of tautomeric equilibrium to the keto-amine form. This absorption band is not observed in non-polar solvents. As the solvent polarity decreases, in solvents the ratio of the keto-amine form is also seen to decrease ( $\text{EtOH} > \text{CHCl}_3 > n$ -hexane) from the UV-Vis spectra. In the present paper, although the phenol-imine/keto-amine tautomeric forms could be expected for (**5** and **6**), only the phenol-imine form is present<sup>24</sup> in DMSO,  $\text{CHCl}_3$ ,  $n$ -hexane, acidic and basic media. However, the phenol-imine/keto-amine tautomeric equilibria are present in EtOH solution, which is perhaps a consequence of the hydrogen bonding character of EtOH. Results of a study of the solvent effect on the phenol-imine/keto-amine tautomerism of crown ether ligands (**5** and **6**) performed by measuring the UV-Vis spectra have shown that the interactions of the Schiff bases with solvent molecules are of local character.

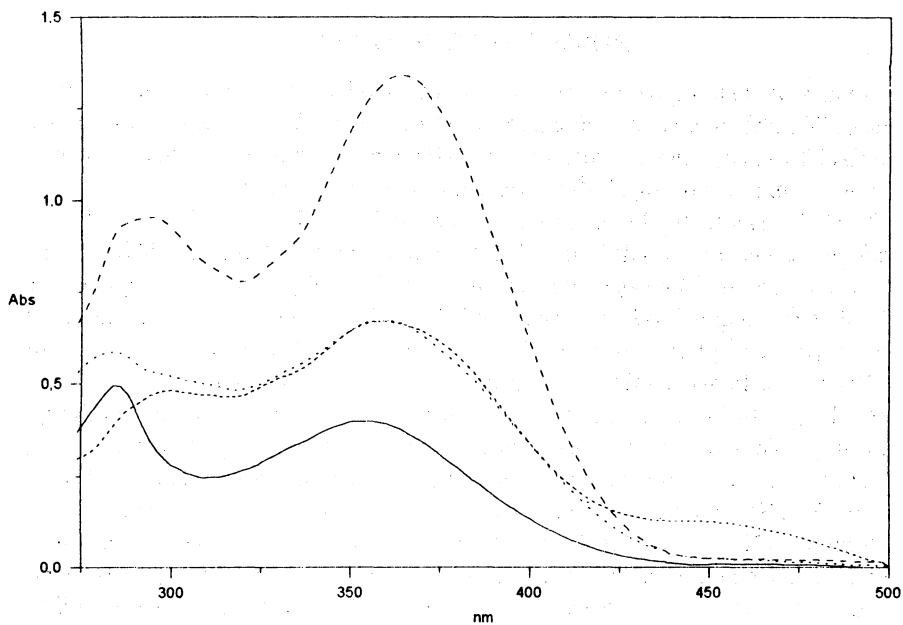


Fig. 1. UV-Vis spectra showing solvent effect on compound (5) (DMSO .....; EtOH ---; CHCl<sub>3</sub> —; *n*-hexane ———),  $C = 5 \cdot 10^{-5} \text{ mol dm}^{-3}$

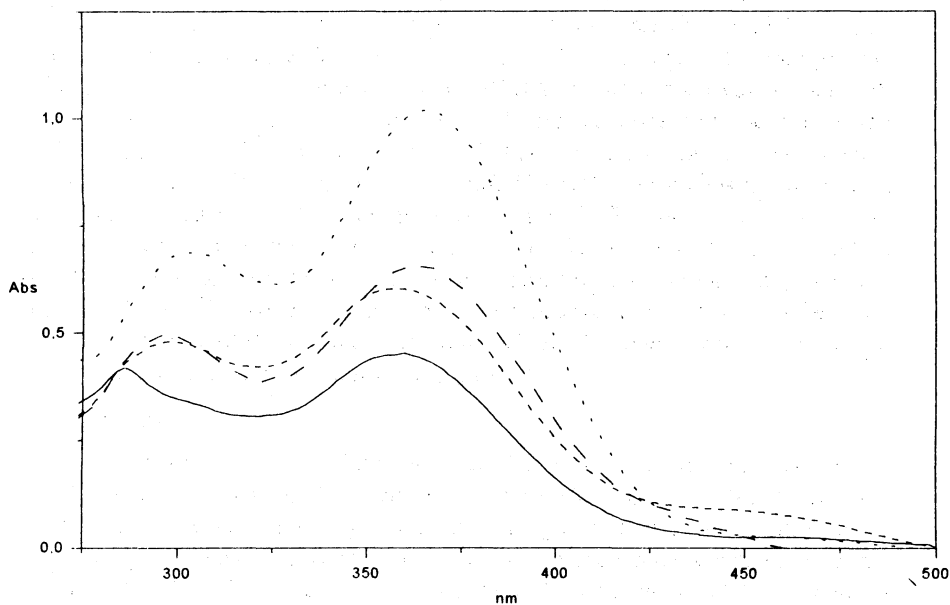


Fig. 2. UV-Vis spectra showing solvent effect on compound (6) (DMSO .....; EtOH ---; CHCl<sub>3</sub> —; *n*-hexane ———),  $C = 5 \cdot 10^{-5} \text{ mol dm}^{-3}$

TABLE-3  
UV-VIS SPECTRAL DATA FOR THE LIGANDS (5-6)

Compd.	Solvent	$\lambda$ [nm](log $\epsilon$ ) <sup>a</sup>	% Keto isomer <sup>b, c</sup> Solvent medium
5	DMSO	360(4.12); 284 (4.06)	0.0
	EtOH	358 (4.12); 446 (3.40)	16.26
	CHCl <sub>3</sub>	354 (3.90); 284 (3.99)	0.0
	n-Hexane	364 (4.42); 292 (4.27)	0.0
6	DMSO	366 (4.30); 304 (4.13)	0.0
	EtOH	358 (4.07); 444 (3.25)	13.29
	CHCl <sub>3</sub>	360 (3.95); 286 (3.92)	0.0
	n-Hexane	364 (4.11); 296 (3.99)	0.0

<sup>a</sup> For the solvent medium.

<sup>b</sup> 0% in acidic medium, attained by addition of CF<sub>3</sub>COOH (1 mL) to the given solution (ligand concentration  $5 \cdot 10^{-5}$  mol dm<sup>-3</sup>).

<sup>c</sup> Per thousand in basic medium, basic medium is attained by addition of NEt<sub>3</sub> (1 mL) to the given solution (ligand concentration  $5 \cdot 10^{-5}$  mol dm<sup>-3</sup>).

### EXPERIMENTAL

The starting compounds, tetraethylene glycol dichloride<sup>25</sup>, benzo-15-crown-5 (1)<sup>1</sup>, 4'-formylbenzo-15-crown-5 (2)<sup>26</sup>, 4'-hydroxybenzo-15-crown-5 (3)<sup>27</sup>, 4'-formyl-5'-hydroxybenzo-15-crown-5 (4)<sup>9</sup> were prepared according to literature methods.

Melting points were determined with a Gallencamp apparatus without correction. The elemental analyzer was a LECO CHNS-932 instrument. IR absorption spectra were obtained from a Mattson 1000 FTIR spectrometer using KBr pellets in the range 4000–400 cm<sup>-1</sup>. <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured in CDCl<sub>3</sub> on a Bruker DPX FT-NMR (400 MHz) spectrometer (SiMe<sub>4</sub>, as internal standard). UV-V is spectra were recorded using a UNICAM UV2-100 series spectrometer.

#### 4'-Formyl-5'-Hydroxybenzo-15-crown with 2-Chloroaniline Schiff Base (5)

A solution of 4'-formyl-5'-hydroxybenzo-15-crown-5 (4) (0.50 g, 1.60 mmol) in dry methanol (50 mL) was added dropwise to a solution of 2-chloroaniline (0.20 g, 1.60 mmol) in methanol (50 mL). The mixture was maintained at a temperature of 60°C for 1 h, then allowed to come to ambient temperature. The raw material was recrystallized from *n*-heptane (0.39 g, 58%); m.p. 109°C. Anal. Calcd. for C<sub>21</sub>H<sub>24</sub>O<sub>6</sub>NCl: C, 59.84; H, 5.74; N, 3.33; Found: C, 59.67; H, 5.59; N, 3.02. IR (KBr): 2936, 2867 (C—H<sub>aliph.</sub>), 1627 (C=N), 1507 (C=C), 1286 (C—O—C<sub>arom.</sub>), 1126–1055 (C—O—C<sub>aliph.</sub>) cm<sup>-1</sup>.

#### 4'-Formyl-5'-Hydroxybenzo-15-Crown-5 with 3-Bromoaniline Schiff Base (6)

A solution of 4'-formyl-5'-hydroxybenzo-15-crown-5 (4) (0.50 g, 1.60 mmol) in dry THF (50 mL) was added dropwise to a solution of 3-bromoaniline (0.27 g, 1.60 mmol) in THF (50 mL). The mixture was refluxed for 1 h, then allowed

to come to ambient temperature. The raw material was recrystallized from n-heptane, yield 0.56 g (67%), m.p. 91°C. Anal. (%), Calcd. for  $C_{21}H_{24}O_6NBr$ : C, 54.18; H, 5.20; N, 3.01; Found: C, 53.94; H, 5.57; N, 3.32. IR (KBr): 2927, 2867 (C—H<sub>aliph.</sub>), 1619 (C=N), 1507 (C=C), 1279 (C—O—C<sub>arom.</sub>), 1130–1054 (C—O—C<sub>aliph.</sub>)  $cm^{-1}$ .

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