

## Synthesis of Macroheterocycles and Complexation With Palladium(II) and Silver(I)

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In present studies, the synthesis of 2-chloroquinoline-3-carbaldehyde derivatives from acetanilide as starting materials, to prepare macroheterocycles and their reaction with heavy metals to test the selectivity of extracting them from their mixtures in the industrial residues are reported.

**Key Words:** Vilsmeier reagent, Quinoline, Wittig reaction, Aldolization, Macrocycles.

### INTRODUCTION

The structure-activity relationship at active sites of metalloenzymes is a matter of continuing interest<sup>1</sup>. Homoleptic thioether crowns are now well known to bind to a wide range of transition-metal ions to give complexes exhibiting unusual stereochemical and redox properties<sup>2</sup>. Mixed donor thioether-aza<sup>3</sup> and thioether-oxa crowns are known, as well as those incorporating aryl **4** and/or heteroaryl **5,6** frameworks within the ring. There are no reports in the literature on mixed quinoline Schiff-base thioether macrocycles. Complexes of mixed aza-thioether ligands represent useful model compounds for metalloenzymes in biological systems<sup>4</sup>. Although bipyridyl and quinolyl moieties have been incorporated into Schiff-base azamacrocycles, crown ethers **1,2**, cryptands and catenands<sup>5</sup>, but no data are available on the other crowns incorporating these fragments.

Vefa Ahsen and co-workers<sup>6</sup> reported that, the 4-({3,4,5-*tris*-[2-(2-ethoxyethoxy)ethoxy]benzyl}oxy) and 4-({3,4,5-*tris*-[2-(2-ethoxyethoxy)ethoxy]benzyl}thio) zinc(II) phthalocyanines have showed photophysical and photochemical properties. These complexes also show potential as type II photosensitizers.

Previously, the synthesis of 2-chloroquinoline-3-carbaldehyde derivatives from acetanilides, using the optimized conditions already described<sup>7</sup>, a variety of quinoline derivatives were synthesized from a series of anilides<sup>8</sup>. These quinoline carbaldehydes

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were subjected to condensation with acetophenone derivatives in presence of NaOH and refluxing in suitable solvent<sup>9</sup> to give a series of chalcone derivatives, some of them are anticancer compounds<sup>10</sup>. In the present work, we used these quinoline derivatives to prepare macroheterocycles and react them with heavy metals to test the selectivity of extracting them from their mixtures.

We report herein the synthesis of the new mixed thia-quinolyl crowns and the preparation and characterization of their Pd(II) and Ag(I) complexes.

### EXPERIMENTAL

All 300 MHz <sup>1</sup>H and 75 MHz <sup>13</sup>C NMR spectra were run on a Bruker AC 300 spectrometer, 200 MHz NMR spectra were run on a Bruker AC 200NMR spectrophotometer. <sup>13</sup>C NMR spectra were recorded using distortionless enhancement by polarization transfer. Both <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded using CDCl<sub>3</sub> as internal standard. Fast atom bombardment (FAB) were recorded with a Kratos MS50 with a *meta*-nitro benzyl alcohol matrix. Accurate mass determinations were carried out on a Kratos Concept IS spectrometer. Elemental analyses were performed using a Carlo-Erba 1106 elemental analyzer. Infrared spectra were recorded using a Perkin-Elmer 783 spectrometer equipped with a PE 600 data station. Melting points were determined using an electrothermal melting point apparatus and were uncorrected. Column chromatography was conducted using silica gel 60 230-400 mesh (Merck & Co.). Silica thin layer chromatography TLC was conducted on precoated aluminium sheets (60 F 254) with a 0.2 mm thickness (Aldrich Chemical Co.).

Synthesis of quinolinecarbaldehydes were carried out by reported methods<sup>3,4</sup>. Spectral data of 2-chloro-3-formyl substituted quinoline and its Schiff bases are given in Tables 1 and 2, respectively.

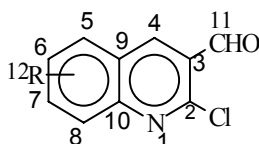
**Synthesis of compound 3:** The quinolinecarbaldehyde **1** (1.03 g, 5 mmol) was dissolved in hot ethanol and ethylenediamine (0.17 mL, 2.5 mmol) was added at room temperature, a white precipitate was formed immediately. The reaction mixture was refluxed for 1 h, it was cooled, the precipitate was washed with ethanol and recrystallized from toluene to give white needles (1.05 g, yield 96 %), m.p. 212 °C, spectral data are shown on Tables 3 and 4.

**Synthesis of compound 4:** The quinoline carbaldehyde **2** was treated as above to obtain a white needles after recrystallization from toluene (1.05 g, yield 90 %) m.p. 215 °C.

**Synthesis of compound 5:** A solution of 60 % NaH in toluene (0.446 g, 4 mmol) was added to a solution of ethylenedithiol in toluene (0.84 g, 2 mmol), then (0.87 g, 2 mmol) of compound **3** was added to the reaction mixture and refluxed for 1 h to give precipitate which recrystallized from toluene to obtain greenish needles.

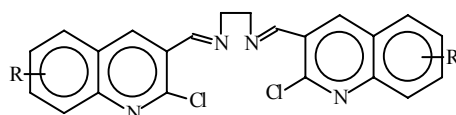
**Synthesis of compounds 6 and 7:** Sodium metal (0.138 g, 6 mmol) was dissolved in a commercial absolute ethanol (10 mL) under dry nitrogen and 1,4,8,11-tetrathiaundecane (0.685 g, 3 mmol) in 20 mL ethanol, was added cautiously. The resulting mixture was heated to reflux for 0.5 h and a solution of compound **1** in ethanol 40 mL

TABLE-1  
<sup>1</sup>H NMR AND <sup>13</sup>C NMR CDCl<sub>3</sub> OF 2-CHLORO-3-FORMYL-SUBSTITUTED QUINOLINE



Compound	H-4	H-5	H-6	H-7	H-8	CHO			
1;R=6Me	8.65 s	7.69d,J 2.5	CH <sub>3</sub> =2.59 s	7.60dd;J 2.5; 8.5	7.95d J 8.5	10.50			
2;R=7MeO	8.65 s	7.86d, 9.5	7.20dd9.5, 2.5	MeO=4.02 s	7.27d 2.5	10.45 s			
Compound	C2	C3	C4	C5	C6	C7,8,9	C10	C11	C12
1;R=6Me	139.52	126.59	140.00	136.00	135.93	128.32	138.00	189.29	21.54
2;R=7MeO	164.16	124.33	139.47	130.78	108.60	121.47	151.91	190.00	55.60

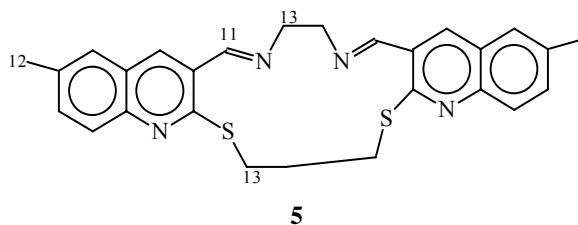
TABLE-2  
<sup>1</sup>H AND <sup>13</sup>C NMR OF SCHIFF BASES



**3**, R= 6 Me, **4**, R= 7 OMe

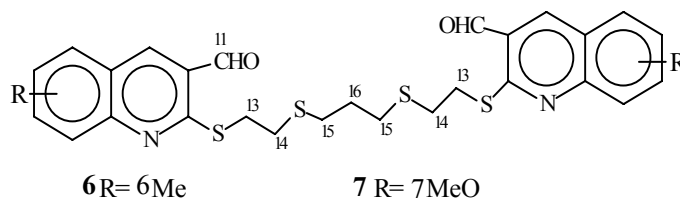
Compd.	H-4	H-5	H-6	H-7	H-8	H-11	CH <sub>2</sub> CH <sub>2</sub>			
3;R=6Me	8.66 s	7.60 d; J 2.5	2.5 s	7.59 dd; J 2.5; 8.5	7.90 d; J 8.5	8.80 s	4.15 s			
4;R=7MeO	8.68 s	7.69d 9.5	7.20 dd, 2.5; 9.5	3.90 s	7.27 d, 2.5	8.85 s	4.10 s			
Compd.	C2	C3	C4	C5	C6	C7,8,9	C10	C11	C12	C13
3;R=6Me	148.77	127.32	136	133.92	137.56	127.32	146.00	158.95	21.54	61.49
4;R=7MeO	149.16	124.33	139.47	130.78	108.60	121.47	147.91	159.84	55.60	61.59

TABLE-3  
<sup>1</sup>H AND <sup>13</sup>C NMR, δ, ppm CDCl<sub>3</sub> OF MACROHETROCYCLE (**5**)



Compd.	H-4	H-5	H-6	H-7	H-8	H-11	2(CH <sub>2</sub> CH <sub>2</sub> )			
5;R=6Me	8.79 s	7.60 m	2.5 s	7.58m	7.95 d J=9.5	8.82 s	4.16 s			
2;R=7MeO	8.68 s	7.69d 9.5	7.20 dd, 2.5; 9.5	3.90 s	7.27 d, 2.5	8.85 s	4.10 s			
Compd.	C2	C3	C4	C5	C6	C7,8,9	C10	C11	C12	C13
5;R=6Me	140.77	127.32	136.79	134.02	137.56	127.42	140	160.60	21.54	61.49

TABLE-4  
<sup>1</sup>H AND <sup>13</sup>C NMR δ ppm, CDCl<sub>3</sub> OF SUBSTITUTED QUINOLINE CARBALDEHYDE



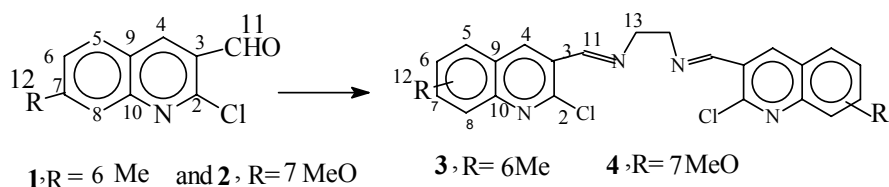
Compd.	H-4	H-5	H-6	H-7	H-8	CHO	
6;R=6Me	8.25s	7.60d; J 2.5	2.45 s; Me	7.59 dd; J 2.5;8.5	7.82 d J 8.5	10.25 s	
7;R=7MeO	8.69 s	7.95 d 9.5	7.10-7.20m	3.95 s	7.10-7.20 m	10.20 s	
Compd.	C2	C3	C4	C5	C6	C7,8,9	C10
6;R=6Me	178.99	127.32	141.61	128.82	137.56	127.32	169.27
7;R=7MeO	165.30	124.69	143.74	130.78	108.60	121.47	147.91
Compd.	C11	C12	C13	C14	C15	C16	
6;R=6Me	189.66	23.47	31.60	36.60	30.95	29.29	
7;R=7MeO	159.84	55.60	31.60	36.60	30.95	29.29	

(1.23 g, 6 mmol) was added drop wise with stirring, a yellowish precipitate was formed, after stirring for 1 h. It was filtered, washed with cold water and dissolved in chloroform, the filtrate was evaporated, the residue was recrystallized from ethanol a yellow needles were formed.

**Synthesis of compounds 8 and 9:** 0.146 g, 0.25 mmol of compound 6 was dissolved in 20 mL. THF, then a solution of AgNO<sub>3</sub> (0.283 g, 0.5 mmol), in THF and few drops of water, then 10 mL of this solution was taken and added to the mixture a white precipitate was formed immediately, it was filtered, washed with THF, it was recrystallized from toluene to give 0.335 g, of compound 8. Similarly, the complexe 9 was also prepared by same procedure.

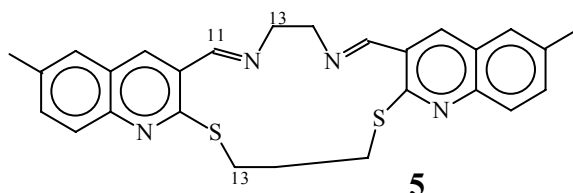
## RESULTS AND DISCUSSION

In the present work, Schiff-bases were prepared by reacting the quinoline carbaldehydes with ethylene diamine, to obtain a new compounds shown on **Scheme-I**.



**Scheme-I**

The compound 3 reacted with HSCH<sub>2</sub>CH<sub>2</sub>SH to give a heteromacrocycle 5, its mass spectrum showed a molecular ion peak at m/z, 456 corresponds to the proposed structure.



These compounds showed a very simple and clean  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra, where H-4 and H-11, appear as a singlets in the region 8.50-8.95 ppm as shown on Tables 1 and 5. Another derivatives were also synthesized by substituting the chlorine atoms with thiols to obtain compounds **6** and **7**.

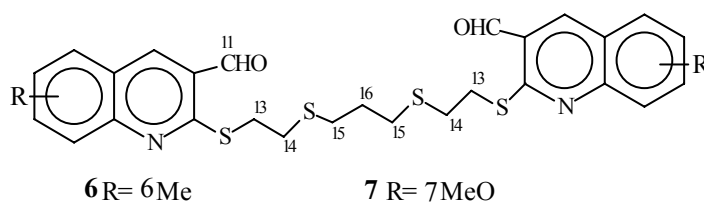
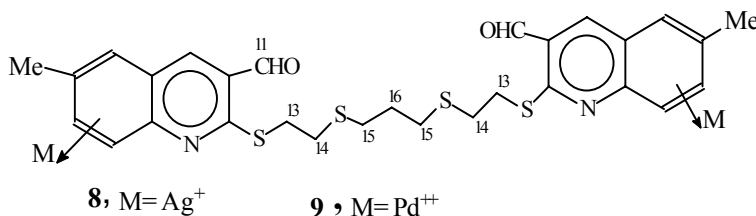
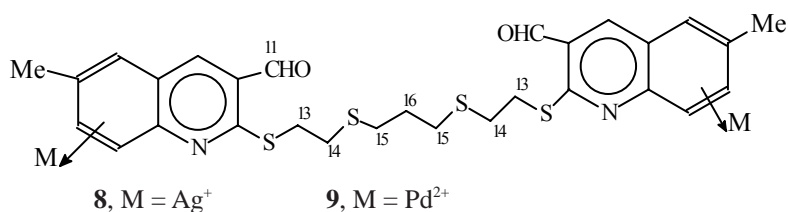


TABLE-5  
 $^1\text{H}$  AND  $^{13}\text{C}$  NMR,  $\delta$  ppm,  $\text{CDCl}_3$  OF  $\text{Ag}^+$  AND  $\text{Pd}^{2+}$  COMPLEXES  
SUBSTITUTED QUINOLENECARBALDEHYDE



Compd.	H-4	H-5	H-6	H-7	H-8	CHO	$(\text{CH}_2\text{CH}_2)_2$	$\text{CH}_2\text{CH}_2$	$\text{CH}_2$
8;M= $\text{Ag}^+$	8.70 s	7.70 m	2.45 s; Me	7.60- 7.80 m	7.60- 7.80 m	10.19 s	3.45 m	2.95- 3.15 m	2.06 m
9;M= $\text{Pd}^{2+}$	8.70 s	7.70 s	2.45 s; Me	7.55- 7.80 m	7.55- 7.80 m	10.19 s	3.95- 3.65m	3.95- 3.65m	2.24m
Compd.	C2	C3	C4	C5	C6	C7,8,9	C10		
8;M= $\text{Ag}^+$	148.80	124.19	144.18	135.24	135.99	126.88	169.27		
9;M= $\text{Pd}^{2+}$	148.76	124.69	143.74	130.78	108.60	127.96	147.91		
Compd.	C11	C12	C13	C14	C15	C16			
8;M= $\text{Ag}^+$	190.89	20.66	31.60	36.60	30.95	29.29			
9;M= $\text{Pd}^{2+}$	159.84	20.65	31.60	36.60	30.95	29.29			

When they reacted with corresponding Ag and Pd salts, a complexed compounds **8** and **9** were obtained in a good yields, which were soluble in organic solvents such as chloroform and toluene.



Characterization of these products involved a combination of methods including elemental analysis (Table-6), the affect of Ag<sup>+</sup> and Pd<sup>2+</sup> on the protons H-7 and H-8 in <sup>1</sup>H NMR. were obvious as shown on the Table-5. The cyclization and complexation of these carbaldehydes with metals are still under going.

TABLE-6  
PHYSICAL PROPERTIES AND ELEMENTAL ANALYSIS OF COMPOUNDS 1-9

Compd.	m.p. (°C)	Yield (%)	Elemental analysis (%)					
			Found			Calcd.		
			C	H	N	C	H	N
<b>1</b>	125	56.00	64.53	3.86	6.74	64.25	3.90	6.80
<b>2</b>	198	60.00	60.20	3.52	6.24	59.60	3.60	6.30
<b>3</b>	212	96.55	66.60	4.68	12.69	66.20	4.59	12.87
<b>4</b>	215	90.36	60.30	4.07	11.33	61.67	4.28	11.99
<b>5</b>	90	15.00	65.72	6.30	9.78	68.42	5.26	6.30
<b>6</b>	140	83.68	64.23	5.08	3.06	61.48	5.30	4.94
<b>7</b>	165	61.54	56.92	4.86	3.92	58.19	5.16	4.69
<b>8</b>	115	60.00	38.26	3.20	3.97	40.51	3.86	3.58
<b>9</b>	180	70.00	44.73	3.75	2.82	43.67	3.88	3.59

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