SYNTHESIS AND BIOLOGICAL STUDIES OF SOME NEW COMPLEXES OF ZR(IV) AND CD(II) WITH 2-PHENYL-4-CARBOXY-1, 8-NAPHTHYRIDINE DERIVATIVES

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Abstract

Complexes of Zr (IV) and Cd (II) of substituted 2- pheny-4-carboxy-1, 8- naphthyridine have been prepared. The synthesis is based on the reaction of $Zr(NO_3)_4 6H_2O$ and $Cd(NO_3)_2 4H_2O$ with naphthyridine derivatives in absolute ethanol. The structures of the complexes obtained were assigned on the basis of their elemental analysis, molar conductance value and Infrared spectral data. Complexes of the type $[Zr(L)_3(H_2O)_3]$ $(NO_3)_4$ and $[Cd(L)_2(H_2O)_2](NO_3)_2$ (where L is a substituted naphthyridine ligands) have been proposed, the ligands in these complexes behave as monodentate. The antimicrobial activities of these complexes have been screened for their antimicrobial activity against eight microorganisms; the results are shown on table 5.

Key words: Synthesis, Complexes, Naphtharidine, Antimicrobial activity

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Introduction

Naphthyridines are the heterocyclic analogues of naphthalene [1] were they contain two N-hetero atoms at positions 1 and 8. The synthetic methods of these compounds are based on the reaction of 2-aminopyridine with benzaldehyde or its derivatives, and then the products were treated with pyruvic acid. Naphthyridine nucleus was prepared for the first time successfully by Bobrenski and Sucharada [2], since then many researchers have succeeded in synthesizing derivatives of these compounds through modification of Dohbner [3], and Pfitzinger [4] reactions and the corresponding 4-carboxynaphthyridine derivatives were obtained.

In this work we have tried to synthesize naphthyridinic acid derivatives (L) by adoption of the Dohbner reaction according to the procedure outlined in the literature [3].

The importance of these compound lies in their uses in drug industries and it has been established that they are biologically active in many aspects [5]. These finding encourage many scientists to concentrate their efforts on modifying these compound for the purpose of using them in treatment of many diseases [6]. It is a matter of interest to determine the extent to which the biological properties of these ligands would be affected by incorporating the Zr (IV) and Cd (II) ions. The results of the biological examination of these various complexes derived from 2-phenyl-4-carboxy-1, 8-naphthyridine derivatives were given in table 5.

Experimental

Melting points were measured by Gallenkamp apparatus and are uncorrected; IR spectra of the ligands and their complexes were recorded on Unicam SP 1100 infrared spectrophotometer using KBr pellets. Elemental analysis were performed on Carlo Erba type 1106 analyzer the metal contents of the complexes are estimated by the literature method [7].

The molar conductivities of 10 □ ³ M solutions of the complexes in absolute ethanol and in dimethyl formamide were measured using an electrolytic conductivity measuring set IF-42.

All the synthesized complexes were tested for antimicrobial activity against eight microorganisms by tube dilution method, the antimicrobial activity measured as described [8].

General procedure for the preparation of ligands (C1, C2, C3, C4) [3]

Benzaldehyde or its derivatives (0.025 mol) were placed in a round bottomed flask provided with $CaCl_2$ tube. Absolute ethanol (10 ml) was added and the mixture was heated in a water bath for 0.5 h. 2-aminopyridine (0.025 mol) in absolute ethanol (5 ml) was added in one portion, followed by drop wise addition of pyruvic acid (0.025 mol) with vigorous stirring. The work up was carried out according to the standard procedure. The physical data of the ligands prepared are shown on table 1.

Preparation of complexes

A solution of (0.0012 mol) of Zr(IV) nitrate and (0.0016 mol) of Cd(II) nitrate in 20 ml absolute ethanol is treated separately with (0.0034 ml) and (0.0033 mol) of each of the ligands, respectively in 10 ml of absolute ethanol. The mixtures were refluxed for 2 h, then evaporated to about half of its volume and cooled. The solid products were filtered and washed with ether then left to dry.

Results and Discussion:

The analytical data (table 2) reveal that the Zr(IV) and Cd(II) complexes possess 1:3 and 1:2 metal to ligand ratio, respectively. The resulting complexes are moderately soluble in methanol and soluble in ethanol, DMF and DMSO. Some of the physical properties of the ligands and their complexes are listed in tables (1) , (2) and (3). The ionic characters of these complexes were estimated by their molar conductivities in absolute ethanol and DMF. The results for the Zr(IV) complexes are in the range 170 – 182 and 310 – 320 Ω^{-1} mol^{-1} cm^2 and that for Cd(II) complexes are in the range 75 – 95 and 140 – 150 Ω^{-1} mol^{-1} cm^2 in absolute ethanol and DMF respectively, which indicate 1:4 and 1:2 electrolytes [9].

The assignment of the infrared spectral bands of the ligands and complexes are listed in (table 4). The infrared spectra for the ligands (C1, C2, C3, C4) showed sharp bands in the regions of 1050- 1150 and 1060 –1150 cm^{-1} which are attributed to $\upsilon_{C\text{-}O\text{-}C}$ and $\upsilon_{C=N\text{-}C}$ groups[10]

respectively. Upon coordination these bands are remained in the same location which supports our conclusion that these groups are not coordinated to the metal ion. The next bands in the ligands are at 1490-1495 and 1600-1590 cm^{-1} which may be assigned to υ_{C-O} and $\upsilon_{C=O}$ groups [11] respectively, on coordination, the υ_{C-O} is shifted to lower frequency. This shift may be interpreted as bonding of the carboxylic oxygen to the metal ion [11]. In comparing the separation between the two υ_{C-O} of the complexes with that of the free acetate [12], it is much larger, as a result naphthyridinic ligands act as unidentate ligands in the resulting complexes. Zr-complexes show bands at 720-740, 560-620 and 420-455 cm^{-1} where as Cd- complexes show bands at 710-770, 620-640 and 425-460 cm^{-1} which may be assigned for the rocking, wagging and MO stretching which support the coordination of water molecule to the metal ions [11]. The bands at about 1370-1380 cm^{-1} in the infrared spectra of the complexes, indicates the presence of ionic nitrate groups [13]. This is in accordance with the conductance values of the complexes. On the other band, the spectra of the complexes show new band around 510-520 cm^{-1} which are likely to be to υ_{M-O} [11]. The presence of this band supports the coordination of the ligands with the Zr(IV) and Cd(II) ions. This data support the formula of the complexes which already been proposed.

The antimicrobial studies

The results of antimicrobial testing revealed that the complexes possess broad spectrum biological activities in vitro, therefore this work would be fruitful for the development of novel class of antimicrobial agents.

Table 1: The physical data of 2-phenyl-4-carboxy-1, 8-naphthridine

No.	Structure	M.F	M.p.^{o} C / Yield (%)	Microanalysis Found (Calc.)			
				C	H	N	Cl
				72.3	3.9	11.2	-

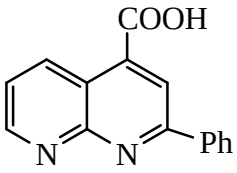
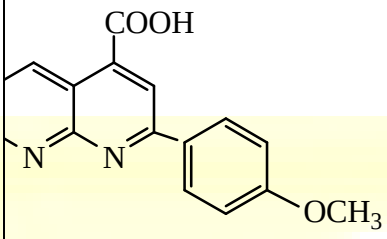
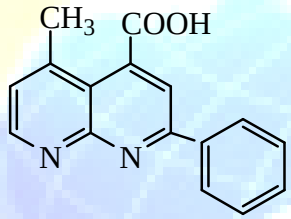
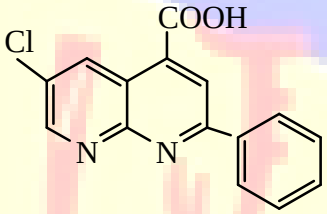
C1		$C_{15}H_{10}N_2O_2$	142d / 36	(72.0)	(4.0)	(11.2)	-
C2		$C_{16}H_{12}N_2O_3$	147d / 33	69 (68.5)	4.4 (4.2)	10.1 (10.0)	- -
C3		$C_{16}H_{12}N_2O_2$	140d / 42	72.8 (72.7)	4.6 (4.5)	11.0 (10.6)	- -
C4		$C_{15}H_9ClN_2O_2$	187 / 57	61.9 (63.2)	3.0 (3.1)	9.7 (9.8)	12.11 (12.47)

Table 2: Elemental analysis of complexes.

Compound No.	Complexes	Mole ratio M/L	Micro analytical data Found(Calc.)				
			C	H	N	Cl	M
		1:3	46.99	3.06	12.00	-	7.49

1	[Zr(C1)3(H2O)3](NO3)4		(47.24)	(3.15)	(12.25)	-	(7.98)
2	[Zr(C2)3(H2O)3](NO3)4	1:3	46.5 (46.7)	3.2 (3.4)	11.11 (11.35)	- -	7.2 (7.4)
3	[Zr(C3)3(H2O)3](NO3)4	1:3	48.2 (48.6)	3.32 (3.54)	11.24 (11.81)	- -	7.23 (7.7)
4	[Zr(C4)3(H2O)3](NO3)4	1:3	43.01 (43.3)	3.31 (2.65)	11.62 (11.23)	8.46 (8.51)	7.11 (7.32)
5	[Cd(C1)2(H2O)3](NO3)2	1:2	46.02 (46.61)	2.99 (3.11)	10.23 (10.88)	- -	14.11 (14.55)
6	[Cd(C2)2(H2O)3](NO3)2	1:2	45.01 (45.7)	3.11 (3.33)	9.88 (10)	- -	13.21 (13.37)
7	[Cd(C3)2(H2O)3](NO3)2	1:2	47.11 (47.97)	3.19 (3.49)	10.22 (10.5)	- -	14.23 (14.04)
8	[Cd(C4)2(H2O)3](NO3)2	1:2	42.89 (42.79)	2.11 (2.61)	9.96 (9.98)	8.29 (8.44)	13.22 (13.36)

Table 3: Some physical properties of complexes

Complexes	Colour	M.P ^{o}C	A	
			DMF	Ethanol
$[Zr(C1)_3(H_2O)_3](NO_3)_4$	Yellow	269	310	170
$[Zr(C2)_3(H_2O)_3](NO_3)_4$	Pale Yellow	188	315	175
$[Zr(C3)_3(H_2O)_3](NO_3)_4$	Yellow	210	310	173
$[Zr(C4)_3(H_2O)_3](NO_3)_4$	Yellow	203	320	182
$[Cd(C1)_2(H_2O)_3](NO_3)_2$	White	219	150	80
$[Cd(C2)_2(H_2O)_3](NO_3)_2$	Pale Yellow	189	155	95
$[Cd(C3)_2(H_2O)_3](NO_3)_2$	Yellow	195	160	90
$[Cd(C4)_2(H_2O)_3](NO_3)_2$	Yellow	213	140	75

($\Omega^{-1}mol^{-1}cm^{-1}$)at 25^{o}Cof 10^{-3}m solution in DMF and absolute ethanol

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Table 4: Characteristic bands in the infrared spectra of the ligands and their complexes

Ligands / and Complexes	υ C-O*	υ C=O **	ΔCO	υ H_2O Coordinated			υ NO_3	υ C-O-C	υ C=N-C	υ M-O
				wagging	rocking	M-O*** ionic				
C1	1490	1600	110	-	-	-	-	1060-1150	1530	-
$[Zr(C1)_3(H_2O)_3](NO_3)_4$	1430	1590	162	620	740	440	1370	1060-1150	1530	515
$[Cd(C1)_2(H_2O)_3](NO_3)_2$	1435	1592	162	620	750	460	1375	1060-1155	1530	520
C2	1495	1600	110	-	-	-	-	1060-1150	1525	-
$[Zr(C2)_3(H_2O)_3](NO_3)_4$	1430	1590	160	570	760	455	1370	1060-1155	1530	515
$[Cd(C2)_2(H_2O)_3](NO_3)_2$	1430	1595	165	635	770	465	1380	1060-1150	1535	515
C3	1490	1610	110	-	-	-	-	1060-1150	1520	-
$[Zr(C3)_3(H_2O)_3](NO_3)_4$	1430	1590	160	570	750	435	1380	1060-1155	1525	520
$[Cd(C3)_2(H_2O)_3](NO_3)_2$	1435	1580	160	640	770	425	1380	1055-1150	1525	515
C4	1495	1590	110	-	-	-	-	1050-1150	1520	-
$[Zr(C4)_3(H_2O)_3](NO_3)_4$	1440	1610	160	560	720	420	1380	1055-1150	1530	520
$[Cd(C4)_2(H_2O)_3](NO_3)_2$	1445	1600	160	620	710	430	1370	1050-1150	1535	520

* Corresponding to COO□ (S)

**Corresponding to COO□ (as)

Corresponding to the coordination the oxygen of water molecule with metal ion

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Table 5: Antimicrobial activity of the complexes

Complexes	Gram negative bacteria			Gram positive bacteria			Fungi	
	Bacillus subtilis	Bacillus magateriju m	Bacillus cereus	Sarcina lutea	Escherichia coli	Pseudomonas aeruginosa	Candida utilis	Aspergilus niger

	A	MIC	A	MIC	A	MIC	A	MIC	A	MIC	A	MIC	A	MIC	A	MIC
$[Zr(C1)_3(H_2O)_3](NO_3)_4$	+ +	330	-	-	-	-	-	-	-	-	+	400	+ + +	320	-	-
$[Zr(C2)_3(H_2O)_3](NO_3)_4$	+ +	400	-	-	-	-	-	-	-	-	++	150	+ +	340	++	350
$[Zr(C3)_3(H_2O)_3](NO_3)_4$	+ +	350	-	-	-	-	-	-	-	-	++	370	+ +	360	+++	400
$[Zr(C4)_3(H_2O)_3](NO_3)_4$	+ +	375	-	-	-	-	-	-	-	-	-	-	+ +	400	++	320
$[Cd(C1)_2(H_2O)_3](NO_3)_2$	+ + +	280	-	-	-	-	-	-	-	-	+++	200	+ + +	425	+++	380
$[Cd(C2)_2(H_2O)_3](NO_3)_2$	+ + + +	190	-	-	+	450	-	-	-	-	++	100	+ +	375	+++	400
$[Cd(C3)_2(H_2O)_3](NO_3)_2$	+ + +	100	-	-	-	-	-	-	-	-	+++	120	+ + +	425	+++	370
$[Cd(C4)_2(H_2O)_3](NO_3)_2$	+ + + +	180	-	-	+	460	-	-	-	-	+++	130	+ + +	440	+++	420

A= activity MIC - Minimum Inhibitory Concentration Calculated as mg / ml

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