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Preparation, Biological Activity and Characterisation of Novel Macroacyclic (N_2O_4 and N_2O_2) Schiff Base Ligands and Their Zn(II), Cd(II) and Hg(II) Complexes

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New macroacyclic $N_2O_4(L_1)$ and $N_2O_2(L_2)$ Schiff base ligands have been synthesized from 1,4-di-(4-fluoro-2-aminophenoxy)butane(DFAB)withsalicylaldehyde and 1,4-di-(4-fluoro-2-aminophenoxy)butane(DFAB)with anthracene-9-carbaldehyde, respectively. Zn(II), Cd(II) and Hg(II) complexes of the Schiff base ligands have also been prepared and all compounds have been characterised by IR, ^{1}HNMR , ^{13}CNMR spectroscopy and mass spectrometry. We are also especially interested in the antibacterial activity of these new complexes. The in vitro antibacterial activity of the metal ions, free ligands and their complexes were tested against the gram-positive bacteriaand gram-negative bacteriaby paper disc diffusion and minimum inhibitory concentration (MIC)methods. It is apparent the metal complexeshave good antibacterial activity but related free ligands and metal ions have not antibacterial activity.

Key words: Schiff base, Macroacyclic, Antibacterialactivity.

Schiff bases and their complexes, a typically of chelators are capable of forming coordinate bonds with many metal ions through azomethine group and phenolic group or via its azomethine or phenolic groups[1-2]. The chemistry of Schiff base ligands and their metal complexes have attracted increasing interest owing to their role in the understanding of molecular processes occurring in biochemistry, antifungal, antibacterial, anticancer, catalytic fields and as encapsulating ligands for radiopharmaceuticals[2-11]. Therefore, The chemistry of Schiff base ligands and their metal complexes have attracted a lot of interest due to their facile synthesis and wide range of applications including pigments, intermediates in organic synthesis and as polymer stabilizers[12-15].

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MATERIALS AND METHODS

4-fluorophenolis commercially available from Merck and is used without any changes.All other solvents and materials were of reagent grade and used without further purification. IR spectra were recorded (KBr) on a BrukerVERTEX 70 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker- AV400MHz. Mass spectra were recorded on a 5973 Tecnology Agilent (HP) spectrometer (EI = 70 eV).

RESULTS

Synthesis

In this work, a new diamine 1,4-di-(4-fluoro-2aminophenoxy)butane has been synthesized by modified previous procedure[16]. Then, macroacyclic (N_2O_4 and N_2O_2) Schiff base ligands and their complexes have been synthesized and characterized by IR, ^{1}H-NMR and ^{13}C-NMR spectroscopy and mass spectrometry.

Synthesis of 1,4-di-(4-fluoro-2-nitrophenoxy) butane (DFNB)

To a solution of 0.16 g 4-fluoro-2-nitrophenol (1mmol) in 50 cm^3 ethanol was added 0.04 g NaOH (1mmol) in 5 cm^3 water under stirring at room temperature. After the color of solution changed from yellow to red, a solution of 0.1 g 1,4-dibromo butane (0.5mmol) in 10 cm^3 ethanol was added dropwise and was refluxed for 48 h according to scheme 1. After completion of the reaction, the cream solid crude was filtered and washed with ethanol.mp: 121 °C. IR (KBr, í, cm^{-1}): 1518 $í_{as}$(N–O), 1342 $í_s$(N–O), 1194 í(C–O), 1020 í(C-F).m/z: 368 [M^+]. ^{1}H NMR (ä, DMSO-d_6, MHz): 1.63 (4H; H_a), 3.15 (4H; H_b), 7.15-732 (6H; H_d, H_e, H_g). ^{13}C NMR (ä, DMSO-d_6, MHz): 23.22 (2C; C_a), 65.43 (2C; C_b), 117.53-132.71 (12C; C_c, C_d, C_e, C_f, C_g, C_h).

Synthesis of 1,4-di-(4-fluoro-2-aminophenoxy) butane (DFAB)

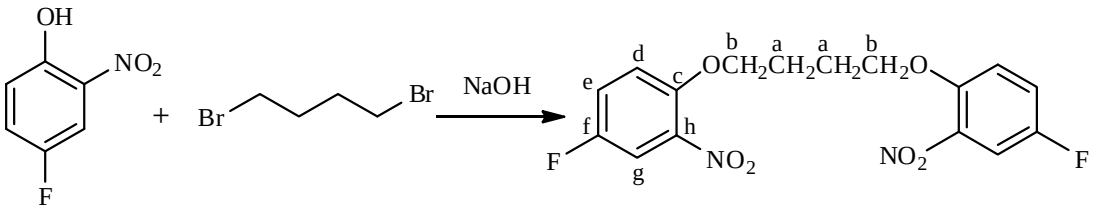
0.37 g 1,4-di-(4-fluoro-2-nitrophenoxy)butane (1mmol) was dissolved in 50 cm^3HCl (5 N) at temperature of 40-50°C. Then 2.3 g $SnCl_2.2H_2O$ (10mmol) was gradually added to the mixture of reaction. After the addition of $SnCl_2.2H_2O$, a turbid solution was formed. The mixture of reaction was refluxed till the solution become colorless and transparent (24 h) according to scheme 2. After completion of the reaction, the white solid crude was filtered and washed with cold ethanol. Yield:mp: 132-133 ÚC. IR (KBr, í, cm^{-1}), 1022 í(C-F), 3505 $í_s$(N–H),1223 í(C–O).m/z: 395 [M^+].

Synthesis of macroacyclic Schiff base ligand (L_1)

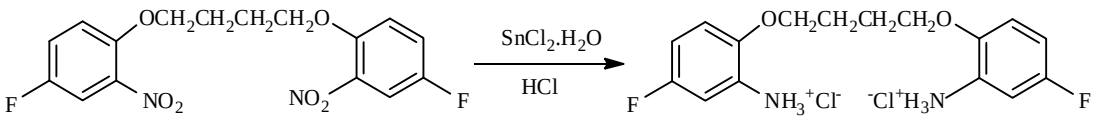
To a solution of 0.12 g salicylaldehyde (1 mmol) in 20 cm^3 ethanol was added dropwise a solution of 0.2 g diamine salt (0.5 mmol) in 10 cm^3 water and 30 cm^3 ethanol over 30 minutes. Then the solution of NaOH (5M) was added drop by drop until pH of the mixture of reaction reached 7. The reaction was stirred at room temperature for 24 h to be completed according to scheme 3. After completion of the reaction, the whity precipitate was filtered and washed with acetonitrile and cold methanol. mp 150-151 ÚC. IR (KBr, í, cm^{-1}): 3470 $í_s$(C–H_{iminic}), 1618 $í_s$(C=N),1115 í(C–O), 1021 í(C-F). m/z: 517 [M^+].^{1}H NMR (ä, DMSO-d_6, MHz): 1.93 (4H; H_a), 4.14 (4H; H_b), 6.94-7.59 (14H; H_d, H_e, H_g, H_k, H_l, H_m, H_n), 8.99 (2H; H_i), 13.7 (2H; $H_{phenolic}$). ^{13}CNMR (ä, DMSO-d_6, MHz): 25.88 (2C; C_a), 68.85 (2C; C_b), 106.42-155.76 (24C; C_c, C_d, C_e, C_f, C_g, C_h, C_j, C_k, C_l, C_m, C_n, C_o), 167.15 (2C; C_i).

Template synthesis of metal complexes of L_1 with M^{2+} (M = Zn, Cd and Hg)

To a solution of 0.12 g salicylaldehyde (1mmol) in 20 cm^3 ethanol was added appropriate amount of M^{2+} (1 mmol) and it was stirred at room temperature for 2 h. After that dropwise a solution of 0.2 g diamine salt (0.5mmol) in 10 cm^3 water and 30 cm^3 ethanol over 30 minutes. Then the solution of NaOH (5M) was added drop by drop until pH of the mixture of reaction reached 7. The mixture of reaction was refluxed for 36 h. After completion of the reaction, the whity precipitate was filtered and washed with acetonitrile and cold methanol.



Scheme 1. Outcome of 1,4-di-(4-fluoro-2-nitrophenoxy)butane condensation between 4-fluoro-2-nitrophenol and 1,4-dibromo butane



Scheme 2. Outcome of 1,4-di-(4-fluoro-2-aminophenoxy)butane condensation between 1,4-di-(4-fluoro-2-nitrophenoxy)butane and $SnCl_2.2H_2O$

Complex (1)

$[Zn(L_1)](NO_3)_2$;Yield 91 %; m.p> 200 ºC; FAB MS (positive FAB in nitrobenzyl alcohol): m/z578 $[C_{30}H_{24}F_2ZnN_2O_4]^+$. IR (KBr, í, cm^{-1}): 2954í(C–$H_{aromatic}$), 2933 í(C–$H_{aliphatic}$), 2875 $í_s$(C–H_{iminic}), 1619 í(C=N), 1227 í(C-O). ^{1}H NMR (ä, DMSO-d_6, MHz): 1.89 (4H; H_a), 3.96 (4H; H_b), 5 (4H; H_e, H_g) 6.21-6.74 (10H; H_d, H_k, H_l, H_m, H_n), 8.99 (2H; H_i). ^{13}C NMR (ä, DMSO-d_6, MHz): 26.09 (2C; C_a), 68.58 (2C; C_b), 100.57-156.36 (24C; C_c, C_d, C_e, C_f, C_g, C_h, C_j, C_k, C_l, C_m, C_n, C_o), 167.4 (2C; C_i).

Complex (2)

$[Cd(L_1)](NO_3)_2$ Yield 75 %; m.p=190-192 ºC; FAB MS (positive FAB in nitrobenzyl alcohol): m/z 627 $[C_{30}H_{24}F_2CdN_2O_4]^+$. IR (KBr, í, cm^{-1}): 2956 í(C–$H_{aromatic}$), 2932 í(C–$H_{aliphatic}$), 2879 $í_s$(C–H_{iminic}), 1618 í(C=N), 1217 í(C-O). ^{1}H NMR (ä, DMSO-d_6, MHz): 1.92 (4H; H_a), 4.09 (4H; H_b), 6.94-7.59 (14H; H_d, H_e, H_g, H_k, H_l, H_m, H_n), 8.99 (2H; H_i). ^{13}C NMR (ä, DMSO-d_6, MHz): 25.88 (2C; C_a), 68.86 (2C; C_b), 106.33-156.36 (24C; C_c, C_d, C_e, C_f, C_g, C_h, C_j, C_k, C_l, C_m, C_n, C_o), 163.86 (2C; C_i).

Complex (3)

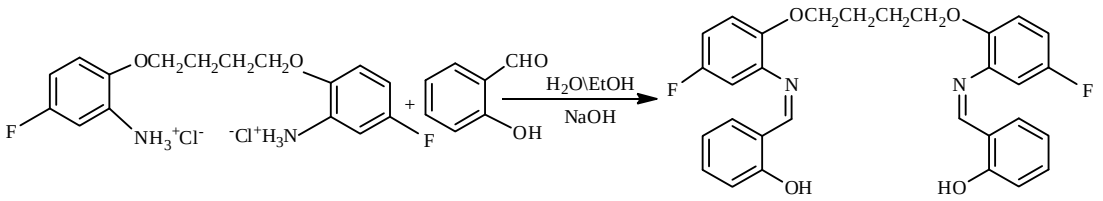
$[Hg(L_1)]Cl_2$; Yield:90 %; m.p > 200 ºC, FAB MS (positive FAB in nitrobenzyl alcohol): m/z 715 $[C_{30}H_{24}F_2HgN_2O_4]^+$. (IR (KBr, í, cm^{-1}): 2954 í(C–$H_{aromatic}$), 2933 í(C–$H_{aliphatic}$), 2875 $í_s$(C–H_{iminic}), 1619 í(C=N), 1227 í(C-O), 1025 í(C-F). ^{1}H NMR (ä, DMSO-d_6,MHz): 1.93 (4H; H_a), 3.35 (4H; H_b), 6.6-7.03 (14H; H_d, H_e, H_g, H_k, H_l, H_m, H_n), 8.99 (2H; H_i), 13.63 (2H; $H_{phenolic}$). ^{13}C NMR (ä, DMSO-d_6, MHz): 25.88 (2C; C_a), 68.86 (2C; C_b), 106.33-156.36 (24C; C_c, C_d, C_e, C_f, C_g, C_h, C_j, C_k, C_l, C_m, C_n, C_O), 163.86 (2C; C_i).

Synthesis of macroacyclic Schiff base ligand (L_2)

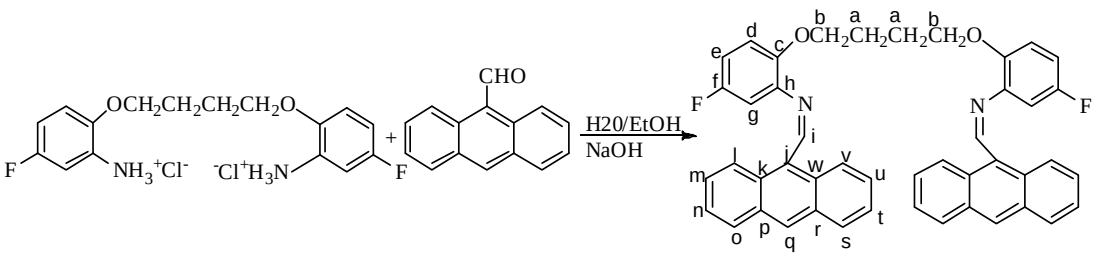
To a solution of 0.2 g anthracene-9-carbaldehyde (1 mmol) in 20 cm^3 ethanol was added dropwise a solution of 0.2 g diamine salt (0.5 mmol) in 10 cm^3 water and 30 cm^3 ethanol over 30 minutes. Then the solution of NaOH (5M) was added drop by drop until pH of the mixture of reaction reached 7. The reaction was stirred at room temperature for 24 h to be completed according to scheme 4. After completion of the reaction, the whity precipitate was filtered and washed with acetonitrile and cold methanol. Yield: 91%. mp 142-143 ÚC. IR (KBr, í, cm^{-1}): 3501$í_s$(C–H_{iminic}), 1622$í_s$(C=N), 1213í(C–O), 1017 í(C-F). m/z: 683 $[M^+]$.^{1}H NMR (ä, DMSO-d_6, MHz): 1.73 (4H; H_a), 3.73 (4H; H_b), 6.72-7.43 (24H; H_d, H_e, H_g, H_l, H_m, H_n, H_o, H_q, H_s, H_t, H_u, H_v), 8.87 (2H; H_i). ^{13}CNMR (ä, DMSO-d_6, MHz): 23.75 (2C; C_a), 59.94 (2C; C_b), 103.13-172.56 (40C; C_c, C_d, C_e, C_f, C_g, C_h, C_j, C_k, C_l, C_m, C_n, C_o,C_p, C_q, C_r, C_s, C_t, C_u, C_v, C_w), 178.17 (2C; C_i).

Template synthesis of metal complexes of L_2 with M^{2+} (M = Zn, Cd and Hg)

To a solution of 0.2 g anthracene-9-carbaldehyde (1 mmol) in 20 cm^3 ethanol was added appropriate amount of M^{2+} (1 mmol) and it was



Scheme 3.Outcome of ofmacroacyclic Schiff base ligand (L_1) condensation between 1,4-di-(4-fluoro-2-aminophenoxy)butane and salicylaldehyde



Scheme 4.Outcome of ofmacroacyclic Schiff base ligand (L_2) condensation between 1,4-di-(4-fluoro-2-aminophenoxy)butane and anthracene-9-carbaldehyde

stirred at room temperature for 2 h. After that dropwise a solution of 0.2 g diamine salt (0.5mmol) in 10 cm^3 water and 30 cm^3 ethanol over 30 minutes. Then the solution of NaOH (5M) was added drop by drop until pH of the mixture of reaction reached 7. The mixture of reaction was refluxed for 36 h. After completion of the reaction, the whity precipitate was filtered and washed with acetonitrile and cold methanol.

Complex (4)

$[Zn(L_2)](NO_3)_2$;Yield 91 %; m.p> 200 ºC; FAB MS (positive FAB in nitrobenzyl alcohol): m/z747 $[C_{46}H_{33}F_2ZnN_2O_2]^+$. IR (KBr, í, cm^{-1}): 2943í(C–$H_{aromatic}$), 2922í(C–$H_{aliphatic}$), 2864í$_s$(C–H_{iminic}), 1620 í(C=N), 1214 í(C-O), 1016 í(C-F).^{1}H NMR (ä, DMSO-d_6, MHz): 1.84 (4H; H_a), 3.86 (4H; H_b), 6.83-7.51 (24H; H_d, H_e, H_g, H_l, H_m, H_n, H_o, H_q, H_s, H_t, H_u, H_v), 8.87 (2H; H_i). ^{13}CNMR (ä, DMSO-d_6, MHz): 23.92 (2C; C_a), 60.12 (2C; C_b), 104.18-170.66 (40C; C_c, C_d, C_e, C_f, C_g, C_h, C_j, C_k, C_l, C_m, C_n, C_o,C_p, C_q, C_r, C_s, C_t, C_u, C_v, C_w), 178.13 (2C; C_i).

Complex (5)

$[Cd(L_2)](NO_3)_2$ Yield 89 %; m.p> 200 ºC; FAB MS (positive FAB in nitrobenzyl alcohol): m/z 797$[C_{46}H_{33}F_2CdN_2O_2]^+$. IR (KBr, í, cm^{-1}): 2942í(C–$H_{aromatic}$), 2920í(C–$H_{aliphatic}$), 2870í$_s$(C–H_{iminic}), 1620 í(C=N), 1217 í(C-O), 1015 í(C-F). ^{1}H NMR (ä, DMSO-d_6, MHz): 1.85 (4H; H_a), 3.90 (4H; H_b), 6.81-8.12(24H; H_d, H_e, H_g, H_l, H_m, H_n, H_o, H_q, H_s, H_t, H_u, H_v), 8.87 (2H; H_i). ^{13}CNMR (ä, DMSO-d_6, MHz): 23.86 (2C; C_a), 60.23 (2C; C_b), 103.18-171.66 (40C; C_c, C_d, C_e, C_f, C_g, C_h, C_j, C_k, C_l, C_m, C_n, C_o,C_p, C_q, C_r, C_s, C_t, C_u, C_v, C_w), 180.14 (2C; C_i).

Complex (6)

$[Hg(L_2)]Cl_2$; Yield: 78 %;m.p> 200 ºC, FAB MS (positive FAB in nitrobenzyl alcohol): m/z 885 $[C_{46}H_{33}F_2HgN_2O_2]^+$. (IR (KBr, í, cm^{-1}): 2965 í(C–$H_{aromatic}$), 2941 í(C–$H_{aliphatic}$), 2878í$_s$(C–H_{iminic}), 1621 í(C=N), 1214 í(C-O), 1016 í(C-F). ^{1}H NMR (ä, DMSO-d_6,MHz): 1.91 (4H; H_a), 3.92 (4H; H_b), 6.82-8.21 (24H; H_d, H_e, H_g, H_l, H_m, H_n, H_o, H_q, H_s, H_t, H_u, H_v), 8.92 (2H; H_i). ^{13}CNMR (ä, DMSO-d_6, MHz): 24.13 (2C; C_a), 60.23 (2C; C_b), 103.54-171.27 (40C; C_c, C_d, C_e, C_f, C_g, C_h, C_j, C_k, C_l, C_m, C_n, C_o,C_p, C_q, C_r, C_s, C_t, C_u, C_v, C_w), 178.17 (2C; C_i).

Antibacterial activity

The in vitro antibacterial activity of the metal ions, free ligands and their complexes were tested against the gram-positive bacteria; Bacillus anthracis (RTCC 1036), Staphylococcus epidermidis (PTCC 1114), Staphylococcus aureus (RTCC 1885), Enterococcus faecalis (RTCC 2121),

Table 1. Antibacterial activity of M^{2+}complexes, N_2O_4 (L_1), metal ions, Gentamycine(GE) and Tetracycline(TE)as standard compounds

Bacterial	Complex (1)	Complex (2)	Complex(3)	Disk diffusion (mm) L_1	$Zn(NO_3)_2$	$Cd(NO_3)_2$	$HgCl_2$	TE	G M
B. anthracis	30	25	98	-	-	-	-	20	25
S. epidermidis	40	44	20	-	-	-	-	25	25
S.aureus	40	40	86	-	-	-	-	25	30
E. faecalis	20	-	80	-	-	-	-	30	15
B. subtilis	30	35	25	-	-	-	-	20	20
P. aeruginosa	20	-	25	-	-	-	-	-	15
K. pneumonia	50	25	100	-	-	-	-	20	25
E. aerogenes	30	25	74	-	-	-	-	20	15
E. coli	30	25	73	-	-	-	-	18	10
			Minimum inhibitory concentration or MIC (mg/ml)						
B.anthracis	6.25	12.5l	82.51	-	-	-	-	-	-
S.epidermidis	1.56	1.56	25	-	-	-	-	-	-
S.aureus	1.56	1.56	25	-	-	-	-	-	-
E. faecalis	25	-	100	-	-	-	-	-	-
B. subtilis	6.25	3.12	84	-	-	-	-	-	-
P.aeruginosa	25	12.5	16	-	-	-	-	-	-
K.pneumonia	0.75	-	97	-	-	-	-	-	-
E.aerogenes	6.25	12.5	25	-	-	-	-	-	-
E. coli	6.25	12.5	84.5	-	-	-	-	-	-

Bacillus subtilis (PTCC 1715) and gram-negative bacteria; Pseudomonas aeruginosa(RTCC 1547), Klebsiella pneumonia (RTCC 1247), Enterobacteraerogenes (PTCC 1221), Eschericha coli (RTCC1330) by paper disc diffusion and minimum inhibitory concentration (MIC)methods. Bacteria cultures were obtained from Tehran islamicazad university hospital, microbiology department. Microbial strains were cultured overnight at 310 ÚK in Nutrient Broth. During the survey, these stock cultures were stored in the dark at 277 ÚK. Tetracycline and Gentamycine were used as standard compounds to determine the sensitivityof one strain/isolate in each microbial species tested. Antibacterial activity in the disc diffusion assay was evaluated by measuring the zone of inhibition against the test organisms. Each assay in this experiment was repeated twice. For investigation of antimicrobial activity of as prepared metal ions, free ligands and their complexes. The inhibitory effect of complexes on the growth of microbes were studied. The results can be seen in Table 1 and Table 2.

The results showed that antibacterial activity of the complexes exceeded the Tetracycline and Gentamycine used as standard compounds.

DISCUSSION

Structural analysis

A potentially macroacyclic Schiffbase ligand (L_1) was prepared by condensation reaction of 1,4-di-(4-fluoro-2-aminophenoxy)butane (DFAB)and salicylaldehyde in ethanol. A potentially macroacyclic Schiff base ligand (L_2) was prepared by condensation reaction of 1,4-di-(4-fluoro-2-aminophenoxy)butane (DFAB) and anthracene-9-carbaldehyde in ethanol. DFAB was also synthesized by nucleophilic substitution reaction (SN_2) of 4-fluoro-2-nitrophenole (DFNB) and 1,4-dibromo butane. The complexation of L_1 and L_2 were carried out toward M^{2+} (M= Zn, Cd and Hg) using one-pot template reactions. The resulted complexes were investigated by IR, ^{1}HNMR, ^{13}CNMR spectroscopy and mass spectrometry.

IR, NMR and mass data gives useful information on the structure of DFAB, DFNB, Schiffbase ligands (L_1 and L_2) and its metal complexes. The spectrum of the free ligands were compared with the spectrum of the metal complexes. The structurally significant IR, NMR and mass spectral data of free ligands and its metal complexes have been reported in the experimental section.

Table 2. Antibacterial activity of M^{2+}complexes, N_2O_2 (L_2), metal ions, Gentamycine(GE) and Tetracycline(TE)as standard compounds

	disk diffusion (mm)								
Bacterial	Complex (4)	Complex (5)	Complex(6)	L_2	$Zn(NO_3)_2$	$Cd(NO_3)_2$	$HgCl_2$	TE	GM
B. anthracis	50	47	70	-	-	-	-	20	25
S. epidermidis	66	40	80	-	-	-	-	25	25
S.aureus	12	90	40	-	-	-	-	25	30
E. faecalis	45	93	42	-	-	-	-	30	15
B. subtilis	100	97	45	-	-	-	-	20	20
P. aeruginosa	-	75	68	-	-	-	-	-	15
K. pneumonia	75	100	68	-	-	-	-	20	25
E. aerogenes	46	72	97	-	-	-	-	20	15
E. coli	73	89	92	-	-	-	-	18	10
	Minimum inhibitory concentration or MIC (mg/ml)								
B.anthracis	43	57	76	-	-	-	-	-	-
S.epidermidis	100	14	46	-	-	-	-	-	-
S.aureus	100	90	47	-	-	-	-	-	-
E. faecalis	75	46	73	-	-	-	-	-	-
B. subtilis	42	85	95	-	-	-	-	-	-
P.aeruginosa	98	85	91	-	-	-	-	-	-
K.pneumonia	65	37	83	-	-	-	-	-	-
E.aerogenes	17	74	56	-	-	-	-	-	-
E. coli	75	19	27	-	-	-	-	-	-

The vibration bands that appeared in the IR spectrum of DFNB at 1342 cm^1 and 1518 cm^1 are assigned to symmetric and asymmetric stretching vibrations of the NO_2 groups in the molecule, respectively. The disappearance of vibration band at 3500 cm^1 related to stretching vibration of phenolic OH groups confirmed the formation of DFNB. The band at 3505 cm^{-1} in the IR spectrum of DFAB is ascribed to the N-H stretching vibration. The vibration band at 1223 cm^1 indicates that etheric bond cleavage has not occurred through reduction of NO_2 groups. The vibration band related to stretching vibrations of the NO_2 groups is absent showing the reduction of NO_2 groups has been completed. The strong absorption bands at approximately 1618 $cm^{-1}$and 1622 cm^{-1}in the IR spectrums of L_1 and $L_2$are ascribed to the stretching vibration of iminic C=N bond, respectively . The ^{1}HNMR spectrum of the ligand L_1showed signals at 1.93 (4H); 4.14 (4H), 6.94-7.59 (14H), 8.99 (2H), 13.7 (2H) ppm which are attributed to methylene H_a; methylene H_b, iminic and phenolic hydrogens, respectively. The ^{13}CNMR spectrum of L_1 showed signals at 25.88 (2C); 68.85 (2C), 106.42-155.76 (24C) and 167.15 (2C) ppm which are attributed to methylene C_a; methylene C_b, aromatic and iminic carbons, respectively. The ^{1}HNMR spectrum of the ligand L_2 showed signals at 1.73 (4H); 3.73 (4H), 6.72-7.43 (24H), 8.87 (2H), 13.7 (2H) ppm which are attributed to methylene H_a; methylene H_b, iminic and phenolic hydrogens, respectively. The ^{13}CNMR spectrum of L_2 showed signals at 23.75 (2C); 59.94 (2C), 103.13-172.56 (40C) and 178.17 (2C) ppm which are attributed to methylene C_a; methylene C_b, aromatic and iminic carbons, respectively.

The IR spectra of Zn(II), Cd(II) and Hg(II) complexes exhibited vibration bands at 1619 cm^{-1}, 1618 cm^{-1} and 1619 cm^{-1} respectively which can be assigned to the C=N stretching vibration of L_1. The frequency of this vibration for Zn(II) complex is the same as Hg(II) complex. Also, vibration bands at 1227 cm^{-1}, 1217 cm^{-1} and 1227 cm^{-1} confirmed the maintenance of C-O bonds of L_1 for Zn(II), Cd(II) and Hg(II) complexes, respectively. The frequency of this vibration for Zn(II) complex is the same as Hg(II) complex. These results in addition to mass results clearly indicate the formation and coordination of macroacyclic ligand (L_1) to metal ions through one-pot template reaction. The IR spectra of Zn(II), Cd(II) and Hg(II) complexes exhibited vibration bands at 1620 cm^{-1}, 1620 cm^{-1} and 1621 cm^{-1} respectively which can be assigned to the C=N stretching vibration of L_2. The frequency of this vibration for Zn(II) complex is the same as Cd(II) complex. Also, vibration bands at 1214 cm^{-1}, 1217 cm^{-1} and 1214 cm^{-1} confirmed the maintenance of C-O bonds of L_1 for Zn(II), Cd(II) and Hg(II) complexes, respectively. The frequency of this vibration for Zn(II) complex is the same as Hg(II) complex. These results in addition to mass results clearly indicate the formation and coordination of macroacyclic ligand (L_2) to metal ions through one-pot template reaction.

Because single crystals of these complexes could not be isolated from any solvents, no definitive crystal structures could be assigned. However, on the basis of characterization results, the molecular ratio of the L_1 and L_2 to metal ions could be confirmed as 1:1.

Antibacterial activity test

The inhibition effect on bacteria growth was determined by disc diffusion method [17-20]. Each compound was dissolved in methanol as a solvent (1g/10 ml) and 50 ìl of each solution applied on the paper disc (the disc diameter was 6 mm). The impregnated discs with different solutions were left for complete evaporation of the solvent. Then disc papers were placed on the inoculated plates with the bacteria of interest. After incubation in the standard upside down position in 40 °C for 24 h, zones of growth inhibition around each of the discs were measured to the nearest millimetre. A blank, containing only methanol, showed no inhibition in a preliminary test. The macrodilutionbrot susceptibility assay was used for the evaluation of minimal inhibitory concentration (MIC). It is apparent the metal complexes have greater antibacterial activity but related free ligands and metal ions have not antibacterial activity. The results showed that in some cases the antibacterial activity of this complexes exceeded of other Schiff base complexes[21-24]. Tweedy's chelation theory is a good clarification for this phenomenon.

CONCLUSION

A new macroacyclic Schiff base ligands derived from condensation of 1,4-di-(4-fluoro-2-

aminophenoxy)butane withsalicylaldehyde and 1,4-di-(4-fluoro-2-aminophenoxy)butane withanthracene-9-carbaldehyde have been synthesized and it's complexation capacity towards Zn^{2+}, Cd^{2+} and Hg^{2+}has been studied by adopting one-pot template method. The structures of the complexes were confirmed by ^{1}HNMR, ^{13}CNMR, IR spectroscopy and mass spectrometry. We are also especially interested in the antibacterial activity of these new complexes, free ligands (L_1 and L_2) and metal ions. The results showed that in the metal complexes have greater antibacterial activity but related free ligands and metal ions have not antibacterial activity.

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