Synthesis of Benzoazolyl-*N,N*-dimethylformamidines: Complexation and Biological Activity

Abdel-Zaher A. Elassar

Chemistry Department, Faculty of Science,
Helwan University, AinHelwan,
Cairo, Egypt
E-mail: aelassar@yahoo.com

Abstract
2-aminobenzimidazole and 2-aminobenzthiazole were transferred to their corresponding benzoazolyl formamidines. The synthesized formamidines were used in the synthesis of six different bioactive derivatives. Using ofN'-(1H-benzo[d]imidazol-2-yl)-N,N-dimethyl-formamidine (L) and N'-(benzo[d]thiazol-2-yl)-N,N-dimethyl-formamidine (L^1)as a ligand was investigated, where aqueous solution of metal salts are treated with L or L^1togive themetal complexes. TGA of ligand and corresponding complexes were also studied. The structure of the ligand and different synthesized formamidines was established based on elemental analysis and spectral data. Biological activity of the formamidines and metal complexes was testedagainst fungus, gram positive and gram negative bacteria.

Keywords:2-aminobenthiazole, 2-aminobenzimidazole, formamidine, complex, biological activity.

1. Introduction

The sulfur containing compounds such as 2-aminobenzothiazole derivatives have been a topic of interest for research for over a century because they have important biological activities and have been developed for the treatment of muscle relaxants, diabetes, tuberculosis, epilepsy, analgesia, inflammation and viral infection (Keri *et al.*, 2015; Hisamoddin, 2014;Abdul Rouf, 2014). Benzothiazole derivatives were showed inhibitory effect against human laryngocarcinoma (Shi *et al.*2004) , anticancer (Huang *et al.* 2006; Kamal, 2006), antitumoractivity (Yongseog, *et al.* 2004), fungicidal activities (Singh *et al.*1988), antihelmintic (Suresh *et al.* 2013), antiviral (Akhtar *et al.* 2008), and antimicrobial activity (Abdel-Rahman *et al.* 2007).
In this article, we have reported a new and efficient method for the synthesis of benzothiazolylformamidine derivatives. Complexation of benzothiazolyl and benzoimidazolylformamidines with different metal ion salts were studied. The benzothiazolylformamidine derivatives reacted with heterocyclic aminesto give biologically active heterocyclic compounds.

2. Experimental

All melting points are uncorrected. IR spectra were recorded in KBr with an IR spectrophotometer Shimadzu408.^{1}H NMR and ^{13}C NMR spectra were recorded on Varian EM-390 MHz spectrometer using

TMS as internal reference and chemical shifts are expressed as δ ppm. Mass spectra were measured ona Shimadzu GCMS-QP 1000 Ex mass spectrometer. Microanalytical data were obtained from the Microanalytical Data Unit at Cairo University, Egypt.

Synthesis of *N′*-(benzo[d]thiazol-2-yl)-N,N-dimethylformamidine (1a) and *N*'-(1*H*-benzo[d]imidazol-2-yl)-*N,N*-dimethylformamidine (1b)

A solution of 2-aminobenzothiazole or 2-aminobenzimidazole (0.01 mol) in absolute ethanol was mixed with DMFDMA (0.01 mol) and left overnight at room temperature in case of 2-aminobenzothiazole while in case of 2-aminobenzimidazole the reaction mixture was heated under reflux for 6h. The solid product, so formed, in case of 2-aminobenzothiazole was collected by filtration, while in case of 2-aminobenzimidazole the reaction mixture was kept 24h in fridge and the collected the solid product by filtration.

***N′*-(benzo[d]thiazol-2-yl)-N,N-dimethylformamidine (1a)**

Compound **1a** was obtained as white crystals (97.79 %) from EtOH; mp 98^{o}C (Lit. (Richter *et al* 1970, Landreau*et al* 2002) mp 99^{o}C and (Al-zaydi*et al* 2003) mp 111^{o}C; IR: 1618 (C=N), 1491 (HC=), 1103 cm^{-1} (C-N); ^{1}H NMR: δ 7.26 (t, 1H, aromatic-H, *J*= 6.8Hz), 7.30 (t, 1H, aromatic-H, *J*=6.8 Hz), 7.74 (d, 1H, aromatic-H, *J*=8 Hz), 7.68 (d, 1H, aromatic-H, *J*=8 Hz), 8.33 (s, 1H, CH=N), 3.08, 3.05 ppm (2s, 6H, 2NMe).^{13}C NMR δ173.60 (CH=N), 157.62 (thiazole–C2), 152.48, 133.11, 125.87, 122.92, 121.30, 120.32 (aromatic –Cs), 40.87 (N-Me), 35.14 ppm (N-Me) ppm. MS (EI): *m/z* 205.06 [M$^{\bullet+}$]. Anal.Calcd for $C_{10}H_{11}N_3S$ (205.28): C: 58.51; H: 5.40; N: 20.47, S, 15.62; Found: C: 58.41; H: 5.45; N: 20.33; S, 15.66.

***N*'-(1*H*-benzo[d]imidazol-2-yl)-*N,N*-dimethylformamidine (1b)**

Compound **1b** was obtained as white crystals (95.13 %) from diethyl ether; mp 240^{o}C (Lit. mp 248-250^{o}C, Shaaban et al; mp 225-228^{o}C, Sakamoto et al); IR: 3153 (NH), 1630 (C=N), 1541 (HC=), 1119 cm^{-1}(C-N); ^{1}H NMR: δ11.56 (br, 1H , NH- D_2O-exchange), 8.67 (s, 1H, CH=NMe_2), 7.23 (t, 2H, aromatic-H, *J*= 8.8Hz), 6.99 (d, 2H, aromatic-H, *J*=6 Hz),3.09, 2.99 ppm (s, 6H, 2NMe_2).^{13}C NMR δ 158.07 (CH=N), 159.04 (imidazole–C2), 138.88, 120.32, 113.13 (aromatic –Cs), 39.28 (N-Me), 34.71 ppm (N-Me). MS (EI): *m/z*188.10 [M$^{\bullet+}$]. Anal.Calcd for $C_{10}H_{12}N_4$ (188.23): C: 63.81; H: 6.43; N: 29.77; Found: C: 63.68; H: 6.21; N: 29.78.

Synthesis of *N,N′*-di(benzo[d]thiazol-2-yl)formamidine (4a); *N′*-(1H-benzo [d]imidazol-2-yl)-*N*-(benzo[d]thiazol-2-yl)formamidine (4b); 1-((benzo[d] thiazol-2-ylimino)methyl)-3-methyl-1H-pyrazol-5(4H)-one (5a);1-((1H-benzo [d]imidazol-2-ylimino)methyl)-3-methyl-1H-pyrazol-5(4H)-one (5b); *N′*-(benzo[d]thiazol-2-yl)-*N*-(thiazol-2-yl)formamidine (6a) and *N′*-(1H-benzo[d]imidazol-2-yl)-*N*-(thiazol-2-yl)formamidine (6b)

To a solution of **1a** or **1b** (0.01 mol) in DMF (30 mL), 2-aminobenzothiazole or 2-aminothiazole or 3-methyl-1H-pyrazol-5(4H)-one (0.01 mol) was added. The reaction mixture was heated under reflux for 3h. The solvent was evaporated under vacuum and left overnight in fridge. The solid product was collected by filtration and crystallized from proper solvent.

***N,N′*-di(benzo[d]thiazol-2-yl) formamidine (4a)**

Compound **4a** was obtained as beige crystals (72 %) from EtOH; mp 88-90^{o}C; IR: 3233 (NH), 1640 cm^{-1}(C=N); ^{1}H NMR: δ 11.44 (br, 1H , NH, D_2O-exchange), 8.23 (s, 1H, CH=N), 7.57 (t, 4H, aromatic-H, *J*= 8.8Hz), 7.22 (d, 4H, aromatic-H, *J*=6 Hz). ^{13}C NMR δ 158.28 (CH=N), 154.78, 138.88, 125.78, 121.68 ppm

(aromatic carbons). MS (EI): *m/z* 310.10 [$M^{\bullet+}$]. Anal.Calcd for $C_{15}H_{10}N_4S_2$ (310.40): C: 58.04; H: 3.25; N: 18.05, S: 20.66; Found: C: 57.98; H: 3.21; N: 17.88, S, 20.48.

***N'*-(1H-benzo[d]imidazol-2-yl)-*N*-(benzo[d]thiazol-2-yl)formamidine (4b)**

Compound **4b** was obtained as yellow crystals (67 %) from DMF; mp185^oC; IR: 3235 (NH), 1642 cm^{-1}(C=N); ^1H NMR: δ 11.12, 10.89 (br, 2H , NH, D_2O-exchange), 8.33 (s, 1H, CH=N), 7.66-7.14 (m, 8H, aromatic-H).^{13}C NMR δ160.21 (CH=N), 158.67, 138.80, 124.23, 113.89 (benzimidazole carbons), 161.23, 149.66, 126.07,125.24, 121.55 ppm (benzothiazole carbons). MS (EI): *m/z*293.1 [$M^{\bullet+}$]. Anal.Calcd for $C_{15}H_{11}N_5S$ (293.35): C: 61.42; H: 3.78; N: 23.87, S: 10.93; Found: C: 61.35; H: 3.67; N: 24.01, S, 11.05.

1-((benzo[d]thiazol-2-ylimino)methyl)-3-methyl-1H-pyrazol-5(4H)-one (5a)

Compound **5a** was obtained as yellow crystals (66 %) from EtOH/DMF(1:1); mp 228-230^oC; IR: 1656 (CO), 1641cm^{-1} (C=N); ^1H NMR: δ 8.33 (s, 1H, CH=N), 7.86, 7.56 (d,t, 4H, aromatic-H), 2.34 (s, 2H, CH_2), 1.12 (s, 3H, Me) .^{13}C NMR δ165.32 (CO), 163.21 (CH=N), 161.43, 148.36, 135.34, 126.07,121.55(benzothiazole carbons), 159.28, 43.12, 23.23 ppm (pyrazolone carbons). MS (EI): *m/z*258.06 [$M^{\bullet+}$]. Anal.Calcdfor $C_{12}H_{10}N_4OS$ (258.30): C: 55.80; H: 3.90; N: 21.69, S: 12.41; Found: C: 56.11; H: 3.89; N: 21.75, S, 12.51.

1-((1H-benzo[d]imidazol-2-ylimino)methyl)-3-methyl-1H-pyrazol-5(4H)-one (5b)

Compound **5b** was obtained as beige crystals (68 %) from DMF; mp 210^oC; IR: 3332 (NH), 1659 (CO), 1641cm^{-1} (C=N); ^1H NMR: δ10.23 (br, 1H, NH, D_2O-exchange), 8.33 (s, 1H, CH=N), 7.74, 7.43 (d,t, 4H, aromatic-H), 2.35 (s, 2H, CH_2), 1.13 (s, 3H, Me) .^{13}C NMR δ165.45 (CO), 162.69 (CH=N), 160.63, 138.36, 125.52,116.32 (benzimidazole carbons), 159.26, 42.98, 23.33 ppm (pyrazolone carbons) ppm. MS (EI): *m/z*241.1 [$M^{\bullet+}$]. Anal.Calcd for $C_{12}H_{11}N_5O$ (241.25): C: 59.74; H: 4.60; N: 29.03; Found: C: 59.42; H: 4.51; N: 28.89.

***N'*-(benzo[d]thiazol-2-yl)-*N*-(thiazol-2-yl)formamidine (6a)**

Compound **6a** was obtained as dark red crystals (62 %) from EtOH; mp101^oC; IR: 3324 (NH), 1641cm^{-1} (C=N); ^1H NMR: δ11.03 (br, 1H, NH, D_2O-exchange), 8.23 (s, 1H, CH=N), 7.78, 7.62 (d,t, 4H, aromatic-H), 7.54, 6.67 (d, 2H, thiazole-H).^{13}C NMR δ163.24 (CH=N), 161.43, 149.66, 135.34, 125.57,122.01(benzothiazole carbons), 159.36, 138.25, 110.21ppm (thiazole carbons). MS (EI): *m/z*260.01 [$M^{\bullet+}$]. Anal.Calcd for $C_{11}H_8N_4S_2$ (260.34): C: 50.75; H: 3.10; N: 21.52, S: 24.63; Found: C: 50.66; H: 2.89; N: 21.42, S, 24.42.

***N'*-(1H-benzo[d]imidazol-2-yl)-*N*-(thiazol-2-yl)formamidine (6b)**

Compound **6b** was obtained as dark red crystals (68 %) from DMF/EtOH(1:1); mp143^oC; IR: 3334-3341 (NH), 1642 cm^{-1}(C=N); ^1H NMR: δ11.02, 10.23 (br, 2H, NH, D_2O-exchange), 8.26 (s, 1H, CH=N), 7.74, 7.43 (d,t, 4H, aromatic-H), 7.66, 6.89 (d, 2H, thiazole-H).^{13}C NMR δ163.24 (CH=N), 161.53, 138.22, 123.57,116.14 (benzimidazole carbons), 159.45, 138.44, 111.12ppm (thiazole carbons).. MS (EI): *m/z*243.1 [$M^{\bullet+}$]. Anal.Calcd for $C_{11}H_9N_5S$ (243.29): C: 54.31 H: 3.73; N: 28.79; S, 13.18 Found: C: 54.44; H: 3.65; N: 28.78; S, 12.97.

Method of Complexation

To a solution of ligand L or L^1 (0.01 mol) in ethanol (20 mL), a filter solution of metal salt in the same solvent, mixed with 2 mL of water, was added. The reaction mixture was refluxed for 3h. The solvent

evaporated under vacuum and the solid product, so formed. After cooling was collected by filtration and crystallized from proper solvent. The elemental analysis and spectral data were collected in Tables1 and 2.

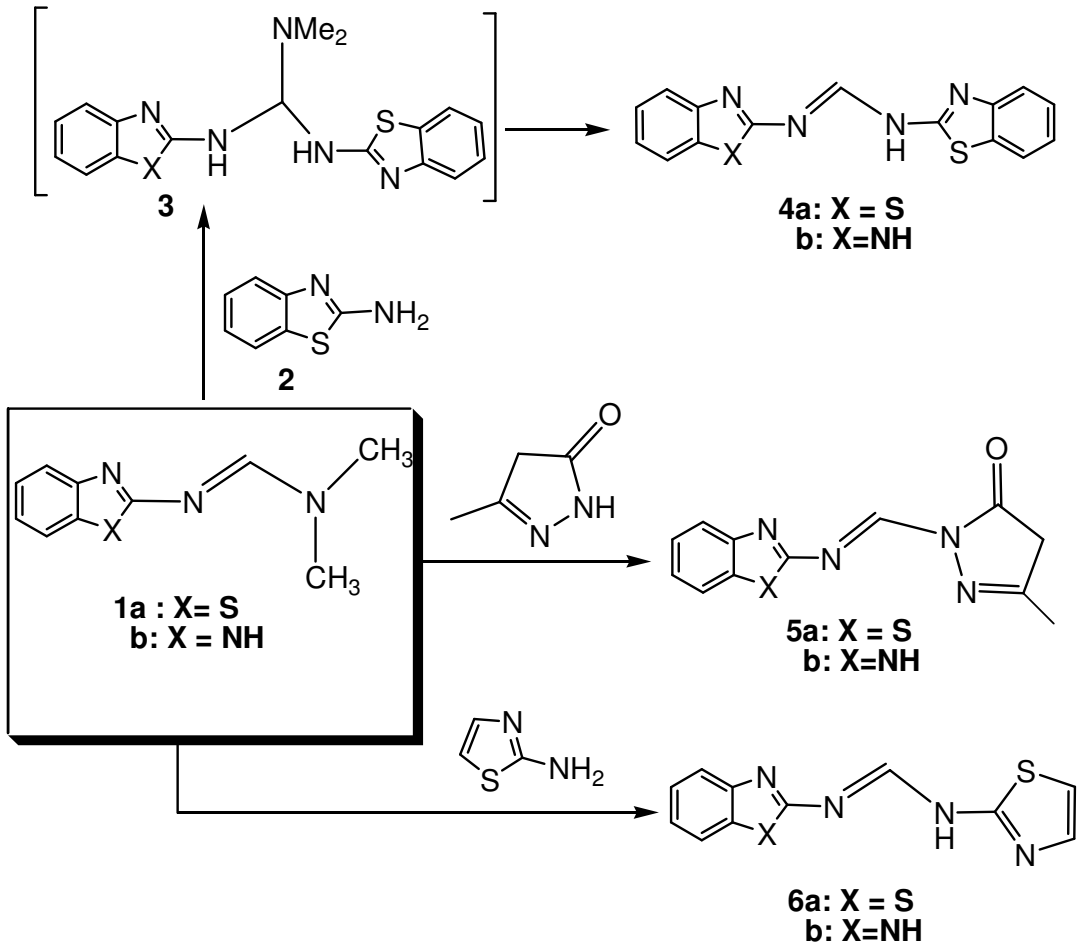
Biological activity*:*

Tested compounds were screened for their antibacterial activity against gram positive, gram negative and fungus (*Bacillus sp., Staphylococcus aureus*, *Escherichia Coli*, *Salmonella sp. and Candida albicans*. The MIC (minimum inhibitory concentration) was evaluated by the turbidity method. A loopful of bacteria was inoculated in 100 mL of nutrient broth at 37^0C for 20 h in a test-tube shaker at 150 rev min^{-1}. The test compounds were prepared by dissolving in a minimal volume of DMSO and were serially diluted in Mueller-Hinton broth at concentrations in the range of 1–100 mg mL^{-1}. The 24h bacterial cultures were then transferred into 10 mL of Muller–Hinton broth (control and test compounds) and incubated at 37^0C for 24 h. The growth of the bacteria was determined by measuring the turbidity after 24 h. Thus, the MIC was generally read as the smallest concentration of drug in the series that prevents the development of visible growth of test organism. All the experiments were done in triplicate.

3. Results and Disscusion

3.1 Synthesis

Literature describes the reaction of 2-aminobenzothiazole **1**with formamides in the presence of $POCl_3$ (1:5:2) gave formamidinederivative (Livshits*et al* 1982). The synthesis of *N*'-(benzo[d]thiazol-2-yl)-*N,N*-dimethylformamidine**1b** with yield 83%. It is of value to report here that reaction yield was improved to be 97.79%. Similarly, 2-aminobenzimidazole reacted with DMFDMA to give *N'*-(1*H*-benzo[d]imidazol-2-yl)-*N,N*-dimethylformamidine**1b**. Both formamidines**1a** and **1b** are treated with heterocyclic amines to give the bioactive products. Thus, compound **1a,b** reacted with 2-aminobenzothiazole, 2-aminothiazole, and 3-methyl-1H-pyrazol-5(4H)-one to give formamidine derivatives **4a,b**to **6a,b** (*cf.* Scheme 1). The reaction was assumed to be proceed *via* addition of amino group in amines to the double bond of formamidine to give the non isolated intermediate followed by lose of one molecule of dimethylamine to give the final isolated products. For example,2-aminobenzothiazole,**2** reacted with formamidine derivatives **1a,b**to give **4a,b** through the non isolatedintermediate **3.**The structure of compounds **1a,b**and **4a,b**-**6a,b** was established based on the elemental analysis and spectral data. For example, the mass spectrum of**4a**was showed*m/z* at 310.10 which agree with the molecular formula $C_{15}H_{10}N_4S_2$. It is^{1}H NMR shows peaksatδ 8.23 (s, 1H, CH=N); triplet at 7.57 ppm for four aromatic protons in addition toδ7.22 ppm as a doublet for another four aromatic protons. Furthermore, ^{13}C NMR shows cabons at δ 158.28 (CH=N), 154.78, 138.88, 125.78, 121.68 ppm (aromatic carbons). Similarly, compounds **4b, 5a,b** and **6a,b** were established (*cf.* experimental).



Scheme 1

3.2Complexation

Using of compound **1a,b** as a ligand for metal complexation was investigated. The complexation of bidentate ligand**1a (L)** and **1b (L^1)** with different metal salts e.g. Co(II), Cd (II), Cu(II), Fe(III), Ni(II) and Zn (II) produced metallo-organic complexes with 1:2 ratio (Metal: Ligand, respectively) in the form $L_2MX_2.nH_2O$ (X= NO_3^- except in case of Fe,X = acetlyacetonate) (*cf.* Scheme 2). Thus, compound **1a** reacted with different metal salt solution to give the complexes $L_2NiCl_2.8H_2O$, $L_2CdCl_2.4H_2O$, $L_2CuCl_2.H_2O$,$L_2CoCl_2.5H_2O$, $L_2ZnCl_2.H_2O$ and$L_2Fe(C_5H_7O_2)_3.H_2O$. On the other hand, **1b** reacted with metal salts with behavior similar to that with **1a** to give the complexes $L^1{}_2NiCl_2.2H_2O$, $L^1{}_2CdCl_2.3H_2O$, $L^1{}_2CuCl_2.4H_2O$, $L^1{}_2CoCl_2.H_2O$, $L^1{}_2ZnCl_2.2H_2O$, and $L^1{}_2Fe(C_5H_7O_2)_3$. Tables 1 and 2 are including elemental analysis and spectral data of the prepared complexes.

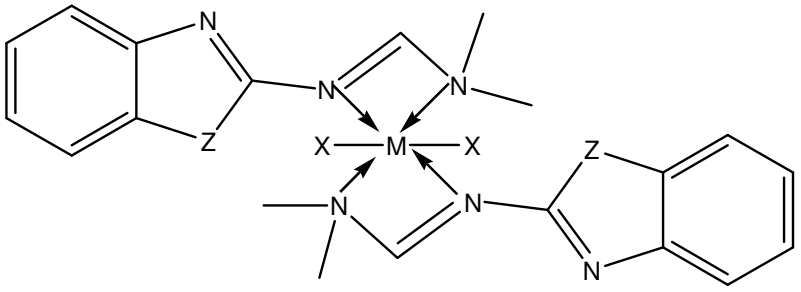
Table (1): Elemental analysis and physical properties of ligands (L and L^1) and there complexes

compound	colour	mp (^oC)	Elemental Analysis Found % (Calcd %)			
			C%	H%	N%	S%
L	White	87	58.42 (58.51)	5.55 (5.40)	20.46 (20.47)	15.66 (15.62)
$L_2CoCl_2.5H_2O$	Blue	142	37.80 (38.10)	4.87 (5.12)	13.02 (13.33)	10.05 (10.17)
$L_2CdCl_2.4H_2O$	White	145	36.18 (36.07)	4.50 (4.54)	12.81 (12.62)	9.59 (9.63)
$L_2CuCl_2.H_2O$	Green	192	43.01 (42.66)	4.27 (4.30)	14.84 (14.93)	11.38 (11.39)
$L_2Fe(C_5H_7O_2)_3.H_2O$	Red	93	53.51 (53.77)	6.12 (5.80)	10.35 (10.75)	7.98 (8.20)
$L_2NiCl_2.8H_2O$	Green	125	34.89 (35.10)	5.85 (5.60)	12.39 (12.28)	9.50 (9.37)
$L_2ZnCl_2.H_2O$	White	238	42.53 (42.53)	4.56 (4.28)	14.67 (14.88)	11.59 (11.58)
L^1	White	240	63.76 (63.81)	6.21 (6.43)	29.78 (29.77)	
$L^1{}_2CoCl_2.H_2O$	Blue	182	45.90 (45.82)	5.18 (5.00)	21.48 (21.37)	
$L^1{}_2CdCl_2.3H_2O$	White	245	38.94 (39.13)	4.91 (4.93)	18.28 (18.26)	
$L^1{}_2CuCl_2.4H_2O$	Green	132	40.96 (41.21)	5.61 (5.53)	19.56 (19.22)	
$L^1{}_2Fe(C_5H_7O_2)_3$	Red	175	57.71 (57.62)	6.36 (6.22)	15.37 (15.36)	
$L^1{}_2NiCl_2.2H_2O$	Green	164	43.97 (44.31)	5.56 (5.21)	20.33 (20.67)	
$L^1{}_2ZnCl_2.2H_2O$	White	>300	44.01 (43.77)	5.31 (5.14)	20.64 (20.42)	

Table (2): ^{1}H NMR and ^{13}C NMR of ligands and there complexes

compound	IR (cm^{-1})	^{1}H NMR (ppm)
L	3053 (CH-Ar); 1618 (C=N of thiazole), 1528 (=CH-NMe_2), 1103 (C-N)	8.33 (s, 1H, CH=N), 7.26 (t, 1H, Ar-H, *J*= 6.8Hz), 7.30 (t, 1H, Ar-H, *J*=6.8 Hz), 7.74 (d, 1H, Ar-H, *J*=8 Hz), 7.68 (d, 1H, Ar-H, *J*=8 Hz), 3.08, 3.05 (2s, 6H, 2NMe).^{13}C NMR δ 173.60 (amidine-C), 157.62 (thiazole –C2), 152.48, 133.11, 125.87, 122.92, 121.30, 120.32 (Ar–Cs), 40.87 (NMe), 35.14 (NMe)
$L_2CoCl_2.5H_2O$	3435 (H_2O);1633C=N of thiazole; 1589(=$CHNMe_2$), 1123 (C-N)	8.71 (s,1H,=CH–N), 7.867, 7.33, 7.31, 7.15 (Ar-H), br, 2.85-2.82 (H_2O). ^{13}C NMR δ157.79, 122.68, 121.75, 120.34, 114.15, 39.33, 35.11
$L_2CdCl_2.4H_2O$	3423(H_2O); 1638 (C=N); 1576 (=$CHNMe_2$); 1103 (C-N)	8.33 (s, 1H, =CH-N), 7.74 (d, 1H, Ar-H, *J*= 5.2Hz), 7.59 (d, 1H, Ar-H, *J*=5.2 Hz), 7.32 (t, 1H, Ar-H, *J*=5.2 Hz), 7.17 (t, 1H, Ar-H, *J*=5.2 Hz), 3.11, 2.99 (2s, 6H, 2NMe).^{13}C NMR δ 173.79 (=CH-), 158.06 (thiazole –C2), 151.52, 132.63, 126.19, 123.19, 121.87, 120.20 (aromatic –Cs), 40.87 (N-Me), 35.36 (N-Me) ppm.
$L_2CuCl_2.H_2O$	3436(H_2O); 1634 (C=N); 1588 (=$CHNMe_2$); 1123 (C-N)	8.33 (s, 1H, =CH-N), 7.61-6.90 (m, 4H,Ar-H), 3.98, 3.86 (2s, 6H, 2NMe).^{13}C NMR δ 173.79 (=CH-), 158.16 (thiazole –C2), 153.98, 132.63, 128.35, 123.03, 122.74, 121.13 (aromatic–Cs), 42.41 (N-Me), 36.87(N-Me) ppm.
$L_2Fe(C_5H_7O_2)_3.H_2O$	3421 (H_2O); 1712 (CO); 1619 (C=N); 1572 (=$CHNMe_2$); 1097 (C-N)	8.30 (s, 1H, =CH-N), 7.85-6.89 (m, 4H, Ar-H), 6.57 (2H, ETHYLENIC); 3.23, 3.34 (2s, 6H, 2NMe), 2.31 (s, 9H, 3Me); 1.73 (s, 9H, 3Me).^{13}C NMR δ 173.79 (=CH-), 158.16 (thiazole –C2), 153.98, 132.63, 128.35, 123.03, 122.74, 121.13 (aromatic–Cs), 42.41 (N-Me), 36.87 (N-Me); 197.10, 189.89, 101.30, 30.35, 25.32 (acetylacetonate carbons)
$L_2NiCl_2.8H_2O$	3423(H_2O); 1638 (C=N); 1576 (=$CHNMe_2$); 1103 (C-N)	8.44 (s, 1H, =CH-N), 7.51-6.72 (dd, tt, 4H, Ar-H), 2.95, 2.84 (2s, 6H, 2NMe).^{13}C NMR δ 172.04 (=CH-), 157.46 (thiazole–C2), 125.40, 124.41, 122.32, 121.45, 120.88, 119.80 (aromatic–Cs), 40.53 (N-Me), 34.64 (N-Me) ppm.
$L_2ZnCl_2.H_2O$	3411 (H_2O); 1630 (C=N); 1588 (=$CHNMe_2$); 1122 (C-N)	8.44 (s, 1H, =CH-N), 7.78-7.03 (dd, &tt, 4H, Ar-H), 3.18, 2.99 (2s, 6H, 2NMe).^{13}C NMR δ 173.42 (=CH-), 157.44 (thiazole –C2), 151.29, 132.11, 129.74, 125.60, 122.41, 121.36, (aromatic–Cs), 40.44 (N-Me), 34.74 (N-Me) ppm.
L^1	3230 (NH), 1630 (C=N); 1541(=$CHNMe_2$); 1119 (C-N)	11.56 (br, 1H, NH, D_2O-Exchange), 8.67 (s, 1H, =CH-N), 7.24, 6.97 (dd,4H, Ar-H), 3.12, 3.01 (2s, 6H, 2NMe).^{13}C NMR δ159.04 (=CH-), 158.07 (thiazole–C2), 138.88, 120.32, 113.15, (aromatic–Cs), 39.28 (N-Me), 34.71 (N-Me) ppm.

$L^1_2CoCl_2.H_2O$	3428(H_2O); 3206 (NH), 1636 (C=N); 1585 (=$CHNMe_2$); 1120 (C-N)	11.45 (br, 1H, NH, D_2O-Exchange), 8.65 (s, 1H, =CH-N), 7.34, 6.88 (dd,4H, Ar-H), 3.14, 3.01 (2s, 6H, 2NMe).^{13}C NMR δ 159.33 (=CH-), 157.35 (thiazole–C2), 138.73, 120.12, 113.36, (aromatic–Cs), 39.27 (N-Me), 34.74 (N-Me) ppm.
$L^1_2CdCl_2.3H_2O$	3420(H_2O); 3194 (NH); 1634 (C=N); 1597 (=$CHNMe_2$); 1121 (C-N)	11.80 (br, 1H, NH, D_2O-Exchange), 8.57 (s, 1H, =CH-N), 7.33, 6.98 (dd,4H, Ar-H), 3.08, 2.93 (2s, 6H, 2NMe).^{13}C NMR δ 159.98 (=CH-), 158.08 (thiazole–C2), 138.88, 120.45, 113.15, (aromatic–Cs), 39.35 (N-Me), 34.74(N-Me) ppm.
$L^1_2CuCl_2.4H_2O$	3396 (H_2O); 3177 (NH); 1639 (C=N); 1596 (=$CHNMe_2$); 1124 (C-N)	11.71 (br, 1H, NH, D_2O-Exchange), 8.87 (s, 1H, =CH-N), 7.44, 6.86 (dd,4H, Ar-H), 3.13, 3.04 (2s, 6H, 2NMe).^{13}C NMR δ 159.14 (=CH-), 158.22 (thiazole–C2), 138.90, 120.22, 113.45, (aromatic–Cs), 39.27 (N-Me), 34.72 (N-Me) ppm.
$L^1_2Fe(C_5H_8O_2)_3$	3169 (NH);1711 (CO); 1631 (C=N); 1570 (=$CHNMe_2$); 1119 (C-N)	11.56 (br, 1H, NH, D_2O-Exchange), 8.50 (s, 1H, =CH-N), 7.77, 7.18 (dd,4H, Ar-H), 3.32, 3.06 (2s, 6H, 2NMe); 2.51 (s, 9H, 3Me); 1.73 (s, 9H, 3Me).^{13}C NMR δ 173.12 (=CH-), 157.29 (thiazole –C2), 152.82, 132.68, 125.34, (aromatic–Cs), 39.43 (N-Me), 35.05 (N-Me); 197.10, 189.89, 117.89, 30.35, 25.32 (acetylacetonate carbons)
$L^1_2NiCl_2.2H_2O$	3396(H_2O); 3178 (NH); 1640 (C=N); 1587 (=$CHNMe_2$); 1125 (C-N)	11.44 (br, 1H, NH, D_2O-Exchange), 8.47 (s, 1H, =CH-N), 7.35, 6.98 (dd,4H, Ar-H), 3.13, 3.11 (2s, 6H, 2NMe).^{13}C NMR δ 159.25 (=CH-), 157.44 (thiazole–C2), 138.32, 120.12, 113.45, (aromatic–Cs), 39.37 (N-Me), 34.55 (N-Me) ppm.
$L^1_2ZnCl_2.2H_2O$	3414(H_2O); 3195 (NH); 1638 (C=N); 1555 (=$CHNMe_2$); 1118(C-N)	11.23 (br, 1H, NH, D_2O-Exchange), 8.23 (s, 1H, =CH-N), 7.38, 6.98 (dd,4H, Ar-H), 3.17, 3.15 (2s, 6H, 2NMe).^{13}C NMR δ 162.78 (=CH-), 158.97 (thiazole–C2), 138.73, 121.05, 119.15, (aromatic–Cs), 39.36 (N-Me), 34.52 (N-Me) ppm.



Z=S or NH ; X= NO_3^- or acetylacetonate

Scheme 2

3.3 Thermogravimetry Analysis (TGA) of Ligand and Complexes:

The thermogravimetric analysis (TGA) of ligands and their metal complexes are shown in Table 3. Thermal stability of complexes as compared by ligands are studied. The data are obtained under nitrogen with heating rate; 10˚C per min. The weight loss (w%) for the ligands and thier complexes in the temperature range 25 – 200 ^{o}C is due to the loss of water absorbed or adsorbed within the analyzed compound. The total weight loss (100%) of *N'*-(benzo[d]thiazol-2-yl)-*N,N*-dimethylformamidine, L and *N*'-(1*H*-benzo[d]imid-azol-2-yl)-*N,N*-dimethylform-amidine, L^1 are appeared at temperature 700^{o}C and 895^{o}C, respectively. This data reflect that the ligand of benzimidazolylformamidine is more stable than that of benzothiazolylformamidine. In the light of data reported in Table (3) the thermal stability of ligands and their complexes could be arranged as follows:

$L_2ZnCl_2.H_2O$ (800^{o}C) > $L_2CdCl_2.4H_2O$ (760^{o}C), >L (700^{o}C) > $L_2CuCl_2.H_2O$ (680^{o}C) >$L_2Fe(C_5H_8O_2)_3.H_2O$ (675^{o}C) > $L_2NiCl_2.8H_2O$ (660^{o}C) > $L_2CoCl_2.5H_2O$ (650^{o}C),

L^1 (895^{o}C) > $L^1{}_2ZnCl_2.2H_2O$ (820^{o}C) > $L^1{}_2CdCl_2.3H_2O$ (680^{o}C) >$L^1{}_2Fe(C_5H_8O_2)_3$ (675^{o}C) > $L^1{}_2NiCl_2.2H_2O$ (665^{o}C) >$L^1{}_2CoCl_2.H_2O$ (650^{o}C) > $L^1{}_2CuCl_2.4H_2O$ (575^{o}C),

The data above revealed that L-Zn-complex and L-Cd-Complexes are more stable than the ligand (L), while L-Co-complex is the least stable. Moreover, the second ligand (L^1), is the most stable followed by L^1-Zn-complex, while the L^1-Cu-complex is the least stable. The metal residual of L-M-complex, as nitride, reported in Table 3 reflected that the metal uptake is different from metal to metal and it can be arranged as follows:

Cu-complex > Ni-complex > Zn-complex > Co-complex > Fe-complex > Cd-complex.

On the other hand, metal nitride residue of the metal-L^1- complexes are arranged as follows:

Co-complex > Zn-complex > Ni-complex > Cu-complex > Fe-complex > Cd-complex

This difference in the metal uptake is may be due to the nature of the metal and the ligand.

Table (3): TGA of ligands and there complexes under nitrogen

compound	No. of decomp steps	Decomposition temperature & (%)	Total Loss (%)	Residue (%)
L	1	276.77 (93.545%); 700.0 (100%)	100	0.00
$L_2CoCl_2.5H_2O$	5	45.73 (1.18); 289.52 (35.79); 468.39 (10.95); 585.16 (36.43); 650.00 (7.68)	92.03	7.97
$L_2CdCl_2.4H_2O$	4	50.00 (0.22); 314.44 (26.78); 653.23 (65.06); 760.00 (96.14)	96.14	3.86
$L_2CuCl_2.H_2O$	8	53.97 (0.22); 106.68 (0.36); 170.91 (8.74); 254.81 (19.61); 331.34 (12.91); 579.43 (32.52); 680 (13.17)	87.53	12.47
$L_2Fe(C_5H_8O_2)_3.H_2O$	5	72.83 (1.06); 212.87 (55.92); 448.67 (33.13); 575.64 (0.54); 675.00 (2.22)	92.87	7.22
$L_2NiCl_2.8H_2O$	6	132.96 (5.41); 183.51 (23.32); 33.41 (14.34); 460.08 (8.39); 548.05 (32.01); 660 (5.89)	89.36	10.64
$L_2ZnCl_2.H_2O$	5	50.02 (0.24); 382.93 (50.19); 449.47 (6.59); 611.50 (29.29); 800.00 (5.63)	91.94	8.06
L^1	5	283.14 (78.45); 580.65 (20.07); 711.01 (0.54); 895.42 (0.94)	100	0
$L^1{}_2CoCl_2.H_2O$	3	321.51 (8.99); 385.12 (36.87); 491.04 (11.18) 650.00 (19.51)	76.55	23.45

$L^1_2CdCl_2.3H_2O$	2	314.44 (26.76); 653.23 (65.06); 680.00 (4.32)	96.14	3.86
$L^1_2CuCl_2.4H_2O$	5	52.81 (2.98); 207.66 (7.67); 345.56 (7.29); 531.65 (67.72); 575.00 (6.17)	91.83	8.17
$L^1_2Fe(C_5H_8O_2)_3$	5	72.83 (1.06); 212.87 (53.92); 448.67 (35.13); 575.64 (0.54); 675.00 (4.22)	94.87	5.13
$L^1_2NiCl_2.2H_2O$	6	133.34 (2.41); 183.51 (25.32); 33.41 (14.34); 460.08 (10.39); 548.05 (30.01); 665 (5.89)	88.36	11.64
$L^1_2ZnCl_2.2H_2O$	7	52.61 (1.41); 195.15 (4.92); 301.92 (15.43); 464.17 (11.21); 550.46 (46.37); 777.64 (0.29); 820.00 (5.38)	85.01	14.99

3.4 Biological Activity of Synthesized Compounds*:*

The well known diverse biological activities of compounds containing sulfur as components of heterocyclic ring system (Keri et al 2015, Hisamoddin 2014, Yang 2014, Anuradha 2014, Bhoi 2014), in addition to metal complexes with such ring systems prompted us to test and study the antibacterial activities and anti-fungus of some of the synthesized compounds. Table 4 shows that most of the tested compounds had low to high activity against tested microorganisms. A high effect against *Bacillus sp.* was observed with compounds **4a,b**to **6a,b,** in addition with L-M-complex, where M = Cd, Cu, Zn and Co. While high effect against *Staphylococcus aureus* was observed with compounds **5a,b** and **6a,b**. Compounds **4a. 6a, 6b**, and L-M-complex, where M = Ni, Cd, and Fe are showed high effect against grame negative *Escherichia Coli.* High effect with *Salmonella sp* was observed with **6a, 6b,** and L-M-complex, where M = Ni, Cd and Zn. High effect against tested fungus was observed with **6a, 6b,** and L-M-complex, where M = Ni, Cu and Fe. A moderate to low effect was observed in other assays. A non effect against tested fungus was observed with **4b** and **5b** only.

Table (4): Biological activity of the synthesized compounds

Compound	*Bacillussp.*	*Staphylococcus aureus*	*Escherichia Coli*	*Salmonella sp*	*Candida albicans*
1a	21	20	22	24	18
1b	15	13	10	11	Nil
4a	22	12	20	19	12
4b	10	12	11	10	Nil
5a	25	24	14	13	15
5b	20	23	10	12	Nil
6a	24	23	20	21	21
6b	22	23	22	21	20
$L_2NiCl_2.8H_2O$	23	18	23	24	20
$L_2CdCl_2.4H_2O$	24	19	22	22	14
$L_2CuCl_2.H_2O$	21	12	12	21	Nil
$L_2CoCl_2.5H_2O$	23	14	19	18	20
$L_2ZnCl_2.H_2O$	24	15	18	21	22
$L_2Fe(C_5H_7O_2)_3.H_2O$	18	13	22	19	20

Severe effect: 25-20mm; moderate effect:15-19mm; low effect: 1-14mm

4. Conclusion

Benzoazolylformamidine derivatives were used for synthesis of other biologically active different derivatives. Metal up take of benzoazolylformamidine derivatives was studied to show that the complex was formed in 1:2 ratio of liganid to metal, respectively. The TGA of metal complex and ligand was studied and showed that the ligand more stable than metal complexes except that of L-Zn-complex. The bioactivity of the tested compounds showed a high to low effect.

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