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Synthesis, Spectral Characterizations and Antimicrobial Activity of 5-methoxy-2-(5-H/Me/F/Cl/Br/NO_2/OMe-1*H*-benzimidazol-2-yl)-phenols and Their $ZnCl_2$ Complexes

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Abstract

5-Methoxy-2-(5-H/Me/F/Cl/Br/NO_2/OMe-1*H*-benzimidazol-2-yl)-phenols (HL_1– HL_7) and their complexes with $ZnCl_2$ were synthesized. The structures of the ligands and the complexes were confirmed on the basis of elemental analysis and FT-IR, FT-Raman, ^{1}H-NMR and fluorescence spectroscopic techniques. In addition, molar conductivity was carried out for the $ZnCl_2$ complexes. In the complexes, the ligands acted as bidentate, via the imine nitrogen and the phenolate oxygen atoms. Fluorescence characteristics of the compounds were observed in ethanol: The ligands fluoresce as dual or triple whereas the complexes give dual or single fluorescence and most of them blue shifted. In addition, fluorescence spectra of HL_1 were investigated in various solvents. The compounds were screened for *in vitro* antimicrobial activities against *S. aureus, E. faecalis, E. coli I, E. coli II, K. pneumoniae, P. aeruginosa, A. baumannii* and for antifungal activity against *C. albicans*. The compounds HL_4, $[Zn(\mathbf{HL_4})_2Cl_2]\cdot 2H_2O$, HL_5, HL_6 and $[Zn(\mathbf{HL_6})_2Cl_2]\cdot 4H_2O$ exhibit antibacterial and antifungal activity against *S. aureus, E. faecalis* and *C. albicans*. It is observed that the Cl, Br and NO_2 groups increase the antimicrobial activity toward *S. aureus, E. faecalis* and *C. albicans*. These results can be considered as selective activity.

***Keywords*:** Benzimidazole; Methoxyphenol; Zinc(II) Complexes; Fluorescence; Antimicrobial activity

1.Introduction

The benzimidazole nucleus and its derivatives are known to play crucial roles in the structures and functions of a number of biologically important molecules, generally by virtue of their being coordinated to metal ions [1]. The high therapeutic properties of the related drugs have encouraged the medicinal chemist to synthesize the large number of novel chemotherapeutic agents [2]. Pharmaceutical properties including: antiviral [3] and antitumoral [4]; antifungal and antimycotic [5]; antihistaminic and antiallergic [6]; antimicrobial [7] and antihelminthic activity [8]; all are unique characteristics know from benzimidazole derivatives. Recently, some chloroaryloxyalkyl derivatives showed considerable bactericidal activity against *Salmonella typhi* O-901 and *Staphylococcus aureus* A 15091 [9]. Also these compounds are used extensively in industrial processes as corrosion inhibitors for metal and alloy surfaces [10,11]. These different applications have attracted many experimentalists and theorist to investigate the spectroscopic and structural properties of benzimidazole [12–14] and some of its derivatives [15]. In our previous studies, we found that various benzimidazolyl-phenol and benzimidazoly-pyridinyl derivatives and some of their complexes showed antimicrobial activity against several microorganisms [16–26]. For instance, 2-(5-H/Me/Cl/NO_2-1*H*-benzimidazol-2-yl)-4-Br/NO_2-phenols were effective especially on *S. aureus*; their Ag(I) and Hg(II) complexes showed high antimicrobial activity toward six bacteria in the study [16]. The Fe(III) complexes of 2-(5-H/Me-1*H*-benzimidazol-2-yl)-4-Br/NO_2-phenols exhibited considerable activity against *S. aureus* and *S. epidermidis* [17]. 2-(5-H/Me/Cl-1*H*-benzimidazol-2-yl)-phenols and their Fe(III) complexes showed considerable activity on some bacteria and fungi [18]. 2-Methoxy-6-(5-H/Me/Cl/NO_2-1*H*-benzimidazol-2-yl)-phenols and their some transition metal complexes were synthesized and characterized. Some ligands and Cu(II) and Zn(II) complexes showed antibacterial activity against Gram+ bacteria [20]. It was reported that 4-methoxy-2-(1*H*-benzimidazol-2-yl)-phenol and its Ag(I) and Cu(II) complexes are effective on *S. epidermidis*, *S. aureus* and *B. subtilis*. Also, 4-methoxy-2-(5-methyl/chloro-1*H*-benzimidazol-2-yl)-phenols showed antibacterial activity toward *S. aureus* [21]. Ag(I) and Zn(II) complexes of 2-methyl-6-(1*H*-benzimidazol-2-yl)-phenol showed antibacterial effect toward *K. pneumoniae*, *S. epidermidis* and *S. aureus* bacteria whereas the ligand itself had no any activity [22]. Pd(II), Ag(I) and Au(III) complexes of 4-(1*H*-benzimidazol-2-yl)-benzene-1,3-diol showed considerable antibacterial and antifungal activity while ligand itself has no any activity [23]. 2-(5-H/Me/F/Cl/NO_2-1*H*-benzimidazol-2-yl)-benzene-1,4-diols (HL_X: X=1–5) and HL_1 complexes with $Fe(NO_3)_3$, $Co(NO_3)_2$, $Ni(NO_3)_2$, $Cu(NO_3)_2$, $Zn(NO_3)_2$ showed considerable antimicrobial activity [24]. 3-(5-H/Me/Cl/NO_2-1*H*-benzimidazol-2-yl)-benzene-1,2-diols (HL_X : X=1-4) ligands and HL_3 complexes with $Fe(NO_3)_3$, $Cu(NO_3)_2$, $Co(NO_3)_2$, $Zn(NO_3)_2$ have been synthesized and characterized. HL_1, HL_2, HL_3 and $[Cu(\mathbf{L_3})_2]\cdot(H_2O)_2$ show considerable antimicrobial activity toward *S. epidermidis* and *C. albicans* [25]. Spectral characterizations and antibacterial effect of 2-(5-H/Cl/Me/NO_2-1*H*-benzimidazol-2-yl)-4-Me/Br-phenols (HL_1 – HL_5) and their some transition metal complexes were reported by us: While HL_1 ligand has considerable antibacterial activity on *B. cereus* only; it's Ag(I) complex show antibacterial effect toward almost to the all bacteria. HL_5 and $[Zn(\mathbf{L_5})_2]\cdot HClO_4$ exhibited considerable high antibacterial activity toward *K. pneumoniae*, *B. cereus*, *S. epidermidis* and *B. subtilis* [26]. In this study, 5-methoxy-2-(5-H/Me/OCH_3/F/Cl/Br/NO_2-1*H*-benzimidazol-2-yl)-phenols (HL_X, X = 1 – 7, Fig. 1.) and their $ZnCl_2$ complexes were synthesized and characterized by means of analytical data and FT-IR, FT-Raman, NMR and fluorescence spectroscopic techniques.

Fig. 1. Schematic view of the compounds in the study R = H, HL_1; R = CH_3, HL_2; R = F, HL_3; R = Cl, HL_4; R = Br, HL_5; R = NO_2, HL_6; R = OCH_3, HL_7.

2.Experimental

All chemicals and solvents are of reagent grade and were used without further purification.

Elemental analysis data were obtained with a Thermo Finnigan Flash EA 1112 analyzer. Decomposition points were determined using an Electro thermal melting-point apparatus. Molar conductivity of the complexes was measured on a WTW Cond315i conductivity meter in dimethylformamide (DMF) at 25 °C. ^{1}H-NMR spectra were run on a Varian Unity Inova 500 NMR spectrometer. The residual DMSO-d_6 signal was also used as an internal reference. FT-IR spectra were recorded on a Bruker Optics Vertex 70 spectrometer using Attenuated Total Reflection (ATR) techniques between 400 and 4000 cm^{-1}. The FT-Raman spectra were also recorded in the same instrument with a R100/R RAMII Raman module equipped with Nd:YAG laser source operating at 1064 nm line with 200 mW power and a spectral resolution of ±2 cm^{-1}. Fluorescence spectra were performed on a Shimadzu RF-5301 PC Spectrofluorophotometer

Synthesis of the Ligands

The ligands were prepared according to literature procedures [27, 28], by reacting 2-hydroxy-4-methoxybenzaldehyde (1.52 g, 10 mmol) and an equivalent amount of $NaHSO_3$ (1.04 g, 10 mmol) at room temperature in ethanol (25 mL) for 4–5 hours. The mixture was treated with appropriate 4-(H/Me/F/Cl/Br/NO_2/OCH_3)-1,2-phenylenediamine (for example 1,2-phenylenediamine 1.08 g for HL_1, 10 mmol) in DMF (15 mL) and gently refluxed for 2 hours. The reaction mixture was then poured into iced water (500 mL), filtered and crystallized from ethanol.

Synthesis of the Complexes

General Procedure: 0.5 mmol ligand (e.g. 120 mg of HL_1) was suspended in 15 mL ethyl acetate. Then equivalent amount of $ZnCl_2 \cdot 6H_2O$ (123 mg, 0.5 mmol) in 10 mL ethyl acetate was added to the ligand solution. After 2 h reflux, a precipitate was formed; it was filtered and dried at room temperature.

Determination of antimicrobial activity

Antimicrobial activity against *Stapyhlococcus aureus* ATCC29213, *Enterococcus faecalis* ATCC 29219, *Pseudomonas aeruginosa* ATCC 27853, *Acinetobacter baumannii* ATCC BAA-747, *Klebsiella pneumoniae* ATCC 700603, *Escherichia coli* ATCC 25922 (E. coli 1), *Escherichia coli* ATCC 35218 (E. coli 2) and *Candida albicans* ATCC 64548 were determined by the microbroth dilutions technique [29]. Sensitivity of the microorganism origin was investigated and quality control strains were used to determination of substances activities. The substances were taken 15 mg of each and were diluted with 1000 microliters of dimethyl sulfoxide AR (DMSO). 50 microliter Mueller Hinton Broth was added to each of microplate wells. 50 microliters diluent of substances was added to first wells. Serial dilutions were performed and positive and negative controls were studied. Then 50 microliters were added from the stock suspension of microorganisms to each of well. The process was repeated for each microorganism. Plates were covered by parafilm in order to prevent dryness and at 37 °C were incubated for 24 hours. Concentration of the reproduction to inhibit by visible was evaluated as minimum inhibitory concentration (MIC). 0.5 Mc Farland of bacteria was diluted with distilled water to 1/100 for bacterial suspension preparing and was obtain to $5x10^5$ cfu/mL concentration of bacterial suspensions. 2 Mc Farland of *Candida albicans* was diluted with distilled water to 1/100 for candida suspension preparing. Certain chemicals used as standard strain sensitivity of certain bacteria and *Candida albicans* from yeast were investigated against.

3.Results and Discussion

The analytical data and physical properties of the compounds are summarized in Table 1.

Table 1. The analytical data and physical properties of the ligands and the complexes

Compound	Found (calcd) %			M.p.[1]	Yield	Λ^2	Color
	C	H	N	°C	%		
HL_1	70.32	4.81	11.43	227	78	-	creamy
$C_{14}H_{12}N_2O_2$	(70.00)	(5.03)	(11.66)				
$[Zn(\mathbf{L_1})Cl(H_2O)]$	47.39	3.59	7.77	245	80	15.0	dirty
$C_{14}H_{13}ClN_2O_3Zn$	(46.95)	(3.66)	(7.82)				white
HL_2	70.59	5.80	10.68	218	91	-	dark
$C_{15}H_{14}N_2O_2$	(70.85)	(5.55)	(11.02)				yellow
$[Zn(\mathbf{HL_2})_2Cl_2]\cdot 2H_2O$	52.52	4.99	7.61	235	95	19.5	soil
$C_{30}H_{32}Cl_2N_4O_6Zn$	(52.92)	(4.74)	(8.23)				color
HL_3	65.32	4.51	10.67	255	86	-	dark
$C_{14}H_{11}FN_2O_2$	(65.11)	(4.29)	(10.85)				grey
$[Zn_2(\mathbf{L_3})_2Cl_2]$	47.22	3.39	7.69	274	68	18.1	dark
$C_{28}H_{20}Cl_2F_2N_4O_4Zn_2$	(46.96)	(2.81)	(7.82)				grey
HL_4	61.53	3.91	9.95	262	94	-	soil
$C_{14}H_{11}ClN_2O_2$	(61.21)	(4.04)	(10.20)				color
$[Zn(\mathbf{HL_4})_2Cl_2]\cdot 2H_2O$	46.97	3.73	7.61	334	94	38	grey
$C_{28}H_{26}Cl_4N_4O_6Zn$	(46.60)	(3.63)	(7.76)				
HL_5	52.76	3.19	8.78	261	81	-	cream
$C_{14}H_{11}BrN_2O_2$	(52.69)	(3.47)	(8.78)				
$[Zn(\mathbf{HL_5})_2Cl_2]\cdot 2H_2O$	41.82	3.43	6.68	297	73	44	light
$C_{28}H_{24}Br_2Cl_2N_4O_5Zn$	(41.43)	(3.35)	(6.90)				brown
HL_6	59.24	4.10	14.48	266	75	-	light
$C_{14}H_{11}N_3O_4$	(58.95)	(3.89)	(14.73)				brown
$[Zn(\mathbf{HL_6})_2Cl_2]\cdot 4H_2O$	43.70	3.96	9.86	301	93	26.5	light
$C_{28}H_{30}Cl_2N_6O_{12}Zn$	(43.18)	(3.88)	(10.79)				brown
HL_7	66.79	5.45	10.08	206	78	-	light
$C_{15}H_{14}N_2O_3$	(66.66)	(5.22)	(10.36)				brown
$[Zn(\mathbf{HL_7})_2Cl_2]\cdot H_2O$	52.16	5.04	7.34	224	81	21.0	brown
$C_{30}H_{30}Cl_2N_4O_7Zn$	(51.85)	(4.35)	(8.06)				

[1], decomposition

[2], Λ, Molar conductivity, $\Omega^{-1}cm^2mol^{-1}$ (in DMF, 25±1°C)

Melting point order of the ligands is: $HL_6 > HL_4 > HL_5 > HL_3 > HL_1 > HL_7$. The compound HL_7, includes two methoxy groups at the both rings, has lowest melting point (m.p.) among the ligands. The highest m.p. belongs to the nitro derivative (HL_6). It is observed that the methyl and methoxy groups decrease the m.p. whereas electronegative groups (F, Cl, Br, NO_2) increase m.p. compared to HL_1. Molar conductivity of the complexes varies between 15 and 44 $\Omega^{-1}cm^2mol^{-1}$ in DMF. According to the molar conductivity data, the all complexes are non-electrolyte in DMF [30].

The M:L (metal:ligand) ratio is 1:1 in the HL_1 and HL_3 complexes; and 1:2 in the other complexes. On the basis of analytical data and the molar conductance, it can be proposed that the HL_3 complex, $Zn_2(\mathbf{L_3})_2Cl_2$, has chloride-bridged structure.

FT-IR Spectra

Table 2. Prominent FT-IR (ATR) and FT-Raman bands (frequencies) for the compounds

Compound	FT-IR (cm^{-1})	FT-Raman (cm^{-1})
HL_1	3334 m, 3060 w, 2931 w, 2834 w, 1639 m, 1606 m, 1590 m, 1490 m, 1453 m, 1398 s, 1269 s, 1200 s, 1136 m, 1035 m, 955 m, 818 m, 721 vs, 580 m, 524 m, 460 m	3063 m, 2931 w, 2829 w, 1639 m, 1604 m, 1545 s, 1482 m, 1451 s, 1393 m, 1330 m, 1275 s, 1169 w, 1146 w, 1067 w, 1005 m, 966 m, 809 w, 731 m
$[Zn(\mathbf{L_1})Cl(H_2O)]$	3234 m, 3005 w, 1614 m, 1532 m, 1504 m, 1462 m, 1381 m, 1308 m, 1243 m, 1221 m, 1156 s, 1087 m, 1034 m, 828 m, 777 m, 742 s, 590 m, 546 m, 514 m, 453 m	3073 m, 2996 w, 2839 w, 1610 m, 1572 s, 1530 m, 1501 w, 1459 m, 1379 w, 1289 w, 1260 m, 1238 w, 1084 w, 1003 m, 965 w, 731 w
HL_2	3349 m, 3020 w, 2921 w, 2857 w, 1640 m, 1604 m, 1592 sh, 1442 m, 1396 s, 1270 s, 1201 m, 1032 m, 953 m, 822 m, 788 vs, 561 m, 525 m, 458 m	3069 w, 3023 w, 2938 w, 1644 w, 1623 m, 1572 w, 1547 m, 1485 w, 1462 w, 1332 w, 1279 m, 1169 w, 1075 w, 972 m, 771 w, 736 m
$[Zn(\mathbf{HL_2})_2Cl_2]\cdot 2H_2O$	3218 m,br, 2979 w, 1611 s, 1559 m, 1504 m, 1475 m, 1455 m, 1427 m, 1289 m, 1244 m, 1212 s, 1143 m, 1086 m, 1026 m, 971 m, 800 s, 736 m, 590 m, 463 m, 430 m	Could not be obtained
HL_3	3333 m, 3069 w, 2974 w, 2845 w, 1640 m, 1601 m, 1548 m, 1455 m, 1396 s, 1270 s, 1201 s, 1135 s, 1030 m, 953 m, 818 s, 795 s, 577 s, 528 m, 478 m	3074 m, 3036 w, 2943 w, 1643 m, 1620 m, 1548 m, 1485 w, 1456 m, 1396 w, 1355 w, 1291 m, 1231 w, 1169 w, 1082 w, 972 m, 774 m, 736 m
$[Zn_2(\mathbf{L_3})_2Cl_2]$	3224 s,br, 3081 w, 2941 w, 1613 s, 1533 m, 1503 m, 1456 s, 1374 m, 1294 m, 1221 s, 1141 s, 1035 m, 962 m, 829 m, 796 m, 736 m, 610 m, 504 m, 460 m, 430 m	Could not be obtained
HL_4	3330 m, 3010 w, 2934 w, 2838 w, 1640 m, 1604 m, 1547 m, 1442 m, 1392 s, 1293 m, 1270 m, 1201 s, 1148 m, 1033 m, 927 m, 821 s, 788 s, 567 m, 524 m, 458 m	3071 m, 3006 w, 2935 w, 2832 w, 1640 m, 1605 m, 1544 s, 1448 m, 1390 w, 1327 w, 1279 m, 1230 w, 1059 w, 963 m, 928 w, 825 w, 735 m
$[Zn(\mathbf{HL_4})_2Cl_2]\cdot 2H_2O$	3204 m,br, 3094 w, 2941 w, 1613 s, 1536 m, 1456 m, 1374 m, 1294 m, 1224 s, 1141 m, 1085 m, 1035 m, 972 m, 925 m, 829 m, 799 s, 733 m, 567 m, 504 w, 460 m, 427 m.	Could not be obtained
HL_5	3322 s, 3013 m, 2972 m, 2936 m, 1638 m, 1602 m, 1491 m, 1462 m, 1437 m, 1393 s, 1300 m, 1270 m, 1197 m, 1140 m, 1029 m, 954 m, 919 m, 818 m, 790 s, 633 m	3072 m, 2932 w, 1639 m, 1606 m, 1542 s, 1433 s, 1388 m, 1324 m, 1276 m, 1168 w, 1048 w, 965 m, 917 w, 820 w, 734 m
$[Zn(\mathbf{HL_5})_2Cl_2]\cdot 2H_2O$	3227 m,br, 2943 w, 1615 s, 1573 m, 1504 m, 1456 m, 1374 m, 1301 m, 1221 s, 1153 s, 1034 m, 971 m, 917 m, 789 m, 732 m, 588 m, 511 m, 459 m, 424 m	3067 m, 2949 w, 2842 w, 1613 s, 1568 s, 1529 m, 1455 m, 1430 m, 1378 w, 1266 m, 1227 m, 1093 w, 961 w, 916 w, 807 w, 736 m
HL_6	3310 m, 3098 w, 2937 w, 2841 w, 1633 m, 1617 m, 1590 m, 1484 m, 1442 m, 1382 m, 1336 s, 1290 s, 1260 s, 1171 m, 1138 m, 1032 m, 801 m, 735 m, 643 m, 541 m, 468 m	3080 w, 2985 m, 1632 m, 1615 m, 1592 m, 1541 m, 1494 m, 1439 m, 1333 s, 1278 m, 1244 m, 1138 w, 1060 m, 960 m, 875 w, 820 w, 735 w
$[Zn(\mathbf{HL_6})_2Cl_2]\cdot 4H_2O$	3344 m,br, 3202 m,br, 3089 w, 2944 w, 1607 m, 1587 m, 1520 m, 1477 m, 1338 s, 1220 m, 1141 m, 1067 m, 1026 m, 973 m, 819 m, 732 s, 609 m, 568 m, 539 m, 459 m	3086 w, 2939 w, 1613 m, 1571 m, 1523 m, 1453 m, 1343 s, 1324 s, 1292 m, 1251 m, 1177 w, 1087 m, 1064 m, 955 m, 817 w, 737 w
HL_7	3314 m, 3254 m, 2997 w, 2937 w, 2835 w, 1637 m, 1604 m, 1584 m, 1458 m, 1392 m, 1293 m, 1194 s, 1151 s, 1030 s, 917 m, 822 m, 788 s, 646 m, 587 m, 557 m, 461 m	3063 w, 2938 w, 1639 m, 1617 m, 1600 sh, 1542 m, 1478 w, 1446 w, 1385 w, 1309 w, 1283 m, 1174 w, 1090 w, 965 w, 901 w, 792 w, 731 w
$[Zn(\mathbf{HL_7})_2Cl_2]\cdot H_2O$	3198 m,br, 2939 w, 1611 m, 1505 m, 1482 m, 1457 m, 1275 m, 1247 m, 1202 m, 1160 m, 1117 m, 1026 s, 949 m, 830 m, 803 m, 735 m, 609 m, 508 w, 465 w	Could not be obtained

* m medium; br broad; s strong; w weak.

FT-IR spectral data of the ligands and the complexes are given in Table 2. The characteristic ν(O–H) and ν(N–H) vibration frequencies of the ligands exhibit only a single strong band at the 3310 – 3350 cm^{-1} range in the IR spectra,

probably caused by doubly intramolecular hydrogen bonding between the phenoxyl hydrogen atom and one of the imine nitrogen atoms (Table 2, Figure 2) [18,31,32]. In the complexes, the band appears at 3198 – 3234 cm^{-1} range should be belong to the ν(N–H) vibration only due to removing of the phenolic OH hydrogen atom on complexation. The characteristic ν(C–H) and δ(C–H) modes of ring residues and aliphatic groups (methyl and methoxy substituents) are observed in the wave region between 3100 – 2900 cm^{-1} and 1500 – 700 cm^{-1} (Table 2). The ν(C=C) frequencies for the ring residue are observed at the 1605 – 1640 cm^{-1} range with their own characteristics for the ligands in the IR spectra. These frequencies are expected to shift to lower frequency upon complex formation. Similarly the (C=N) asymmetric stretching frequencies are appeared at the 1584 – 1604 cm^{-1} range. It is observed that the ν(C=N) bands also shift to the lower frequencies, i.e. 1587 – 1532 cm^{-1} range upon complex formation. The corresponding bands for these frequencies in the IR spectra are observed as weak in most of the compounds. Probably reason of this is weakening of the C=N bond and having of it a form between the single and double bonds. These changes in the frequencies support the argument that coordination possibly occurs *via* imine nitrogen atom.

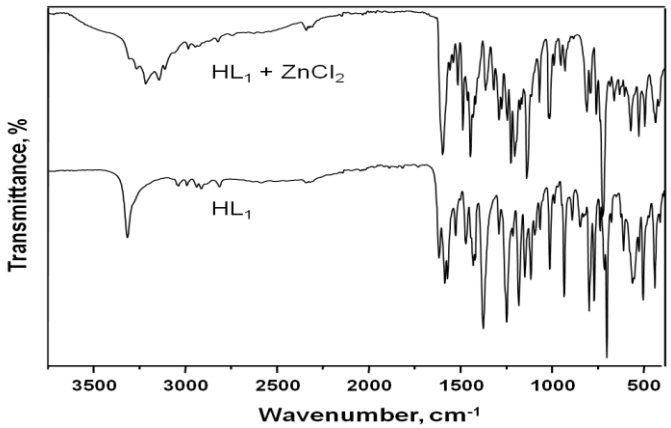


Fig. 2. FT-IR spectra of HL_1 and its Zn(II) complex.

The characteristic ν(C–H) modes of ring residues are observed in the range of 3005 – 3095 cm^{-1}, particularly in the Raman spectra of the compounds (Figs 2 and 3). The aliphatic ν(C–H) bands are appeared as weak or medium at the range of 2800 – 2985 cm^{-1} in both of the IR and Raman spectra. In the FT-Raman spectra of the compounds, the aliphatic and aromatic ν(C–H) groups are seen clearly at the 2900 – 3086 cm^{-1} range because of the NH and OH bands are absent in FT-Raman (Figure 3). The FT-Raman spectra of the Zn(II) complexes of HL_2, HL_3, HL_4 and HL_4 are not smooth probably due to disturbing fluorescence effect.

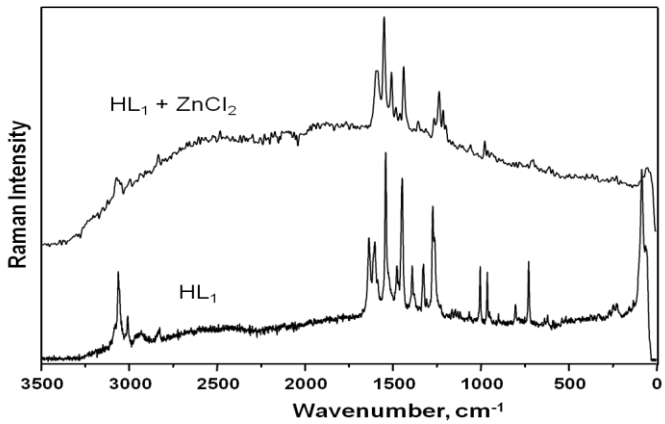


Fig. 3. FT-Raman spectra of HL_1 and its Zn(II) complex.

NMR Spectra

^{1}H-NMR spectral data are given in Table 3. The OH and NH protons show only a broad single band in the spectra of the ligands between 12.32 and 13.37 ppm values except HL_2. This observation results from strong hydrogen bonding between the imine nitrogen with double bond and phenolic hydrogen atoms (Figure 4) [24,33]. In the spectra of HL_2, the OH and NH protons are appeared separately at 13.37 (NH) and 12.90 ppm (OH): This may be considered as evidence for an isomeric structure as shown in Figure 4. Comparison of the ^{1}H-NMR spectra between HL_3 and its Zn(II) complex is shown in Figure 5.

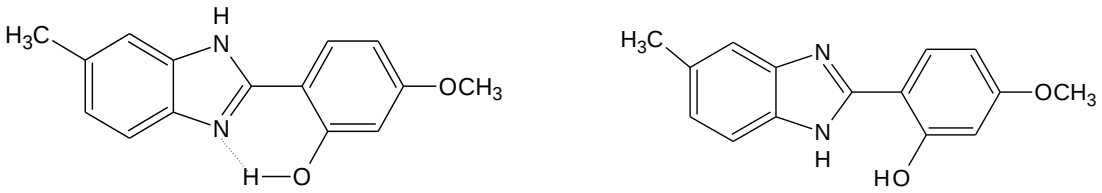
Table 3. ^{1}H-NMR spectral data of the ligands and their Zn(II) complexes (δ_H, ppm; in DMSO-d_6)

Compound	----------Benzimidazole protons----------					----------Phenolic protons----------				
	H4	H5	H6	H7	NH	H3'	H5'	H6'	OH	OCH_3
HL_1	7.61 m,br	7.24 m	7.24 m	7.61 m,br	13.17 s,br	6.59 d J=2.4	6.62 dd J=8.5,2.4	7.96 d J=8.5	13.17 s,br	3.80 s
[Zn(**L_1**)Cl(H_2O)]	7.65 dd J=6.2,3.2	7.30 dd J=6.2,3.2	7.30 dd J=6.2,3.2	7.65 dd J=6.2,3.2	--	6.60 s	6.65 d J=8.3	7.96 d J=8.8	--	3.81 s
HL_2	7.49 s, br	2.44 s[a]	7.40 d J=8.8	7.81 d,br J=7.8	13.37 s,br	6.58 d J=2.4	6.62 dd J=8.8,2.4	7.93 d J=8.3	12.90 s,br	3.81 s
[Zn(**HL_2**)$_2$Cl_2]·$2H_2O$	7.40 s	2.44 s[a]	7.09 d J=7.8	7.50 d J=8.3	13.07 s,br	6.57 s,br	6.60 s,br	7.91 d J=8.4	--	3.80 s
HL_3	7.60 s,br	--	7.43 s,br	7.10 d-t J=9.3,2.4	13.08 s	6.59 d J=2.4	6.63 dd J=8.8,2.4	7.94 d J=8.8	13.08 s	3.81 s
[Zn_2(**L_3**)$_2Cl_2$]	7.60 dd J=8.8,4.9	--	7.42 dd J=9.3,2.0	7.10 td J=9.3,1.9,2.4	13.06 s,br	6.57 s	6.60 d J=8.8	7.92 d J=8.8	--	3.80 s
HL_4	7.64 s,br	--	7.58 d J=8.5	7.23 dd J=8.5, 1.9	13.03 s,br	6.58 d J=2.5	6.62 dd J=8.8,2.5	7.93 d J=8.8	13.03 s,br	3.79 s
[Zn(**HL_4**)$_2$Cl_2]·$2H_2O$	7.64 d J=1.0	--	7.59 d J=8.3	7.25 dd J=8.8,2.0	13.05 s,br	6.57 s	6.60 d J=8.8	7.92 d J=8.8	--	3.80 s
HL_5	7.78 s,br	--	7.54 d J=8.3	7.35 dd J=8.3, 2.0	13.02 s,br	6.58 d J=2.4	6.62 dd J=8.8,2.4	7.93 d J=8.8	13.02 s,br	3.80 s
[Zn(**HL_5**)$_2$Cl_2]·$2H_2O$	7.80 s	--	7.57 d J=8.8	7.38 dd J=8.8,2.0	13.05 s,br	6.59 s	6.63 d J=8.3	7.95 d J=8.8	--	3.81 s
HL_6	8.85 s	--	7.91 dd J=9.3,1.9	6.79 d J=9.3	12.32 s,br	6.50 d J=2.4	6.58 dd J=8.8,2.4	7.67 d J=8.3	12.32 s,br	3.81 s
[Zn(**HL_6**)$_2$Cl_2]·$4H_2O$	8.37 s	--	8.07 dd J=8.8, 2.4	7.92 d J=8.8	--	6.54 d J=2.0	6.59 dd J=8.8,2.0	7.68 d J=8.8	--	3.80 s
HL_7	7.11 s,br	3.79 s[b]	6.86 dd J=8.8,2.4	7.49 d J=8.8	13.05 s,br	6.56 d J=2.4	6.60 dd J=8.8,2.4	7.90 d J=8.8	13.05 s,br	3.81 s
[Zn(**HL_7**)$_2$Cl_2]·H_2O	7.13 d J=2.0	3.81 s[b]	6.91 dd J=8.8,2.4	7.53 d J=8.8	--	6.59 d J=2.0	6.63 d J=8.8	7.91 d J=8.8	--	3.83 s

a, 3H (CH_3); b, 3H (OCH_3)

In ^{1}H-NMR spectrum of HL_1 and its Zn(II) complex, H5 and H6, and H4 and H7 protons appear to be identical. However, in the other compounds (HL_2 – HL_7 and their complexes), the identicalness is disappeared because of 4-position substituents. Benzimidazole benzene ring protons appear in the 6.59 – 8.85 ppm range. In the ^{1}H-NMR spectrum of the HL_1 complex, two doublets of doublets of AA'XX' system at δ_H 7.65 (2H) and 7.30 (2H) ppm are attributed for the benzimidazole benzene ring protons (The dd system does not observed in the HL_1 spectrum because of broadness). There are considerable differences between HL_6 (nitro derivative, and its complex) and the other benzimidazole derivatives (and their complexes) in terms of H4 and H6 protons because of the nitro group's strong withdrawing effect. For example, H4 appears at 8.85 ppm and 8.37 ppm in HL6 and its complex, respectively, as a singlet (the H4 signal is observed in the 7.49 – 7.80 ppm range for the other ligands and the complexes).

The OH proton is disappeared in the ^{1}H-NMR spectra of the complexes. This shows that the OH proton is removed on complexation or possesses acidic character and dissociated, consequently it disappears in the ^{1}H-NMR spectra. Thus, the elemental analysis and molar conductivity data indicate that the OH proton does not remove in the HL_2, HL_4, HL_5, HL_6 and HL_7 complexes because of dissociation. In the ^{1}H-NMR spectra of the complexes, some prominent changes are observed in the characteristics of the phenolic and benzimidazole benzene ring protons with respect to the ligand. For instance, the shifting and the characteristics of H4, H6 and H7 protons of some complexes were changed considerably. They show upfield shifting generally on complexation and some changings were observed such as from multiplet to doublet of doublet; from doublet to singlet etc because of Zn(II) ion's perturbing effect.



Isomer A Isomer B

Fig. 4. Schematic presentation of the isomeric structures for HL_2.

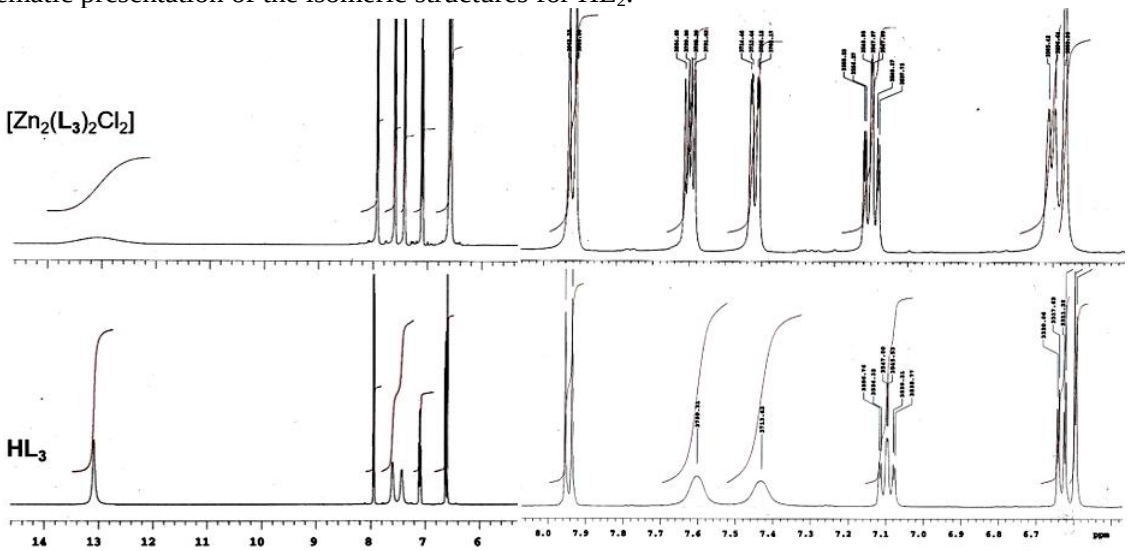


Fig. 5. Comparison of the ^{1}H-NMR spectra of HL_3 (below) and its Zn(II) complex (above).

Fluorescence Spectra

Excitation and emission spectra of the compounds were obtained in ethanol at room temperature (excitation wavelength: 354 nm; concentration: ~10^{-4} M). The fluorescence data of the compounds in ethanol are given in Table

4. The fluorescence spectra of HL_2 and its Zn(II) complex in ethanol are shown in Figure 6. In addition, fluorescence spectra of HL_1 were obtained in various solvents such as acetone, acetonitrile, acetic acid, dichloromethane, dimethylformamide and tetrachloroethylene (Table 5, Fig. 7). The ligands HL_1 – HL_4 and HL_7 show triple fluorescence and HL_5 and HL_6, bromo and nitro derivatives, dual fluorescence. It is known that 2-(2'-hydroxyphenyl)benzimidazole (HPBI) can undergo an excited-state intramolecular proton transfer (ESIPT) from the acidic (hydroxyl proton) to the basic site (aromatic nitrogen) when photoexcitation changes their charge density distribution [34–36]. Based on the ESIPT theory, the shoulder or weak bands are attributed to the emission from a weak enol form of the ligand, while the main band is attributed to the emission from tautomer form (i.e. keto form, Fig. 8) via ESIPT process. The fluorescence band maximum of HL_2 – HL_7 are red-shifted with respect to that of HL_1 in ethanol. -It is remarkable that all of the complexes have fluorescence characteristic as dual or single in ethanol in spite of decreasing the fluorescence intensity (the complexes of HL_6 and HL_7 give single fluorescence, the others are dual). This is expected behavior due to the enol-keto system is removed on complexation and the enol structure becomes dominant. The blue shifting is observed in the complexes of HL_1 – HL_5 whereas the complexes of HL_6 and HL_7 are red-shifted compared to the ligands.

Table 4. Emission maximum wavelengths of the compounds in ethanol

Compound	Emission maximum wavelength (nm)	Compound	Emission maximum wavelength (nm)
HL_1	378 sh, 393 m,br, 426 m,br	$[Zn(\mathbf{L_1})Cl(H_2O)]$	380 sh, 393 m,br
HL_2	376 sh, 393 w, 432 m,br	$[Zn(\mathbf{HL_2})_2Cl_2]\cdot 2H_2O$	381 sh, 391 m,br
HL_3	381 sh, 394 w, 438 m,br	$[Zn_2(\mathbf{L_3})_2Cl_2]$	382 sh, 393 m,br
HL_4	381 sh, 393 w, 443 m,br	$[Zn(\mathbf{HL_4})_2Cl_2]\cdot 2H_2O$	427 sh, 441 m,br
HL_5	394 w, 444 m,br	$[Zn(\mathbf{HL_5})_2Cl_2]\cdot 2H_2O$	392 m,br, 407 sh
HL_6	431 m,br, 447 sh	$[Zn(\mathbf{HL_6})_2Cl_2]\cdot 4H_2O$	458 m,br
HL_7	369 w, 394 w, 434 m,br	$[Zn(\mathbf{HL_7})_2Cl_2]\cdot H_2O$	451 m,br

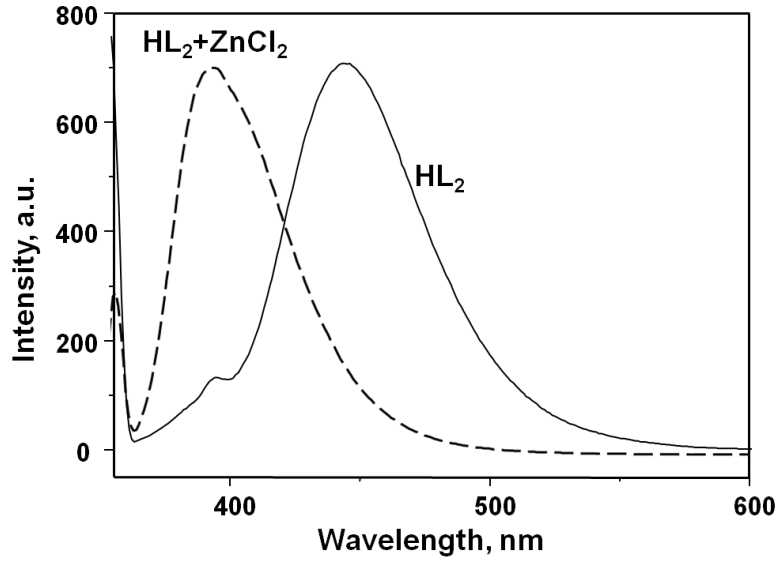


Fig. 6. Fluorescence spectra of HL_2 and its Zn(II) complex in ethanol

Table 5. Emission maximum wavelengths of HL_1 in various solvents

Solvent	Emission maximum wavelength (nm)
Acetic acid	371 s, 388 sh, 414 m,br
Acetone	398 m,br, 442 m,br
Acetonitrile	395 m,br, 435 m,br
Dichloromethane	450 s
Dimethylformamide	395 m, 407 sh
Ethanol	378 sh, 393 m,br, 426 m,br
Perchloroethylene	458 s

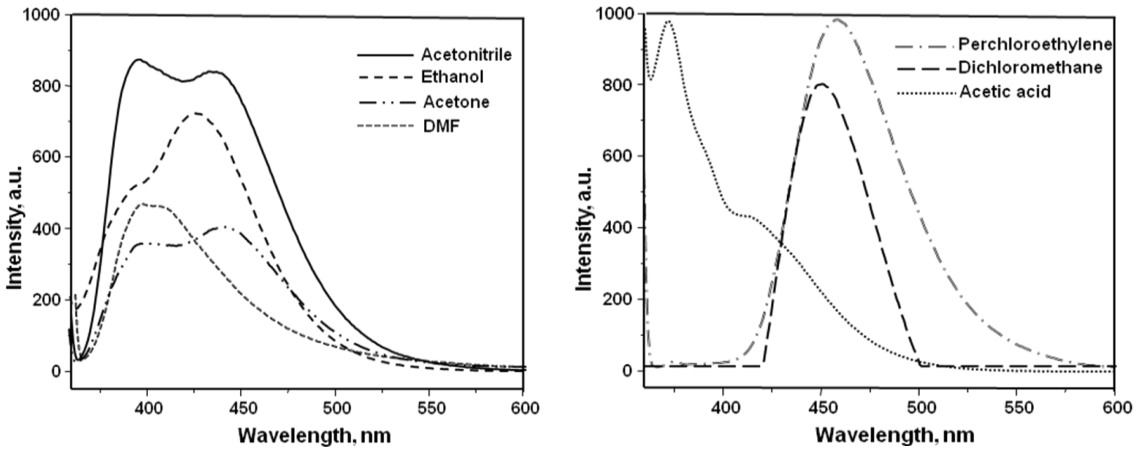
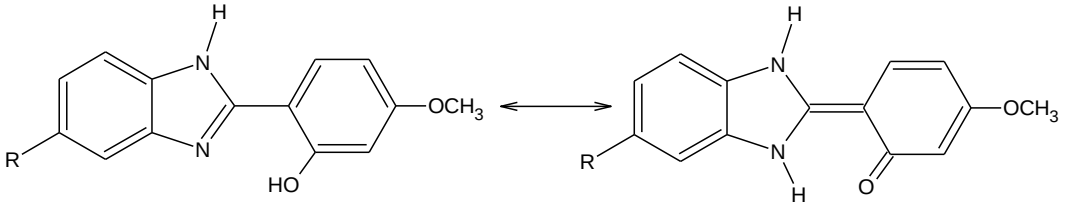


Fig. 7. Fluorescence spectra of HL_1 in various solvents



enol keto

Fig. 8. Enol-keto tautomerism in the ligands.

The fluorescence behavior of HL_1 in various solvents is observed: It fluoresces as dual or triple in the polar solvents. Only one strong peak near 450 nm is observed in the non-polar solvents i.e. perchloroethylene and dichloromethane with high fluorescence intensity (red-shifting according to the polar solvents). But it exhibits different behavior in acetic acid fluorescing at 371 nm (s) with 388 nm (sh) and 414 nm (m,br) compared to the other solvents (blue shift). The behavior of HL_1 in acetic acid may results from forming of acetate structure as $H_2L_1{\cdot}CH_3COO$. The fluorescent emission for all of the compounds is observable in the visible region. Thus, these compounds have potential applications as a luminescent material in light-emitting devices.

Antimicrobial Activity

The results concerning *in vitro* antimicrobial activity of the complexes together with MIC values of compared antibiotic and antifungal are presented in Table 6. Actually seven bacteria and only one fungus have been studied in the antimicrobial activity tests. The compounds HL_1, HL_2, HL_3, HL_7 and their complexes and also $ZnCl_2$ salt have no significant enough antimicrobial activity toward the microorganisms used in the study. However, it is observed that

the other compounds, HL_4 and its Zn(II) complex, HL_5, HL_6 and its Zn(II) complex, exhibit antibacterial and antifungal activity against *S. aureus*, *E. faecalis* and *C. albicans*. Considering the HL_4, HL_5 and HL_6 include Cl, Br and NO_2 substituents, it can be concluded that the Cl, Br and NO_2 groups increase the antimicrobial activity toward *S. aureus*, *E. faecalis* and *C. albicans* that *S. aureus*, *E. faecalis* are Gram+ bacteria and *C. albicans* is yeast. These results can be considered as selective activity.

Table 6. *In vitro* antimicrobial activity of the compounds (MIC, µg/mL)

Compound	Microorganisms							
	Sa[a]	*Ef*[a]	*Ab*[b]	*Kp*[b]	*Pa*[b]	*Ec I*[b]	*Ec II*[b]	*Ca*
HL_4	–	256	–	–	–	–	–	128
HL_4+$ZnCl_2$	–	128	–	–	–	–	–	64
HL_5	64	256	–	–	–	–	–	64
HL_6	64	256	–	–	–	–	–	–
HL_6+$ZnCl_2$	128	1024	–[c]	–	–	–	–	–
$ZnCl_2$	–	–	–	–	–	–	–	–

Sa Staphylococcus aureus ATCC 29213 *Ef Enterococcus faecalis* ATCC 29212
Ab Acinetobacter baumannii ATCC BAA-747 *Kp Klebsiella pneumoniae* ATCC 700603
Pa Pseudomonas aeruginosa ATCC 27853 *Pm Proteus mirabilis* ATCC 14153
Ec I Escherichia coli ATCC 25922 *Ec II Escherichia coli* ATCC 35218
Ca Candida albicans ATCC 10231

[a], Gram(+); [b], Gram(-); [c], □ : Antimicrobial activity value is higher than 1024 µg/mL

It is interesting that HL_5 is effective on *S. aureus*, *E. faecalis* and *C. albicans* and its activity was removed on complexation. It is observed that the Zn(II) complex of HL_4 increase the antimicrobial activity slightly compared to HL_4 itself. In case of the HL_6 complex, complexation decreases the antimicrobial activity with respect to that of HL_6.
It can be seen from Table 6 that the antimicrobial activity of the compounds in this study is focused on *S. aureus*, *E. faecalis* (Gram + bacteria) and *C. albicans* microorganisms. The results of our study indicate that the compounds having antimicrobial activity are effective on Gram + bacteria and fungus. These effects can be considered as selective activity as conclusion.

Conclusion

5-Methoxy-2-(5-H/Me/F/Cl/Br/NO_2/OMe-1*H*-benzimidazol-2-yl)-phenols (HL_1 – HL_7) and their complexes with $ZnCl_2$ were synthesized. The structures of the ligands and the complexes were confirmed on the basis of elemental analysis and FT-IR, FT-Raman, ^{1}H-NMR and fluorescence spectroscopic techniques. Molar conductivity was also measured in DMF for the complexes. It is observed that the ligands acted as bidentate, via the imine nitrogen and the phenolate oxygen atoms. Fluorescence characteristics of the compounds were investigated in ethanol: The ligands fluoresce as dual or triple whereas the complexes give dual or single fluorescence and most of the complexes blue shifted according to the ligands. In addition, fluorescence spectra of HL_1 were investigated in various solvents. The compounds were screened for *in vitro* antimicrobial activities against *S. aureus*, *E. faecalis*, *E. coli I*, *E. coli II*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii* and for antifungal activity against *C. albicans*. The compounds HL_1, HL_2, HL_3, HL_7 and their complexes do not show antimicrobial activity toward the microorganisms whereas HL_4 and its

Zn(II) complex, HL_5, HL_6 and its Zn(II) complex exhibit antibacterial and antifungal activity against *S. aureus*, *E. faecalis* and *C. albicans*. Considering the HL_4, HL_5 and HL_6 include Cl, Br and NO_2 substituents, it can be concluded that the Cl, Br and NO_2 groups increase the antimicrobial activity toward *S. aureus*, *E. faecalis* and *C. albicans* that *S. aureus*, *E. faecalis* are Gram+ bacteria and *C. albicans* is yeast. These results can be considered as selective activity. The proposed structures for the complexes of HL_1, HL_3 and HL_6 ligands are shown in Figure 9 as exemplary for 1:1, 1:1 by bridge and 1:2 M:L ratio complexes. They are in best accord with the experimental data obtained from the analytical data, molar conductivity measurements, NMR, FT-IR, Raman and UV-visible spectroscopic techniques. In addition, the ball-stick structures of the complexes are shown in Figure 10.

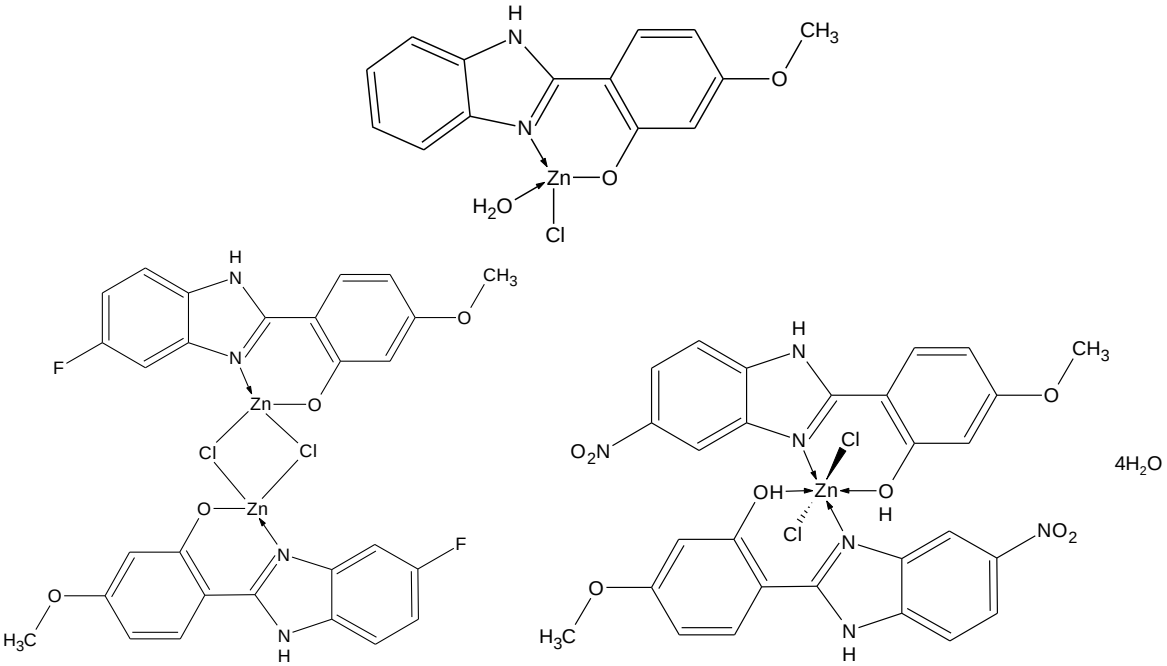
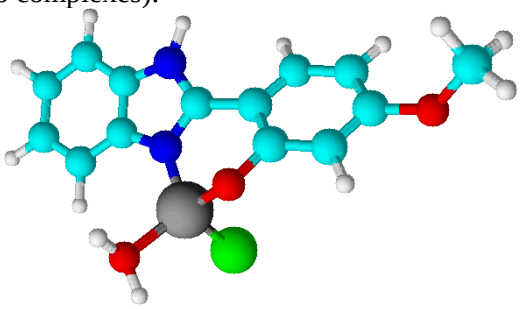


Fig. 9. The proposed structures for the Zn(II) complexes with HL_1, HL_3 and HL_6 ligands (exemplary for 1:1, 1:1 by bridge and 1:2 M:L ratio complexes).



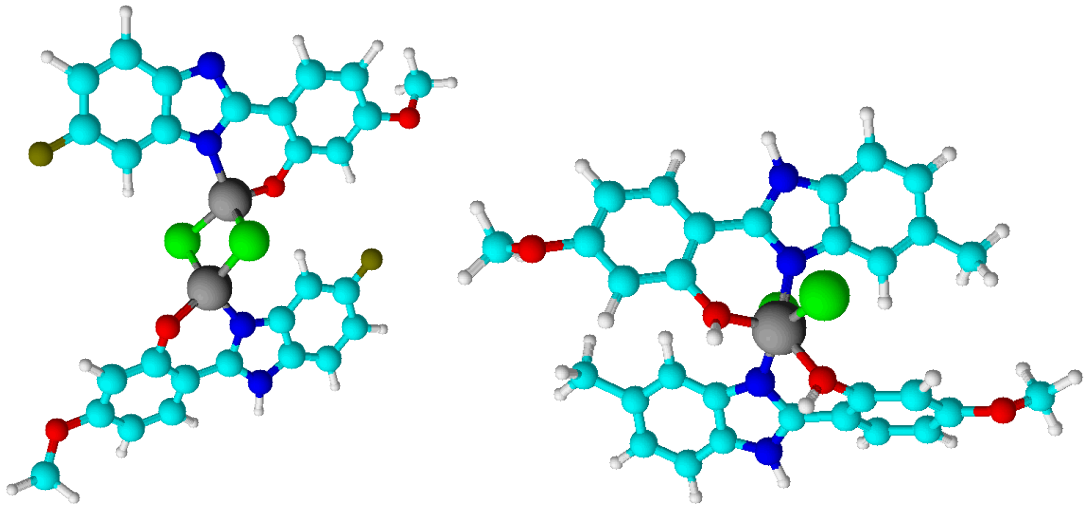


Fig. 10. The ball-stick structures of the HL_1, HL_3 and HL_6 complex (these figures were obtained by ACD/ChemSketch software program).

Acknowledgements

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