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Synthesis and Antibacterial Activity of a Series of Heterocyclic Sulfonate Ligands and Their Metal Complexes

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A series of heterocyclic sulfonate ligands and their barium(II), silver(I), manganese(II), zinc(II) and cobalt(II) coordination compounds have been synthesized. Through antibacterial activities experiments of these complex compounds, metal salts as well as ligands, the rational conclusion is arrived that antibacterial activities of these compounds come from metal ions.

Key Words: Heterocyclic sulfonate ligand, Antibacterial activity, Coordination complex.

INTRODUCTION

Though organic sulfonate and their metal complexes have been studied by chemists[1-8], in pharmacy, the antibacterial activities of these compounds are explored scarecely. To perfect coordination and broad-spectrum antibacterial ability, sulfonic acid is modified with pyrimidine.

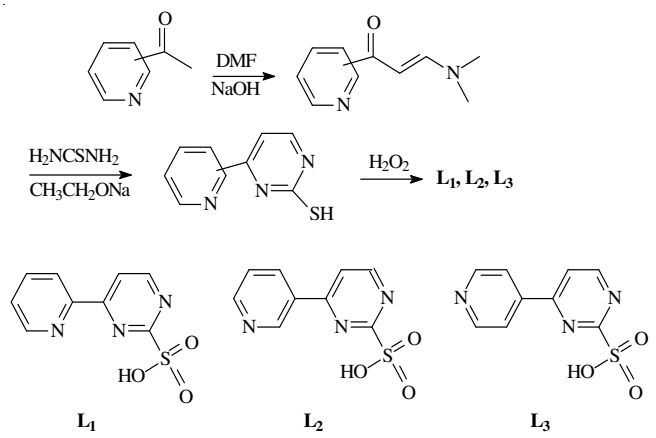
EXPERIMENTAL

All the solvents and chemicals were used without further purification. Infrared spectra (4000-400 cm^{-1}) were recorded with a Bruker Vector 22 FTIR spectrophotometer on KBr disks. Elemental analyses were done by using a Perkin-Elmer 1400C analyzer. The microbial strains were from Agricultural Culture Collection of China (ACCC).

Synthesis of L_{1-3}: The series of ligands{4-pyridin-2-yl-pyrimidine-2-sulfonate (L_1), 4-pyridin-3-yl-pyrimidine-2-sulfonate (L_2), 4-pyridin-4-yl-pyrimidine-2-sulfonate (L_3)} were synthesized according to the literature method[9-11] with synthetic route below (**Scheme-I**).

Synthesis of complexes: $[BaL_1(NO_3)(H_2O)]_n$ (**1**), $\{[Ba(L_1)_2(H_2O)]\cdot 2H_2O\}_n$ (**2**), $[BaL_2(H_2O)(ClO_4)]_n$ (**3**), $[Ag_3(L_1)_3(H_2O)_2]_n$ (**4**), $[Ag_3(L_2)_3(H_2O)_2]_n$ (**5**), $[Ag_3(L_1)_3(H_2O)_2]_n$ (**6**), $[Mn(L_1)_2\cdot H_2O]$ (**7**), $[Mn(L_2)_2\cdot H_2O]$ (**8**), $[Mn(L_3)_2\cdot 4H_2O]\cdot 2H_2O$ (**9**), $[Zn(L_1)_2\cdot H_2O]$ (**10**), $[Zn(L_2)_2\cdot H_2O]$ (**11**), $[Zn(L_3)_2\cdot 4H_2O]\cdot 2H_2O$ (**12**), $[Co(L_1)_2\cdot H_2O]$ (**13**), $[Co(L_2)_2\cdot H_2O]$ (**14**), $[Co(L_3)_2\cdot 4H_2O]\cdot 2H_2O$ (**15**).

The single crystals of complexes **1-3** were used for detection of antibacterial activity directly (CCDC: **1**, 760305; **2**, 760306; **3**, 760307). Synthesis, characterization, crystal data and structure were reported in earlier thesis[12].



Scheme-I: Synthetic route of title ligands

NaL_1, NaL_2, NaL_3 (26.0 mg, 0.1 mmol) were added, respectively in water (5 mL), then triplicate solutions of $AgNO_3$ (8.5 mg, 0.05 mmol) in acetonitrile (5 mL)were very slowly dropped in. Crystal products (**4**, **5**, **6**) formed after two-three weeks standing in darkness. The structures of **4**, **5** were confirmed by Liu and Hu[13].

4: Yield 78 %. Anal. calcd. (%) for $Ag_3(L_1)_3(H_2O)_2$ $\{[Ag_3(C_9H_6N_3O_3S)_3(H_2O)_2]\}$: C, 30.35; H, 2.08; N, 11.80. Found. (%): C, 30.34; H,2.10; N, 11.77. Main IR absorption (KBr, ν_{max}, cm^{-1}): 3431 (m), 1615 (m), 1578 (s), 1533 (m), 1496 (m), 1385 (m), 1225 (s), 1197 (s), 1043 (s).

TABLE-1
DETECTION OF ANTIBACTERIAL ACTIVITY ("+" IS POSITIVE RESULT, "–" IS NEGATIVE RESULT)

Compound	Bacteria															
	Escherichia coli (ACCC01555)					*Bacillus subtilis* (ACCC01430)					*Staphylococcus aureus* (ACCC01331)					
L_1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
L_2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
L_3	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
$BaCl_2$	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
3	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
$AgNO_3$	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
4	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
5	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
$MnCl_2$	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
7	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
8	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
$ZnCl_2$	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
10	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
11	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
12	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
$CoCl_2$	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
13	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
14	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
15	–	–	–	–	–	+	+	+	+	+	+	+	+	+	+	+

5: Yield 64 %. Anal. calcd. (%) for $Ag_3(\mathbf{L_2})_3(H_2O)_2$ $\{[Ag_3(C_9H_6N_3O_3S)_3(H_2O)_2]\}$: C, 30.35; H, 2.08; N, 11.80. Found (%): C, 30.33; H, 2.10; N, 11.83. Main IR absorption (KBr, ν_{max}, cm^{-1}): 3431 (m), 1617 (m), 1573 (s), 1530 (m), 1495 (m), 1386 (m), 1225 (s), 1197 (s), 1044 (s).

6: Yield 71 %. Anal. calcd. (%) for $Ag_3(L_3)_3(H_2O)_2$ $\{[Ag_3(C_9H_6N_3O_3S)_3(H_2O)_2]\}$: C, 30.35; H, 2.08; N, 11.80. Found. (%): C, 30.37; H, 2.07; N, 11.78. Main IR absorption (KBr, ν_{max}, cm^{-1}): 3432 (m), 1615 (m), 1574 (s), 1533 (m), 1495 (m), 1381 (m), 1222 (s), 1195 (s), 1041 (s).

The preparation of complexes (**7-15**) with similiar way, the process as followed: the ligand ($\mathbf{L_1}$-$\mathbf{L_3}$, 0.0472 g, 0.2 mmol) in warm water (15 mL) and an aqueous solution (10 mL) of metal salt (0.1 mmol) [$MnCl_2{\cdot}4H_2O$; $Zn(ClO_4)_2{\cdot}6H_2O$; $Co(ClO_4)_2{\cdot}6H_2O$] were mixed. The mixture was stirred for 1 h, the crystals were obtained in filtrate when the solution cooled to room temperature. CCDC: 9, 681493; 12, 681494; 15, 681495. The general formulas of these complexes are $[M(L)_2]{\cdot}H_2O$ (L = $\mathbf{L_1}$, $\mathbf{L_2}$)[14] and $[M(L)_2{\cdot}4H_2O]{\cdot}2H_2O$ (L = $\mathbf{L_3}$)[15]. The structures of complexes **7**, **10**, **13** were reported by Dong *et al.*[14].

8: Yield 86 %. Anal. calcd. (%) for $C_{18}H_{14}MnN_6O_7S_2$ $\{[Mn(\mathbf{L_2})_2]{\cdot}H_2O\}$: C, 40.99; H, 2.29; N, 15.93. Found. (%): C, 40.97; H, 2.28; N, 15.89. Main IR absorption (KBr, ν_{max}, cm^{-1}): 3442 (vs), 1616 (w), 1577 (s),1534 (m), 1430 (m), 1418 (m), 1370 (w), 1249 (vs), 1197 (s), 1034 (s).

11: Yield 63 %. Anal. calcd. (%) for $C_{18}H_{14}ZnN_6O_7S_2$ $\{[Zn(\mathbf{L_2})_2]{\cdot}H_2O\}$: C, 38.89; H, 2.54; N, 15.12. Found. (%): C, 38.85; H, 2.53; N, 15.10. Main IR absorption (KBr, ν_{max}, cm^{-1}): 3445 (vs), 1614 (w), 1579(s), 1533(m), 1432(m), 1416(m), 1374(w), 1246(vs), 1199(s), 1034(s).

14: Yield 62 %. Anal. calcd. (%) for $C_{18}H_{14}CoN_6O_7S_2$ $\{[Co(\mathbf{L_2})_2]{\cdot}H_2O\}$: C, 39.35; H, 2.57; N, 15.30. Found. (%): C, 39.33; H, 7.59; N, 15.32. Main IR absorption (KBr, ν_{max}, cm^{-1}): 3448 (vs), 1617 (w), 1574 (s), 1531 (m), 1434 (m), 1420 (m), 1372 (w), 1245 (vs), 1196 (s), 1032 (s).

Detection of antibacterial activity: After materials for detection of antibacterial activity antoclaved, each petri dish was infused proper nutrient agar *ca.* 40 ºC. When the nutrient agar was cooled to room temperature, a solution of bacterial and a piece of circular paper (0.5 cm in diameter) carrying with sample were placed on it in order. Then petri dish were put into electro-thermal incubator at 36 ºC for 24 h. The control group (n = 5) was established with every compound. At the same time, a blank control group (n = 5) without any sample was cultured.

As good water-solubility of $\mathbf{L_{1\text{-}3}}$ and inorganic compounds, their solutions (0.001 g/mL) were used in detecting antibacterial activity. The rest of samples (**1-15**) were performed in solid on watery papers for their poor solubility. The positive result is that the inhibition zone was present and *vice versa*. The blank control group assumed negative result.

RESULTS AND DISCUSSION

Three kinds of bacterias are not inhibited by ligends ($\mathbf{L_{1\text{-}3}}$) and anions (Cl^-, ClO_4^-, NO_3^-). Complexes and corresponding metal ions exhibits similar antibacterial activity. Enough metal ionic concentration is the cause of antimicrobial activity expect two kinds complexes that are Co(II)-$\mathbf{L_3}$ and Mn(II)-$\mathbf{L_{1\text{-}3}}$. It is possible that dissociation constant of this two kinds metal complexes is too low to inhibit increase of microbe. These coordination compounds are potential sustained-release antibacterial drugs for their low dissociation constant.

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