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Studies on antimicrobial effects of four ligands and their transition metal complexes with 8-mercaptoquinoline and pyridine terminal groups

Li-Jie Zhang [a,b,†], Jing-An Zhang [a,b,*,†], Xun-Zhong Zou [a,b], Ya-Jie Liu [a,b], Ning Li [a], Zi-Jie Zhang [a], Yu Li [c,*]

[a] *School of Pharmacy, Guangdong Pharmaceutical University, Guangzhou 510006, People's Republic of China*
[b] *College of Traditional Chinese Medicine, Guangdong Pharmaceutical University, Guangzhou 510006, People's Republic of China*
[c] *Department of Environmental Engineering, Guangdong Industry Technical College, Guangzhou 510300, People's Republic of China*

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ABSTRACT

Four types of ligands (Q1–Q4) and their complexes (**1–36**) with transition metal ions have been synthesized, in which two new complexes (**15** and **20**) have been prepared and tested. In vitro antimicrobial activities of the ligands and their complexes were investigated against a representative panel of strains including two Gram positive bacteria (*Sarcina ureae*, *Staphylococcus aureus*), two Gram negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*) and three fungi (*Aspergillus niger*, *Saccharomyces cerevisiae*, *Fusarium oxysporum* f. sp. *cubense*). The relationship between the structure and the antibacterial activities was discussed. Our study results indicated that some compounds have preferred antibacterial activities that may have potential pharmaceutical applications.

As human living habits and environment consistently change, bacterial infection has been a major cause of death in both developing and developed countries. Bacteria drug resistant is a growing issue in treatment. In order to prevent this serious medical problem, the discovery of new types of antimicrobial agents or the expansion of bioactivity of the previous drugs is a very important but challenging task.[1] Therefore, in recent years, research has been focused on the development of novel antibacterial agents, which may act through structure design, to overcome the problem of acquired resistance. In a long period of time, the quinoline terminal group is found in a large variety of natural compounds and also chemically mediates diverse bioactivities.[2–8] Yet, no one can ignore the important role of pyridine as an imperative heterocyclic for its countless derivatives and antimicrobial activity.[9] Moreover, multicomponent reactions were employed as a powerful tool to synthesize diverse and complex heterocyclic compounds due to their advantages of the intrinsic atom economy, simpler procedures, structural diversity, and reduced waste.[1] Therefore many chemists have carried out research on the compounds containing pyridine or quinoline terminal group ligands and their complexes because of their potential applications in biological recognition, electrochemistry and functional materials.[10–14] However, reports on the bioactivities of such kinds of ligands and their complexes still remain largely missing.

Based on a literature survey and our research, we have synthesized and reported a series of semi-rigid monothioether and dithioether ligands Q1–Q4 (Chart 1), 8-((pyridin-2-yl)methylthio) quinoline (Q1),[15,16] 8-((pyridin-3-yl)methylthio)quinoline(Q2),[16,17] 8-((pyridin-4-yl)methylthio)quinoline(Q3),[16,18] 2, 6-bis(8-quinolinylthiomethyl)pyridine(Q4)[16,19,20] and their transition metal complexes $[Cu(Q1)Cl_2]$(**1**), $[Co(Q1)(NO_3)_2]$(**2**), $[Cd(Q1)(NO_3)_2]$(**3**), $[Cd(Q1)I_2]$(**4**), $[Cu(Q1)_2](BF_4)_2(H_2O)_2$(**5**), $[Cu(Q1)_2](ClO_4)_2(CH_3COCH_3)_2$(**6**), $[Zn(Q1)_2](ClO_4)_2(H_2O)_2$(**7**), $[Cd_2(Q1)_2Br_4]$(**8**), $[Ag_2(Q1)2(ClO_4)_2]$(**9**), $[Ag_2(Q1)_2(NO_3)_2]$(**10**),[15] $[Ag_2(Q2)_2(NO_3)_2]$(**11**), $[Ag_2(Q2)_2(CF_3CO_2)_2]$(**12**), $\{[Ag_2(Q_2)_2](CF_3SO_3)_2(H_2O)\}_n$(**13**),[17] $[Cd_2(Q3)_2I_4]$(**18**), $[Cd_2(Q3)_2(NO_3)_4]$(**19**), $[Cd(Q3)Br_2]$(**22**), $[Cd(Q3)](ClO4)_2$(**23**),[18] $[Cu(Q2)(CF_3CO_2)_2]$(**14**), $[Ni(Q3)(H_2O)(CF_3CO_2)_2]$(**16**), $[Zn(Q3)(H_2O)(CH_3OH)](ClO_4)_2(CH_3OH)]$(**17**), $[Ag(Q3)](CF_3SO_3)(CH_3CN)$(**21**), $[Cu(Q4)(CF_3CO_2)](CF_3CO_2)(H_2O)_2$(**24**), $[Zn(Q4)(H_2O)](ClO_4)_2(H_2O)(CH_3CN)$(**28**), $[Mn(Q4)(CF_3SO_3)](CF_3SO_3)$(**30**), $[Ag_2(Q4)(CF_3COO)_2]$(**35**), $[Ag(Q4)](CF_3SO_3)$(**36**),[16] $[Hg(Q4)](ClO_4)_2$(**32**), $[Hg_2(Q4)_2](ClO_4)_2H_2O$(**33**),[19] $[Cu(Q4)(CF_3SO_3)](CF_3SO_3)$(**25**), $[Co(Q4)CoCl_4]CH_3OH$(**26**), $[Zn(Q4)(CO_2CF_3)](ClO_4)CH_3CN$(**29**), $[Cd(Q4)](ClO_4)_2(H_2O)_2$(**31**),[20] $[Ni(Q4)(H_2O)](CF_3SO_3)_2$(**27**) and $[Cu(Q4)(NO_3)]Cu(NO_3)_4$(**34**) (the structures of **27** and **34** will be published in another Letter), which

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* Corresponding authors. Tel.: +86 20 39352141.
E-mail addresses: zhangja@126.com (J.-A. Zhang), liyuletter@163.com (Y. Li).

† These authors equally contributed to this work. Li-Jie Zhang and Jing-An Zhang.

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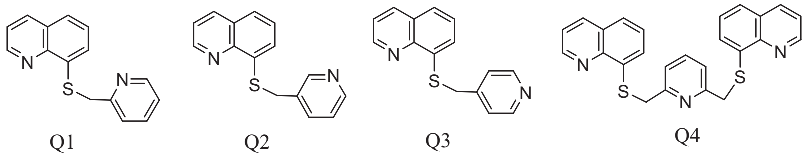

Chart 1. The structures of ligands Q1–Q4.

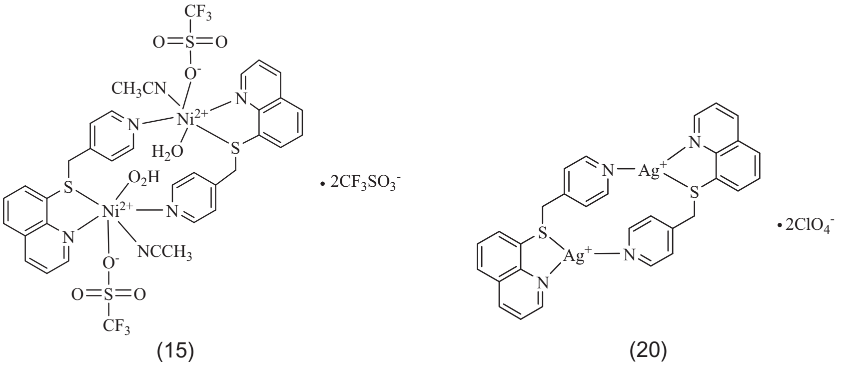

Chart 2. The structures of complexes **15** and **20**.

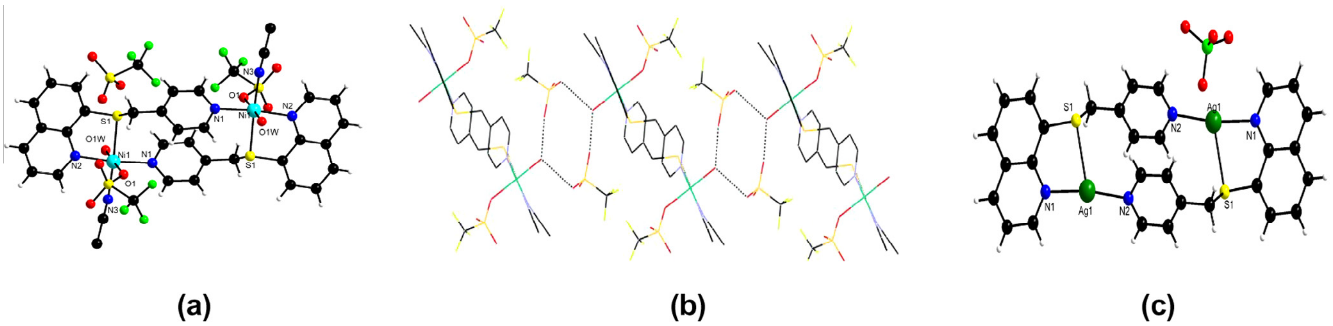

Figure 1. (a) View of the coordination environment of Ni(II) ions in complex **15**. (b) The intermolecular hydrogen bond of complex **15**. (c) View of the coordination environment of Ag(I) ions in complex **20**.

contained both quinoline and pyridine terminal groups with closely correlated structures and different coordination behaviors yet, showed some good antimicrobial effects. Therefore we also synthesized other two new complexes (detailed experiment referred to references and notes[21]) namely $[Ni(Q3)(H_2O)(CF_3SO_3)(CH_3CN)](CF_3SO_3)$(**15**) and $[Ag(Q3)](ClO_4)$(**20**) (Chart 2), and we compared the MIC of these complexes with those compounds in order to find some factors affecting the antimicrobial activities against various bacteria and fungi.

The two new complexes were characterized by elemental analysis (EA), infrared spectra (IR) and single-crystal diffraction. In the complex $[Ni(Q3)(H_2O)(CF_3SO_3)(CH_3CN)](CF_3SO_3)$(**15**), the asymmetric unit consisted of one Ni(II) atom, one Q3 ligand, one coordinated water molecule and CF_3COO^- anion and one free CH_3CN molecule and CF_3COO^- anion. The central Ni(II) ion was eight coordinated by one S atom (Ni–S = 2.447(1) Å), one quinoline N atom (Ni–N = 2.085(9) Å) from one ligand, and one pyridyl N atom (Ni–N = 2.080(9) Å) from another Q3 ligand, one O atom (Ni–O = 2.076(9) Å) from water molecule, one N atom (Ni–N = 2.076(9) Å) from CH_3CN molecule and one O atom (Ni–O = 2.086(9) Å) from trifluoroacetate anions, forming a very stable dinuclear building block which contained a 14-membered ring of two Ni(II) centers and the corresponding atoms on the two ligands (Fig. 1a). The intermolecular hydrogen bond of complex **15** is shown in Figure 1b. The selected bond lengths [Å] and bond angles [°] for **15** were listed in Table S1 (Supplementary material).

The complex $[Ag(Q3)](ClO_4)$ (**20**) was composed of two nuclear Ag atoms, two Q3 ligand and one ClO_4^- anion, formed a M_2L_2 coordination model, in which each Ag(I) atom was coordinated in a T-shaped tri-coordinated geometry coming from one S atom (Ag–S = 2.682(1) Å), one quinolinyl N atom (Ag–N = 2.237(8) Å) and from one ligand and one pyridyl N atom (Ag–N = 2.237(1) Å) from another Q3 ligand. Similarly, the complex **20** formed a 14-membered ring of two Ag(I) centers and the corresponding atoms on the two ligands (Fig. 1c). The selected bond lengths [Å] and bond angles [°] for **20** were listed in Table S2. The crystallographic data and the structure refinement summary for **15** and **20** were listed in Table S3 (Supplementary material).

The antimicrobial activities of the ligands and their transitional metal complexes were tested. The antibacterial activities of the compounds were evaluated by a microdilution method using the G^+ bacteria *Staphylococcus aureus* ATCC 27154 and *Sarcina ureae* and the G^- bacteria *Pseudomonas aeruginosa* and *Escherichia coli* ATCC 25922. Cultures of bacteria were incubated under vigorous shaking. The effects of the prepared compounds on the fungi *Aspergillus niger*, *Fusarium oxysporum* f. sp. *cubense* and