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2-Quinoxalinol salen ligands incorporated into functionalized resins for selective solid-phase extraction of copper(II)

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ABSTRACT

In exploring selective extraction systems for use in environmental remediation or in metal scavenging agents for use in combinatorial chemistry, a novel reagent for the selective extraction of copper(II) has been developed. 2-Quinoxalinol salen ligands supported on an aminomethyl-polystyrene resin has been shown to efficiently and selectively extract copper(II) ions from organic solvents within 30 min under a variety of experimental conditions. Mild reducing conditions allow for metal ion recovery.

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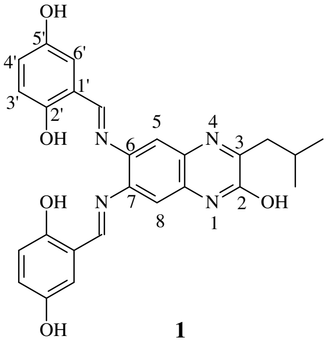
Solid-phase extraction (SPE) technologies are being used in a wide number of areas including environmental chemistry, medicinal chemistry, combinatorial chemistry, agriculture, and food science. This technology has been used in environmental applications to monitor or extract toxic heavy metal cations such as Hg^{2+}, Pb^{2+}, and As^{3+}.[1–7] Others have applied solid-phase microextraction (SPME) techniques to analyze biological fluids in diagnostic medicine.[8] In food science, SPE technologies are used extensively in food analysis and quality control.[9–12] Currently, the most common application of SPE technology in use is in the identification of drug components.[13,14] One promising area of SPE technology not as widely investigated is as a scavenging agent to remove excess catalysts or metal ions used in synthetic methods or combinatorial chemistry.[15–17]

Copper salts are often applied as catalysts in a variety of organic synthetic procedures. An overabundance of copper in the environment is of concern due to possible harmful effects to agriculture, fish, or wildlife.[18–22] SPE technology for the selective recovery of copper has not previously been described in the literature. Such technology has considerable potential and would allow many catalytic or coupling reactions commonly used in the synthetic laboratory to be more accessible for use in combinatorial processes or in industrial applications, where excess or trace metal ions are likely to complicate subsequent reactions. In addition, because of the high cost of copper reagents, this would create a more efficient and more readily recyclable system thereby limiting the need for costly copper reagents.

In our previous research, both symmetric and unsymmetric 2-quinoxalinol salen ligands have been prepared (see structure **1** as an example).[23,24] It has been found that these ligands can coordinate +2 metal cations. This made us consider the possibility of incorporating these 2-quinoxalinol salen ligands into solid-phase resins. Here, we will detail the methods of preparing solid-phase reagents and their application in the selective extraction and recovery of copper cations.

Polystyrene (PS) aminomethyl resin was selected as solid carrier, because this resin can swell in many organic solvents. Glutaric anhydride was selected as linker between solid carrier and 2-quinoxalinol salen ligand. The isopropyl-2-quinoxalinol salen ligand (**1**) was selected as the coordination ligand, both because the 5′-hydroxyl group on the outer portion of the salen is a convenient site for incorporating the resin, and because its yield is the highest of the symmetric library.[23]



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Presented in Scheme 1 is the optimized method for the synthesis of solid reagents PLG1 or PLG2. Different molar ratios and various solvents were investigated to optimize the acylation of the amino group onto the (PS) aminomethyl resin. Finally, a molar ratio of glutaric anhydride to (PS) aminomethyl resin 5:1 using dichloromethane as solvent at room temperature for 24 h was found to be the optimum conditions for acylation of the amino group. After acylation was completed, the resin was washed with DCM, DMF, and MeOH, three times each. The loaded resin PL can be further acylated with 1.5 equivalent of ligand **1** by using 2.2 equivalents of 4-dimethyl-aminopyridine (DMAP) and 2.2 equiv

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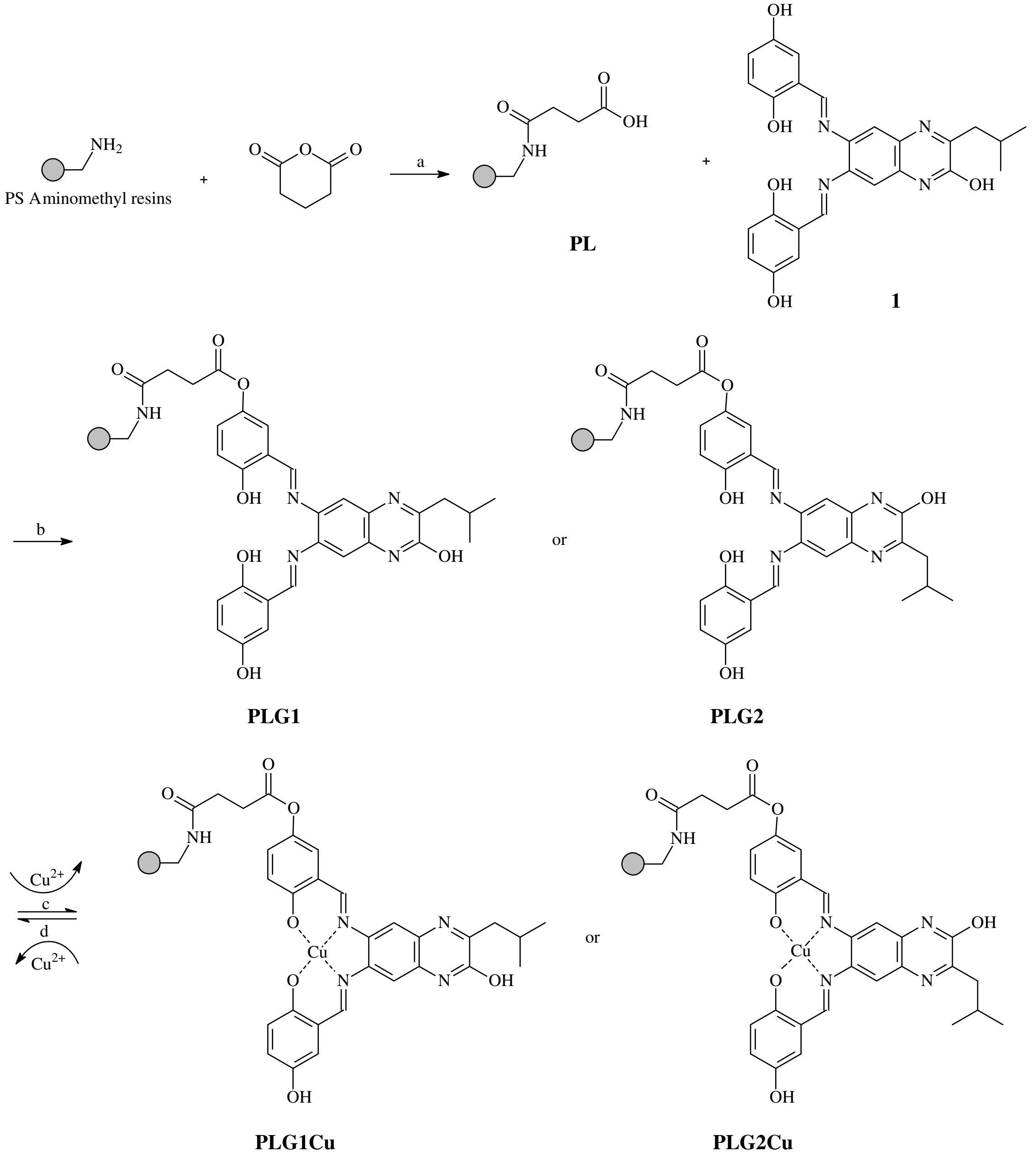

Scheme 1. Reaction route for solid reagents PLG1 and PLG2. Reagents and conditions: (a) 5 equiv, glutaric anhydride, DCM, rt, 24 h; (b) 2.2 equiv, DMAP, 2.2 equiv, DIC, DMF, rt, 72 h; (c) Cu^{2+}, DCM, MeOH, rt, 30 min; (d) $NaBH(OAc)_3$, DCM, AcOH, rt, 4 h.

of *N*,*N*′-diisopropyl-carbodiimide (DIC) in distilled, dry DMF at room temperature for three days. Extending the reaction time does not increase loading. Without DMAP, the loading is very low. If wet DMF was used, the loading capability is decreased, because DIC can be decomposed easily by moisture.

There are three potential binding sites (the 2, 2′, and 5′ positions) for the carboxylic acid linker to attach to ligand **1**. Positions 2 and 2′ cannot react with the carboxylic acid moiety due to reactive inertia of the 2 position and steric hindrance at the 2′ position. Hydrogen bonding also limits the reactivity of the hydroxyl group on the 2′ position.[25] Reaction with the hydroxyl groups in the two 5′ positions results in two possible products (i.e., PLG1 and PLG2). They have the same coordination capability to bind +2 valence metal cations, because the salen coordination cavity is not affected by their position. By this procedure, PL was obtained with 100.0% loading by ninhydrin test, and PLG1 and PLG2 were obtained with 60.0–65.0% loading, as determined by mass. Identification of resins PLG1 and PLG2 was made by comparing the major peaks of an IR spectra of ligand **1** (3381.2, 1658.8, 1622.3, 1577.8, 1489.1, 1278.8 cm^{-1}).

With this solid ligand functionalized reagent in hand, extraction studies were run in several different solvent combinations: DMF, DMF/MeOH, MeOH, THF/MeOH, DCM/MeOH, and DCM/EtOH. Finally, we found that DCM/MeOH is the best combination for our extraction experiment, because the DCM can best swell the PS resins while MeOH still readily dissolves the metal salts. Metal salts of Cu^{2+}, Mn^{2+}, and Ni^{2+} were used in extraction studies. Solutions containing these metal ions were prepared using copper acetate, manganese acetate, and nickel nitrate salts in a 50:50 solution of DCM/MeOH. To determine extraction capability, 3 ml of a prepared solution of 2×10^{-4} mol/l Cu^{2+} was mixed with 5 mg, 10 mg, 15 mg, 20 mg prepared PLG**1(2)** (The molar ratio of Cu^{2+} to PLG**1(2)** is

1:3, 1:6, 1:9, 1:12), respectively, at room temperature with stirring for 40 min. The extraction results for Cu^{2+} metal are shown in Figure 1. It was found that 20 mg PLG1 and PLG2 resins may completely extract 3 ml Cu^{2+} 2×10^{-4} mol/l solution at 40 min. Further optimization of extracting time using 20 mg PLG1 and PLG2 resins with 3 ml 2×10^{-4} mol/l concentration copper cations solution at room temperature (Fig. 2) showed that the shortest time for 100% extraction is 30 min. Complexed resin can be directly filtered off to separate from the organic solvent.

For nickel, 20 mg of prepared PLG1 or PLG2 was mixed with 3 ml of the nickel (2×10^{-4} mol/l) salt solution at room temperature. After 24 h, only 30% of nickel was extracted, and after 72 h, only 45.7% of the nickel was extracted. (The final metal ion concentrations were determined using atomic absorption.) For Mn, the Mn salt solution must be prepared as a 1×10^{-4} mol/l solution, because the detection limit for Mn by atomic absorption using a hollow cathode lamp is limited. A 3 ml 1×10^{-4} mol/l manganese salt solution was extracted at room temperature by 10 mg PLG1 and PLG2 resins for 24 h. It was found that 63.0% of the manganese was removed by the resin.

This lead us to a surprising conclusion. The PLG1 and PLG2 resins might *selectively* extract Cu^{2+} within a short time (30 min). To confirm this, we combined 3 ml 2×10^{-4} mol/l Cu^{2+} and 3 ml 2×10^{-4} mol/l Ni^{2+} solution to prepare a 6 ml 1×10^{-4} mol/l Cu^{2+} and Ni^{2+} mixed solution; 3 ml 2×10^{-4} mol/l Cu^{2+} solution and 3 ml 1×10^{-4} mol/l Mn^{2+} solution were combined to obtain a 6 ml 1×10^{-4} mol/l Cu^{2+} and 5×10^{-5} mol/l Mn^{2+} solution. To these mixed solutions, 20 mg of the prepared PLG1 and PLG2 resins was added at room temperature and allowed to extract for 45 min. After filtering off the PLG1 and PLG2 resins, the extraction solution was analyzed by atomic absorption. It was found that 80.0% of the Cu^{2+} was removed, but only 7.8% Ni^{2+} in the Cu^{2+}/Ni^{2+} solution, and only 22.0% Mn^{2+} was extracted in the Cu^{2+}/Mn^{2+} mixed solutions.

For the recovery of copper from the PLG1Cu and PLG2Cu resins, several different conditions were tried (Scheme 1). Routine cleavage or recovery conditions, DCM with different organic acids including trifluoroacetic acid were not found to release copper ions, nor were strong bases.

Because sodium triacetoxyborohydride can efficiently reduce the imine group (C═N) to amino group (C–N) which coordinates only weakly with the metal, the 20 mg PLG1Cu and PLG2Cu resins were mixed with 3 ml DCM/CH_3COOH (2:1). To this, 10 mg sodium triacetoxyborohydride was added, and the reaction progress was measured over time (Fig. 3).[26] The results show that after 4 h the maximum amount of Cu^{2+} can be recovered (70.0%). Extending the reaction time or increasing the amount of sodium triacetoxyborohydride does not increase this recovery rate.

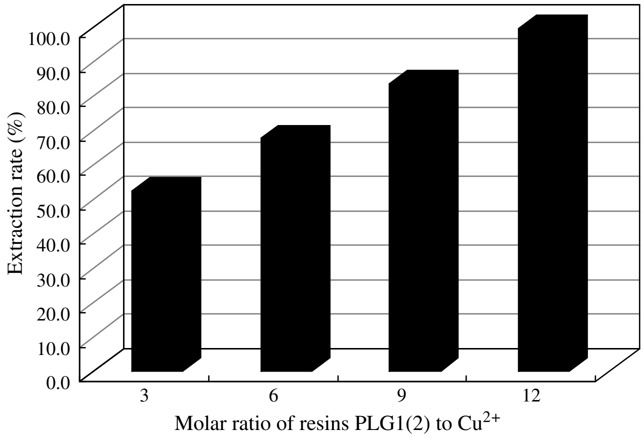

Figure 1. Cu^{2+} extraction bar graphs indicating the different molar ratios of PLG1(2) resin to Cu^{2+} extracted. (Quantified using atomic absorption.)

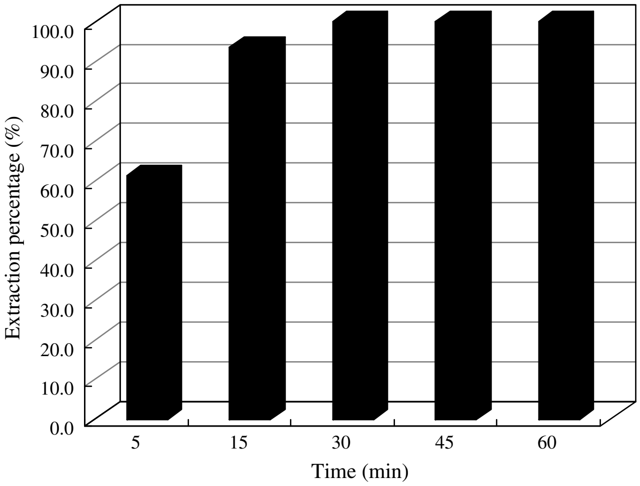

Figure 2. Cu^{2+} extraction with PLG1(2) resin with respect to agitation time. (Quantified using atomic absorption.)

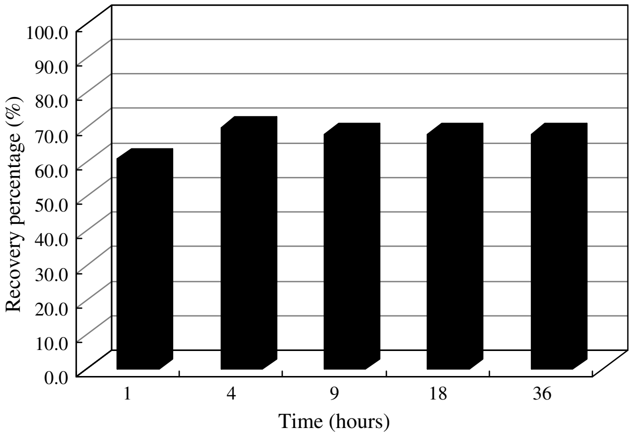

Figure 3. Cu^{2+} recovery with time. (Quantified by atomic absorption.)

To conclude, an optimized synthetic route for resins PLG1 and PLG2 was obtained. This kind of resin can selectively extract copper(II) cation within short time. The copper can then be recovered using simple reducing conditions from the resin. This has the potential to enable the selective extraction of copper even from a mixture containing other metals. PLG1 and PLG2 resins could also be applied in environmental or materials chemistry to remove copper or in combinatorial chemistry as a metal scavenging agent to remove excess copper. In the future, design new solid reagents to selectively extract other metals or improve on the selectivity or application of this system.

Supplementary data

All organic solvents were from Aldrich Scientific and were used directly for synthesis. Metal salts and other reagent for synthesis were from Acros reagent Inc. Polystyrene (PS) aminomethyl resin (1% DVB, 0.59 mol/g loading and 100–200 mesh.) was from ChemPep Inc. IR, Prestige-21 Fourier transform infrared spectrophotometer and KBr solid samples. Atomic absorption spectrum (VarianAA240), its software (AA240FS) and hollow cathode lamp (HLC; Ni 232.0 nm, optimum working range: 0.1–20 mg/L; Mn 279.5 nm, optimum working range: 0.02–5 mg/L; Cu 324.8 nm, optimum working range: 0.03–10 mg/L) from Varian, Inc.

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