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Synthesis and Binding Properties of New Tripodal Hexadentate Ligands Having Three Quinolinol Moieties for Trivalent Metal Cations

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Abstract:

Tripodal hexadentate ligands, having three 8-hydroxyquinolyl or 2-methyl-8-hydroxyquinolyl groups as binding sites, were successfully prepared from the corresponding tris(isobutenyl 8-quinolyl ether) via the Claisen rearrangement. The 2-methyl-8-hydroxyquinolyl derivative exhibited binding ability for several kinds of trivalent metal cations to form 1:1 complexes, and showed selective extractability for Ga^{3+} among trivalent cations of Group 13 elements.

Keywords: host compounds; ionophores; rearrangement; gallium and compounds

Various chelating agents have been developed for the detection, separation, and/or purification of a target metal cation for a mixture of several kinds of metal cations. Although most of them are chelating agents for monovalent or divalent metal cations, tripodal chelating agents, having a bidentate binding site in each pod, have been also developed for trivalent metal cations upon mimicking naturally-occurring siderophores such as enterobactin. [1–3]

In the preceding paper, we have demonstrated that the Claisen rearrangement was very useful for the introduction of a bidentate binding site in each pod in the synthesis of a tripodal hexadentate ligand. [4] On the other hand, 8-hydroxyquinoline and its derivatives are well-known to be excellent chelating agents for various metal cations, [5] and on the basis of this fact, one of the authors has prepared dipodal tetradentate ligands and demonstrated that they exhibit excellent extractability for heavy metal cations. [6]

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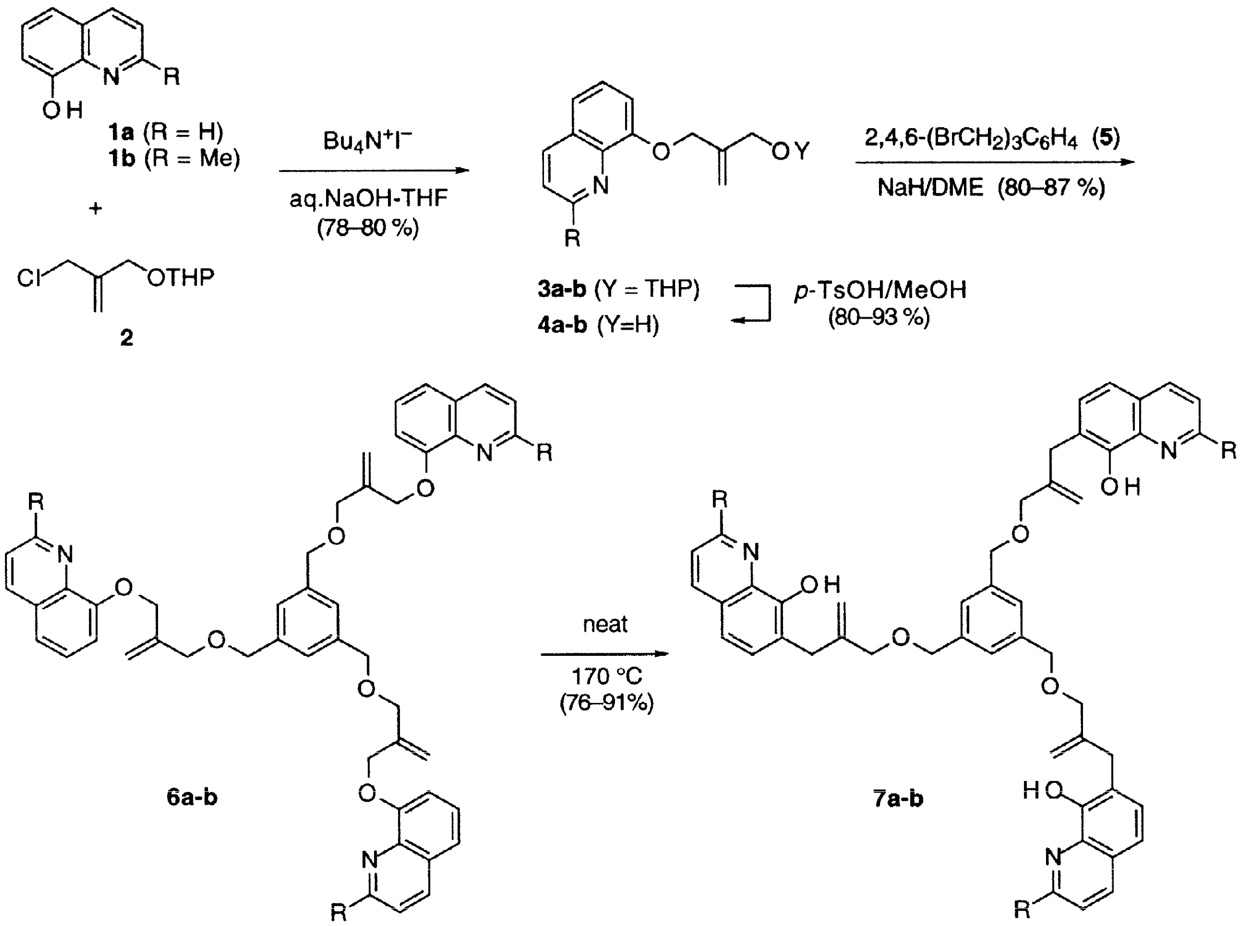
In this communication, we would like to report the synthesis and binding properties of tripodal hexadentate ligands having three 8-hydroxyquinolyl or 2-methyl-8-hydroxyquinolyl groups as binding sites. [7]

We designed tripodal hexadentate ligands **7**, referring to the structure of the hexadentate ligand reported in the preceding paper. [4] The synthesis of **7** was similarly carried out by using 8-hydroxyquinoline (**1a**) or 2-methyl-8-hydroxyquinoline (**1b**), 2-(chloromethyl)-2-propen-1-yl 2-tetrahydropyranyl ether **2**, [4] and tris(bromomethyl)benzene (**5**) as the starting materials. The condensation of **1** with **2** in tetrahydrofuran/aq. NaOH in the presence of a catalytic amount of tetrabutylammonium iodide proceeded smoothly to give **3** (**a**: 80% yield, **b**: 78% yield), which were converted into **4** upon treatment with *p*-toluenesulfonic acid in methanol (**a**: 80% yield, **b**: 93% yield). Allyl alcohols **4** were converted into their sodium salts and allowed to react with **5** in dimethoxyethane to afford precursor **6** (**a**: 87% yield, **b**: 80% yield). The final key step, the Claisen rearrangement, smoothly proceeded upon heating **6** at 170 °C for several hours under reduced pressure to give **7** [8] in high yields, even though the conversion required the triple Claisen rearrangement (**a**: 91%, **b**: 76%).



Scheme 1.

We first examined the complexation behavior of **7** in solutions by choosing Ga^{3+} (GaCl$_3$) and Fe^{3+} (FeCl$_3$) as trivalent metal cations. The Job plots by UV-Vis or ^{1}H-NMR spectrometry for four combinations [9] of **7** with Ga^{3+} and Fe^{3+} showed that **7b** formed 1:1 complexes with the metal cations, while **7a** afforded complexes with a molar ratio of 3:2. Although the reason for the difference in molar ratio between the complexes of **7a** and **7b** is not clear at present, **7a** may produce a mixture of several kinds of complexes upon complexation with Ga^{3+} or Fe^{3+}. The Job plots for the complexes of **7b** with Ga^{3+} and Fe^{3+} are shown in Fig. 1.

As mentioned above, **7b** clearly formed 1:1 complexes with Ga^{3+} and Fe^{3+}. We then examined the extractability of **7b** for trivalent metal cations such as Ga^{3+}, Fe^{3+}, Al^{3+} (AlCl$_3$), and La^{3+} (La(OTf)$_3$) upon changing the pH of their solutions. The results are shown in Fig. 2.

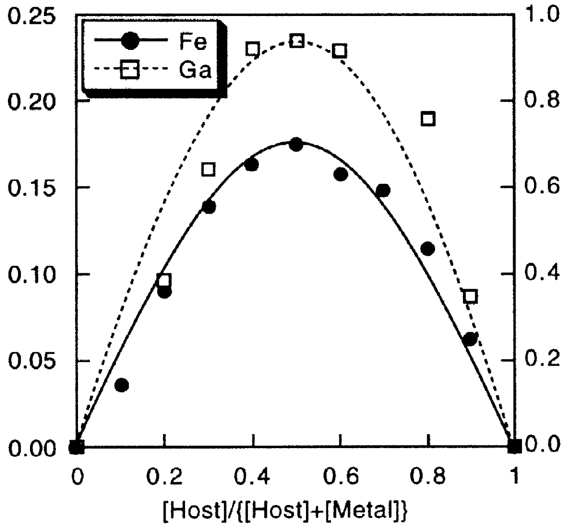


Figure 1. Job's Plots of **7b** with GaCl$_3$ and FeCl$_3$. The vertical axis is the complex concentration (mM) calculated from the induced shifts in the ^{1}H NMR (Ga^{3+}, right) or absorbance at 620 nm (Fe^{3+}, left).

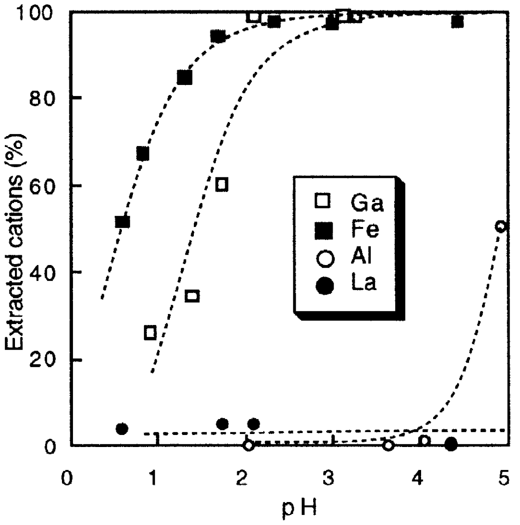


Figure 2. Extractability of **7b** for the trivalent metal cations. Conditions: 1 mM ligand solution (5 mL, CHCl$_3$), 0.1 mM solution of metal ion (5 mL acetate buffer), 12 h, 20 °C.

As can be seen from Fig. 2, the extractability of **7b** for the trivalent metal cations was highly dependent on the pH of the solutions. The dependency of the extractability on the pH indicates that **7b** liberates three protons upon complex formation, and that **7b** forms neutral 1:1 complexes with trivalent metal cations. Moreover, the pH regions corresponding to the large change in extractability for the metal cations were different from each other. These phenomena indicate that **7b** would be able to discriminate the trivalent metal cations at appropriate pH. Thus, we carried out competitive extraction experiments for mixtures of two kinds of trivalent metal cations. The results are summarized in Fig. 3.

By using **7b** as a chelating agent, Ga^{3+} was selectively extracted from mixtures of Ga^{3+} and Al^{3+}, and Ga^{3+} and In^{3+}. These results indicate that Ga^{3+} forms a relatively stable complex with **7b** among the trivalent metal cations of Group 13 elements. In contrast, selective extraction by **7b** from a mixture of Ga^{3+} and Fe^{3+} could not be achieved at higher pH region, where the almost quantitative extraction of both metal cations was observed in extraction experiments of the respective cations (Fig. 2).

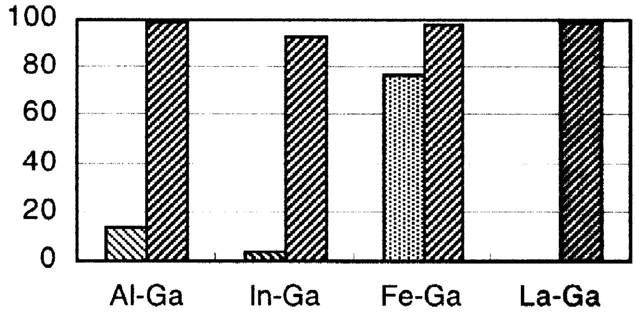


Figure 3. Competitive extraction of several metal cations with **7b**. Conditions: 2 mM host solution (5 mL, $CHCl_3$), solutions of metal ion (0.2 mM each, 5 mL acetate buffer, pH 3.6), 18 h, 20 °C. In the case of In-Ga, pH 1.9.

In conclusion, we have synthesized new tripodal hexadentate chelating agents having three 8-hydroxyquinolyl or 2-methyl-8-hydroxyquinolyl groups as the binding site. The 2-methylated derivative formed 1:1 complexes with Ga^{3+} and Fe^{3+}, and showed selective extractability for Ga^{3+} among the metal cations of Group 13 elements.

References and Notes

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[8] Spectral data for **7a**: ^1H NMR (300 MHz; CDCl3) δ 2.69 (s, 9H), 3.64 (s, 6H), 4.01 (s, 6H), 4.48 (s, 6H), 4.93 (s, 3H), 5.15 (s, 3H), 7.3-7.2 (m, 12H), 7.96 (d, J=8.6, 3H); ^{13}C-NMR (67.5 MHz; CDCl3) 24.8, 33.4, 71.7, 72.8, 113.1, 116.8, 120.5, 121.9, 125.1, 126.2, 128.9, 135.9, 137.4, 138.6, 144.7, 149.0, 156.6; FABMS 760 (M+H); IR (neat) 3390, 1615, 1440, 1100, 910, 843.

Spectral data for **7b**: ^1H-NMR (300 MHz; CDCl3) δ 2.38 (s, 9H), 3.60 (s, 6H), 3.97 (s, 6H), 4.47 (s, 6H), 4.83 (s, 3H), 5.09 (s, 3H), 7.2 (m, 3H), 7.3 (m, 6H), 8.02 (dd, J=1.7, J=8.3, 3H), 8.68 (dd, J=1.4, J=4.4, 3H); ^{13}C-NMR (75 MHz; CDCl3) 15.9, 33.5, 67.1, 73.2, 113.2, 117.2, 120.8, 121.1, 127.1, 130.1, 132.6, 135.9, 138.2, 138.3, 144.9, 147.8, 149.6; FABMS 802 (M+H); IR (KBr) 3400, 1578, 1503, 1483, 1378, 1100, 835.

[9] The solvent and spectroscopy: **7a**/Fe^{3+} and **7a**/Ga^{3+}, 0.18 mM in $CHCl_3$ and UV-Vis; **7b**/Fe^{3+}, CH_3CN and UV-Vis; **7b**/Ga^{3+}, 2.3 mM in CD_3CN and ^1H-NMR.