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# Formation of Host-guest Complexes of Amino Acids and Cucurbit[7]uril

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Interaction of amino acid hydrochlorides (guests) by cucurbit[7]uril (Q7, host) has been studied by $^1$H NMR. UV-vis spectra titration are employed in present study and the interaction models of 1:1 between guests and host is obtained. The binding constants (Ka) of TryHCl, PheHCl and TyrHCl for Q7 are $3.73 \times 10^5$, $8.15 \times 10^5$, and $2.33 \times 10^5$ L/mol, respectively.

**Key Words: Cucurbiturils, Molecular recognition, Inclusion complex, Amino acid, Supramolecular.**

## INTRODUCTION

Cucurbit[n]urils (n = 5-8,10), Qn, are macrocyclic-caged compounds, which are made of glycoluril units interconnected with methylene bridges (Fig. 1). Its hydrophilic character is unique and cucurbit[7]uril (Q7) is the optimal hereinto[1]. The hydrophobic cavity is accessible from the exterior and therefore inclusion complexes with molecules and ions can be formed. It was known that phenyl and pyridine group are appropriate guests[2]. The molecular container or pseudorotaxane structures have been investigated by the inclusion of guest-host[3]. This provides unique opportunities to study the molecular recognition in the microenvironments[4].

The junction of amino acids and macrocycle molecular with non-covalent bond is an important topic both to understand the mechanism of process in recognizing and transferring a specific amino acid by t-RNA and to research kinds of interaction modes in the chemistry of molecular recognition. Inclusion complexes of amino acids and cyclodextrin, aza macrocycle or crown ethers have been reported[5-7]. In this paper, the interactions between Q7 and L-tryptophan, L-phenylalanine or L-tyrosine hydrochlorides (TryHCl, PheHCl and TyrHCl, respectively) have studied and reported.

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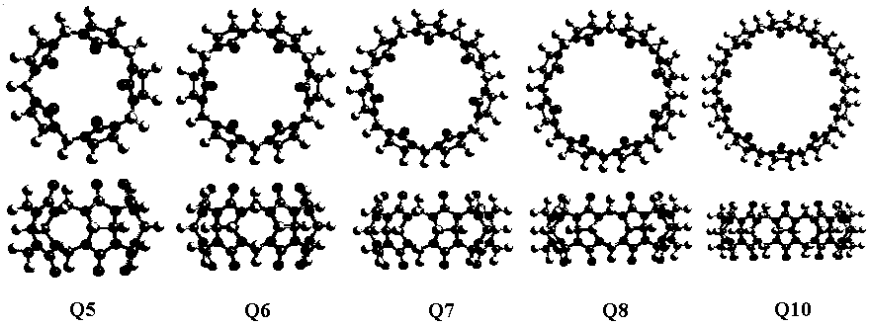


Fig. 1. The models of cucurbit[n]urils (n = 5-8, 10).

## EXPERIMENTAL

Amino acids are purchased from Sinopharm Chemical Reagent Co., Ltd.. Solids of amino acid hydrochlorides were obtained from the concentrated hydrochloric acid acidified solution of amino acids.

$^1$H NMR spectra were recorded at 300K on a Bruker 500 spectrometer in $D_2O$. UV-vis spectra were measured on a Unico UV-2102 instrument at 25°C.

## RESULTS AND DISCUSSION

$^1$H NMR spectra and the peak assignments of the protons on TryHCl, PheHCl and TyrHCl are shown in Fig.2. The β-H appears double-double shape because of the chiral α-C atoms. The broadener of the peak shapes implies inclusion formations of the stable host-guests. The peaks of guests are splitted clearly. However, it can hardly find any set of proton resonance signals for free amino acid in the spectra of inclusion complexes. On account of difference of half band width between inclusion and Q7 host, the broad peak of interacted complexes may be reveal that the frequency that guests entry or leave cavity of host is fast far from NMR time scale, so the intermediate states from free guests to inclusion complexes are observed here[8]. Exceptionally, the signals of side-group proton of binding TyrHCl shift upfield relative to the free one. The appearance of two peaks at $\delta$ = 6.0 ppm and $\delta$ = 6.4 ppm illustrates that the phenyl moiety of tyrosine is now located inside cucurbit[7]uril.

Inclusion ratios and binding constants of amino acids and cucurbit[7]uril have been measured with UV-Vis spectra titration and the results are exhibited in Fig. 3. The concentration of the guests is fixed during the measurements and the spectra are recorded with the increasing concentration of Q7 along with the arrow in Fig. 3(a-c).

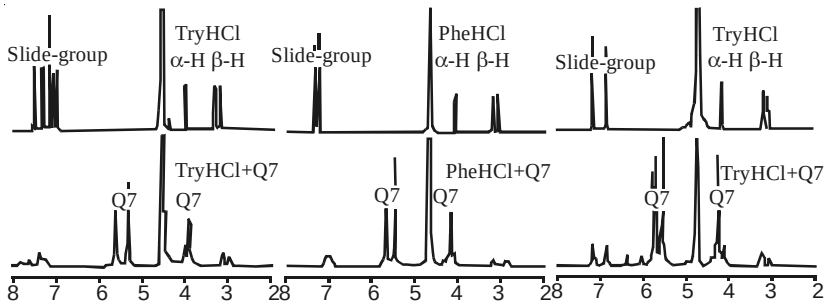


Fig. 2. $^{1}$H NMR spectra of guests and inclusion complexes of guests-Q7

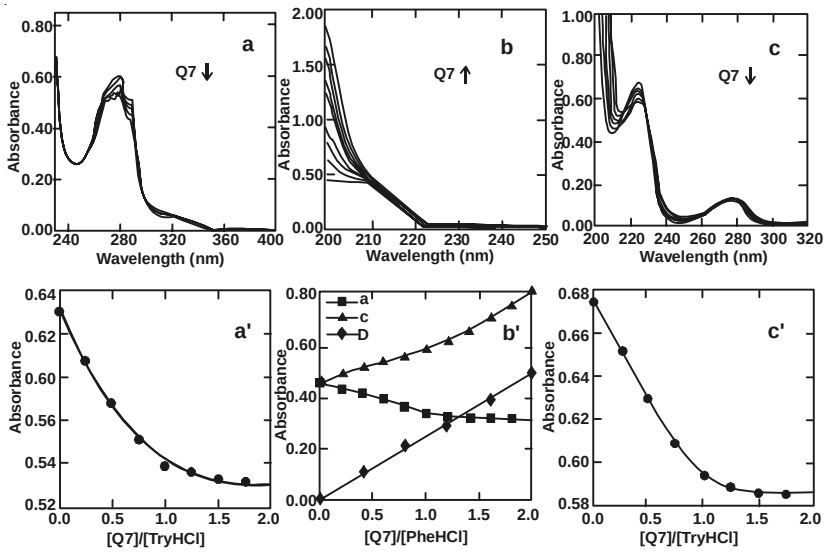


Fig. 3. The absorption spectra changes of the mixtures of guest-host (a, b ,c) and curve-fitting analysis for the inclusion complexes (a', b', c')

a) [TryHCl] = $1.00 \times 10^{-4}$ mol/L, [Q7]: $2.50 \times 10^{-5} - 2.00 \times 10^{-4}$ mol/L; a') $\lambda$ = 280 nm
b) [PheHCl] = $5.00 \times 10^{-5}$ mol/L, [Q7]:$2.00 \times 10^{-5} - 1.00 \times 10^{-4}$ mol/L; b') $\lambda$ = 206 nm
c) [TyrHCl] = $1.00 \times 10^{-4}$ mol/L, [Q7]: $2.50 \times 10^{-5} - 2.00 \times 10^{-4}$ mol/L; c') $\lambda$ = 223 nm

The wavelength at the maximum absorbance of L-TryHCl guest is observed at 280 nm ($\varepsilon = 6.10 \times 10^{3}$ L mol$^{-1}$ cm$^{-1}$) from Fig. 3a. The 1:1 interaction model with Q7 can be gained by fitting the absorbance *vs.* host concentrations as shown in Fig. 3a'. Thus, the 1:1 interaction equilibrium of Q7(H) and amino acid guest(G) is expressed by eqn. 1:

$$\mathbf{H} + \mathbf{G} \xrightarrow{K_a} \mathbf{H \cdot G} \qquad (1)$$

The steady constant ($K_a$) was found to be $3.73 \times 10^{5}$ L/mol (R = 0.99) with non-linear least square fitting according to curve fitting eqn. 2:

$$\Delta A = \frac{\Delta\varepsilon([H]_0 + [G]_0 + 1/K_a) \pm \sqrt{\Delta\varepsilon^2([H]_0 + [G]_0 + 1/K_a)^2 - 4\Delta\varepsilon^2[H]_0[G]_0}}{2} \quad (2)$$

where $\Delta A$ is the change in the absorbance of guest on gradual addition of Q7, whereas the $\Delta\varepsilon$ refers to difference of molar absorptivity between junctional complex and free amino acid guest, the total concentration of cucurbituril host and guest is denoted by $[H]_0$ and $[G]_0$ accordingly.

Similar experiment and data analysis with TyrHCl as the guest yielded the values of $K_a = 8.15 \times 10^5$ L/mol (R = 0.99) at $\lambda_{max} = 223$ nm and $\varepsilon = 6.75 \times 10^3$ L mol$^{-1}$ cm$^{-1}$ and a 1:1 binding model for its Q7 complex was shown in Fig. 3c and c', respectively. The titration curve C in Fig. 3b' was drawn according to the absorbance change of shoulder peak along with increasing concentration Q7 for L-phenylalanine at 206 nm (Fig. 2b, $\varepsilon = 8.98 \times 10^3$ L mol$^{-1}$ cm$^{-1}$). The difference (Fig. 3b' curve B) of the curve (curve C) drawn in experiment data and its corrected line (curve D) deduced from the absorbance of host at the same wavelength shows the best fit with the 1:1 binding model. It were also treated with nonlinear curve-fitting with $K_a = 2.33 \times 10^5$ L/mol (R = 0.99).

In words, the evidences of $^1$H NMR and UV-Vis titration indicate the interactions of aromatic amino acid hydrochlorides and cucurbit[7]uril host in water. The binding model of the host with the guests is 1:1.

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