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Zenzo Tamura and Motoichi Miyazaki : Metal Complexes of D-Glucosamine and its Derivatives. VI.*1 Determinations of Stability Constants of Copper Complexes of Methyl-β-D-glucosaminide and of 3,4,6-Tri-O-methyl-D-glucosamine by pH Titration Method.

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Following after the investigations of the metal complexes of D-glucosamine (I), two methyl derivatives of I, methyl-β-D-glucosaminide (II) and 3,4,6-tri-O-methyl-D-glucosamine (III) were studied on the complex formation with cupric ion.

Considering from the results obtained with the copper complexes of II and III, they were found to be the most stable complexes among the metal complexes of II and III, therefore, the stability constants and hydrolysis constants were determined by the pH titration method reported previously and compared with those of copper complex of I.

Experimental

Materials and Solutions——Methyl-β-D-glucosaminide (II) and 3,4,6-tri-O-methyl-D-glucosamine (III) were the same preparations reported in the previous paper.[1] $Cu(NO_3)_2$ of analytical grade was used to make the stock solutions having a concentration of $10^{-2}M$ of cupric ion. This stock solution was standardized by EDTA titration with a metal indicator in the similar manner as described previously.[2]

Apparatus and Procedure——The apparatus and the equipments for the pH titration were the same ones and the similar procedure was also employed to that described in the previous publications.[1]

Treatments of Data of pH Titrations——The treatments of the data for the calculation of the stability constants of copper complexes of II and III were as same as the case of metal complexes of I.[2] Bjerrum's method[3] was used for calculations, after its applicability being examined in the similar manner previously described.[2]

Acid dissociation constants of II and III used for the calculations were 7.15 and 6.92, respectively, which were determined and reported in the previous publication.[1]

Results and Discussion

The titration curves of II and III in the presence of cupric ion are shown in Fig. 1 as denoted II′ and III′. They are the curves of having a 1:1 ratio of II or III to cupric ion and are very similar to that of copper complex of (I) system. During the pH titrations, the bluish green color of the sample solution turned to deep blue as an increase of pH of the solution. The pH depression was also observed and either cupric hydroxide or hydrolysis product was perceived as was seen in the case of copper complex of (I).

Bjerrum's method was examined for its applicability to the calculation of stability constants of these complexes and results are shown in Fig. 2.

As was the same in the case of copper complex of I, a linear relationship was obtained between $\bar{n}$ and $(1-\bar{n})[G]$ of these complexes.

Consequently, it is clearly seen that copper complex having a 1:1 ratio of either II or III to cupric ion is formed in the solution.

*1 Part V : This Bulletin, **13**, 345 (1965).
*2 Hongo, Tokyo (田村善蔵, 宮崎元一).
1) Part III : This Bulletin, **13**, 330 (1965).
2) Part IV : *Ibid.*, **13**, 333 (1965).
3) J. Bjerrum : "Metal Ammine Formation in Aqueous Solutions" (1941), Haase & Son, Copenhagen.

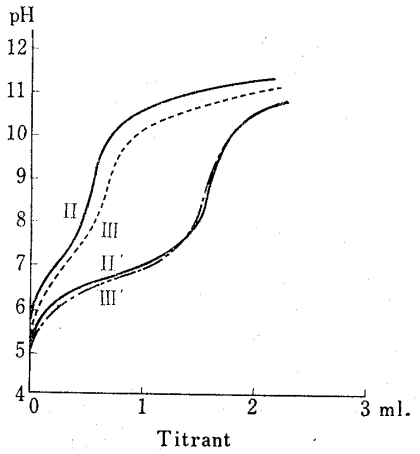

Fig. 1. Titration Curves of Methyl-β-D-glucosaminide (II) and 3,4,6-Tri-O-methyl-D-glucosamine (III) in the Presence of Cupric Ion

II : (II)
II′: (II)+cupric ion
III : (III)
III′: (III)+cupric ion
Ligand to cupric ion 1 : 1
Ligand concentration : $1\times10^{-3}M$
titrant : 0.1M NaOH
temp. : 30±0.5°, μ=0.1(KNO_3)

The stability constants and hydrolysis constants of these two copper complexes were calculated in the same manner as described in the previous paper.[2] In Table I, the stability constants log K_1 and hydrolysis constants $pK_{LCu(OH)}$ are listed.

The magnitude of obtained values for log K_1 of these two copper complexes are of the same order, and both of them are slightly smaller than that of copper complex of I.

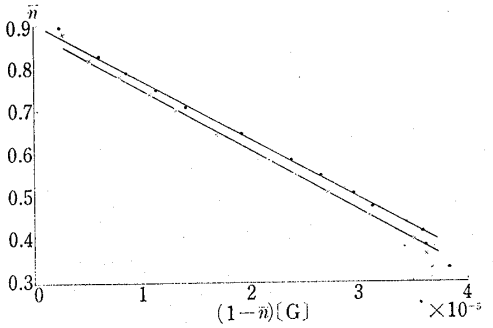

Fig. 2. Relation between $\bar{n}$ and $(1-\bar{n})$ [G]

×——× II-copper complex
●——● III-copper complex

TABLE I. Stability and Hydrolysis Constants of Copper Complexes of D-Glucosamine (I), Methyl-β-D-glucosaminide (II) and 3,4,6-Tri-O-methyl-D-glucosamine (III)

Material	Stability constant log K_1	Hydrolysis constant $pK_{LCu(OH)}$[a]	Concentration (M)
D-Glucosamine (I)	5.0	7.7	1.028×10^{-3}
Methyl-β-D-glucosaminide (II)	4.5	7.5	1.041×10^{-3}
3,4,6-Tri-O-methyl-D-glucosamine (III)	4.5	7.3	1.026×10^{-3}

Ligand to cupric ion=1:1, temp. 30±0.5°, μ=0.1 (KNO_3).
a) Suffix L means each ligand (I), (II) and (III) respectively.

Hydrolysis constants of copper complexes of II and III are almost of the same magnitude, and they are almost equal to that of copper complex of I. Considering from log K_1 values of copper complexes of II and III, it may be deduced that the position and numbers of methoxyl group at a carbon atom of glucosamine moiety do not influence on the magnitude of their copper complexes.

However, both of the copper complexes have smaller log K_1 values than that of copper complex of I at nearly same concentration of ligand.

The effect of the presence of one methoxyl group is so noticeable that the structural change of the ligand will affect the stability of complexes. From this point of view, it may be supposed that a certain steric factor which gives rather larger influence on the complex formation would be present and participate in the complex formation.

For instance, such an assumption may be possible to consider that the methoxyl groups at C_1 and C_3 of glucosamine moiety would prevent the complex formation by interfering the mutual approaching between cupric ion and ligand molecule because of its bulky size or by decreasing the weak coordinating ability of hydroxyl group vicinal to the amino group of glucosamine molecule with the displacement of methoxyl group

for hydroxyl group. In regard to the formation mechanisms, other possibilities might be considered, and much informations should be necessary to interpret the mechanism of complex formation in solutions.

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Summary

Copper complexes of methyl-β-D-glucosaminide (II) and 3,4,6-tri-O-methyl-D-glucosamine (III) were investigated by pH titration method.

The stability constants log K_1 and hydrolysis constants $pK_{LCu(OH)}$ of these two complexes were determined and compared with that of copper complex of D-glucosamine (I).

The magnitude of log K_1 of copper complex of II was the same to that of copper complex of III, but both of them were slightly smaller than that of copper complex of I.

However, the hydrolysis constants of copper complexes of I, II, and III were of the same order in the magnitude.

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Kinji Harada and Sakae Emoto : Condensation of 5-Nitro-2-furaldehyde with 4-Methyl(or 4-Ethyl)pyridine.

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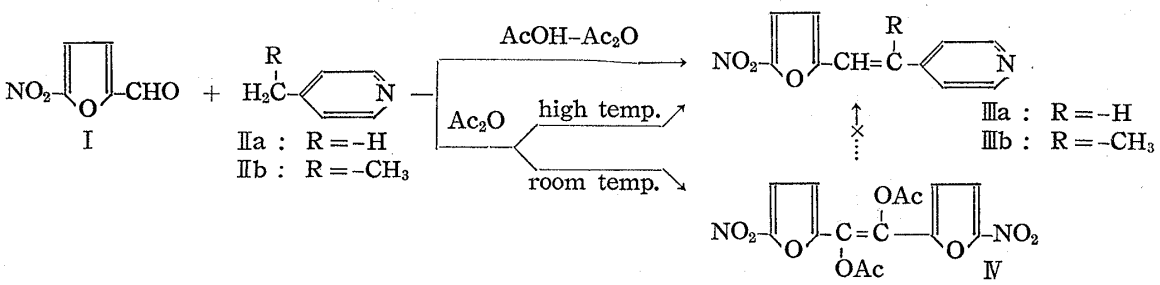
A series of condensation of 5-nitro-2-furaldehyde with 2- or 4-alkylpyridines and lutidines was studied to obtain antibacterial substances.

Recently, Boehringer, *et al.*[1] reported on the condensation of 5-nitro-2-furaldehyde (I) with 4-methyl(or 4-ethyl)pyridine (IIa or IIb) by being heated at 100° for 2 hours in acetic anhydride to give 4-[2-(5-nitro-2-furyl)vinyl]pyridine (IIIa) or 4-[1-methyl-2-(5-nitro-2-2-furyl)vinyl]pyridine (IIIb), however our reinvestigation on their experiments found the yield of IIIa or IIIb was unsatisfactory (about 10%) and its purification was very difficult.



Accordingly, in order to improve the yield of aimed products (IIIa or IIIb), aforementioned condensations were examined again under the following conditions. Using of acetic acid

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1) C. F. Boehringer, Soehne G. m. b. H : C. A., 58, 11333 (1963); Berg. Pat., 615319, Sept. 20, 1962.