

# EFFECTS OF CONFORMATION OF POLYMER LIGANDS IN COPPER(II) COMPLEXES ON CATALYTIC ACTIVITIES AND MECHANISM OF OXIDATIVE COUPLING OF $\beta$ -NAPHTHOL

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## ABSTRACT

Copper(II) complexes of sericin, chitosan, 6- and 2-aminodeoxystarch were used as catalysts in oxidative coupling of  $\beta$ -naphthol, the effects of conformation of the polymer ligands in these complexes on activities of the catalysts and mechanisms of the reaction were studied. It was found that if the catalysts react with the substrate by mechanism similar to the enzymic catalysis they must be composed of polymer ligands with highly coiled, especially with densely helicoidal, conformations. While catalysts composed of loosely coiled or helicoidal ligands react with the substrate through molecular collision and have relatively lower activities only. Under nitrogen, catalysts from sericin and chitosan reacting with  $\beta$ -naphthol give optically active  $\beta$ -binaphthol, rotating polarized light to right, but the stereoselectivities are rather low.

In recent years, polymer metal complex catalysts have been given much attentions. It is well known that the highly active and stereoselective metalloenzymes are aggregates of metal-ion-containing cofactors and apoenzymes polymers. Since the polymer-metal complexes contain both metal and polymers, so it may act as catalysts too, and if optically active ligands are introduced into such complexes the catalysts derived may also be stereoselective and used in asymmetric synthesis. A number of papers in this respect have been published<sup>[1,2,7,9]</sup>, but only little about the effects of factors of the polymer ligands such as conformations, states of aggregation on reactivities, stereoselectivities and reaction mechanisms have been known.

Enzymic proteins are the basic components of all enzymes. Relative positions of functional groups of these proteins in space are essentially important for their activities. The ability of maintenance of those groups in their own positions depends upon the stabilities and completeness of the secondary and the tertiary structures (the conformation). Using different solvents, changes of pH, variation of ionic strength and temperatures may cause some changes in conformations and thus influence the catalytic behaviors. Conformations are, probably, the most important factors of polymers from which the catalysts are to be derived. Thus, it should be very interesting to synthesize polymermetal complexes or chelates from natural or synthtic polymers with different conformations under different conditions, or with unchangeable conformations (different from each other) in all experimental conditions, and examine the effects of such conformations on the reactivities and mechanisms in detail. Sericin, chitosan and aminoderivatives of starch may fulfil these requirements. Accordingly, by using Cu(II) complexes from these ligands as catalysts, oxidative coupling reaction of  $\beta$ -naphthol was carried out. Oxidative coupling of phenols is a key-

step in biosynthesis of many natural products. Study on this reaction may be helpful in comprehension of these processes as well.

## EXPERIMENTAL

### 1. Materials

Silk sericin: It was obtained by treating silkworm cocoon according to the method in Ref. [3]. The extraction with boiling water was carried out under  $N_2$  at  $96^\circ C$  for 5 hrs. Starch is the medicine grade corn starch produced by Chengdu starch factory. Chitosan is obtained from Yuhuan chemical factory of Zhejiang. Glucosamine, biological reagent.  $\beta$ -Binaphthol was synthesized according to the method in Ref. [4] with 80% yield.

Synthesis of amino derivatives of starch: 6-Aminodeoxystarch was synthesized according to the method in Ref. [5]. The N content was 3.72%.

2-Aminodeoxystarch was prepared by method in Ref. [6], and N content was found as 2.95%. Thus the degree of substitution calculated was 0.39.

Synthesis of Cu(II) complexes: Chitosan was dissolved in 2% acetic acid and stirred overnight with  $CuCl_2$  at pH 8. Molar ratio of ligand to Cu was kept at 1:1.5. The suspended product was then filtered out, dehydrated by solvent exchange with alcohol, dried in vacuum desiccator at room temperature, light blue complexes was thus obtained. The content of Cu was 3.27% (wt.) from chelating titration<sup>[7]</sup>. Cu(II) complexes of the other ligands were prepared by mixing aqueous solutions of  $CuCl_2$  and the ligands. After standing for a few hrs., the required amounts of base, salt, ethanol were added, agitated at  $35^\circ C$  for 15 min., then the formed complex was ready for use.

### 2. Oxidative coupling reaction

The reaction was carried out at  $35^\circ C$ , in a specially designed reactor, followed by measurement of oxygen consumed. Air was used as oxidant instead of pure oxygen, but corrected to pure oxygen under standard conditions in the calculation of reaction rates. When substrate solution was added to the reactor, air volume fluctuation in air burette was diminished by keeping the composition of the solvent nearly the same as that in reactor. After 5 min., reading was taken. The volume of oxygen consumed-time curves extended to the origin 0, the initial reaction rates ( $V_0$ ) were measured.

The asymmetric oxidative coupling of the substrate  $\beta$ -naphthol reaction was carried out according to the method in Ref. [8]. The products were analyzed quantitatively by liquid chromatogram without further purification. The yields of products are listed in Tab.1.

Table 1 Yield in asymmetric oxidation of  $\beta$ -naphthol

| Catalysts          | Unreacted raw material (%) | Yield of $\beta$ -binaphthol (%) | By — products (%) | Reaction condition  |
|--------------------|----------------------------|----------------------------------|-------------------|---------------------|
| Glucosamine-Cu(II) | 85.9                       | 12.6                             | 1.5               | $45^\circ C$ 90hrs  |
| Sericin-Cu(II)     | 84.4                       | 13.1                             | 2.5               | $28^\circ C$ 90hrs  |
| Chitosan-Cu(II)    | 53.3                       | 37.6                             | 9.1               | $40^\circ C$ 144hrs |

## RESULTS AND DISCUSSION

### 1. By using sericin-Cu(II) complexes as catalyst

#### (1) Effects of reaction media

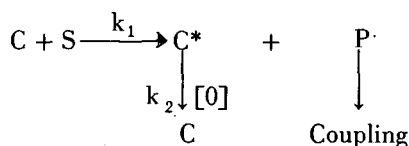


without salt added. In the absence of salt,  $V_0$  has one maximum at  $0.003\text{ }M$  KOH. But in the presence of salt, there are two maxima at  $0.003$  and  $0.007\text{ }M$  respectively. It may be held that in the presence of KCl, the condition of the first maximum  $V_0$  are actually the same as those for maximum  $V_0$  in the absence of salt, and the conditions for the two maxima differ only in the concentration of KOH: one, at  $0.003\text{ }M$ ; the other, at  $0.007\text{ }M$ . As stated above, in  $0.003\text{ }M$  KOH solution (60% ethanol), the molecular chains of the ligand coil up loosely (Condition I). In solution containing  $0.003\text{ }M$  KOH and  $0.5\text{ }M$  KCl(60% ethanol), the molecular chain will be more highly coiled (Condition II).

In solution containing  $0.007\text{ }M$  KOH and  $0.5\text{ }M$  KCl, since the concentration of KOH is higher, more carboxyl and pheolic groups will be changed into corresponding anions, and the molecular chains will be extended from highly coiled state to loosely coiled state again (Condition III). Thus, it has been proved that under different conditions, the reaction takes place with different rates, the catalysts have different conformations and reactivities. So, bear these differences in mind, by studying the kinetics of the reaction under conditions I, II, III, resp., it is possible to ascertain the effects of the conformations of the ligands upon the reaction mechanisms.

## (2) Reactions by molecular collision mechanism

Experimental works confirmed this expectation. It was found that under conditions I and III,  $V_0$  increases proportionally to the concentration of the substrate up to the substrate crystallized out (Fig. 2). The reaction takes place through molecular collision mechanism:



Since free radicals are short-lived,  $C^*$  is reoxidized very fast, and  $C$  is nearly constants, so the following expression for  $V_0$  may be derived:

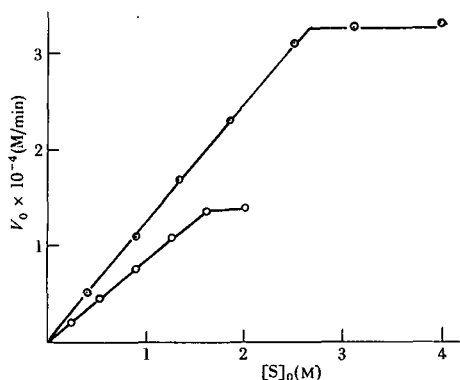


Fig. 2 Relation between  $V_0$  and substrate content in 60% (V/V) ethanol,  
 $[KOH] = 3 \times 10^{-3}\text{ }M(\odot)$   
 and  $7 \times 10^{-3}\text{ }M(O)$   $[KCl] = 0.5\text{ }M$ ,

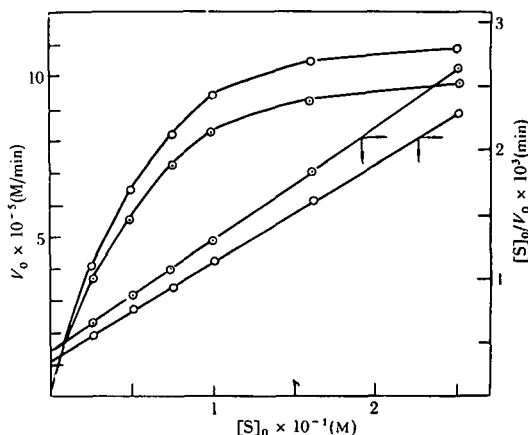


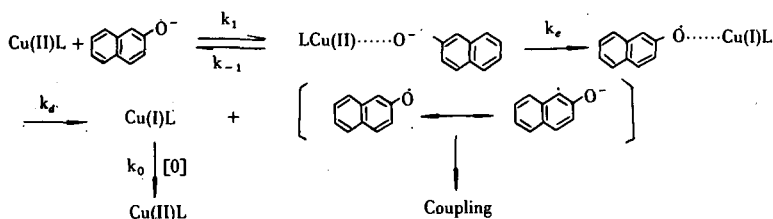
Fig.3 Relation between  $V_0$ ,  $[S]_0/V_0$  and substrate content in 60% (V/V) ethanol,  $[KCl] = 0.5\text{ }M$   
 $[L]/[Cu(II)] = 5(\odot), 10(O)$

$$V_0 = K[S]_0$$

It is quite evident that the reaction is a pseudo-unimolecular process, without formation of catalyst-substrate (CS) intermediate complexes and possesses no characteristic features of enzymic catalysis.

### (3) Reactions with characteristics of enzymic catalysis

However, under condition II, by catalysts of L/Cu molar ratios of 5 and 10, the relationship between  $V_0$  and concentration of substrate can be represented diagrammatically as hyperbolas with distinct substrate saturation phenomena (Fig.3). Thus, it is questionless that the reaction takes place through formation of CS intermediate complexes. A reaction mechanism, as proposed by Tsuchida<sup>[11]</sup>, may be expressed as follows:



The kinetic data may also be treated in the same way.

$$V_0 = \frac{V_m [S]_0}{K_m + [S]_0}$$

where  $K_m = \left( \frac{k_{-1} + k_e}{k_1} \right) \left( \frac{k_d}{k_e + k_d} \right), \quad K_1 = \frac{1}{K_m}$

$$V_m = k_2 [C]_0 = \frac{k_e k_d}{k_e + k_d} [C]_0$$

Taking the reciprocal of  $V_0$  expression, multiplying both sides by  $[S]_0$ , the following equation can be obtained.

$$\frac{[S]_0}{V_0} = \frac{K_m}{V_m} + \frac{[S]_0}{V_m}$$

A plot of the experimental data according to this equation is shown in Fig. 3. From the slope and the intercept of the line,  $V_m$  and  $K_m$  were calculated (Tab.2).

Obviously, the reaction follows Michaelis-Menten kinetics, and possesses characteristics of enzymic catalysis. Probably the inner hydrophobic area in the highly coiled polymers plays an important role in these cases.

Table 2 Kinetics data of Oxidative coupling of  $\beta$ -naphthol under condition II

| [L]/[Cu(II)] | $V_m \times 10^3$<br>(M, min <sup>-1</sup> ) | $k_2$<br>(min <sup>-1</sup> ) | $K_m \times 10^3$<br>(M) | $K_1$<br>(M <sup>-1</sup> ) |
|--------------|----------------------------------------------|-------------------------------|--------------------------|-----------------------------|
| 5            | 1.18                                         | 0.236                         | 54                       | 18.52                       |
| 10           | 1.36                                         | 0.272                         | 54                       | 18.52                       |

## (4) Temperature effects on reaction rates

Variations of  $V_0$  with temperature under condition II may be represented as a common bell-shaped curve (Fig. 4). The higher the temperature, the higher the energy content in the system, the more the molecules acquired activation energy, the higher the reaction rate. But over certain temperature the molecular chains of the ligand more extended, the activity thus lost (from this point, the effect of ethanol content and the expressions in kinetics, it is much like true enzymes.) Plot in  $V_0$  against  $1/T$  (below  $40^\circ\text{C}$ ) one straight line is obtained. It tells that under certain limit, temperature does not affect the equilibrium between C,S and CS complexes. Activation energy approximately estimated is  $35.6 \text{ kJ/mol}$  ( $8.5 \text{ kcal/mol}$ ).

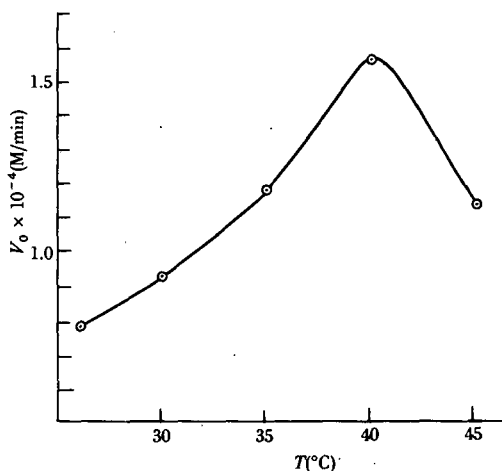


Fig. 4 Relation between  $V_0$  and reaction temperature  
 $[\text{S}]_0 = 1.5 \times 10^{-1} \text{ M}$ ,  $[\text{KCl}] = 0.5 \text{ M}$ , others as those under Fig.1

## (5) Superficial understanding of reaction valley

Fig.1 reveals that in the presence of  $0.5 \text{ M}$  salt and  $0.005 \text{ M}$  KOH,  $V_0$  is the minimum. It is believed that when the alkalinity is increased from  $0.003$  to  $0.005 \text{ M}$ , the molecular chains of the ligand extended more and more, the ability to form CS complexes diminished, the reaction rate decreased quickly. At the transition stage, only a few molecules acquired the loosely coiled conformation, the activity of which is relatively low, and not every collision between C and S can lead to reaction, thus the valley in reaction rate curve appears. In other words, the activities of catalysts with ligands of different conformations are different. When the molecular chains are coiled more compactly, the catalysts are more active; if the molecular chains coiled loosely they are less active.

2. The behaviors of  $\text{Cu(II)}$  complexes of amino-substituted polysaccharides(1) Chitosan- $\text{Cu(II)}$  complex catalyze reaction by molecular collision mechanism

It is apparent from sericin- $\text{Cu(II)}$  complexes tested the effects of conformations of ligands is a more important factor which must be considered. In order to confirm this phenomenon further,  $\text{Cu(II)}$  complexes prepared from crystalline ligands with  $\beta$ -pleated sheet (extremely extended) conformation and helicoidal (specially coiled) conformation were examined, very interesting results were obtained too.

The chain unit of chitosan is  $\beta$ -D-2-aminopyranoglucose. The conformation of this

macromolecule is of  $\beta$ -pleated sheet, as that of cellulose. There are some inter- and intra-molecular hydrogen bonds between chain units, this conformation is very stable. Chitosan and its Cu(II) complexes are all highly crystalline as proved by X-ray diffraction method.

Since the reactivity of chitosan-Cu(II) is very low, for  $V_0$  to be measurable and comparable, [Cu(II)] and [L]/[Cu(II)] equal to 0.015 M and 10, instead of 0.005 M and 5, resp., were used. Even though the  $V_0$  is the lowest. In the presence or absence of salt, the relations between  $V_0$  and concentrations of substrate are all straight lines and there is no distinct difference between them (Fig. 5).

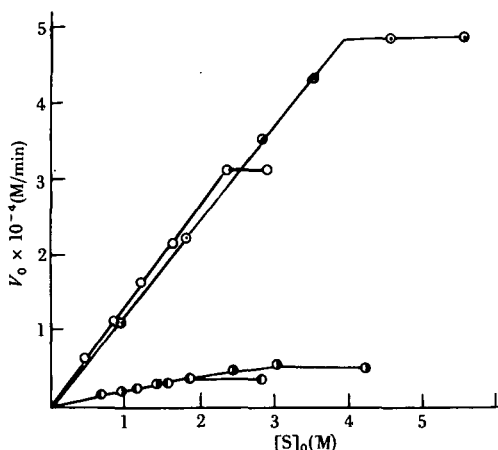


Fig. 5 Relation between  $V_0$  and  $[S]_0^*$  2-aminodeoxystarch-Cu(II) ( $\odot$ ): [Cu(II)] =  $5 \times 10^{-3} M$ , [L]/[Cu(II)] = 5, [NaOH] =  $8 \times 10^{-1} M^{**}$   
glucosamine-Cu(II) ( $\circ$ ): [Cu(II)] =  $8 \times 10^{-3} M$ , [NaOH] =  $1 \times 10^{-2} M$   
chitosan-Cu(II): [L]/[Cu(II)] = 10, [Cu(II)] =  $1.5 \times 10^{-2} M$ , [NaOH] =  $3 \times 10^{-3} M$   
[NaCl] =  $5 \times 10^{-1} M$  ( $\bullet$ ) or absence ( $\odot$ )

\* All reactions were carried out in 60% (V/V) ethanol.

\*\* The upper concentration of NaOH under which the reaction took place with collision mechanism.

Because chitosan and its Cu(II) complexes are all insoluble in reacting medium, the reaction obviously occurs on the surface of the catalyst, and follows molecular collision mechanism. Salt decreases the solubility of  $\beta$ -naphthol only.

(2) Amino-deoxystarches-Cu(II) complexes may catalyze reaction of both molecular collision mechanism and enzyme-like catalysis mechanism

Different from those of chitosan, the chain units of amino substituted starches are  $\alpha$ -D-aminodeoxypyranoglucose, the conformation of which is the same as that of the chain units of starch, so the conformations of these macromolecules, as that of starch, are also left handed helicoidal. It can also form inclusion compounds with KOH, some organic and inorganic compounds, the diameter of their chain  $\alpha$ -helix may be enlarged, and the absolute length per spiral

may be shortened<sup>[12]</sup>, i.e. the Cu(II) complexes along the molecular chain, the active centers, may be more concentrated. With 6-aminodeoxystarch-Cu(II) as catalyst, since, in this case, substrate saturation phenomenon appears too early, for the  $V_0$  to be measurable and comparable,  $[\text{Cu(II)}]$  were properly raised.  $[\text{L}]/[\text{Cu}]$  decreased,  $[\text{NaOH}]$  and  $[\text{NaCl}]$  are varied, several sets of experiments were carried out, no main difference in shape of  $[\text{S}]_0-V_0$  curves were found. Typical results are shown in Fig. 6. It is clear that the oxidative coupling of  $\beta$ -naphthol undergoes with distinct substrate saturation phenomenon(Fig. 6), straight line is obtained by Hane's plotting method (Fig. 6). The kinetics data are listed in Tab. 3.

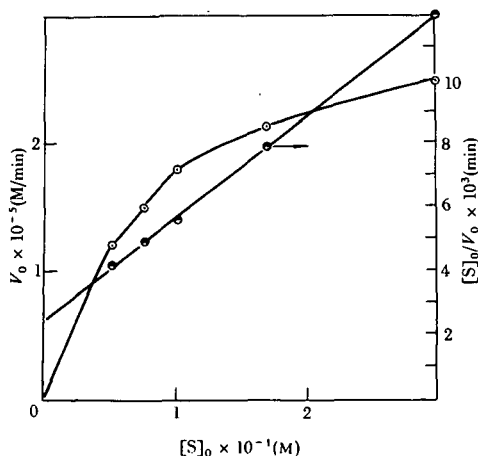


Fig. 6 Relation between  $V_0$ ,  $[\text{S}]_0/V_0$  and  $[\text{S}]_0$   
6-aminodeoxystarch-Cu(II) ethanol content 60% (V/V), 2-aminodeoxystarch-Cu(II): ethanol content 60% (V/V),  
 $[\text{Cu(II)}] = 1.2 \times 10^{-2} \text{ M}$ ,  $[\text{NaOH}] = 0.1 \text{ M}$ ,  
 $[\text{NaCl}] = 0.5 \text{ M}$ , and  $[\text{L}]/[\text{Cu(II)}] = 4$

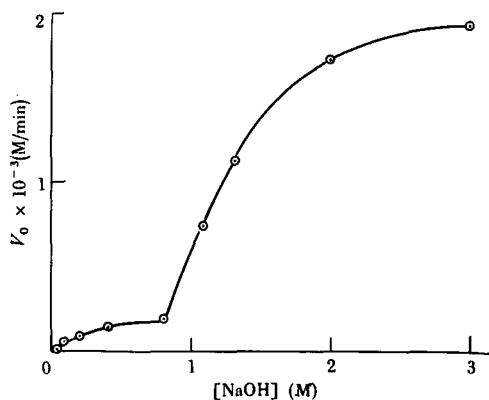


Fig. 7 Relation between  $V_0$  and NaOH content  
 $[\text{Cu(II)}] = 5 \times 10^{-3} \text{ M}$ ,  $[\text{S}]_0 = 1.5 \text{ M}$   
and  $[\text{L}]/[\text{Cu(II)}] = 5$

**Table 3** Kinetics data of oxidative coupling of  $\beta$ -naphthol  
by 6-amino-deoxystarch-Cu(II) complex.

| $V_m \times 10^3 (\text{M} \cdot \text{min}^{-1})$ | $k_2 (\text{min}^{-1})$ | $K_m \times 10^3 (\text{M})$ | $K_1 (\text{M}^{-1})$ |
|----------------------------------------------------|-------------------------|------------------------------|-----------------------|
| 0.322                                              | 0.0644                  | 82                           | 12.2                  |

When 2-amino-deoxystarch-Cu(II) was used as catalyst, very significant results were obtained. Since the molecular chains of this ligand originally helicoidal, insoluble in the experimental medium, the reaction carried out without salt. It was shown that relation between  $V_0$  and alkalinity varies as a combination of two hyperbolas (Fig. 7). The former at relative low alkalinity distinctly differs from the latter at relatively high alkalinity, one is of low reactivity, the other is of high reactivity. It was proved that in the presence of NaOH lower than 0.8M, the reaction takes place through molecular collision mechanism (Fig. 5). It was deduced that under these conditions, every spiral of the ligand, as starch, contains six chain units, with relatively small diameter of the  $\alpha$ -helix and longer spiral length, i.e. with loosely helicoidal conformation, the density of active centers on molecular chains is moderately low. While the catalyst, in presence of

more than 0.8 M NaOH, reacts with  $\beta$ -naphthol with higher  $V_0$  and characteristics of enzymic catalysis. it was deemed that under these conditions the ligand is changed to the conformation with relatively larger spiral diameter and shortened spiral length, i.e. with densely helicoidal conformation, so the density of active centers along the ligand chains is relatively higher, the reaction takes place through the formation of CS complexes. In addition, it may also be possible that the reaction occurs through the formation of inclusion compound where the naphthalene ring of substrate inserted in the spiral tubing, the phenolic anion approached C<sub>2</sub> amino and C<sub>3</sub> hydroxyl groups, i.e. approached the active center, thus the rearrangement of electrons and coupling of the free radicals produced will take place easily. In the case where 6-amino-deoxystarch-Cu(II) was used, inclusion complexes may also be formed, but the active centers embedded on external branches, the phenolic anion approached them with some difficulties and reacted difficultly. This is probably the rational reason why the activity of 6-amino-deoxystarch-Cu(II) is in the midst only.

### 3. Stereoselectivities of some sampled catalysts

There are many asymmetric carbon atoms on the chains of polymer-metal complexes, thus, it is of great interest to study the stereoselectivities of some samples. Liquid chromatography of the oxidative coupling products displayed that  $\beta$ -binaphthol is the main product together with two by-products. Compared with that of the main product, U.V. spectra of these by-products evidently appear in the high field. The products were not further purified by preparative LC, the optical activities were measured in wider range since the color of the solution is very heavy due to by-products and impurities. Table 4 gives the approximate optical activities. All products rotate polarized light to right, contrary to the result of Feringa<sup>[8]</sup> obtained with 1- $\alpha$ -phenylethylamine-Cu(II) as catalyst.

Table 4 Results of asymmetric oxidative coupling of  $\beta$ -naphthol

| Cu(II) complex    | 2-amino-D-glucose-Cu(II) | sericin-Cu(II)      | chitosan-Cu(II)      |
|-------------------|--------------------------|---------------------|----------------------|
| $(\alpha)_D^{22}$ | $81.1 \pm 5.6^\circ$     | $7.8 \pm 3.3^\circ$ | $11.1 \pm 4.4^\circ$ |

### 4. Conclusions

Although all the catalytic systems differ from each other, sericin-Cu(II) are semisuspended in the experimental medium, those from chitosan and amino substituted polysaccharide are insoluble, the conclusions can still be drawn that the reaction mechanisms are different. In the cases where sericin-Cu(II), 2- and 6-amino-deoxystarch-Cu(II) were used as catalysts,  $[S]_0$  equals to or less than 1.0M (before the appearance of substrate saturation) the polymer-Cu(II) complexes composed of ligands of highly coiled conformation, especially with densely helicoidal conformation, may react with  $\beta$ -naphthol with relatively higher activities through mechanism similar to enzymic catalysis, the initial reaction rates may be described by Michaelis-Menten type kinetic equations. Those with loosely coiled or helicoidal conformations react through collision mechanism and with lower reaction rates. Sampled catalysts such as sericin-Cu(II) and chitosan-Cu(II) are stereoselective, the products rotate polarized light to right, but the optical activities are rather low.

**Keywords:**

$\beta$ -naphthol,  $\beta$ -binaphthol, oxidative coupling, polymer-copper(II) complexes, polymeric ligands, conformational effect

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