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ALDOL CONDENSATION WITH COPPER(II) COMPLEX CATALYSTS. MODEL REACTIONS OF CLASS II ALDOLASE

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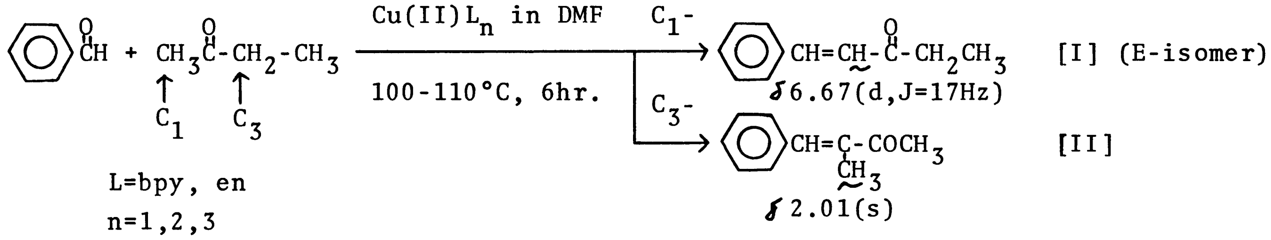
The aldol condensation of benzaldehyde with 2-butanone, catalyzed by 2,2'-bipyridine or ethylenediamine copper(II) complexes, afforded the regioselective reaction product at the C_1-position of 2-butanone. The yield and regioselectivity of the aldol condensation was affected by the ligand species and numbers of ligand molecule.

It was known that zinc(II) ion was essential for the activity of class II aldolase.$^{1)}$ In order to shed light on the role of metal ion in the catalytic mechanism of class II aldolase, we investigated the aldol condensation of benzaldehyde with 2-butanone in the presence of 2,2'-bipyridine copper(II) or ethylenediamine copper(II) complexes as a model for metal ion in the enzyme. In these reactions, the regioselective reaction product[I] at the C_1-position of 2-butanone was obtained.

We wish to report the results of the aldol condensation in this paper.



In a typical procedure, a DMF(10 ml) solution of benzaldehyde(2.8 mmol), 2-butanone(10 ml), and catalyst(4 mmol) was stirred at 100-110°C for 6hr. After the completion of the reaction, the solvent was removed in vacuo and the residue was extracted with ether-water system. The organic layer was dried over anhydrous sodium sulfate and was evaporated to give a mixture of [I] and [II]. The yields and the ratio of [I] to [II] were determined by ^1H-NMR spectra. The results are summarized in Table 1.

It has been known that the aldol condensation of 2-butanone and aldehyde with strong base occurs preferentially at the C_1-position, while mineral acid catalyzed condensation occurs preferentially at the C_3-position.$^{2)}$ Recentry,Iwata and Emoto$^{3)}$ reported that the aldol condensation catalyzed by $CuCl_2 \cdot 2H_2O$ took place

Table 1. Yields and the ratio [I]:[II] in the aldol condensation of benzaldehyde with 2-butanone in the presence of Cu(II)-amine complexes.

Catalyst[4]	Yield	[I]	: [II]
$[Cu(bpy)](NO_3)_2 \cdot 3H_2O$	65	94	6
$[Cu(bpy)_2](NO_3)_2 \cdot H_2O$	10	96	4
$[Cu(bpy)_3](NO_3)_2 \cdot 6H_2O$	0	———	
$Cu(NO_3)_2 \cdot 3H_2O$ + $(en)_1$	25	91	9
$Cu(NO_3)_2 \cdot 3H_2O$ + $(en)_2$	34	92	8
$Cu(NO_3)_2 \cdot 3H_2O$	18	82	18
Ethylenediamine	19	61	39
2,2'-Bipyridine	0	———	

at the C_3-position of 2-butanone to give [II]. On the contrary, our results showed that the condensation catalyzed by Cu(II)-amine complexes took place at the C_1-position of 2-butanone to give [I].[5] Ethylenediamine itself had catalytic activity, but the regioselectivity was low. 2,2'-Bipyridine showed no catalytic activity. On the other hand, high regioselectivity and good yield were obtained in the presence of Cu(II)-amine complexes, particularly $[Cu(bpy)](NO_3)_2 \cdot 3H_2O$. The reaction seemed to take place at the vacant coordination site of the complex since $[Cu(bpy)_3](NO_3)_2 \cdot 6H_2O$ complex did not act as the catalyst. The difference of the yields between Cu(II)-ethylenediamine and Cu(II)-2,2'-bipyridine complexes seemed to be attributed to the stability of the ternary complexes as intermediate in the reactions.[7]

DMF was the best reaction solvent among DMF, DMSO, HMPA, and MeOH. The yields of condensation products differed largely by the kind of counter anion in $[Cu(bpy)]\ X_2$: $X=NO_3$(65%), OAc(29%), ClO_4(12%), and Cl(0%) in DMF.

Further studies on the reactions are now in progress.

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4) Cu(II)-bpy complexes were prepared by the method in the literature: "Shin Jikken Kagaku Koza," Vol. 8-III, Ed. Chem. Soc. of Jpn., Maruzen, Tokyo (1977). Ethylenediamine was added to a solution of Cu(II)-salt. (en; equimolar en for Cu(II)-salt, en_2; two equimolar en for Cu(II)-salt)

5) Purified [I] was identified by comparing its melting point and infrared spectrum with those in the literature.[2a),6]

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