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Ullmann Condensation Reaction of Haloanthraquinone Derivatives with Amines in Aprotic Solvents

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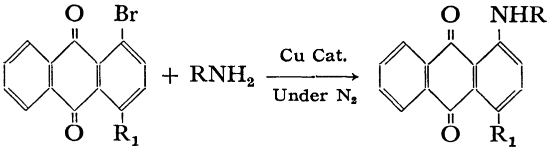
Synopsis. Cuprous catalysts were more effective than cupric ones in the Ullmann condensation of haloanthraquinones with amines in aprotic media. In the presence of Cu(I) catalyst, amines with a hydroxyl group (3-amino-1-propanol and 2-aminoethanol) were more reactive than the higher basic butylamine.

In our previous papers we discussed the mechanism of the Ullmann condensation reaction of haloanthraquinones with amines.[1)] The reaction rate and mechanism were found to be largely affected by the chemical structures of haloanthraquinones, amines, and ligands and by the valence state of copper catalysts.

This paper deals with the reactivities of haloanthraquinones, amines, and catalysts in aprotic media under nitrogen atmosphere.



(**1**) $R_1=H$
(**2**) $R_1=NH_2$

Results and Discussion

As shown in Table 1, cuprous salts were more effective than cupric ones. The catalytic activities of cuprous salts decreased with the increase of Cu(I)–halogen bond strength[2)]: CuCl>CuBr>CuI. The reactivities of 1-bromoanthraquinone (**1**) and 1-amino-4-bromoanthraquinone (**2**) toward some kinds of amines with and without the catalyst are summarized in Table 2. Table 2 suggests that the character of the reaction is largely changed in the presence of the catalyst. Thus in the absence of cuprous catalyst the yields of the condensation products, though very low, increased with increasing basicity of the amines used. This fact can be easily understood by the nucleophilic character of this reaction.

Amines with a hydroxyl group, however, were more reactive than butylamine, stronger as a base, in the presence of cuprous bromide: butylamine<3-amino-1-propanol<2-aminoethanol. It is also noteworthy that 2-aminoethanol was more reactive toward 1-bromoanthraquinone (**1**) than toward 1-amino-4-bromoanthraquinone (**2**) in the absence of cuprous catalyst, but the reverse was found in the presence of the catalyst. Such unexpected results in the presence of the catalyst may be ascribed to the difference in the coordination of haloanthraquinones to cuprous species.

When the reactions of bromoanthraquinones with 2-aminoethanol were carried out in 1,2-dimethoxyethane by use of cuprous catalyst under nitrogen atmosphere, the blue cupric complex deposited. In 1,2-dimethoxyethane–methyl cellosolve solution the blue cupric complex did not deposit very much, since it was more soluble in this solvent. No cupric complex was formed without bromoanthraquinones.

Table 1. Comparison of the catalytic activity in the condensation of 1-bromoanthraquinone with 2-aminoethanol[a)]

Catalyst	t/h	Yield (%)	Solvent
CuCl	2	21.6	THF-EtOH 4:1
CuBr	2	17.7	THF-EtOH 4:1
CuI	2	9.3	THF-EtOH 4:1
$CuBr_2$	2	1.3	THF-EtOH 4:1[b)]
CuBr	2	12.2	THF[b)]
None	3	2.6	THF

a) Reaction temp: 60 °C; [Substrate (**1**)]$_0$=5×10^{-3} mol/l, [Catalyst]$_0$=2×10^{-3} mol/l, [$NH_2CH_2CH_2OH$]$_0$=5×10^{-1} mol/l. b) Heterogeneous system.

Table 2. Comparison of the reactivity in the condensation of haloanthraquinone (**1** or **2**) with amines[a)]

Amine	pK_a	Yield (%) at 5h			
		Substrate (**1**)		Substrate (**2**)	
		CuBr	none	CuBr	none
n-$C_4H_9NH_2$	10.60	9.1	6.0	6.0	0.4
$NH_2CH_2CH_2CH_2OH$	9.96	31.3	6.1	30.9	0.4
$NH_2CH_2CH_2OH$	9.51	43.2	4.3	48.8	0.2

a) Reaction temp: 70 °C; Solvent: 1,2-dimethoxyethane–methyl cellosolve 4:1; [Substrate]$_0$=5×10^{-3} mol/l, [Amine]$_0$=5×10^{-1} mol/l, [Catalyst]$_0$=2×10^{-3} mol/l.

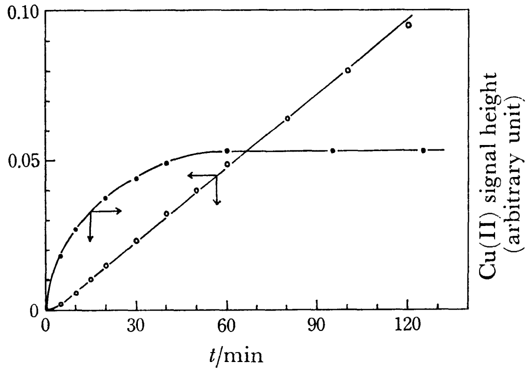


Fig. 1. Pseudo-first order plots and the time dependence of Cu(II) signal height; temp 70 °C under N_2 atmosphere, [substrate (**1**)]$_0$ 5×10^{-3} mol/l, [$NH_2CH_2CH_2OH$]$_0$ 5×10^{-1} mol/l, [CuBr]$_0$ 2×10^{-3} mol/l, solvent 1,2-dimethoxyethane–methyl cellolve 4:1.

The ESR spectra suggested that the Cu(II) species were formed3) and their concentration increased up to a certain amount as the reaction proceeded (Fig. 1). The formation of the Cu(II) species can be understood by an electron transfer from Cu(I) to the haloanthraquinone. In the reaction system of 1-bromoanthraquinone with 2-aminoethanol using CuBr catalyst, the organic paramagnetic species, assumed to be a radical anion of 1-bromoanthraquinone, was indeed observed. As shown in Fig. 1, however, the reaction rate did not decrease in accordance with the formation of Cu(II) species, which is much less active than Cu(I) species.

The formation and the role of Cu(II) species is a very interesting and important problem of the Ullmann condensation reaction in aprotic media. Further examination of this problem will be reported in the near future.

Experimental

Materials and Solvents. 1-Bromoanthraquinone (**1**) was prepared from 1-aminoanthraquinone by Sandmeyer's bromination and purified by column chromatography on alumina (benzene as developing solvent) followed by recrystallization from benzene: λ_{max} (C_2H_5OH) 336 nm (ε 4980); mp 189.6—189.9 °C(cor) (lit, mp 192 °C4)) (Found: C, 58.60; H, 2.20%). 1-Amino-4-bromoanthraquinone (**2**) was prepared by desulfonation of sodium 1-amino-4-bromoanthraquinone-2-sulfonate with 80% sulfuric acid. After being separated from the reaction mixture by column chromatography on alumina (benzene as developing solvent), it was recrystallized from acetic acid: λ_{max} ($CH_3OCH_2CH_2OCH_3$) 474 nm (ε 7100); mp 178.5—179.2 °C(cor) (lit, mp 170—176 °C5)) (Found: C, 55.75; H, 2.56; N, 4.56%). 2-Aminoethanol and 3-amino-1-propanol were dried over sodium hydroxide and distilled under nitrogen atmosphere. Butylamine was dried over sodium and distilled under nitrogen atmosphere. Cuprous halides were prepared by the usual methods.6) All solvents were purified by the usual methods and stored under nitrogen atmosphere.

Spectral Measurements. The UV and visible spectra were measured using a Shimadzu UV-200 spectrophotometer. The ESR spectra were taken on a JEOL JES-PE-3X instrument.

Reaction Procedure. A typical run is as follows. 1-Bromoanthraquinone and the solvent (THF–EtOH) were mixed in a flask. After this solution was brought to the reaction temp, the reaction was initiated by the addition of a homogeneous ethanol solution containing 2-aminoethanol and cuprous bromide. All above operations were performed under a dry and oxygen-free nitrogen atmosphere. At regular time intervals, 0.5 ml portions of the reaction solution was withdrawn and diluted in 25 ml of ethanol. The yields were determined spectrophotometrically.

Products. Products were obtained from the reaction mixture in a following manner. After the solvent was removed under reduced pressure, the reaction mixture was poured into water. After being filtered, washed with water, and dried, the precipitate was chromatographed. The separated amination product was recrystallized.

1-Amino-4-(β-hydroxyethylamino)anthraquinone: λ_{max} (C_2H_5OH) 616 nm (ε 16700); mp 195.3—196.4 °C(cor) (lit, 195—197 °C7)) (Found: C, 67.68; H, 4.96; N, 9.63%).

1-(β-Hydroxyethylamino)anthraquinone: λ_{max}(C_2H_5OH) 503 nm (ε 6700); mp 175.6—175.8 °C(cor) (lit, 171—171.5 °C7)) (Found: C, 71.86; H, 4.70; N, 4.99%).

1-Amino-4-(γ-hydroxypropylamino)anthraquinone: λ_{max} ($CH_3OCH_2CH_2OCH_3$) 615 nm (ε 15300); mp 211.7—212.3°C(cor); Found: C, 68.78; H, 5.43; N, 9.51%. Calcd for $C_{17}H_{16}O_3N_2$: C, 68.91; H, 5.44; N, 9.45%.

1-(γ-Hydroxypropylamino)anthraquinone: λ_{max}($CH_3OCH_2CH_2OCH_3$) 502 nm (ε 6800); mp 184.7—185.4 °C(cor); Found: C, 72.58; H, 5.37; N, 5.03%. Calcd for $C_{17}H_{15}O_3N$: C, 72.58; H, 5.37; N, 4.98%.

1-Amino-4-(butylamino)anthraquinone: λ_{max}(C_2H_5OH) 617 nm (ε 17600); mp 142.6—143.1 °C(cor); Found: C, 73.32; H, 6.01; N, 9.65%. Calcd for $C_{18}H_{18}O_2N_2$: C, 73.45; H, 6.16; N, 9.52%.

1-(Butylamino)anthraquinone: λ_{max}(C_2H_5OH) 507 nm (ε 7090); mp 85.9—86.7 °C(cor) (lit, 80—81 °C8)); Found: C, 77.57; H, 6.20; N, 4.88%.

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3) Very little formation of cupric species was observed in the reaction with butylamine. In the reaction with 3-amino-1-propanol the cupric species were formed in a smaller amount than in the reaction with 2-aminoethanol.

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