

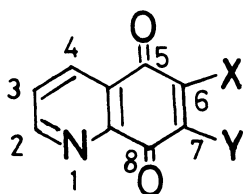
## Catalytic Action of Metal Salts in the Amination of 5,8-Quinolinediones

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The catalytic effects of some metal ions on the amination of 5,8-quinolinedione have been investigated. The reactions were specifically promoted by nickel(II) ion, and 6-aminated products were exclusively obtained. The metal chelate complex was proposed as an activated intermediate.

The reactivities of organic ligands coordinated to metal ions are often quite different from those of the free ligands. Recently, we have reported the novel direct alkylamination of  $\alpha$ -aminoanthraquinones promoted by metal chelate formation.<sup>1)</sup> We now report a catalytic action of metal salt in the amination of 5,8-quinolinedione(1) and the amine displacement of 6-piperidino-5,8-quinolinedione(2).



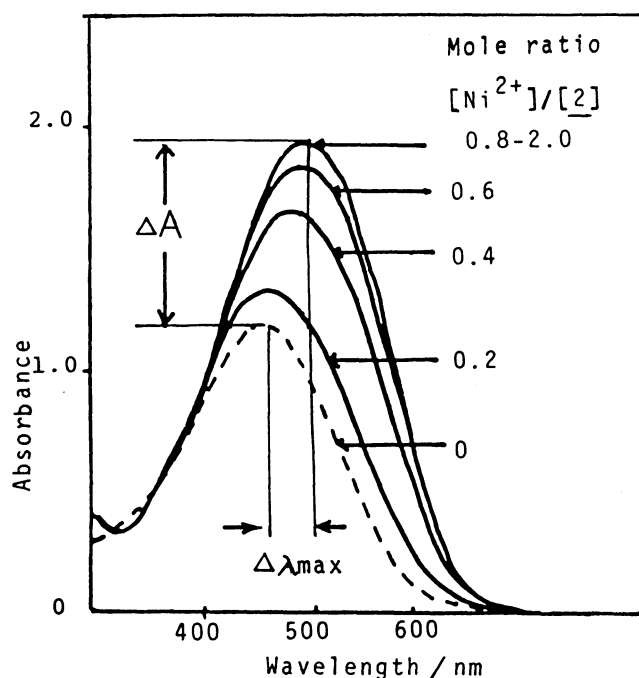
	X	Y
<u>1</u> :	H	H
<u>2</u> :	piperidino	H
<u>3</u> :	H	piperidino
<u>4</u> :	n-BuNH	H
<u>5</u> :	H	n-BuNH
<u>6</u> :	p-(CH <sub>3</sub> ) <sub>2</sub> N-C <sub>6</sub> H <sub>4</sub> -NH	H
<u>7</u> :	H	p-(CH <sub>3</sub> ) <sub>2</sub> N-C <sub>6</sub> H <sub>4</sub> -NH
<u>8</u> :	p-O <sub>2</sub> N-C <sub>6</sub> H <sub>4</sub> -NH	H
<u>9</u> :	H	p-O <sub>2</sub> N-C <sub>6</sub> H <sub>4</sub> -NH

The reaction of 2 with butylamine was found to give 6-butylamino-5,8-quinolinedione(4); the amine exchange reaction proceeded smoothly at 30 °C in the presence of some metal ions, but did not proceed at all without metal ion. The results are summarized in Table 1. Metal chlorides were arranged in the order of the catalytic activity as follows: Ni(II) >> Cu(II) > Co(II) > Al(III). The activity of the Ni(II) ion was particularly superior to those of other metal ions. For the presence of

Table 1. Effect of metal chlorides on the reaction of 2 with butylamine<sup>a)</sup>

Run	Metal salt	Mole ratio [Metal salt]/[ <u>2</u> ]	Time h	Recovery/% <sup>b)</sup> <u>2</u>	Yield/% <sup>b)</sup> <u>4</u>
1	none	0	50	86	0
2	CuCl <sub>2</sub>	1.0	1	0	73
3	CuCl <sub>2</sub>	0.1	25	trace	43
4	CoCl <sub>2</sub>	0.1	45	4	43
5	NiCl <sub>2</sub>	0.1	2.5	0	83
6	AlCl <sub>3</sub>	0.1	25	trace	7

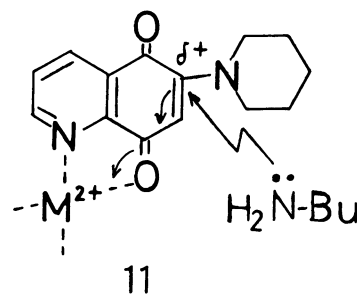
- a) Reactant(2) (0.5 g) was stirred in pyridine(15 ml) with butylamine(5 ml) and metal salt at 30 °C.  
 b) Isolated yield after column chromatography.

Fig. 1. Influence of added Ni(II) ion on the absorption spectra of 2 (----:  $2.5 \times 10^{-4}$  M) in chloroform(10 vol% DMF).Table 2. Influence of added metal ions on the absorption spectra of 2 ( $2.5 \times 10^{-4}$  M) in chloroform(10 vol% DMF)

Metal salt	Mole ratio [Metal salt]/[ <u>2</u> ]	$\lambda_{\max}$ nm	$\Delta \lambda_{\max}$ nm	$\Delta A$
none	—	470 <sup>a)</sup>	—	—
NiCl <sub>2</sub>	1.0	503	33	0.80
CuCl <sub>2</sub>	1.0	500	30	0.77
CoCl <sub>2</sub>	1.0	500	30	0.63

a) 2 ( $2.5 \times 10^{-4}$  M);  $\lambda_{\max} = 470$  nm,  $A = 1.206$ .

0.1 mole ratio of nickel(II) chloride, a 83% yield of 4 was obtained after 2.5 h (Run 5). However, the displacement of piperidino group was not observed when 7-piperidino-5,8-quinolinedione(3) and 2-piperidino-1,4-naphthoquinone(10) were used instead of 2. These results suggest that the formation of a metal chelate(11), in which the 1-nitrogen atom and 8-carbonyl group of 2, probably increases the electrophilicity of the 6-carbon atom and facilitates the nucleophilic substitution of 6-piperidino group by butylamine. This idea was supported by another experimental results; the absorption spectra of 2 are affected by the addition of metal ions, causing red shift( $\Delta\lambda_{\max}$ ) of absorption maximum with increase of absorption intensity( $\Delta A$ ) (Fig. 1). As shown in Table 2, the values of  $\Delta\lambda_{\max}$  and  $\Delta A$  for the metal ions are compatible with the order of catalytic activity in the amine exchange reaction. The absorption spectra of 10, which did not undergo the amine exchange reaction, were not affected at all by the addition of metal ions.



From the above results, it is expected that the reaction of 1 with amines can be well catalyzed by  $\text{NiCl}_2$ . The effects of  $\text{NiCl}_2$  on the amination of 1 were examined and summarized in Table 3. Isomeric mixtures of the products, 6- and

Table 3. Effect of added  $\text{NiCl}_2$  on the amination of 1

Run	Amine	Mole ratio [ $\text{NiCl}_2$ ]/[ <u>1</u> ]	Time h	Yield <sup>d)</sup> %
7 <sup>a)</sup>	piperidine	none <sup>c)</sup>	2.0	<u>2</u> 48 , <u>3</u> 10
8 <sup>a)</sup>	"	1.0	1.5	<u>2</u> 75 , <u>3</u> 6
9 <sup>b)</sup>	p-N,N-dimethyl- aminoaniline	none <sup>c)</sup>	6.0	<u>6</u> 43 , <u>7</u> 37
10 <sup>b)</sup>	"	0.5	2.0	<u>6</u> 71 , <u>7</u> 0
11 <sup>b)</sup>	p-nitroaniline	none <sup>c)</sup>	15.0	no reaction
12 <sup>b)</sup>	"	0.1	7.0	<u>8</u> 36 , <u>9</u> 0

a) Reactant(1) (3.14 mmol) was stirred in chloroform(70 ml) at 0 °C with piperidine(9.42 mmol) and  $\text{NiCl}_2$  under air atmosphere.

b) Reactant(1) (3.14 mmol) was stirred in 95% ethanol(150 ml) at 30 °C with the substituted aniline(9.42 mmol) and  $\text{NiCl}_2$  under air atmosphere.

c) Reactions were conducted without  $\text{NiCl}_2$ .

d) Isolated yield after column chromatography.

7-amino derivatives of 1, were obtained without metal ion(Runs 7 and 9),<sup>2)</sup> whereas the 6-amino derivatives were preferentially obtained in the presence of NiCl<sub>2</sub>(Runs 8 and 10). Atmospheric oxygen plays an important role as an oxidizing agent for the completion of the amination of 1; the adducts formed by the Michael type addition of amines to 1 can be dehydrogenated by both the unchanged 1 and atmospheric oxygen to give the aminated products. The electrophilicity of 6-position of 1 would be so strongly increased by the formation of nickel chelate that the 6-amination of 1 can proceed even in the reaction with p-nitroaniline(Runs 11 and 12).

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#### References

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- 2) The reaction of 1 with aromatic amines to produce the 6- and 7-amino derivatives is known.<sup>3)</sup> Y. T. Pratt has found that cerium ion catalyzes the reaction and the 6-arylamino isomers are preferentially obtained.<sup>4)</sup>
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