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BUTYLAMINATION OF 1-AMINOHALOGENO-ANTHRAQUINONES PROMOTED BY METAL IONS

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SUMMARY

The butylamination of 1-*aminohalogenoanthraquinones was promoted by both copper and cobalt ions. In the presence of cobalt*(II) *chloride the butylamination of* 1-*amino*-4-*bromo*-(**2b**) *or* 1-*amino*-2,4-*dibromo*-*anthraquinone*(**2j**) *proceeded smoothly even at ambient temperature to give the corresponding butylaminated products. It is proposed that the formation of a metal complex*(**1**), *in which the* 1-*aminoanthraquinone moiety coordinates with the metal ion, facilitates the amination.*

1. INTRODUCTION

The nucleophilic substitution of aryl halides by amines in the presence of copper catalyst is well known as the Ullmann condensation reaction.[1] In the field of dye chemistry, the Ullmann amination of halogenoanthraquinones is widely adopted to prepare aminoanthraquinones as dyes and dye intermediates. There are many reports dealing with the mechanism[2] and a variety of syntheses[3] of this reaction.

However, there have been few reports on the amination of halogenoanthraquinones utilizing other metal salts instead of copper salts as a catalyst. Philip and Sunthanker[4] have reported the preparation of 1-amino-4-anilinoanthraquinone from 1-amino-4-chloroanthraquinone with aniline in the presence of aluminium(III) chloride with 85% yield.

On the other hand, we have recently reported a new direct 4-alkylamination of 1-aminoanthraquinones promoted by metal ions:[5] e.g. the reaction of

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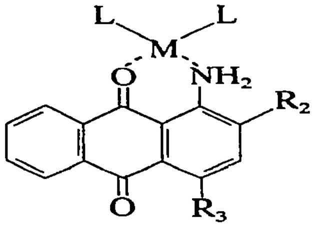
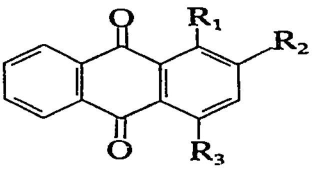
1-aminoanthraquinone(**2a**) with butylamine in the presence of an equimolar amount of a metal salt under atmospheric oxygen gave 1-amino-4-butylaminoanthraquinone(**2d**) in a good yield.

The activities of metal salts in the reaction were in decreasing order as follows: $CoCl_2 \gg NiCl_2 > CuCl_2 > AlCl_3$. In the reaction the formation of a metal complex(**1**), in which the 1-aminoanthraquinone moiety coordinates with the metal ion, increases the electrophilicity of the substituted anthraquinone nucleus and facilitates the nucleophilic attack of butylamine at the 4-position. Therefore, the amination of 1-aminohalogenoanthraquinones appeared to be likely to be promoted by some metal ions. In this paper, we describe the reactions of some 1-aminohalogenoanthraquinones and related compounds with butylamine in the presence of some metal salts, and evaluate the role of the metal ions on this reaction. The reactants and the products may be represented as compound **2**.



(1)



(2)

M: Metal ion
L: Amine or other ligands

Compound No.	*Substituent* R$_1$	R$_2$	R$_3$
2a	NH$_2$	H	H
2b	NH$_2$	H	Br
2c	NH$_2$	H	NH$_2$
2d	NH$_2$	H	NHBu
2e	Cl	H	H
2f	NHBu	H	H
2g	Cl	H	Cl
2h	NHBu	H	Cl
2i	NHBu	H	NHBu
2j	NH$_2$	Br	Br
2k	NH$_2$	NHBu	Br
2l	NH$_2$	Br	NHBu
2m	NH$_2$	NHBu	NHBu

2. RESULTS AND DISCUSSION

2.1. *Butylamination of* 1-*Amino*-4-*bromoanthraquinone*(**2b**)

The reaction of **2b** with butylamine hardly proceeded without metal salt (run 1) (Table 1). However, in the presence of an equimolar amount of a copper or cobalt salt the reaction proceeded smoothly to give 1-amino-4-butylaminoanthraquinone(**2d**) along with a trace of 1,4-diaminoanthraquinone(**2c**) and small amounts of 1-amino-anthraquinone(**2a**). Compound **2c** was obtained by the debutylation of **2d**, and **2a** was derived from **2b** by the debromination. These side reactions, dealkylation and dehalogenation, have been previously noted in the anthraquinone series.[6] The activity of cobalt(II) chloride was significantly better than those of other metal salts and the amination proceeded smoothly even at 30°C (run 4).

Nickel(II) chloride did not promote the amination (run 5).

These effects of metal salts were analogous to those observed in the direct amination of **2a**.[5b] It is also proposed that the formation of a metal complex(**1**) facilitates the nucleophilic substitution of butylamine at the 4-position of **2b** to give **2d**.

2.2. *Butylamination of* 1-*chloro*-(**2e**) *and* 1,4-*dichloroanthraquinone*(**2g**)

The reaction of **2e** with butylamine readily proceeded even in the absence of metal salt to give 1-butylaminoanthraquinone(**2f**) (run 6) (Table 2). An addition of copper salt was rather disadvantageous, because small amounts of by-products such as **2d** and **2i** were obtained (runs 7 and 8). 1,4-Bis(butylamino)anthraquinone(**2i**) was produced by the direct butylamination of **2f**. Similar direct alkylamination of **2a** or alkylaminoanthraquinones in the presence of some metal salts have been reported in previous papers.[5] 1-Amino-4-butylaminoanthraquinone(**2d**) was obtained from **2i** by debutylation.

A prolonged reaction time decreased the yield of **2f** and increased those of **2i**

TABLE 1

BUTYLAMINATION OF 1-AMINO-4-BROMOANTHRAQUINONE(**2b**) IN THE PRESENCE OF METAL SALT

	Reaction conditions			*Product (% yield)*			*Recovery (%)*
Run	*Metal salt*	*Temperature* (°C)	*Time* (h)	**2a**	**2c**	**2d**	**2b**
1	none	80	8	0	0	2·0	91
2	$Cu(OCOCH_3)_2$	80	4	4·4	trace	37	0·8
3	$CuCl_2$	80	8	0·9	trace	34	5·5
4	$CoCl_2$	30	4	3·4	1·1	39	24
5	$NiCl_2$	80	8	4·2	trace	3.4	82

TABLE 2

BUTYLAMINATION OF 1-CHLORO-(**2e**) AND 1,4-DICHLOROANTHRAQUINONE(**2g**) IN THE PRESENCE OF METAL SALT

		Reaction conditions						
			Temperature	*Time*	*Product* (% *yield*)			
Run	*Reactant*	*Metal salt*	(°C)	(h)	**2d**	**2f**	**2h**	**2i**
6	**2e**	none	80	6	0	95	—	0
7	**2e**	$Cu(OCOCH_3)_2$	80	6	trace	86	—	0·4
8	**2e**	$Cu(OCOCH_3)_2$	80	30	0·4	61	—	4·1
9	**2e**	$CoCl_2$	80	8	0	98	—	0
10	**2g**	none	80	8	0	—	92	3·0
11	**2g**	$Cu(OCOCH_3)_2$	80	8	trace	—	73	16

and **2d** (run 8). However, an addition of cobalt(II) chloride did not give **2d** or **2i** (run 9).

In the reaction of **2g** with butylamine, the first chlorine atom was readily displaced by butylamine in the absence of a metal salt, while the second chlorine atom was hardly substituted, and 1-butylamino-4-chloroanthraquinone(**2h**) was obtained as the main product (runs 10 and 11). The introduction of the first butylamino group in **2h** reduces the reactivity of the second chlorine atom at 4-position for the further substitution by butylamine.

However, an addition of copper(II) acetate increased the yield of **2i** (run 11). This result suggests that the conversion of **2h** to **2i** might be promoted by some metal ions, and we examined the reaction of **2h** with butylamine in the presence of metal salts. The results are shown in Table 3. An addition of copper(II) acetate was effective to produce **2i** but cobalt(II) chloride or nickel(II) chloride did not promote the reaction. Similar effects due to metal ions were also observed in the direct 4-butylamination of 1-alkylaminoanthraquinone,[5c] and it was proposed that the alkyl group of the 1-substituent prevents the formation of a cobalt complex(**1**) of **2h**.

2.3. *Butylamination of* 1-*amino*-2,4-*dibromoanthraquinone*(**2j**)

Without a metal salt the reaction of **2j** with butylamine hardly proceeded at 30°C, but it proceeded slowly at 60°C (Table 4).

TABLE 3

BUTYLAMINATION OF 1-BUTYLAMINO-4-CHLOROANTHRAQUINONE(**2h**) IN THE PRESENCE OF METAL SALT

	Reaction conditions						
		Temperature	*Time*	*Product* (% *yield*)			*Recovery* (%)
Run	*Metal salt*	(°C)	(h)	**2d**	**2f**	**2i**	**2h**
12	none	80	8	0	0	4·8	91
13	$Cu(OCOCH_3)_2$	80	8	trace	4·7	20	60
14	$CoCl_2$	30	8	0	0	0	96
15	$NiCl_2$	80	8	trace	0	1·5	95

TABLE 4
BUTYLAMINATION OF 1-AMINO-2,4-DIBROMOANTHRAQUINONE(**2j**) IN THE PRESENCE OF METAL SALT

		Reaction conditions		*Product (% yield)*			*Recovery (%)*
Run	*Metal salt*	*Temperature* (°C)	*Time* (h)	**2k**	**2l**	**2m**	**2j**
16	none	30	24	0	2·4	0	94
17	none	60	24	2·9	21	trace	59
18	CuCl	60	7	2·4	26	trace	25
19	$CoCl_2$	30	1	11	6·7	3·1	37

An addition of copper or cobalt salts was effective for this reaction, especially, in the presence of cobalt(II) chloride when the reaction proceeded smoothly even at 30°C as well as in the case of the butylamination of **2b**. It is generally known that the 4-bromine atom is replaced by amines much more readily than the 2-bromine atom, while the 2-bromine atom was substituted much more readily than the 4-bromine atom in the presence of cobalt salt.

From these results together with others obtained from the direct amination of **2a**,[†] it was found that the formation of a metal complex(**1**) facilitates the nucleophilic amination of 1-aminohalogenoanthraquinones, and copper(II) or cobalt(II) ions are effective for this reaction.

3. EXPERIMENTAL

All the melting points are uncorrected. The visible spectra in methanol solution were measured using a Hitachi EPS-3T spectrometer.

The PMR spectra were taken on a JEOL Model MH-100 spectrometer with TMS as an internal standard. Elemental analyses were recorded on a Yanaco CHN recorder MT-2. Column chromatography was carried out on activated alumina (Sumitomo KCG-30) using xylene as eluent.

Thin layer chromatography was performed on alumina (Merck Aluminiumoxid 60 Art. 5713) or on silica gel (Merck Kieselgel 60 Art. 5724).

3.1. *Materials*

1-Amino-4-bromoanthraquinone(**2b**),[7] 1,4-dichloroanthraquinone(**2g**),[8] and 1-amino-2,4-dibromoanthraquinone(**2j**)[9] were prepared according to the reported methods. 1-Chloroanthraquinone(**2e**) (Wako Pure Chemicals), 1-aminoanthraquinone(**2a**) (Mitsubishi Chemical Industry), and 1,4-diaminoanthraquinone(**2c**) (Mitsui Toatsu Chemicals) were purified by column

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[†] The direct amination of **2a** is remarkably prevented by the substitution of an alkyl group in the 1-amino group of **2a**. Neither anthraquinone or 2-aminoanthraquinone show any sign of the reaction in the same conditions.[5]

chromatography followed by recrystallization. All the metal salts were reagent grade and used without further purification. 1-Butylamine and solvents were purified by the ordinary methods.

3.2. *Butylamination of* 1-*Amino*-4-*bromoanthraquinone*(**2b**)

A mixture of **2b** 1 g ($3{\cdot}3\times10^{-3}$ mole), metal salt ($3{\cdot}3\times10^{-3}$ mole), anhydrous sodium acetate 0·54 g ($6{\cdot}6\times10^{-3}$ mole), 1-butylamine (15 ml), and 1-butanol (50 ml) was heated in a flask fitted with a reflux condenser and a mechanical stirrer. After the solvent and excess amine were distilled off under reduced pressure, the mixture was poured into 3·0% hydrochloric acid. The separated products were filtered, washed with water and dried. The crude product was shown to be a mixture of **2a** ($R_f = 0{\cdot}30$), **2b** ($R_f = 0{\cdot}24$), **2d** ($R_f = 0{\cdot}18$), **2c** ($R_f = 0{\cdot}05$) by t.l.c. on alumina using a ligroin–chloroform mixture in a volume ratio of 5 : 2 as developing solvent. Each component was obtained by column chromatography on alumina and the yields were determined.

3.3. *Butylamination of* 1-*Chloroanthraquinone*(**2e**)

A mixture of **2e** 1 g ($4{\cdot}1\times10^{-3}$ mole), metal salt ($4{\cdot}1\times10^{-3}$ mole), anhydrous sodium acetate 0·67 g ($8{\cdot}2\times10^{-3}$ mole), 1-butylamine (15 ml), and 1-butanol (5 ml) was heated at 80°C in a flask. The following procedures were the same as those described in the butylamination of **2b**. Column chromatography of the crude product gave rise to **2f** along with **2i** and **2d**.

3.4. *Butylamination of* 1,4-*Dichloroanthraquinone*(**2g**)

A mixture of **2g** 1 g ($3{\cdot}6\times10^{-3}$ mole), metal salt ($3{\cdot}6\times10^{-3}$ mole), anhydrous sodium acetate 1·2 g ($1{\cdot}44\times10^{-2}$ mole), 1-butylamine (15 ml), and 1-butanol (50 ml) was heated in a flask. The following procedures were the same as those described for the butylamination of **2b**.

The crude product was shown to be a mixture of **2h** ($R_f = 0{\cdot}61$), **2i** ($R_f = 0{\cdot}34$), and **2d** ($R_f = 0{\cdot}13$) by t.l.c. on silica gel using benzene as developing solvent.

3.5. *Butylamination of* 1-*Butylamino*-4-*chloroanthraquinone*(**2h**)

A mixture of **2h** 1·13 g ($3{\cdot}6\times10^{-3}$ mole), metal salt ($3{\cdot}6\times10^{-3}$ mole), anhydrous sodium acetate 1·18 g ($7{\cdot}2\times10^{-3}$ mole), 1-butylamine (15 ml), and 1-butanol (50 ml) was heated in a flask. The following procedures were the same as those described for the butylamination of **2g**.

3.6. *Butylamination of* 1-*Amino*-2,4-*dibromoanthraquinone*(**2j**)

A mixture of **2j** 1 g ($2{\cdot}6\times10^{-3}$ mole), metal salt ($2{\cdot}6\times10^{-3}$ mole), 1-butylamine (15 ml), and pyridine (50 ml) was heated in a flask.

The mixture was cooled and poured into water, and H_2S gas was then bubbled through the solution to decompose the chelate complex of the products. The separated products were filtered, washed with water and dried. The crude products were shown to be a mixture of **2j** ($R_f = 0·61$), **2l** ($R_f = 0·46$), **2k** ($R_f = 0·12$), and **2m** ($R_f = 0·03$) by t.l.c. on silica gel using benzene as developing solvent.

3.7. *Characterization and identification of products*

Compounds **2a**, **2c**, and **2e** were identified with the authentic samples available as commercial products.

Some properties of the following compounds: **2d**,[5c] **2f**,[7] and **2i**,[10] were already known and these were identified by the data described in the literature.

1-*Butylamino*-4-*chloroanthraquinone* **2h**: m.p. 113–114°C (ethanol); UVmax, nm, methanol ($\varepsilon \times 10^{-4}$), 510 (0·66). Analysis found(%): C, 68·93; H, 5·06; N, 4·38. Calculated for $C_{18}H_{16}NO_2Cl$: C, 68.90; H, 5·14; N, 4·46.

1-*Amino*-2-*butylamino*-4-*bromoanthraquinone* **2k**: m.p. 243–244°C (benzene); UVmax 514 (1·25); PMR (D_6-DMSO); $\delta = 0·96$ (3H, t), 1·1–1·9 (4H, m), 3·22 (2H, q), 6·50 (1H, broad), 6·74 (1H, s), 7·82 (2H, m), 8·11 (2H, m), 8·52 (2H, broad). Analysis found(%): C, 57·67; H, 4·69; N, 7·01. Calculated for $C_{18}H_{17}N_2O_2Br$: C, 57·89; H, 4·59; N, 7·51.

1-*Amino*-4-*butylamino*-2-*bromoanthraquinone* **2l**: m.p. 130–131°C (benzene); UVmax 551^{sh} (0·69), 583 (1·23), 626 (1·31); PMR ($CDCl_3$); $\delta = 1·02$ (3H, t), 1·3–1·9 (4H, m), 3·31 (2H, q), 7·40 (1H, s), 7·5–7·9 (4H, m), 8·25 (2H, m), 10·26 (1H, broad). Analysis found(%): C, 58·10; H, 4·53; N, 7·03. Calculated for $C_{18}H_{17}N_2O_2Br$: C, 57·89; H, 4·59; N, 7·51.

1-*Amino*-2,4-*bis*(*butylamino*)*anthraquinone* **2m**: m.p. 198–200°C (benzene); UVmax 512^{sh} (0·78), 546 (1·74), 585 (2·30); PMR (D_6-DMSO); $\delta = 1·00$ (6H, t), 1·2–1·9 (8H, m), 3·0–3·5 (4H, m), 6·00 (1H, s), 6·60 (1H, broad), 7·75 (2H, m), 8·25 (2H, m), 8·94 (2H, broad), 11·46 (1H, broad). Analysis found(%): C, 72·16; H, 7·43; N, 11·26. Calculated for $C_{22}H_{27}N_3O_2$: C, 72·30; H, 7·45; N, 11·50.

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