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COPPER-CATALYZED AMINATION OF α-SUBSTITUTED ANTHRAQUINONES[1)]

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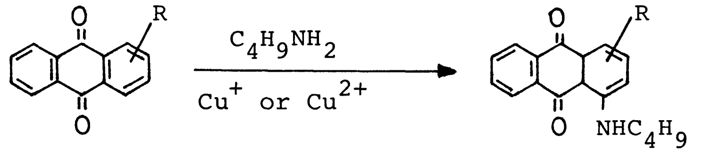
The reaction of 1-aminoanthraquinone with large excess of butylamine in the presence of various copper salts gave 1-amino-4-butylaminoanthraquinone in 15-40% yield. 1,4-Dihydroxyanthraquinone was also aminated at β-position in the same condition. Nucleophilic amination catalyzed with the copper salts of α-substituted anthraquinones was proposed.

It is known that the reaction of halogenoanthraquinones with various amines in the presence of copper catalysts affords aminoanthraquinones. The reaction is known as the Ullmann condensation reaction[2)] and is applied widely to prepare anthraquinone intermediates and dyes. In this communication, we report a new copper-catalyzed amination between α-substituted anthraquinones and alkylamines.

The reaction of 1-aminoanthraquinone 1a with butylamine in the presence of anhydrous cupric acetate affords 1-amino-4-butylaminoanthraquinone 2a, (Scheme 1). The results of a series of reactions are summerized in Table 1.



a, $R=1\text{-}NH_2$
b, $R=1\text{-}C_4H_9NH$
c, R=H
d, $R=2\text{-}NH_2$

Scheme 1

The yield of 2a increased with prolonged reaction time (Run 1-4). The reaction did not proceed at all without catalyst (Run 5). In the case of 1-butylaminoanthraquinone 1b (Run 6), a small amount of 1,4-bisbutylaminoanthraquinone 2b[3)] was obtained together with a trace amount of 2a and 1a. While, both of anthraquinone 1c and 2-aminoanthraquinone 1d did not give any aminated products[4)] (Run 7 and 8).

The effect of copper catalysts on the butylamination of 1a are summerized in Table 2. It is generally observed that the charge of copper salts does not effect so much but the kinds of anion component effects considerably on the yield of 2a.

Table 1. Butylamination of anthraquinone derivatives5)

Run	Substituent	Time(hr)	Recovered 1,(%)	Yield 2,(%)	Conversion(%)a)
1	1-NH_2	8	92.5	2.3	32.5
2	"	16	81.3	6.2	33.4
3	"	24	62.8	14.6	39.1
4	"	48	42.9	15.9	27.8
5b)	"	24	99.0	nonec)	0
6	1-C_4H_9NH	24	71.8	1.2	4.2
7	H	24	98.7	nonec)	0
8	2-NH_2	24	98.2	nonec)	0

a) The yields based on aminoanthraquinones reacted.

b) Without anhydrous cupric acetate.

c) Any of aminated products were not obtained.

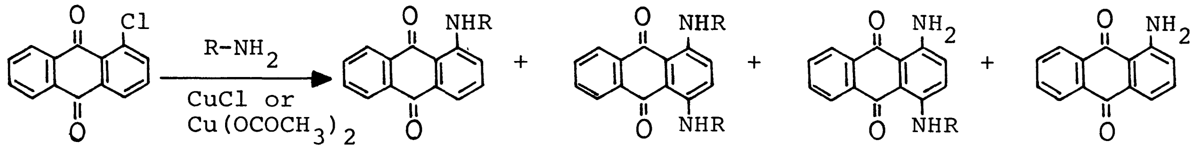
Table 2. Effect of copper salts on the butylamination of 1-aminoanthraquinone5)

Runa)	Copper catalyst	Recovered 1a,(%)	Yield 2a,(%)	Conversion(%)b)
1	none	99.0	none	0
2	CuCl	60.3	9.4	23.7
3	CuBr	51.8	10.2	21.2
4	CuI	65.0	6.2	17.6
5	$CuCl_2$	54.1	11.2	24.3
6	$CuBr_2$	70.9	4.0	13.6
7	$CuSO_4$	51.3	13.5	27.7
8	$Cu(OCOCH_3)_2$	62.8	14.6	39.1
9	$Cu(CH_3COCHCOCH_3)_2$	48.6	15.6	30.4

a) The reaction was carried out under reflux for 24 hr.

b) The yields based on 1-aminoanthraquinone reacted.

In connection with the Ullmann reaction, 1-chloroanthraquinone 3 was alkylaminated in the presence of copper salts. Results are shown in Scheme 2. Alkylamination of 3 in the presence of cuprous6) or cupric salts5) gave 1-alkylaminoanthraquinone 4 and 1,4-bisalkylaminoanthraquinone 5 together with a trace amount of 1a and 6, respectively. Cuprous and cupric salts were also effective in these cases. Alkylamination of 1-alkylaminoanthraquinone 4 at 4-position is found as one of the side-reaction of the Ullmann reaction. Dealkylation is well known in the Ullmann reaction condition7).

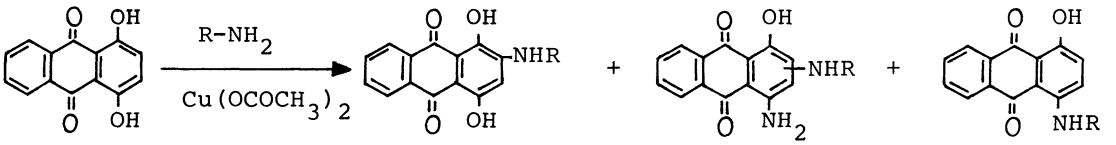


3 4 5 6 1a

Yield(%)		4	5	6	1a
	a, R=CH_3	55.5	0.4	trace	trace
	b, R=C_4H_9	68.0	0.2	trace	trace

Scheme 2

The formation of copper complex between quinone carbonyl group and α-substituent of anthraquinone may play a great role on this amination. To confirm these speculation, 1,4-dihydroxyanthraquinone 7 was aminated with butylamine under the same condition$^{5,8)}$. Two kinds of β-aminated products were isolated$^{9)}$ (Scheme 3).



7 R=C_4H_9 8 (6%)$^{a)}$ 9 (7.3%)$^{a)}$ 10 (trace)$^{a)}$

a) Yield isolated.

Scheme 3

Without the cupric acetate, amination at α-position was proceeded and 1,4-bisbutylaminoanthraquinone 5b was obtained in 50% yield, but none of the β-aminated products were obtained.

The details of the mechanism are currently under investigation and will be reported elsewhere.

References and Notes

1) This work was presented at the 37th Spring Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1978, Abstr. No. 2D29.

2) R.Bacon, H.Hill, Quart. Rev., 19, 95(1965).

3) 2b: m.p. 115-117°C (Ethanol): UVmax(Benzene), 604(13100), 652(15300): Analysis found: C, 75.43; H, 7.51; N, 8.05: Calcd. for $C_{22}H_{26}N_2O_2$: C, 75.40; H, 7.48; N, 7.99.

4) Recently, Hida and his collaborators have reported the preparation of alkylaminoanthraquinones by the amination of anthraquinone by use of rhodium complexes, K.Mita, T.Yamagishi, and M.Hida, Abstr. No. 1D47, the 37th Spring Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1978.

5) Butylamination was carried out in the following manner.

Reactant (9 mmol) was heated in butyl alcohol (5 ml) with butylamine (15 ml), anhydrous sodium acetate (23 mmol) and anhydrous cupric acetate (9 mmol),(or other copper salts) under reflux for some hours mentioned. The mixture was poured into aqueous HCl solution (PH 1) and separated products were filtered, washed with water, dried, chromatographed and identified with authentic samples. The yields were determined by chromatoscanner using callibration curves of authentic samples.

6) Reactant (8.2 mmol) was heated in 40% aqueous methylamine (50 ml) with cuprous chloride (4.1 mmol) under reflux for 15 hr in a glass tube. Following procedure was the same as that of butylamination.

7) W.Bradley, E.Leete, J. Chem. Soc., 1951, 2147.

8) Three times equivalent of anhydrous cupric acetate (27 mmol) was used. The reaction was carried out under reflux for 24 hr.

9) 8: m.p. 160-161°C(Ethanol); UVmax(Benzene), 484(9300), 516(12200), 545(9400): Analysis found: C, 69.06; H, 5.49; N, 4.52: Calcd. for $C_{18}H_{17}NO_4$: C, 69.45; H, 5.47; N, 4.50: MASS, 311(M^+), 268(M^+-43): NMR($CDCl_3$), δ=14.35(1H,s), 14.0(1H,s), 8.2(2H,m), 7.85(2H,m), 6.15(1H,s), 5.6(1H,broad), 3.25(2H,q), 1.6-1.0(7H,m).

9: m.p. 202-203°C(Ethanol): UVmax(Benzene), 480(7600), 514(13500), 552(14900): (Ethanol + $NaOC_2H_5$), 515, 552, 590 nm: MASS, 310(M^+), 267(M^+-43): Analysis found: C, 69.46; H, 5.73; N, 8.80: Calcd. for $C_{18}H_{18}N_2O_3$: C, 69.68; H, 5.80; N, 9.03: The position (2 or 3) of the butylamino group is not determined yet.

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