The Direct Alkylamination of α-Substituted Anthraquinones Promoted by Metal Ions

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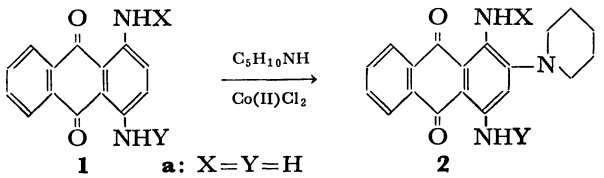
Synopsis. The reaction of 1-amino-4-acylaminoanthraquinones with piperidine in the presence of $CoCl_2$ and atmospheric oxygen gave the 2-aminated products in 75—80%, and similar reaction of 1-hydroxyanthraquinone or 1-aminoanthraquinone-2-sulfonic acid with butylamine gave the corresponding 4-aminated products, respectively. The effects of the α-substituents and the role of metal salts were discussed.

In our previous papers,[1-3] the new metal-promoted direct aminations of anthraquinone nucleus were reported. These are useful methods to prepare some aminoanthraquinone (aminoAQ) derivatives as dyes and dye intermediates.

In this paper, these metal-promoted direct aminations were applied to each of 1,4-diaminoAQs, 1-aminoAQ-2-sulfonic acid, and 1-hydroxyAQ which are the important intermediates for the preparation of some anthraquinonoid dyes.

The results of the reaction of 1,4-diaminoAQs with piperidine are shown in Scheme 1 and Table 1. The reaction of **1a** with piperidine resulted only in recovery of **1a** (Run 1). While, 1-amino-4-acylaminoAQs (**1b** and **1c**) gave the corresponding 2-aminated product (Runs 2 and 3). In the case of **1b**, hydrolysis of the 4-acetylamino group of **2b** was observed during the reaction, forming **2a** in 49.5%. The amination site of **1b** and **1c** were determined by ^{1}H-NMR spectra; the proton at 3(or 2)-position of **2a** was found at 6.40 ppm, while those of **2b** and **2c** were shifted downfield to 8.60, 8.66 ppm respectively, because of the deshielding effect of the neighboring 4-acylamino group. 1,4-Bis(benzoylamino)AQ (**1d**) did not react with piperidine, and **1d** was recovered in 93.6% (Run 4). These results imply that the mechanism of the 2-amination of **1** is the same as our previous case of 1-aminoAQ;[1] activation of 2-position by the formation of cobalt complex and reduction by 4-acylation in deactivating ability of 4-amino group play a cooperative roll for formation of 2-aminated products. Diacylation (**1d**) results in losing the ability of the complex formation and the amination does not take place.



1 **a**: X=Y=H **2**
b: X=H, Y=$COCH_3$
c: X=H, Y=COC_6H_5
d: X=Y=COC_6H_5

Scheme 1.

TABLE 1. THE REACTION OF **1** WITH PIPERIDINE[a]

Run	Reactant	Time/h	**1**(Recovered)	Products (yield/%)
1	**1a**	50	94.0	None
2	**1b**	24	Trace	**2a** (49.5), **2b** (31.5)
3	**1c**	15	5.5	**2c** (74.5)
4	**1d**	50	93.6	None

a) Reactant (**1**, 2.92 mmol) was stirred with piperidine (50 ml) in the presence of $CoCl_2$ (2.92 mmol for **1b**—**1c**, 5.84 mmol for **1a**) at 30 °C.

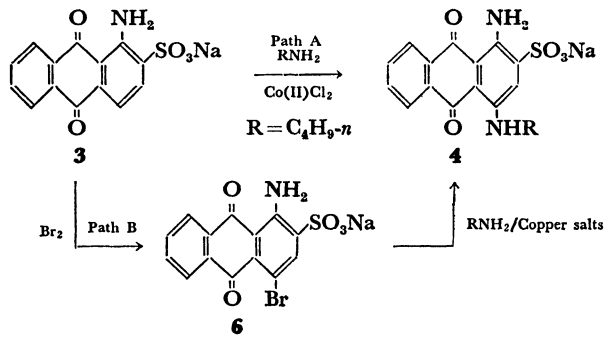
The reaction of 1-aminoAQ-2-sulfonic acid (**3**) with butylamine gave the 4-aminated product (**4**), which is a very important compound as dye intermediate. In industry, **4** is produced by two-step method;[4] the bromination of **3** followed by the Ullmann amination of **6** (Path B in Scheme 2). Thus, the direct 4-amination of **3** affords a useful method for preparation of **4** (Scheme 2). The results are summarized in Table 2. Without $CoCl_2$, the amination did not take place at all (Runs 5 and 9). In the presence of $CoCl_2$, **3** gave rise to **4** in 23% yield together with 43% recovery of **3** (Run 6). The increase in molar ratio of $CoCl_2$ rather depressed the yield of **4** and a trace amount of **5** was formed along with **4** (Run 8). The yield of **4** could not be improved at higher temperature (Run 7).

The reaction of **7** with butylamine mainly afforded three products as shown in Scheme 3. The results are summarized in Table 3. The reaction hardly proceeded at room temperature (Run 15) and was carried out at 80 °C. Without metal salts, the reaction scarcely proceeded (Run 11), but an addition of $CoCl_2$ gave **9** in 23% and **10** in 2.4% yield together with 4-butylated product (**8**) in 48% yield (Run 12). A novel butylation of **7** at 4-position forming **8** was observed, but the mechanism was not obvious. The reaction did not proceed smoothly without solvent (Run 13). In the presence of $CuCl_2$, the reduction of copper ion to metal copper occured quantitatively, and a small amount of **8** (11%) and **10** (3%) were yielded (Run 14). From these results, it was concluded that the 4-amination of **7** hardly proceeds because of the

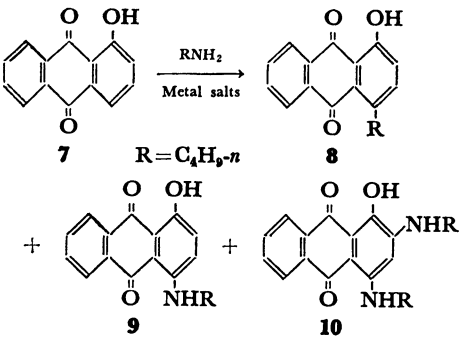
TABLE 2. THE REACTION OF **3** WITH BUTYLAMINE[a]

Run	$CoCl_2$/**3**	Solvent	**3**(Recovered)	Yield/% **4**
5	0	Pyridine	100	0
6	1	Pyridine	43	23
7[b]	1	Pyridine	7	27
8	2	Pyridine	33	11
9	0	1-Butanol	100	0
10	1	1-Butanol	Trace	41

a Reactant **3**(5.0 mmol) and butylamine(20 ml) were stirred with or without $CoCl_2$ at 30 °C for 24 h. b) Reaction was carried out at 80 °C for 24 h. A number of the unidentified by-products were obtained in a low yields.



Scheme 2.



Scheme 3.

Table 3. The reaction of **7** with butylamine[a)]

Run	Metal salts	**7**(Recovered)	Yield/%			
			8	**9**	**10**	Cu°
11[b)]	None	Trace	3.8	0	0	—
12	$CoCl_2$	0	48.0	23.1	2.4	—
13[c)]	$CoCl_2$	53.0	32.0	8.5	0	—
14[b)]	$CuCl_2$	0	11.0	0	2.9	91
15[d)]	$CuCl_2$	58.9	Trace	2.9	0	—

a) Reactant (**7**, 5.0 mmol) was stirred with butylamine (22.5 ml) in 1-butanol(7.5 ml) in the presence of metal salts(5.0 mmol) at 80 °C for 5 h. b) A number of unidentified by-products were mainly obtained. c) Reaction was carried out without 1-butanol. d) Reaction was carried at 30 °C for 24 h.

formation of undesired product (**8**).

Experimental

Melting points are uncorrected. The spectra were measured on the instrumentals reported previously.[1-3)] Column chromatography were carried out on the activated alumina (Sumitomo KCG-30) or silica gel (Wacogel C-300).

*Reaction of **1** with Piperidine. General Procedures*: A mixture of **1c** (1.0 g, 2.92 mmol), $CoCl_2$ (1.37 g, 2.92 mmol), piperidine (50 ml) was stirred in a open flask at 30 °C. After the reaction, the solution was poured into water, and then H_2S gas was passed into the mixture. The precipitate was filtered, washed with water, dried, and extracted with chloroform. The extract was concentrated and chromatographed on alumina using benzene as an eluent.

*1,4-Diamino-2-piperidinoanthraquinone (**2a**)*: Mp 183.5—184 °C (xylene); lit,[5)] 185.5—186 °C. λ_{max} (benzene) (ε): 574 (8260), 538 (10100). Found: C, 71.16; H, 5.90; N, 12.84%. Calcd for $C_{19}H_{19}N_3O_2$: C, 71.01; H, 5.96; N, 13.07%. ^{1}H-NMR ($CDCl_3$) δ 1.70 (6H, m), 2.87 (4H, m), 6.40 (1H, s), 7.14 (2H, broad), 7.58 (2H, m), 7.60 (2H, broad), 8.25 (2H, m).

*1-Amino-2-piperidino-4-acetylaminoanthraquinone (**2b**)*: Mp 186—186.5 °C (xylene). λ_{max} (benzene) 568 (10600), 534 (13100). Found: C, 70.03; H, 5.75; N, 11.10%. Calcd for $C_{21}H_{21}N_3O_3$: C, 69.41; H, 5.82; N, 11.56%. ^{1}H-NMR ($CDCl_3$) δ 1.68 (6H, m), 1.80 (3H, s), 2.95 (4H, m), 7.64 (4H, m), 8.13 (2H, m), 8.60 (1H, s), 12.68 (1H, broad).

*1-Amino-2-piperidino-4-benzoylaminoanthraquinone (**2c**)*: Mp 195—195.5 °C (benzene). λ_{max} (benzene) 574 (10900), 538 (13200). Found: C, 73.00; H, 5.39; N, 9.51%. Calcd for $C_{26}H_{23}N_3O_3$: C, 73.40; H, 5.45; N, 9.88%. ^{1}H-NMR ($CDCl_3$) δ 1.70 (6H, m), 3.00 (4H, m), 7.55 (7H, m), 8.12 (4H, m), 8.66 (1H, s), 13.72 (1H, broad).

*Reaction of **3** with Butylamine. General Procedures*: A mixture of **3** (1.72 g, 5.0 mmol), $CoCl_2$ (0.65 g, 5.0 mmol), butylamine (20 ml) and pyridine (15 ml) or 1-butanol (15 ml) was stirred in a open flask at room temperature for 24 h. After the reaction, the mixture was poured into aqueous 30% HCl solution. The precipitate was filtered, washed with small amount of water, dried, and chromatographed on silica gel using benzene–acetone (5:5) as an eluent to give **4**. Small amount of **4** was also obtained from the filtrate by salting-out with NaCl. The recovery of **3** was determined by means of spectroscopy. The structure of **4** and **5** were determined by comparison with authentic samples.

*Reaction of **7** with Butylamine.* A mixture of **7** (5.0 mmol), metal salts (5.0 mmol), butylamine (22.5 ml) and 1-butanol (7.5 ml) was stirred under reflux for 5 h in a flask equipped with a reflux condenser. After the reaction, the mixture was poured into aqueous 10% HCl solution. The precipitate was filtered, washed with water, dried and chromatographed on silica gel using benzene as an eluent to give the products in the order of **8**, **9** and **10**, respectively.

*1-Hydroxy-4-butylanthraquinone (**8**)*: Mp 119.5—120 °C (benzene). λ_{max} (benzene) 435[s] (5120), 415 (6410), 395[s] (5480). Found: C, 77.16; H, 5.79%. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75%. ^{1}H-NMR ($CDCl_3$) δ 0.95—1.60 (7H, m), 2.73 (2H, t), 7.73 (4H, m), 8.25 (2H, m), 12.92 (1H, s). MS, *m/e* (rel intensity) 280 (M^+, 100), 251 (27), 238 (64), 237 (64).

*1-Hydroxy-4-butylaminoanthraquinone (**9**)*: Mp 122—123 °C (benzene). λ_{max} (benzene) 602 (10000), 561 (10600), 522[s] (6250). Found: C, 73.22; H, 5.82; N, 4.49%. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74%. ^{1}H-NMR ($CDCl_3$) δ 1.00 (3H, m), 1.62 (4H, m), 3.35 (2H, q), 7.15 (2H, s), 7.70 (2H, m), 8.30 (2H, m), 10.18 (1H, broad), 13.65 (1H, s). MS, *m/e* (rel intensity) 295 (M^+, 9), 294 (29), 251 (100), 223 (27).

*1-Hydroxy-2,4-bis(butylamino)anthraquinone (**10**)*: Mp 129—129.5 °C (hexane). λ_{max} (benzene) 598 (10100), 558 (10300), 518[s] (5900). Found: C, 71.45; H, 6.91; N, 7.34%. Calcd for $C_{22}H_{26}N_2O_3$: C, 72.11; H, 7.15; N, 7.64%. ^{1}H-NMR ($CDCl_3$) δ 0.69—2.20 (14H, m), 3.20 (4H, m), 5.30 (1H, broad), 5.77 (1H, s), 7.55 (2H, m), 8.14 (2H, m), 10.75 (1H, broad), 15.00 (1H, s). MS, *m/e* (rel intensity) 366 (M^+, 74), 323 (100), 262 (89).

References

1) K. Yoshida, M. Matsuoka, Y. Yamashita, and T. Kitao, *Chem. Lett.*, **1978**, 1317; *Bull. Chem. Soc. Jpn.*, **53**, 2552 (1980).

2) K. Yoshida, M. Matsuoka, Y. Yamashita, S. Nagamori, and T. Kitao, *Bull. Chem. Soc. Jpn.*, **53**, 3725 (1980).

3) M. Matsuoka, Y. Makino, K. Yoshida, and T. Kitao, *Chem. Lett.*, **1979**, 219; *Dyes and Pigments*, **1**, 27 (1980).

4) K. Venkataraman, "The Chemistry of Synthetic Dyes," Academic Press Inc., New York (1952), p. 840.

5) S. A. Russkikh. V. V. Loskutov, and V. V. Russkikh, *J. Gen. Chem. USSR.*, **44**, 162 (1974).