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SELECTIVE BUTYLAMINATION OF 5,8-DIHYDROXY-1,4-NAPHTHOQUINONE PROMOTED BY COPPER SALTS

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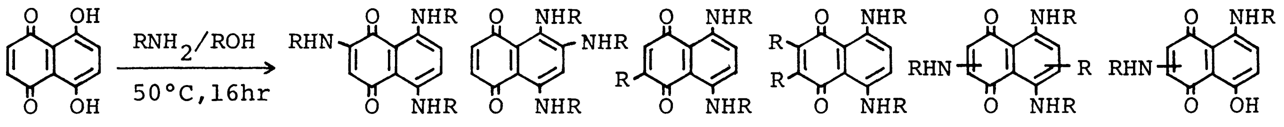
Selective butylamination promoted by copper salts was observed on the reaction of 5,8-dihydroxy-1,4-naphthoquinone(DHNQ) with butylamine. A novel β-butylamination of DHNQ proceeded in the presence of copper salts. A number of β-butylaminated naphthoquinone derivatives were conveniently obtained.

A few synthesis of aminonaphthoquinone derivatives have been reported. In connection with the synthesis of naphthoquinone dyes, Kasai et al.1) reported the multistep process to aminonaphthoquinones from 2,3-dichloro-1,4-naphthoquinone as a starting material, and Klein2) also reported the amination of leuconaphthazarin to 5,8-bisalkylaminonaphthoquinones in the patent. Another methods to prepare the variety of aminonaphthoquinone derivatives have been widely anticipated. In our previous paper3), we reported a new metal promoted convenient synthesis of 2-butylamino-1,4-dihydroxyanthraquinone from 1,4-dihydroxyanthraquinone(DHAQ), in which quantitative and highly selective β-butylamination was observed, while without metal salts none of the β-butylaminated but 1,4-bisbutylaminated products were obtained.

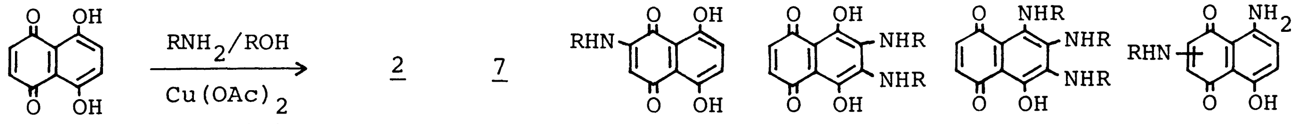
In this paper, we intend to report a new route to aminonaphthoquinone derivatives by means of the selective amination promoted by copper salts. It is generally known that α-hydroxyanthraquinone give α-aminoanthraquinones by usual nucleophilic substitution with amines. The reaction of 5,8-dihydroxy-1,4-naphthoquinone(DHNQ) with excess of butylamine4) also afforded many of 5,8-bisbutylamino-1,4-naphthoquinone derivatives in a low yield, together with many of blue colored unidentified products5). Unless the copper salts presented, α-butylamination proceeded predominantly. Alkylation6) at β-position was also observed as a side reaction. A number of products were separated by column chromatography on silica gel, as shown by Scheme 1.



	$R=CH_2CH_2CH_2CH_3$	2	3	4	5	6	7
1	Yield(%)[7)]	<1	<1	<1	<1	<1	3

Scheme 1

An addition of cupric acetate to the reaction mixture markedly changed the variety of products (Scheme 2)[8)]. β-Butylamination predominantly proceeded instead of α-butylamination. It was interested that compounds 9 and 10, bisbutylaminated at 6- and 7-position, were obtained. In the case of DHAQ, 2-butylamino-DHAQ was exclusively obtained in the similar conditions[3)]. It was concluded that the reactivity of DHNQ for β-butylamination was much more higher than that of DHAQ, and concequently compounds 9 and 10 were obtained. As a result, selective β-butylamination of DHNQ promoted by copper salts was observed comparing with the results of Scheme 1.



1		2	7	8	9	10	11
	Yield(%)	<1	26.5 [9)]	1.7	1.1	1.6	1.8

Total Yield 32.7%

Scheme 2

As it was proposed the formation of copper complex between quinone carbonyl group and α-hydroxyl group of 1 may play a great role on this β-amination as supposed for earlier cases[3)], DHNQ copper complex was previously prepared[10)] and was butylaminated (Scheme 3).

DHNQ-Copper Complex $\xrightarrow[50°C,16hr]{RNH_2/ROH}$	7	8	9	10
Yield(%)[11)]	41.8	4.7	10.3	2.9

Total Yield 59.7%

Scheme 3

Only the four components were isolated. None of the 5,8-bisbutylaminated but β-butylaminated products were exclusively obtained. Each of the products was obtained in a better yield than that of the result of Scheme 2. The amination of DHNQ copper complex was the successful and convenient route to prepare some aminonaphthoquinone derivatives.

Characterization of aminonaphthoquinone derivatives;

2 mp. 102-104°C(petroleum ether): UVmax,nm,benzene(εx10^{-4}), 598(1.60), 649(2.86) Mass, 371(M$^+$), 328(M$^+$-43): NMR(CDCl$_3$), δ=13.66(1H,broad), 11.59(1H,broad), 7.01 (2H,s), 6.27(1H,broad), 5.62(1H,s), 3.28(6H,m): Analysis found(%); C,70.65; H,8.95; N,11.30; Calcd. for $C_{22}H_{33}N_3O_2$; C,71.12; H,8.95; N,11.31.

3 mp. 69-69.5°C(petroleum ether): UVmax, 614(1.13), 662(1.22): Mass, 371(M$^+$), 328(M$^+$-43): NMR, 10.46(2H,broad), 7.09(1H,s), 5.84(1H,broad), 5.69(2H,s), 3.20 (6H,m): Analysis found; C,71.42; H,8.90; N,10.59; Calcd. for $C_{22}H_{33}N_3O_2$; C, 71.12; H,8.95; N,11.31.

4 mp. 60-61°C(petroleum ether): UVmax, 630(1.25), 681(1.25): Mass, 356(M$^+$), 313 (M$^+$-43): NMR, 10.96(2H,broad), 7.18(2H,s), 6.73(1H,s), 3.35(4H,q), 2.58(2H,t).

5 mp. 136-137°C(petroleum ether): UVmax, 602, 652: Mass, 412(M$^+$), 369(M$^+$-43): NMR, 13.35(2H,broad), 7.25(2H,s), 3.61(4H,q), 2.77(4H,t): Analysis found; C, 75.19; H,9.89; N,6.78; Calcd. for $C_{26}H_{40}N_2O_2$; C,75.68; H,9.77; N,6.79.

6 mp. 84.5-86.5°C(petroleum ether): UVmax, 588(1.36), 638(2.75): Mass, 427(M$^+$), 384(M$^+$-43): NMR, 13.55(1H,broad), 11.80(1H,broad), 6.89(1H,s), 6.39(1H,broad), 5.67(1H,s), 3.34(6H,m), 2.74(2H,t).

7 mp. 80-81.5°C(ethanol): UVmax, 555(1.25), 599(1.16): NMR, 14.80(1H,s), 10.10 (1H,broad), 7.24(1H,s), 7.15(1H,s), 6.42(1H,broad), 5.73(1H,s), 3.34(4H,m): Analysis found; C,68.13; H,7.75; N,8.95; Calcd. for $C_{18}H_{24}N_2O_3$; C,68.33; H, 7.65; N,8.85.

8 mp. 127-128°C(ligroin): UVmax, 474(0.78), 500(0.86), 534(0.65): Mass, 261(M$^+$), 218(M$^+$-43): NMR, 13.58(1H,s), 11.97(1H,s), 7.30(1H,s), 7.23(1H,s), 6.15(1H, broad), 5.75(1H,s), 3.24(2H,q): Analysis found; C,64.50; H,6.11; N,6.01; Calcd. for $C_{14}H_{15}NO_4$, C,64.36; H,5.79; N,5.36.

9 mp. 189-190°C(ligroin): UVmax, 463(1.09), 501(1.18), 541(1.28): Mass, 332(M$^+$), 289 (M$^+$-43): NMR, 14.64(2H,s), 6.30(2H,broad), 5.89(2H,s), 3.32(4H,q): Analysis found; C,64.95; H,7.27; N,8.10; Calcd. for $C_{18}H_{24}N_2O_4$, C,65.04; H,7.28; N,8.43.

10 mp. 139-140°C(petroleum ether): UVmax, 523(1.57), 562(2.47): Mass, 387(M$^+$), 344 (M$^+$-43): NMR, 16.72(1H,s), 11.60(1H,broad), 6.90(1H,broad), 6.13(1H,broad), 5.76(1H,s), 5.67(1H,s), 3.24(6H,q): Analysis found; C,68.13; H,8.67; N,10.43; Calcd. for $C_{22}H_{33}N_3O_3$, C,68.19, H,8.58; N,10.84.

11 mp. 148-150°C(ligroin): UVmax, 526(0.90), 558(0.73): Mass, 260(M$^+$), 217(M$^+$-43): NMR, 14.30(1H,s), 7.07(1H,s), 6.89(1H,s), 6.89(2H,broad), 6.29(1H,broad), 5.67

(1H,s), 3.18(2H,q): Analysis found, C,64.21; H,6.13; N,10.31; Calcd. for $C_{14}H_{16}N_2O_3$, C,64.64; H,6.20; N,10.76.

References and Notes

1) T.Kasai, R.Kurabayashi, Y.Suzuki, A.Yoshida, and S.Tsuruoka, Yuki Gosei Kagaku Kyokai Shi, 27, 162(1969).
2) D.X.Klein, U.S. patent 2,399,355. Chem. Abstr., 40, 4530(1946).
3) M.Matsuoka, Y.Makino, K.Yoshida, and T.Kitao, Chem. Lett., 1979, 219.
4) Reactant 1 (10 mmol) was heated in butyl alcohol (10 ml) with butylamine (30 ml) at 50°C for 16 hr. Following procedure was the same as that of our earlier paper$^{12)}$.
5) They have following UVmax but too small to be identified. UVmax(benzene), 634, 685 nm. 615, 664 nm. 626, 675 nm.
6) Alkylation at 4-position in a yield of 48% was also observed in our case of butylamination of 1-hydroxyanthraquinone at 80°C for 4.5 hr in the presence of cobalt dichloride.
7) Main component of product was the black colored unidentified solid which did not soluble in benzene and was supposed to be some kinds of polymeric matters.
8) Reactant 1 (10 mmol) in butyl alcohol (10 ml) was previously stirred with cupric acetate (20 mmol) for 30 min. Butylamine (30 ml) was added to the mixture and then heated at 50°C for 16 hr.
9) An addition of cupric chloride instead of cupric acetate gave better yield(61%) of 7 at ambient temperature.
10) A.Mangini and R.Stratta, Gazz. Chim. ital., 62, 686(1932). Chem. Abstr., 27, 285(1933).
11) The yield based on DHNQ copper complex used. Copper complex (1.43 g) was obtained from 1 (1 g) with cupric acetate (3 g)$^{10)}$. Analysis found; C,30.44; H,2.48; Calcd. for $C_{10}H_4O_4Cu_2 \cdot 4H_2O$, C,31.01; H,3.10.
12) K.Yoshida, M.Matsuoka, T.Ueyama, Y.Yamashita, and T.Kitao, Chem. Lett., 1978, 765.

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