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A NOVEL RING CLOSURE REACTION BETWEEN 1,4-DIHYDROXYANTHRAQUINONE AND ETHYLENEDIAMINE PROMOTED BY COPPER IONS

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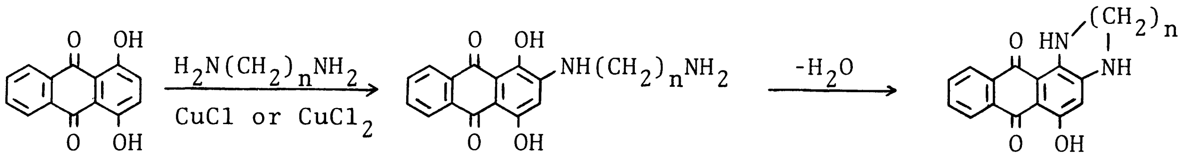
The reaction of 1,4-dihydroxyanthraquinone with ethylenediamine in the presence of Cu(I)Cl or Cu(II)Cl_2 gave 6-hydroxy-1,2,3,4-tetrahydro-naphtho-(2,3-f)-quinoxaline-7,12-dione in quantitative yield at ambient temperature. The reaction was promoted greatly by copper ions. The possible mechanism and the role of copper ions were discussed.

In our previous papers$^{1)}$, quantitative 2-alkylamination of 1,4-dihydroxyanthraquinone 1 promoted by copper ions was reported. In the reaction, copper ions were proposed to play as an effective oxidizing agent to give quinizarinquinone (1,4,9,10-tetrahydroanthracene-1,4,9,10-tetraone) from 1 via copper complex.

In this paper, we wish to report a novel ring closure reaction between 1 and ethylenediamine (ETDA). The reaction of 1 with ETDA in the presence of Cu(II)Cl_2 gave 6-hydroxy-1,2,3,4-tetrahydronaphtho-(2,3-f)-quinoxaline-7,12-dione 3a in 98% yield at ambient temperature. Without copper ion under atmospheric oxygen, 3a was obtained in 47% yield together with 15% yield of leucoquinizarin and 9% recovery of 1. On the other hand, the reaction of 1 with 1,3-propylenediamine in the presence of Cu(II)Cl_2 did not give the cyclic product 3b but 2-(3'-aminopropylamino)-1,4-dihydroxyanthraquinone 2b in 95% yield.



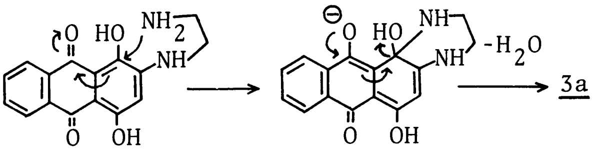
1   2 a: n=2, b: n=3   3 a: n=2, b: n=3

Scheme 1

The facile ring closure with ETDA but not with 1,3-propylenediamine should be ascribed to the steric requirments of 2'-aminoethylamino group in which six-membered ring could be formed by the intramolecular nucleophilic substitution as shown in Scheme 2. Analogous results of ring closures which are dependent on the chain length of alkylenediamine have been reported (Scheme 3)$^{2,3)}$.

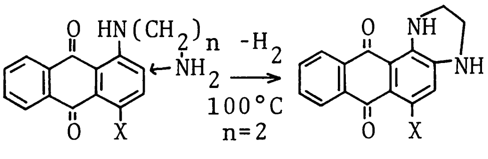
The reaction of 1 with ETDA in the presence of Cu(I)Cl under the conditions without oxygen gave 3a in 96.6% yield together with the deposition of metal copper in 44.1% yield. On the other hand, the reaction of quinizarinquinone with ETDA without copper salts gave 3a in 90.7% yield along with 1.2% yield of 1. These results suggest that the role of copper ions is the same as our previous cases of

2-butylamination of 1[1], that is; copper ions oxidize 1 to quinizarinquinone via copper complex, and copper ions are reduced to metal copper. These findings are taken to support the intermediacy of 2a, i.e., the first amination should take place at 2-position giving 2a, and another possibility of the course of the reaction via 1-(2'-aminoethylamino)-4-hydroxyanthraquinone is not probable.



2a

Scheme 2



Scheme 3

General procedures of the reaction were as follows; reactant 1 (5 mmol) was stirred in pyridine (12 ml) with ETDA (228 mmol) and/or copper salt (10 mmol) at 30°C for 24 h. The mixture was poured into 10% aqueous HCl solution and the separated products were isolated by filtration, washed with water, dried and chromatographed on silica gel column using benzene as eluent. Compound 3a was not developed in this system, but extracted with methanol from the resulting column. Product 2b was partially soluble in water and isolated by salting out with NaCl.

The reaction under the conditions without oxygen was carried out as same as before[1]. The acetylation of 3a gave rise to 4-acetyl derivative. The selective 4-acetylation of similar compounds has been reported[3].

2b: mp. >300°C (Water:Acetone=2:3): UVmax (Methanol), 509, 534^s: Mass (Rel. intensity); 312(M^+, 29), 282(M^+-30 ,100), 268(36), 267(44), 254(67).

3'-Acetyl derivative of 2b: mp. 237-238°C (Methanol): UVmax (Methanol), 514(12200), 534^s(11000): IR (KBr); νco 1640 cm^{-1}: Analysis found; C, 64.82, H, 5.45, N,7.97 Calcd for $C_{19}H_{19}N_2O_5$; C, 64.22, H, 5.39, N, 7.88.

3a: mp. 274-275°C (Pyridine:Water=9:1): UVmax (Benzene), 510^s(11000), 544(19500), 585(19800): NMR (D_6-DMSO); δ= 15.46(1H,s), 10.55(1H,broad), 8.11(2H,m), 7.95 (1H,m), 7.70(2H,m), 6.06(1H,s), 3.50(4H,s): Mass (Rel. intensity); 280(M^+, 100), 279(M^+-1, 83): Analysis found; C, 68.11, H, 4.21, N, 10.12; Calcd for $C_{16}H_{12}N_2O_3$; C, 68.56, H, 4.32, N, 10.00.

4-Acetyl derivative of 3a: mp. 232-233°C (Methanol): UVmax (Benzene), 520^s(7550), 553(14800), 594(12600): IR (KBr); νco 1670 cm^{-1}: Analysis found; C, 66.64, H, 4.59, N, 8.26; Calcd for $C_{18}H_{14}N_2O_4$; C, 67.07, H, 4.38, N, 8.69.

References

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   b: ibid, 1979, 1347.
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3) H.P.Koelliker and P.Caveng, Chimia, 20, 281(1966).

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