On the Synthesis of 8-Hydroxyquinoline

By Akira INOUE, Michio SUGIURA and Yojiro TSUZUKI

(Received May 25, 1954)

Introduction

The object of this investigation is to prepare 8-hydroxyquinoline for the purpose of utilizing quinoline, a constituent of the coal tar bases contained in considerable quantity (ca. 18%). On the synthesis of this substance from quinoline, however, no systematic investigations have been made, in spite of the fact that 8-hydroxyquinoline has been reported to be useful as an organic reagent for the microanalysis of metal irons, as a stabilizer of P.V.A.[1], and a fungicide in the form of its copper salt[2], etc.

The present research was undertaken to find out the best condition of the sulfonation of quinoline, that of the alkali fusion of sulfoquinoline, and that of the preparation of copper 8-hydroxyquinolate in order to obtain 8-hydroxyquinoline as well as its copper salt with good yield.

Sulfonation of Quinoline

The process of sulfonation was adopted as the first stage of the synthesis, because the 8-position of quinoline is, from the view-point of active complex, most active in cationic substitution, is as its highest in electron density (see Fig. 1), and finally because the sulfonic group is expected to enter preferentially into the 8-position considering the previous experimental result.[4]

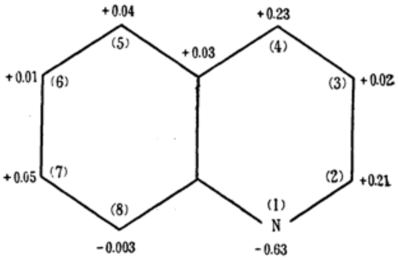

Fig. 1. Electron density of quinoline (C. A. Coulson)

Purification of Material—Crude quinoline was subjected to fractional distillation with a column of 2 cmφ×50 cm under reduce pressure. The boiling point of thus purified quinoline was 113–114°C/17 mm. The content was 65% of the crude material. Isoquinoline distilled at 117–118C°/17 mm; the content was 27%.

Procedure—50 g. of quinoline was dropped gradually in to 150 g. of 50% oleum (fuming sulfuric acid) contained in a 300 cc. flask, equipped with an air-tight stirrer, a dropping funnel, and a reflux condenser. The temperature was kept below 50°C while adding; then the whole was gradually heated to a given temperature, and kept constant there for some hours, as shown in Table I and II. On pouring the reaction product onto ice, 8-sulfoquinoline separated in the form of white precipitate or crystals (m.p. 312°C), while 5-sulfoquinoline (m.p. 59°C), the main by-product, was dissolved into water.

Results—The influence of the temperature on the yield of 8-sulfoquinoline is shown in Table I. The maximum yield (80.3%) was obtained at 140°C. When the reaction is carried out above this temperature, the product is colored brown, the purification becomes difficult and hence the yield is reduced.

---

1) F. W. Cox, U.S.P. 2,396,555, March 12 (1946).

2) P. G. Benignus, *Ind. Eng. Chem.* **40**, 1426 (1948).

TABLE I
INFLUENCE OF REACTION TEMPERATURE ON THE YIELD OF 8-SULFOQUINOLINE
(The reaction time: 2 hrs.)

Temp. (°C)	Yield (%)	Temp. (°C)	Yield (%)
100	40.7	130	61.7
110	49.4	135	70.4
120	63.9	140	80.3

The influence of the reaction time on the yield of 8-sulfoxuinoline was investigated at 120° and 140°C. The results are shown in Table II.

TABLE II
INFLUENCE OF REACTION TIME ON THE YIELD OF 8-SULFOQUINOLINE

Time (hr.)	Yield	
	120°C	140°C
1	41.7	54.9
2	63.9	80.3
3	53.1	42.4
4	46.9	32.1

G. M. McCasland[3] obtained a lower yield (54%) in the sulfonation of quinoline with 30% oleum at 90°C and 40 hrs. The unfavorable result is probably due to the long heating by which 7- and 5-sulfoquinoline and disulfoquinolines,[4] all soluble in water, are formed. It may be attributed to the formation of these reaction products that the yield decreases, when the reaction is continued further than 2 hrs., as observed in our case (Table II).

Alkali Fusion of 8-Sulfoquinoline

To a quantity of molten (260°C) sodium hydroxide in a graphite crucible is gradually added 20.9 g. (1/10 mol) of 8-sulfoquinoline, and the whole is kept at 300-310°C for 10 to 15 min. Table III shows how the yield of 8-hydroxyquinoline varies with the quantity of sodium hydroxide, which is expressed by a unit of the theoretical quantity, 3 moles of NaOH being theoretically required for one mole of 8-sulfoquinoline.

$$C_9H_6NSO_3H+3NaOH$$
$$=C_9H_6NSO_3Na+Na_2SO_3+2H_2O.$$

The yield of 8-hydroxyquinoline is expressed by the quantity obtained by distilling with steam for 1.5 hrs.* after alkali fusion.

TABLE III
INFLUENCE OF THE QUANTITY OF SODIUM HYDROXIDE ON THE YIELD OF 8-HYDROXQUINOLINE

NaOH	Yield (%)	NaOH	Yield
1	0	3	38.6
1.5	38.6	3.5	29.0
2	40.7	4	22.1

8-Hydroxyquinoline and its Copper Salt

In order to isolate 8-hydroxyquinoline from the product of alkali fusion the following procedure was adopted:

acid decomposition→neutralizaton→steam distillation→8-hydroxyquinoline.

However, complete isolation is not realized by such a simple method, since 8-hydroxyquinoline is slightly soluble in water, and readily soluble both in acid and concentrated alkali, namely, 8-hydroxyquinoline remains in the residue as well as in the filtrate of steam distillation. The following modifications were, therefore, to be made: the product of alkali fusion was decomposed by dilute sulfuric acid, the liquid was carefully neutralized with both concentrated sodium hydroxide and sodium carbonate to a *p*H 7.2, the isoelectric point[5] of 8-hydroxyquinoline, where the solubility in water is the minimum.

These processes were carried out always below 35°C in order to prevent the evaporation of 8-hydroxyquinoline with steam and also to prevent the formation of a cake from the black body formed by the neutralization. The steam distillation is continued for 1.5 hrs. (the quantity of water ca. 1.7 l.), the distillate is cooled, and 8-hydroxyquinoline filtered. The filtrate from 8-hydroxyquinoline, (I), is combined with the filtrate (II), mentioned below. The residue of steam distillation is, after cooling, acidified with dilute sulfuric acid to a *p*H 2.8, so as to precipitate the ferrous 8-hydroxyquinolinate completely, where 8-hydroxyquinoline itself is soluble. The filtrate of ferrous 8-hydroxyquinolinate, (II), is combined with the filtrate (I), and a calculated quantity of crystalline copper sulfate is added, in the state of warm solution, to this combined filtrate, in order to prepare the copper salt of 8-hydroxyquinoline. The crystalline powder of the copper salt, thus formed is filtered at *p*H 2.7–3.2 by treating the mixture with concentrated sodium hydroxide, solution at which *p*H the solubility of the copper salt is least and the precipitate of cupric hydroxide dissolved[6]. The copper salt is washed with warm water, and dried at 100°C in an air-bath. The copper salt is prepared from 8-hydroxyquinoline in the following: an aqueous solution containing a little more than the calculated quantity (0.86 times the weight of 8-hydroxyquinoline) of $CuSO_4 \cdot 5H_2O$ is warmed at 80° to 100° and 8-hydroxyquinoline is gradually added to this warm solution, the precipitate is filtered, while still not, at *p*H 2.7–3.2, and dried at 100°C. The yield of the copper salt is nearly 100%.

In Table IV is shown the yield of 8-hydroxyquinoline including copper salt from 8-sulfoquinoline. Even in respect of the yield the present method is superior to the most

---

[3] *J. org. Chem.*, **11**, 277 (1946).

[4] Claus, Stelzner *J. prakt. Chem.*, [2], **53**, 390 (1896).

* It takes more than one hour, for the black product formed by neutralization with NaOH to turn entirely to a tarry precipitate.

[5] I. M. Kolthoff, *Chem. Weekblad*, **24**, 606 (1927).

[6] H. Gotô, *Sci. Rept. Tôhoku Imp. Univ.*, 1 ser., **26**, 391 (1937).

recent method (67%) of Skraup synthesis[7] from *o*-aminophenol as well as from *o*-nitrophenol.

TABLE IV

NaOH (theoret. quantity=1)	Yield		Experimental condition at the max. yield	
	max. (%)	mean (%)	temp. (°C)	time (min.)
2	61.4	50.3	300–325	5
2.5	77.9	59.3	300–310	10
3	84.1	62.6	300–313	10

8-Hydroxyquinoline obtained from the steam distillate was always pure colorless needles, m.p. 73–74°C. Found: C, 74.64; H, 4.93; N, 9.77. Calc. for C_9H_7NO (145.15): C, 74.48; H, 4.83; N, 9.65%. The copper 8-hydroxyquinolinate obtained from the filtrate was a yellowish green crystalline powder, changed to a brown power on heating and carbonized completely at 245°C. Found: CuO, 21.67; calc. for $C_{18}H_{12}N_2O_2Cu \cdot 1/2\ H_2O$[8] (360.84): 22.05%.

Summary

1) 8-Sulfoquinoline has been obtained with a yield of 80.3% by sulfonating quinoline with 50% oleum at 140°C for 2 hrs.

2) 8-Hydroxyquinoline has been synthesized by fusing 1 mole of 8-sulfoquinoline with 9 moles of NaOH at 300–315°C for 10 to 15 minutes, decomposing the with dilute sulfuric acid, neutralizing with sodium hydroxide and soda to a *p*H 7.2, and by distilling with steam for 1.5 hrs. The remaining 8-hydroxyquinoline in the residue and in the filtrate was collected in the form of its copper salt. The highest yield of 8-hydroxyquinoline including its copper salt was 84.14%.

3) Copper 8-hydroxyquinolinate has been obtained with a yield of nearly 100% by heating 8-hydroxyquinoline with 0.86 times its weight of crystalline copper sulfate together with a large quantity of water at 80° to 100°C.

The authors are deeply indebted to Mr. K. Arakawa of the Nippon Steel Co., Kawasaki, for his suggestions and help.

Tokyo College of Science
Shinjuku-ku, Tokyo

---

[7] W. R. Ashford, *U.S.P.*, 2,591,553, July 24 (1951).

[8] Y. Nakatsuka. This Bulletin, **11**, 47 (1936).