

A Study of the Preparation of 8, Mercapto, Quinoline

- by -

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This thesis is dedicated to Dr. John Robert Taylor,  
a man possessing vast and surprising amounts of  
wisdom, science, and information. To his  
students, he has been a guide, en-  
couragement and inspiration.

W. L. B.

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Edinger in 1908 reported in the German journal, Berichte  
der Deutschen Chemischen Gesellschaft <sup>(1)</sup>, that he had prepared  
8, mercapto, quinoline <sup>by reacting 8, quinoline</sup> sulfonic acid with phosphorous penta-  
chloride, thus obtaining the acid chloride of the sulfonic  
acid. The acid chloride he reduced with stannous chloride in  
a hydrochloric acid solution, and obtained the tin double salt  
of 8, mercapto quinoline. The free mercaptan was obtained by  
its extraction with ether from an alkaline solution.

This paper is a description of the results obtained by  
its author when he attempted to duplicate Edinger's results,  
starting, however, with the preparation of quinoline, then  
preparing the sulfonic acid, the acid chloride, and finally  
the mercaptan. It was, also, hoped to be able to prepare the  
mercaptan by making 8, nitro, quinoline and reducing this to  
the amino compound, then diazotizing and adding potassium  
acid sulfide. The author was, however, successful only to  
the point of roughly identifying the 8, amino quinoline.



### Preparation of Quinoline

Quinoline was prepared by the Skrop synthesis<sup>(2)</sup>, using ferrous sulfate, glycerol, anilin, nitrobenzene and concentrated sulfuric acid. These were refluxed together for six hours and then diluted with water and steam distilled. The distillate was discarded and the residue was made alkaline with sodium hydroxide and again steam distilled. The distillate was made acid with concentrated sulfuric acid and the remaining anilin diazotized by adding sodium nitrite. This solution was heated until there was no longer an evolution of gas and it was steam distilled. The distillate was discarded and the residue was made alkaline with sodium hydroxide and steam distilled. The distillate contained water and quinoline. The water was decanted and the quinoline was steam distilled several more times. Finally the quinoline was separated from any remaining water in a separatory funnel. 110 grams of crude quinoline were obtained.

Preparation of 8, Sulfonic Acid, Quinoline (3)

10 grams of quinoline were placed in a three-necked 500 ml. round bottom flask, equipped with an electrically operated stirrer, a small reflux condenser, and a thermometer. To the 10 grams of quinoline were added 99 grams of 20% fuming sulfuric acid, which was prepared by adding to 100 grams of 96% sulfuric acid, 95 grams of 60% fuming sulfuric acid. An oil bath was brought under the flask and the solution was stirred and heated at 160 degrees for 20 hours. It was then poured into a 2 l. beaker and diluted with water to about 500 ml. This solution, dark brown in color, was heated on a ring stand over a burner and 97 grams of barium carbonate were added to precipitate the sulfate ions from the solution. The solution was not yet neutral and 70 grams of barium chloride were added. The solution, now, gave a neutral reaction to litmus. The barium sulfate precipitate was filtered off in three batches, each being well washed with cold water and the washings being added to the filtrates. The combined filtrates were evaporated to about 500 ml. and cooled. The excess barium chloride precipitated

and was filtered off. The clear solution was evaporated to about 5 ml. It was light yellow in color and slightly viscous. Ammonium hydroxide was added slowly and the solution produced large amounts of light brown crystals. As more ammonium hydroxide was added, the solution became reddish brown and the solid dissolved. The solution was now alkaline to litmus and carbon dioxide was passed into it to precipitate any excess barium. The solution remained clear. The solution was then placed on a steam bath until all of the free water had evaporated leaving behind a moist light brown mass. A portion of this was scraped onto another watch glass which was placed in a vacuum oven and heated at about 100-120 degrees for 45 minutes. The watch glass was removed from the oven and the light brown solid powdered with a spatula. Similar treatment was given the rest of the moist mass in four more batches.

The powdered solid weighed 28 grams. A portion of the solid was dried in an oven at 110 degrees for 24 hours, showing a loss in weight of 4.62% . It takes up moisture readily as shown by increasing weight on a balance, and by the accompanying change in color to a darker brown from a very light



brown. An ignition test showed 98.28% volatile material. Sodium hydroxide added to a solution of the substance gave an evolution of ammonia, detected by its odor. A melting point was not obtained although the mixture darkened at 220 degrees. A chloride determination was made. Assuming the chloride to be combined with the ammonia, it was found that there was 8.46% of ammonium chloride. The substance was found to be very soluble in water. Its solution is amber colored and gives a reaction with universal indicator paper, showing a pH of about 4 or 5.

It was assumed that this was the ammonium salt of the 8, sulfonic acid, quinoline mixed with a little of the barium salt, some small quantities of the salts of other quinoline sulfonic acids, and ammonium chloride.



(1)  
Preparation of the Acid Chloride

Two attempts were made to prepare the acid chloride of 8, sulfonic acid, quinoline. In the first attempt the results were somewhat similar to those in the second, but the procedures differ. The acid chloride was not identified in the first attempt.

The first time, 5 grams of the salt of the acid were weighed on a balance, as were 5 grams of phosphorous pentachloride, and these were dumped together into a 50 ml. distilling flask. This was placed in an oil bath with a thermometer suspended in it and heated under a hood at 130-150 degrees for 10 minutes. At the end of this time all of the phosphorous oxychloride had apparently come off and the mixture was cooled and about 15 ml. of water was added and shaken in the flask. This mixture was poured into a beaker. White globules of oil floated on top of the water while at the bottom of the beaker was an insoluble sticky mass, a light brown in color. This was stirred with a stirring rod to allow the water to come into contact with as much of it as possible, thus dissolving any remaining pentachloride of phosphorous, salts of acids, and ammonium chloride. The water was decanted from the brown insoluble mass and this mass was scraped onto a suction filter,

where it had air sucked through it for 5 minutes, and then scraped off the filter paper onto a watch glass and placed in a vacuum oven where it was heated at 50 degrees for an hour. It was removed from the oven, hard, perforated with holes and air bubbles. A portion of it was scraped from the watch glass, with difficulty, into a test tube. Several milliliters of concentrated ammonium hydroxide were added to the test tube. The mixture was stirred and the chunks of acid chloride in the bottom of the tube were broken into small pieces. There was an evolution of heat and a white crystalline solid formed, which when filtered became gray. This was placed on a porcelain plate after washing several times with concentrated ammonium hydroxide. The gray colored mass became soggy with water after several hours standing. The remainder of the acid chloride on the watch glass had become very moist. Concentrated ammonium hydroxide was poured on the watch glass and brown crystals formed momentarily and then dissolved.

5 grams of the salt of the acid were again weighed on a balance and approximately 5 grams of phosphorous pentachloride were added to it in a casserole. This mixture was thoroughly mixed with a stirring rod and held in an oil bath under a hood.

The mixture was stirred while it was being heated. It became moist at 120 degrees. The oil bath was allowed to continue to grow hot, the temperature of the bath reaching a final temperature of 190 degrees. Fumes of phosphorous oxychloride were given off at 138 degrees. When the mass had become solid and no more fumes were being driven off, 190 degrees was the temperature of the oil bath at this point, the casserole was taken from the bath and the mass was washed with three small portions of water. The brown sticky mass was rinsed with ether into a separatory funnel, the small amount of water ran back into the casserole and the ether poured onto a watch glass. This was immediately placed in a vacuum oven where it was heated at 50 degrees for an hour. It was then removed. It appeared the same as it had in the first attempt. A portion was scraped onto two smaller watch glasses and placed in an oven at 110 degrees for 30 hours. The rest was hurriedly scraped from the watch glass and weighed - 1 gram - and then dropped into 8 ml. of concentrated hydrochloric acid for use in the preparation of the mercaptan.

The portion which had been placed in the oven at 110 degrees was removed. No change in appearance was noted. A portion of this was scraped from the watch glass into a test



tube and a few milliliters of concentrated ammonium hydroxide were added. A white precipitate formed with an amber colored solution above it. This was heated over a free flame and more concentrated ammonium hydroxide was added. The white crystalline precipitate remained. This was filtered and dried for thirty minutes by suction. The white crystals were transferred to a porcelain plate and allowed to remain for a short time. A melting point was taken. A small portion melted around 172 degrees, and the rest melted sharply at 179 degrees. The recorded value of the melting point of 8, quinoline sulfonamide<sup>(4)</sup> is 183 - 184 degrees. By adding a stem correction of three degrees, this gives a melting point of 182 degrees to the experimental results.



(1)  
Reduction of Acid Chloride

1 gram of the acid chloride was dissolved in 8 ml. of concentrated hydrochloric acid. This was poured into 8 grams of stannous chloride in 20 ml. of concentrated hydrochloric acid. These are the figures given by Edinger for 2.5 grams of the pure acid chloride of 8, sulfonic acid, quinoline. The 8 grams of stannous chloride did not dissolve to give a perfectly clear solution, but rather one which was a milky suspension. The acid chloride dissolved in the concentrated hydrochloric acid to give a clear solution. This clear solution was filtered into the acid containing the stannous chloride. The solution turned a greenish yellow. It was allowed to stand overnight, by which time it had become a clear yellow. There was no precipitate. It was evaporated to about 15 ml. over a free flame. A few ml. were then added to a test tube containing several ml. of cold water. There developed a yellow suspension, which upon standing became a yellow flacculent precipitate. This was filtered and washed with several portions of 6 N hydrochloric acid. It had air sucked through it for several minutes at the end of which time it appeared light brown in color. This was scraped onto a porcelain plate where it appeared orange. It was allowed to remain on the plate until dry - about 5 minutes - and a

melting point was taken. Half of the mixture which was a deep orange melted at 52 - 54 degrees. The rest, which was a bright yellow did not melt by 190 degrees. The filtrate developed more of the yellow flacculent precipitate. This was placed on a porcelain plate to dry and gave a melting range of 185-190 degrees.

The melting point of 52-54 degrees was indicative of the presence of the 8, mercapto, quinoline which is red in color and melts at 58-59 degrees <sup>(1)</sup>. The yellow flacculent precipitate is somewhat like Edinger's disulfide, which he says came down as a yellow flacculent precipitate and melts at 206 degrees. However, he obtained both his mercaptan and disulfide from an alkaline solution.

(5)

Nitration of Quinoline

To 10 grams of quinoline in a 400 ml. beaker was added from a buret 3.43 ml. of fuming nitric acid. The mixture became a gray solid mass which was broken up with a stirring rod and, under a hood, was added in 5 portions to 10 ml. of concentrated sulfuric acid. 2 ml. of fuming sulfuric acid were added after each addition of the solid nitrate to the concentrated sulfuric acid solution. The mixture was kept cool and was well stirred. It was allowed to stand for 45 minutes, and from time to time a drop of it was added to a few ml. of water on a watch glass. This was neutralized with sodium hydroxide. At the early part of the reaction, a milky suspension appeared in the watch glass. At the end of 45 minutes, however, numerous yellow crystals separated on the watch glass before the sodium hydroxide was added. Dufton says that the reaction is completed when a mass of crystals separates on the watch glass with the addition of sodium hydroxide. This did not happen, but because of the large amount of insoluble yellow crystals, which separated before the addition of sodium hydroxide, it was thought best to stop the reaction. Dufton describes these crystals as the dinitroquinoline. The mixture which was a dark reddish brown in



color was neutralized slowly with a sodium hydroxide solution, care being taken to keep the mixture cool. Dark yellow needles precipitated first and were filtered off by suction. They were dried on a porcelain plate and weighed and a melting point was taken. They weighed 0.2 grams and melted at 84-85 degrees. (8, nitroquinoline melts at 89 degrees <sup>(5)</sup>.) The solution continued to produce needles which were filtered off. They showed a melting point range of 70-80 degrees and weighed 1.3 grams. The solution in the beaker was allowed to stand overnight. About 5 ml. of a dark oil formed on the bottom. This oil was separated from the upper aqueous layer and was poured onto a clean porcelain plate and allowed to stand for four days. 2 grams of a yellowish green mass had appeared when the oil had disappeared. A portion of the mass was dissolved in a dilute solution of nitric acid, filtered and extracted from the solution with ether which was allowed to evaporate on a watch glass. Green colored needles appeared. No definite melting point could be determined.

Another portion of the mass was heated in alcohol and filtered while hot, then to the filtrate was added a few drops of water until a precipitate appeared. This was filtered and again recrystallized several times from alcohol. A cream



colored solid was obtained which melted at 49-50 degrees. Dufton states that when equal portions of ana and ortho nitro-quinolines are mixed they give a melting point of 53-54 degrees.

Another portion of the yellowish green mass was added to water and shaken well. A yellow suspension resulted. This was centrifuged, yielding on the bottom of the test tube a dark oil, above it a cream colored precipitate and above that a yellow suspension from which yellow needles crystallized. These were filtered off and dried. They melted from 48-52 degrees.

This method of preparation of the 8, nitro, quinoline involved too much time in the separation of the 8 nitro compound from the by-products. It was used by Dufton to obtain the ana nitro quinoline.

Preparation of 8, Nitro, Quinoline by the Skraup Synthesis (6)

This method involved the preparation of 8, nitro, quinoline from o-nitroanilin. Kneuppel uses 51.5 grams of arsenic oxide, 100 grams of concentrated sulfuric acid, 110 grams of glycerol, and 50 grams of o-nitroanilin. This is per mol of o-nitroanilin, 0.5 mol arsenic oxide or 1.0 mols of arsenic acid, 2.5 mols of sulfuric acid and 3 mols of glycerol.

On the basis of 10 grams of o-nitroanilin or 0.07 mols, 10.6 grams of arsenic acid, 17.2 grams of sulfuric acid (9.4 ml of sp. gr. 1.84), and 19.3 grams (15.3 ml.) of glycerol were used. These quantities were added to a 500 ml. round bottom flask in the order named. The flask was equipped with a free flame, a pan of cold water being used to cool the flask when the reaction became too violent. After the first reaction had subsided, the flame was adjusted to boil the mixture gently and it was left in this condition for 3 hours. Then it was diluted with water, poured into a beaker and allowed to stand over night. It was then filtered and the filtrate, which was a dark brown solution, was treated with a 40% sodium hydroxide solution. The sodium hydroxide was added slowly and the solution was still acid when the first brown turbidity appeared. The solution was filtered by suction and the precipitate dried.

Sodium hydroxide was added in 3 more portions and 3 more times a precipitate was filtered off. Each time the precipitant was darker than before. The last addition of sodium made the solution alkaline and the precipitate this time was black. The first batch of precipitate was recrystallized from alcohol and gave 1 gram of grayish green needles which melted at 87-88 degrees. This was used in an attempt to prepare the 8 amino compound of quinoline.

A portion of the last batch was recrystallized from alcohol by filtering while hot, cooling the filtrate, adding water, filtering off the precipitate and dissolving it in hot alcohol, then repeating the procedure 5 times. There was finally obtained a small amount of straw colored needles which melted at 87.5-88 degrees. 8 nitroquinoline melts at 89  
(5)  
degrees .



(7)  
Preparation of 8, Amino, Quinoline

1 gram of 8, nitro, quinoline was dissolved in about 5 ml. of concentrated hydrochloric acid in a 50 ml. beaker. 1.1. grams of stannous chloride was dissolved in about 5ml. of concentrated hydrochloric in a second 50 ml. beaker and the contents of the first beaker were poured into the second. The contents of the first beaker were a dark red while those of the second were clear. When mixed, a mass of light brown crystals separated. The mixture was poured into a casserole and a sodium hydroxide solution was definitely alkaline. The light brown crystals did not dissolve. Ether was added and the entire solution suddenly turned red with dark lumps of solid in it. More ether was added until there was a distinct ether layer, which was a light yellow in color. It was poured into a separatory funnel, shaken with a portion of of the aqueous solution. The aqueous solution was run back into the casserole and the ether layer was poured onto a watch glass. This procedure was repeated twice more. The solution in the casserole was made acid with concentrated hydrochloric acid and was allowed to stand over night. The ether solution on the first produced an outer ring of a dark red liquid, as more ether evaporated a ring of orange needles appeared, and when all the ether had evaporated there appeared in the middle



of the watch glass transparent needles. In a short while all of the needles had become a dark gray in color. These were placed on a porcelain plate to dry. About the edges appeared a yellow color. A portion of this was recrystallized from cold alcohol in a test tube which was revolved in an ice bath. A metallic gray substance separated. This was filtered, dried by suction, and pressed on a porcelain plate. A melting point was taken showing it to melt at 83-84 degrees. The 8, amino,<sup>(8)</sup> quinoline melts at 70 degrees .

The casserole which had stood over night had about its walls red crystals from the acid solution. These were scraped onto a porcelain plate, dried, and their melting point determined. They melted at 200 degrees, stem correction of 6 degrees makes the experimental value 206 degrees. The mono hydrochloride of 8, amino, quinoline is red and melts at<sup>(9)</sup> 208-209 . An ether extraction of the acid solution was made and a yellow flacculent precipitate was obtained. It was assumed this was the dihydrochloride of the amine, but it was insoluble in water and an attempt to convert it into the red mono hydrochloride by heating in a vacuum oven at 90<sup>(9)</sup> degrees was unsuccessful.

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