A CONTRIBUTION TO THE PREPARATION AND CHEMISTRY OF 6-AMINOQUINOLINE.*

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Para or 6-aminoquinoline was originally desired as a possible source of the 5,6-quinoline quinone either by direct oxidation in a manner similar to the corresponding hydroxy compound (1) or indirectly by conversion into the hydroxy compound by diazotization and hydrolysis. The 6-nitro compound is readily prepared in fairly good yields in the Skraup reaction on *p*-nitraniline. 6-Aminoquinoline was originally prepared by LaCoste (2) by the reduction of the corresponding nitro compound with tin and hydrochloric acid and decomposing the tin double salt formed with hydrogen sulfide. A modification of this method, using stannous chloride, was found to be impractical when workng with as much as ten Gm. quantities because of the poor yields and the difficulty encountered in the precipitation and removal of the tin sulfide. This problem was solved by decomposing the tin double salt with alkali and extracting the amino compound with ether. Reduction with powdered iron and glacial acetic acid according to Claus and Schnell (3) was not satisfactory, neither was the use of alcoholic ammonium sulfide as employed by Magidson and Strukow (4) with the 6-alkoxy-8-nitroquinolines. Sulfonation of 6-aminoquinoline was studied in an attempt to produce a quinoline type of sulfanilamide. The 6-amino-5-sulfonic acid has been made by Cybulski and co-workers (5) using 25–40% oleum. Attempts to sulfonate 6-amino-quinoline with concentrated sulfuric acid and with oleum below this strength were unsuccessful. It, however, was found to react readily with chlorosulfonic acid. The action of chlorosulfonic acid on other aminoquinolines is also being studied in this laboratory.

6-Nitroquinoline.—This was prepared by Knueppel's (6) modification of the Skraup reaction as revised by Capps (7) using technical *p*-nitraniline. Yields as high as 50% were obtained. Recrystallized from dilute alcohol, it melts at 149°. It was found best to use the recrystallized product in the subsequent reduction as higher yields of a better product were obtained than when the crude nitro compound was used.

6-Aminoquinoline.—17.4 Gm. of 6-nitroquinoline was dissolved in 100 cc. of hot conc. HCl and to it was slowly added 90 Gm. of stannous chloride dissolved in 100 cc. of conc. HCl. After allowing the mixture to cool, the precipitated crystalline tin double salt was filtered off and sucked as dry as possible, dissolved in 75 cc. of water, made faintly alkaline with $5N$ NaOH solution and completely extracted with ether in a separatory funnel. 6-Aminoquinoline dissolves readily in ether forming solutions with a strong bluish fluorescence which serves as an indicator in the extraction. This fact has not been previously reported in the literature. The ether was distilled from the combined extracts and the crystalline residue dissolved in as small a quantity of hot alcohol as possible and poured into an evaporating dish for crystallization. Yield 13 Gm. or 90%. Melting point 114°.

6-Aminoquinoline has also been prepared by reduction of the nitro compound with powdered iron in alcoholic solution in the presence of calcium chloride (8), from 6-hydroxyquinoline by heating with ammoniacal zinc chloride in a tube at 270–280° (9) and by warming the hydrochloride of 6-nitroso-1,2,3,4-tetrahydroquinoline with water (10).

Diazotization of 6-Aminoquinoline.—4.8 Gm. ($^1/_{10}$ mole) of 6-aminoquinoline was dissolved in 100 cc. of water and 10 cc. of conc. HCl. The solution was allowed to cool and enough ice added to bring the temperature range within 0–5°. A cold solution of 20% sodium nitrite was then added until a slight excess was indicated by starch-iodide paper.

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Definite proof of the diazotization of this compound was demonstrated in this laboratory by Bostick (11) who prepared several azo dye derivatives, the quinoline-6-azo-betanaphthol compound being a red crystalline substance melting at 199°.

Attempted Replacement of the Diazonium Group by Hydroxyl.—The diazonium solution was poured into 50 cc. of boiling 6*N* HCl. Nitrogen was evolved and the addition required several minutes to avoid boiling over the solution. The resulting solution was cooled and neutralized with sodium hydroxide solution. The slight cloudy precipitate formed, when filtered, proved to be a red tarry mass, difficult to filter and upon standing resulted in a plastic-like substance of a deep red color. No melting point could be obtained from the tar-like substance.

This method was varied by gradually decreasing the acid concentration to 0.1*N* HCl and finally substituting distilled water but the results were the same in every case. The use of sulfuric acid in the diazotization and attempted hydrolysis gave the same results. This is similar to the results obtained by Claus (12) with 5-amino-6,8-dibromquinoline.

When 2*N* NaOH was substituted for the hydrochloric acid, a white amorphous precipitate was obtained. Attempts at purification gave no clue as to its identity. No hydroxyquinoline could be isolated from the mass.

Attempts to replace the diazonium group with chlorine and the arsonic acid group were also unsuccessful.

Oxidation of 6-Aminoquinoline.—Oxidation of 6-aminoquinoline with lead peroxide and dilute sulfuric acid (1) yielded deep red solutions which did not give the characteristic green color with ammonia and from which no quinone sulfate could be isolated. This reaction is still being studied.

Action of Chlorosulfonic Acid on 6-Aminoquinoline.—20 Gm. of chlorosulfonic acid was poured cautiously onto 4 Gm. of the aminoquinoline and allowed to stand for 15 minutes. The reaction mixture was then heated over a low flame for 5 minutes. On cooling, it was poured cautiously onto 50 Gm. of cracked ice. A yellow precipitate resulted which was collected and thoroughly washed with cold water. Yield 5.5 Gm. or 92–93%. Melting point 173–174°. This substance is only very slightly soluble in water and alcohol and practically insoluble in ether, acetone, chloroform and benzene. In the absence of a satisfactory analysis, it is being tentatively reported as 6-aminoquinoline-5-sulfonechloride.

6-Aminoquinoline-5-sulfonic acid.—The compound obtained above was dissolved in 10% NaOH solution and then made slightly acid with HCl. A precipitate of yellow crystalline scales resulted in practically a quantitative yield. It decomposed above 230°. This agrees with the data of Cybulski and co-workers (5). It is only very slightly soluble in water and alcohol and practically insoluble in ether, chloroform, acetone and benzene. Its water solution has a greenish fluorescence.

SUMMARY.

1. 6-Aminoquinoline is produced in good yields by the reduction of the corresponding nitro compound with stannous chloride, decomposing the tin double salt with alkali and extracting with ether.

2. The amino compound is readily diazotized but attempts to convert the diazonium compound to the hydroxy compound have been unsuccessful.

3. Oxidation of the aminoquinoline in a manner similar to the hydroxy compound does not yield the 5,6-quinone.

4. 6-Aminoquinoline is not sulfonated by concentrated sulfuric acid or oleum of less than 20% but it reacts readily with chlorosulfonic acid.

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THE ASSAY OF SPIRIT OF CAMPHOR.*

BY O. GISVOLD.**

The U. S. P. XI method of assay for camphor in spirit of camphor has proven very unsatisfactory. E. M. Plein and C. F. Poe[1] report studies of this assay, show that the official method is unsatisfactory and recommend a method that is very similar to the one presented in this paper. Since this problem was under investigation at the time Plein and Poe reported their results, it seemed desirable to present the findings in this laboratory.

The dinitrophenylhydrazine reagent when prepared according to the U. S. P. XI is very unstable. About one-half of the reagent crystallizes out upon standing over night. When this half-strength reagent was used in the assay of spirit of camphor, very low results were obtained. *First*, because the camphor sublimed into the reflux condensor and *second*, because an insufficient amount of dinitrophenylhydrazine was present to insure complete combination with all camphor. A freshly prepared one and one-half per cent reagent also gave very unsatisfactory results.

The addition of either methyl or ethyl alcohol increased the yield of the dinitrophenylhydrazone. It was found that 25 per cent methyl alcohol was a very satisfactory solvent for the preparation of the one and one-half per cent dinitrophenylhydrazine reagent of the U. S. P. XI. This reagent is stable for some time.

The following procedure gave good results. Two cc. of the spirit of camphor were pipetted into 75 cc. of the reagent. The mixture was refluxed on a steam-bath for two hours. A Hoffmann distilling head was attached to the flask and the mixture heated at such a rate that 15 to 17 cc. of alcohol were distilled in a period of one-half hour. Fifty cc. of 5 per cent sulfuric acid were added to the flask and the mixture allowed to cool. An additional 150 cc. of 5 per cent sulfuric acid were added and the mixture allowed to stand over night. The derivative was collected in a tared fritted-glass filter funnel (No. 3) and dried to constant weight at 100°.

The derivative can readily be washed from the fritted-glass filter funnel with chloroform and the funnel can be used repeatedly without retaring.

This procedure was used in the analyses of accurately prepared 8, 10 and 12 per cent spirits. These results, together with those obtained using the U. S. P. XI and the Plein and Poe methods, are tabulated below.

U. S. P. XI Method.	Plein and Poe Method.	Modified Method.
	Eight per cent spirit.	
6.44	7.91	7.88
7.66	7.92	7.81
6.49	8.00	7.95
7.72	8.02	7.85
Av. 7.08	Av. 7.96	Av. 7.87

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