

SOME STUDIES IN COUPLING
OF ALIPHATIC NITROCOMPOUNDS

A thesis submitted to the Chemistry
Department of Washington and Lee
University as a partial fulfillment
of the requirements for the degree
of Bachelor of Science in Chemistry.

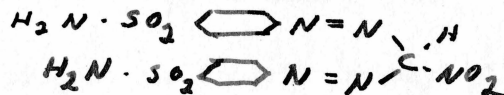
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Under the direction of Professor J.R. Taylor

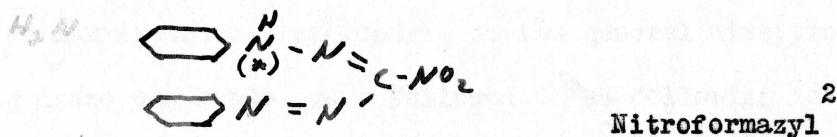
INTRODUCTION

The object of this thesis was the production and isolation of a new compound. The structural formula of this compound is:



This problem ^{was} set forth by Merck and Co. because they believe that this compound may have properties similar to sulfanilamide.

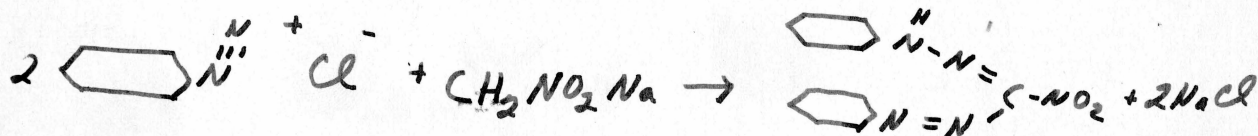
In an article by Hass and Riley¹, a coupling product similar to the one desired was mentioned. Its formula is,



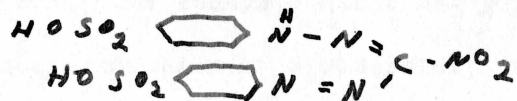
Thinking along the lines that the hydrogen on N (*) is mobile i. e. that it could easily jump over to the methane carbon (depending on conditions of acidity) causing the double bond to move in between the two N's, thereby giving the exact molecular arrangement desired. The method of producing this compound was looked into.

² Bamberger worked on this compound and his general outline was used in trying to produce the new compound.

Although the homologues of nitromethane will not yield a di-coupling product, nitromethane will. The compound was obtained by the action of benzene diazonium chloride on sodium nitromethane.



By the substitution of diazotized sulfanilic acid for diazotized aniline it is hoped to produce the product,

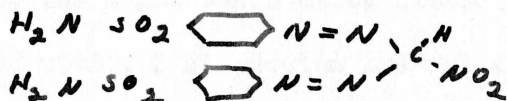


This product reacted with thionyl chloride or phosphorous pentachloride should yield the corresponding sulfonyl chloride. The sulfonyl chloride added to ammonia will yield the compound desired.

The literature ² did not give any detailed account of the procedure for making the nitroformazyl, so the general directions ⁴ for coupling diazo compounds were followed. The following is a detailed account of the experimental procedure followed in trying to make the desired compound.

EXPERIMENTATION

The object of this thesis, as it was pointed out in the introduction, was the production of a completely new compound with the following structural formula.



As there were no definite directions to work by, the first step in the preparation was to find out what the best hydrogen ion concentration would be to carry out the coupling of the diazotized sulfanilic acid with the sodium nitromethane.

The sodium salt of sulfanilic acid was made and dried in an oven at 100-105°C. 5 gm. (.025 moles) of sodium sulfanilate was dissolved in 17 ml. of water, 2 gm. of sodium nitrite was added and the solution was cooled to 0-5°C. Simultaneously 25 ml. of 4N hydrochloric acid was cooled to 0-5°C. The sulfanilic acid solution was slowly added to the hydrochloric acid, the temperature being held down to 5°C. or below. 1.5 gm. (.025 mole.) of nitromethane was divided into approximately three parts and added to .5 ml., 1 ml., and a large excess of 20% sodium hydroxide. Then the cold diazotized sulfanilic acid was added to the three solutions of sodium nitromethane. The first concentration of sodium nitromethane yielded a yellow color and a precipitate which disappeared later. In the second there was an orange color and precipitate. The third was dark brown in color with no precipitate. Benzene and ether extractions were tried on second solution plus precipitate, but the precipitate wasn't taken up in

either case. Evaporation of both solvents yielded nothing. The precipitate was then filtered off but was not soluble in hot alcohol. Upon dissolving precipitate in hot water and evaporating to dryness the substance left no residue on ignition.

The coupling was tried again using nitric acid instead of hydrochloric acid with 1.5 ml. sodium hydroxide (20%) to 1.5 gm. nitromethane, and 5 gm. of sodium sulfanilate. The precipitate was filtered, dissolved in water, refiltered, chilled, a very small amount of crystals were obtained and filtered off. They didn't melt up to 240°C. but apparently left no residue on ignition.

The coupling was tried again as above, but in a more acid solution in hopes of increasing yield. There was no yield and only a slight coloring of solution.

Following a suggestion made by Dr. Taylor, .05 moles of cold diazonium nitrate was suspended in 30 ml. of cold ethyl alcohol and added to .05 moles of sodium nitromethane in 20 ml. of 30 % methyl alcohol containing .1 moles of potassium hydroxide, a reddish brown substance precipitated. The precipitate was filtered, but wouldn't dissolve or be extracted by hot ethyl alcohol, ether, acetone, or benzene. It was very soluble in water. The precipitate was dissolved in a minimum amount of water, but hot alcohol didn't precipitate anything. The solution was made acid and evaporated on a water bath. The residue was extracted with alcohol and the alcohol became colored leaving almost a white residue. When alcohol was chilled crystals came out of solution. These crystals were put on a filter paper to dry. By the next morning there was nothing on the filter paper. It had sublimed and completely disappeared.

The mother liquor was evaporated yielding a very viscous substance. This viscous substance upon addition of absolute alcohol yielded yellow orange crystals insoluble in hot alcohol. When filtered these crystals were insoluble in benzene, ligroin, ether, and ethyl acetate. On treatment with ethyl acetate the color changed to the red of the original solution. Working on the assumption that only the pure salt of product was left, a weighed amount was added to a weighed amount of camphor in order to get an estimation of the molecular weight.⁵ The crystals proved to be insoluble in the camphor. Then a regular freezing point depression method⁶ was tried, but as solution got cold yellow crystals came down. This ruined the determination and no molecular weight could be obtained.

In hopes that maybe a neutral solution would yield a precipitate, .1 moles (17.3 gm.) of sulfanilic acid was diazotized by first dissolving in .200 moles of sodium hydroxide, adding 10 gms. of sodium nitrate and cooling to 0-5°C. .05 moles (3.05 gm.) of nitromethane was added to .300 moles of sodium hydroxide. Sulfanilic acid solution was added to .400 moles (33ml. of concentrated diluted to 100 ml.) hydrochloric acid, which was previously cooled to 0-5°C. The temperature of the whole was kept at 0-5°C. and solution was allowed to stand overnight. As usual nothing came out of solution.

The solution was evaporated to about 200 ml. on a water bath, filtered, took residue (crystals), and using a continuous extractor extracted (about 5 hours) with acetone (dried over calcium chloride).

The small amount of white precipitate in bottom of boiling flask contained no nitrogen when subjected to a sodium fusion. The acetone was evaporated to a very little bit, absolute alcohol was added, and crystals appeared which turned red litmus blue. Elementary analysis showed presence of nitrogen and sulfur.

Weighed crystals for a molecular weight determination, dissolved in a weighed amount of water using a Beckmann thermometer to measure freezing point change.

Wt. of material = .0901 gm.
Wt. of water = 13.075 gm.

F. P. of pure water by Beckmann = 1.553
F. P. of solution by Beckmann = 1.658
Freezing temperature change = .105

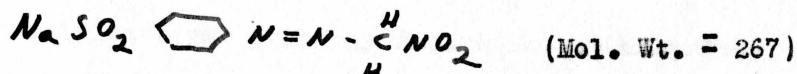
$$M = \frac{1000 K_f W_{\text{salt}}}{W_{\text{water}} \Delta T}$$

$$M = \frac{1000(1.855)(.0901)}{(13.08)(.105)} = 121.7 \text{ gm.}$$

Solution looked like it had suspended particles in it. The solution was filtered, a given amount was weighed out (10.4965 gm.) water was evaporated off, weight of crystals was gotten (.0768 gm.), and weight water was gotten by subtraction (10.42 gm.).

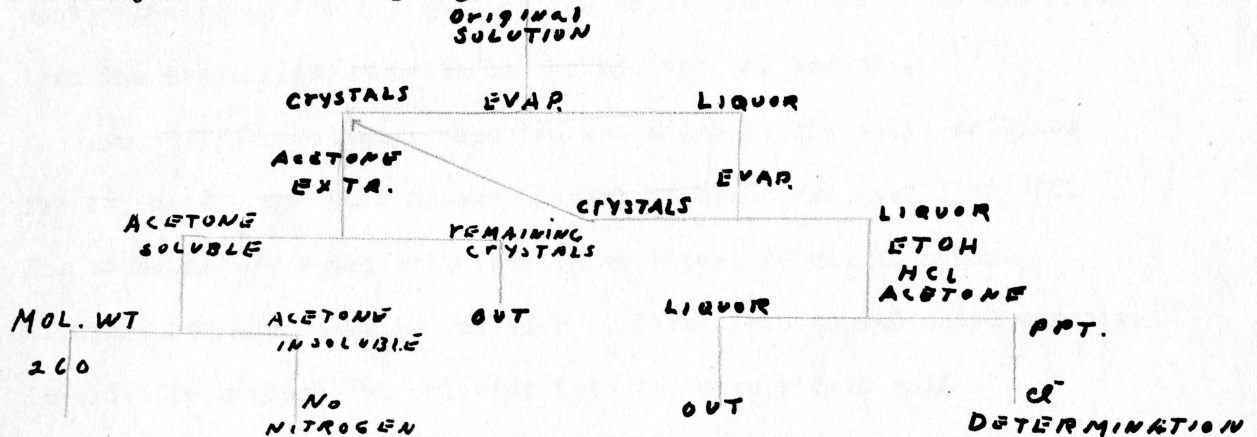
$$M = \frac{1000 (1.855)(.0768)}{(10.42)(.105)} = 130.0 \text{ gm.}$$

The material was a sodium salt therefore the M is an average of two ions i.e. molecular weight is 260.0 gm. (2X130). The single coupling product would be a possibility for this molecular weight.



A nitrogen determination by a modified Kjeldahl method was tried which converted all the nitrogen to Ammonia. .0609 gm. of salt, 1 gm. salicylic acid, 10 gm. of sodium thiosulphate, and .5 gm. copper sulphate were put into a reaction flash with 25 ml. of concentrated sulphuric acid. This was boiled until all of the carbon was oxidized off. Then solution was made basic with 20% sodium hydroxide and ammonia was driven off into standard hydrochloric acid. Something went wrong because more nitrogen came off than anything theoretically possible (approx. 24.6%)

The following diagram indicates the steps taken in separation and analysis of this coupling.



The precipitate gotten by the addition of alcohol, acetone, and hydrochloric acid was dried and tested for chloride ions. This test was positive and a chloride determination was run.

$$\begin{aligned}
 .2727 \text{ gm. salt} &= .6364 \text{ gm. AgCl} \\
 .6364 \text{ gm. AgCl} &= .1571 \text{ gm. Cl} \\
 \frac{.1571}{.2727} \times 100 &= 57\% \text{ Cl}
 \end{aligned}$$

The percentage chlorine in sodium chloride is 61.8%. It was decided that the precipitate was probably impure sodium chloride. An elementary analysis showed no sulphur. Then it was decided to attack the problem differently.

Another lot of sulfanilic acid was diazotized exactly as before, except the temperature was kept at -10°C . and in the whole reaction was not allowed to rise above -4°C . After the coupling the color was a brighter red than before, so the temperature must have had some effect on the reaction. Every bit of solution was evaporated and dried in an oven at $100-105^{\circ}\text{C}$.

If the acid group of the sulfanilic acid is converted into the chloride it is highly possible that benzene would extract the sulfonyl chloride from impurities. Sulfonic acids are converted into their chlorides by the action of thionyl chloride or phosphorous pentachloride on the dry salt of the acid. The chloride is converted into the corresponding amide by the addition of ammonia.

An excess of thionyl chloride was added to the salt, refluxed for two hours, and then excess thionyl chloride was distilled off. The resultant mass was extracted three times, 20 ml. at a time, with dry benzene, solution was then filtered into concentrated ammonia. in order to convert the chloride into the more stable amide.

The supposed amide was not soluble in benzene, but it was soluble in ammonia water. Evaporation to dryness gave a mixture of amide and ammonium chloride. Fractional crystallization was tried with very little success. Absolute alcohol was added to the mixture of crystals and a low yield of white crystals were obtained (these were turned into Dr. Taylor).

As thionyl chloride is not as strong chlorinating agent as phosphorous pentachloride, it was decided to try the action of this compound on the remainder of the salt. The salt (53 gm.) was redried

and mixed intimately with phosphorous pentachloride (45 gm.).

On warming the mixture (125°C.) the reaction got out of hand, reacted violently and charring occurred.

A small amount of the solid was put on ice and added to concentrated ammonia but nothing visible happened i. e. none of the white fumes of reaction.

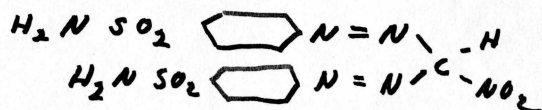
Then the whole of the reacted mass was extracted with dry benzene, and benzene solution was charcoaled, leaving a cherry-red solution. This solution was added to concentrated ammonia and the benzene layer turned cloudy and muddy looking. On evaporation of benzene a red viscous oil was obtained, soluble in ether and acetone, but no crystallization from either. It was decided that the charring might have effected result, so the diazotization was started again.

.1 moles of sulfanilic acid was diazotized and coupled exactly as before. The resulting solution was evaporated and salt dried 100-105°C. 45 gm. of phosphorous pentachloride was added to 49 gm. of dry salt. At this point the dry salt, one fourth mixed, started to get hot and a gas started to evolve. Luckily the reaction subsided, then dry benzene was added to the mixture. Then the rest of the salt and chloride were mixed and added to the flask. The benzene mixture was refluxed four hours. The benzene was poured off and salt was extracted twice with dry benzene. The benzene solution was filtered and dry ammonia was added to the red colored benzene. Voluminous precipitation occurred from the benzene. The precipitate was dried and put in a continuous extractor using dry benzene. The benzene solution was evaporated to a small volume and no crystallization occurred, (This was turned into Dr. Taylor along with crystals used

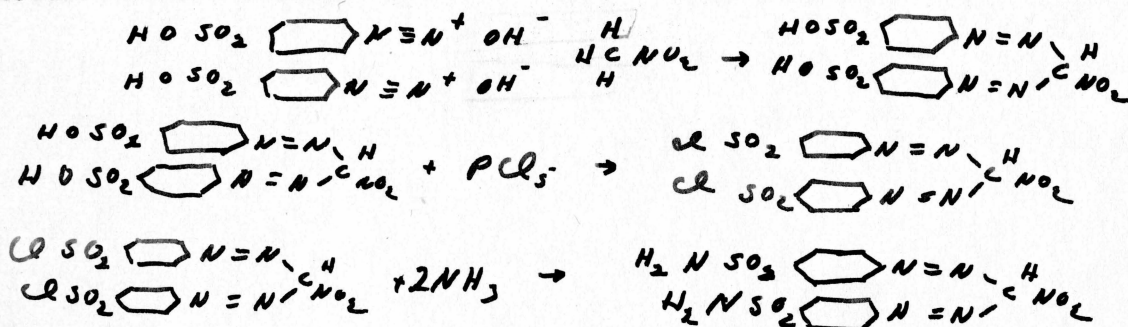
in the benzene extraction). It is interesting to note that when water was added to the phosphorous pentachloride brown fumes came off similar to nitrogen dioxide. This concluded the experimental work.

SUMMARY

It is advisable here to review the reactions in the formation of the new compound. It was desired to make the compound.



by the action of diazotized sulfanilic acid on sodium nitromethane. Then forming the corresponding sulfonyl chloride which is easily converted into the amide.



The di-sulfonic acid formed, if it is formed, is so water soluble that it cannot be separated from the inorganic salts formed in its formation. The corresponding chloride, if formed, is evidently soluble in dry benzene. The amide obtained, if obtained, is apparently very slightly soluble in benzene, but extremely water soluble.

From the reactions, the change in color upon coupling, and violent reaction with phosphorous pentachloride, show that it is not impossible to make this compound although the author couldn't isolate definite compounds. The author firmly believes that time is the only factor that hinders the isolation of the desired compound.

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