

THE SANDMEYER REACTION (NITRILE)  
WITH  
P-TOLUIDIN-META-SULFONIC ACID

Thesis

by

Earl D. Stewart

In partial fulfillment of the requirements  
for the degree of Bachelor of Science  
in Chemistry

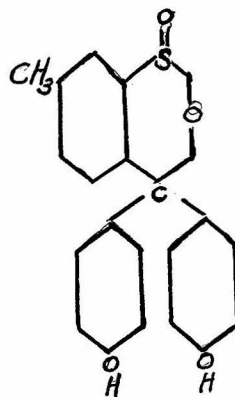
California Institute of Technology

Pasadena, California

1925

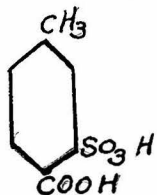
The Sandmeyer Reaction (nitrile) with Para-toluidin-  
meta-sulfonic acid

The original purpose of this work was to study  
compounds of the type,

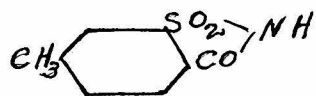


with a view to their use as indicators. The homologous  
compounds prepared from benzenesulfonic acid are of  
course well known, being first prepared by Remsen and  
his pupils who gave them the name "sulfonethaleins".  
The compound, whose formula is given above, was prepared  
by Lyman in 1894 ( Am. Chem. J. 16, 513 et seq.). He  
called it "phenol-para-methyl-sulfon-phtalein" and noted  
that "in alkaline carbonates, more readily than in caustic  
alkalies, it dissolves to a red liquid much like an alka-  
line solution of phenolphthalein", (loc, cit. p. 516). No  
further reference to the compound has been found in the  
literature.

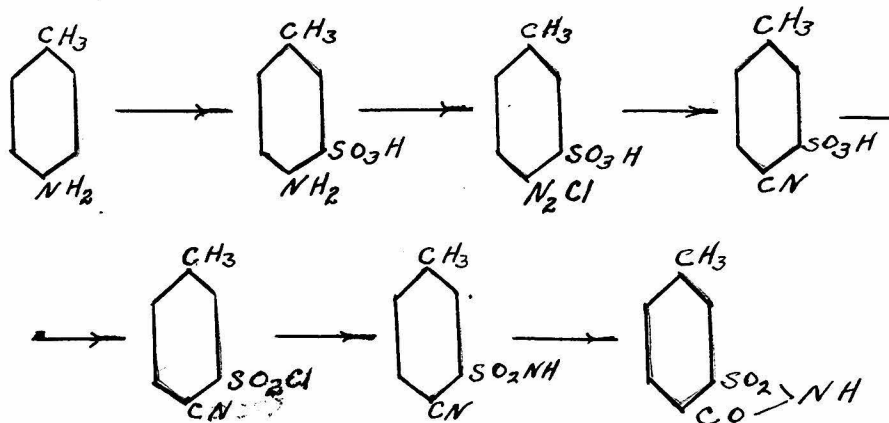
Lyman prepared this substance from sulfo-toluic acid,  
which he prepared according to the method de-  
scribed by Randall in 1891 ( Am. Ch. J. 13, 256  
et seq.). Randall prepared the acid from meth-

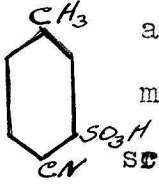
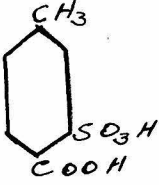
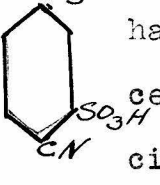


yl saccharin,



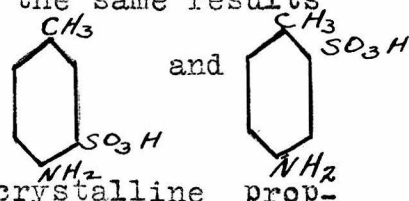
which he obtained from the Badische Anilin Soda Fabrik, the owners of the patent on the substance, (D.R.P. 48583). The process described is as follows, (B. 22, vol. 3, Ref. 719),



It seemed likely that it might be possible to follow this procedure as far as the compound,  and by hydrolysis to form, . Inasmuch as  had not been described except in the patent literature, (loc. cit.), it was thought desirable to attempt to isolate it.

The first step, the sulfonation of p-toluidine, was first carried out by von Pechman (A. 173,195 etseq.). His method was to use fuming sulfuric acid, heating the sulfonating mixture to 180° until SO<sub>2</sub> began to come off.

This method was tried with substantially the same results as von Pechman describes. The two acids were formed in about equal quantities.



( The acids are differentiated by their crystalline properties and form, the ortho acid being heavy rhombic crystals and the meta acid light, fluffy needles. See v. Pechman, loc.cit. 197, also Metcalf, Am. Ch. J. 15, 303) Considerable residue without easily identifiable crystalline form remained and there was evidence of considerable charring. The yield was very poor - less than 20%.

Neville and Winther also investigated the sulfonation of p-toluidine ( B. 13,1947.). Their method seemed on the whole the most satisfactory and with some modifications was used in this work. The reaction was less violent and more easily controlled. Charring was practically eliminated, the acid was lighter in color and the yield was much improved - 30 - 35%.

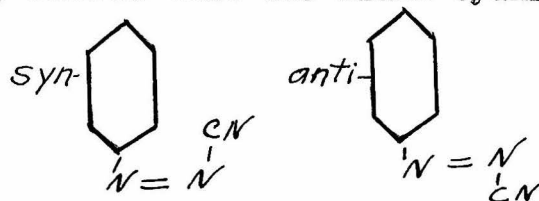
Separation of the sulfonic acid by the use of barium hydroxide seemed most satisfactory although both lead and calcium salts were also tried. The lead salt of the sulfonic acid refused to crystallize out. Only a sticky, oily liquid resulted.(For Ca see experimental part). Since some toluidine sulfate is also present the acid cannot be crystallized from the first solution, while the alkali salts are all so soluble that they can be crystallized only with difficulty.

(see Metcalf loc. cit.)

It was decided, at first, to carry out the diazo-reaction in alcoholic solution as described by Metcalf (loc. cit. 304). A trial showed that the method was slow, unsatisfactory and rather wasteful of sodium nitrite. In subsequent experiments the sulfonic acid was diazotised in aqueous solution very satisfactorily. The diazonium compound is quite soluble in water at room temperature but is only slightly soluble in water at 0 - 5°. At the latter temperature it separated out as a pinkish white, granular to flocculent precipitate.

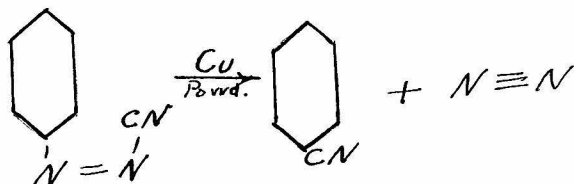
The Sandmeyer reaction was first attempted according to the method used for the formation of p-tolunitrile, given by Harry Fisher. (Laboratory Manual of Organic Chemistry, p. 187). Dark colored solutions were the result, showing much tarry matter and gummy material on evaporation. No crystallization of any value could be performed from any of these preliminary experiments.

Hantsch (B. 28, 666) showed that the diazo cyanides may exist in two forms,

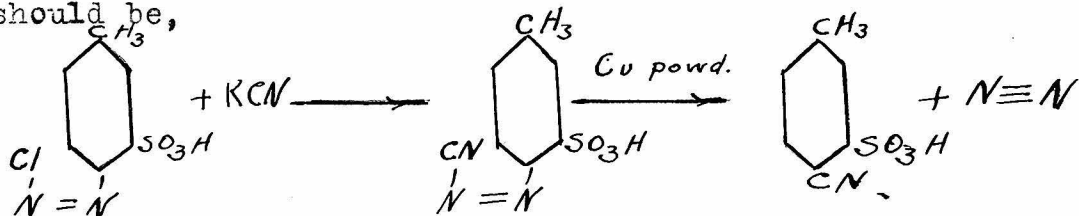


He further showed that the syn- forms are formed at low temperatures (below 5°) and that they go over on standing to the anti- forms especially at higher temperatures. He also showed that the syn- forms decompose on the addit-

ion of copper powder according to the equation,



(loc. cit.) Since the ordinary Sandmeyer reaction gave such inconclusive results, the formation of Hantsch's syn-diazo cyanide was attempted. Theoretically the reaction should be,



However no gas was given off even on heating the solution. It would seem probable that this is a case of steric hindrance and that the rate of formation of the syn-compound at these low temperatures is very small. Hantsch worked principally with sulfanilic acid in his experiments and as far as I have been able to determine, the reaction has not been carried out with a sulfonic acid group ortho to the amino group.

Since Hantsch's method gave no useful results a method for making *p*-tolunitrile given in Organic Syntheses Vol IV p. 69 was used. This involved first forming a solution of  $\text{NaCu}(\text{CN})_2$ . Four runs were made varying the conditions as follows,

1. Diazonium solution neutralized and run into alkaline  $\text{NaCu}(\text{CN})_2$ .

2.  $\text{Na}_2\text{CO}_3$  added to the  $\text{NaCu}(\text{CN})_2$  solution and diazonium salt suspension added at room temperature. Mixture heated to boiling.
3. Same as 2 except that the cyanide solution was boiling when the diazonium salt was added. Boiling continued for five hours.
4. Same as three except that evaporation was done in a more acid solution.

The first method was not satisfactory. There was apparently little or no decomposition. The second method was also unsatisfactory, but not for the same reason. The copper salts crystallized out along with the product and were difficult to remove. The third method yielded a considerable quantity of paper thin, dark red, hexagonal plates. These plates fused to a brown liquid on platinum foil and finally charred, giving an odor resembling nitrobenzene. They became opaque and white on standing but retained their crystalline form. Qualitative tests gave the following results,

N -- present

S -- present

Halogen = a trace.

The halogen test was very faint and might easily have been due to  $\text{NaCl}$  occluded or dried on the surface of the crystals.

The fourth method was essentially the same as the

third. A fresh  $\text{NaCu}(\text{OH})_2$  solution was made up and the solution boiled as before. More acid was added to precipitate the copper salts than in run No. 3. Consequently boiling to remove  $\text{H}_2\text{S}$  and to evaporate was done in a more acid solution. Concentration was carried further than in previous experiments and on cooling the dish became filled with long thin needles almost forming a thin jelly. On filtering off and redissolving and allowing them to recrystallize slowly from dilute solution the same thin hexagonal plates appeared as before. These, however, were lighter in color (nearly colorless). On drying they lost water and became opaque. This phenomenon was also noticed on dissolving them in water by the aid of heat. They first seemed to lose water and then to dissolve. In cold water they dissolved without becoming opaque.

An analysis for nitrogen by the Gunning-Arnold-Dyer modification of the Kjeldahl method gave the following results,

I 6.25% N

II 3.4%

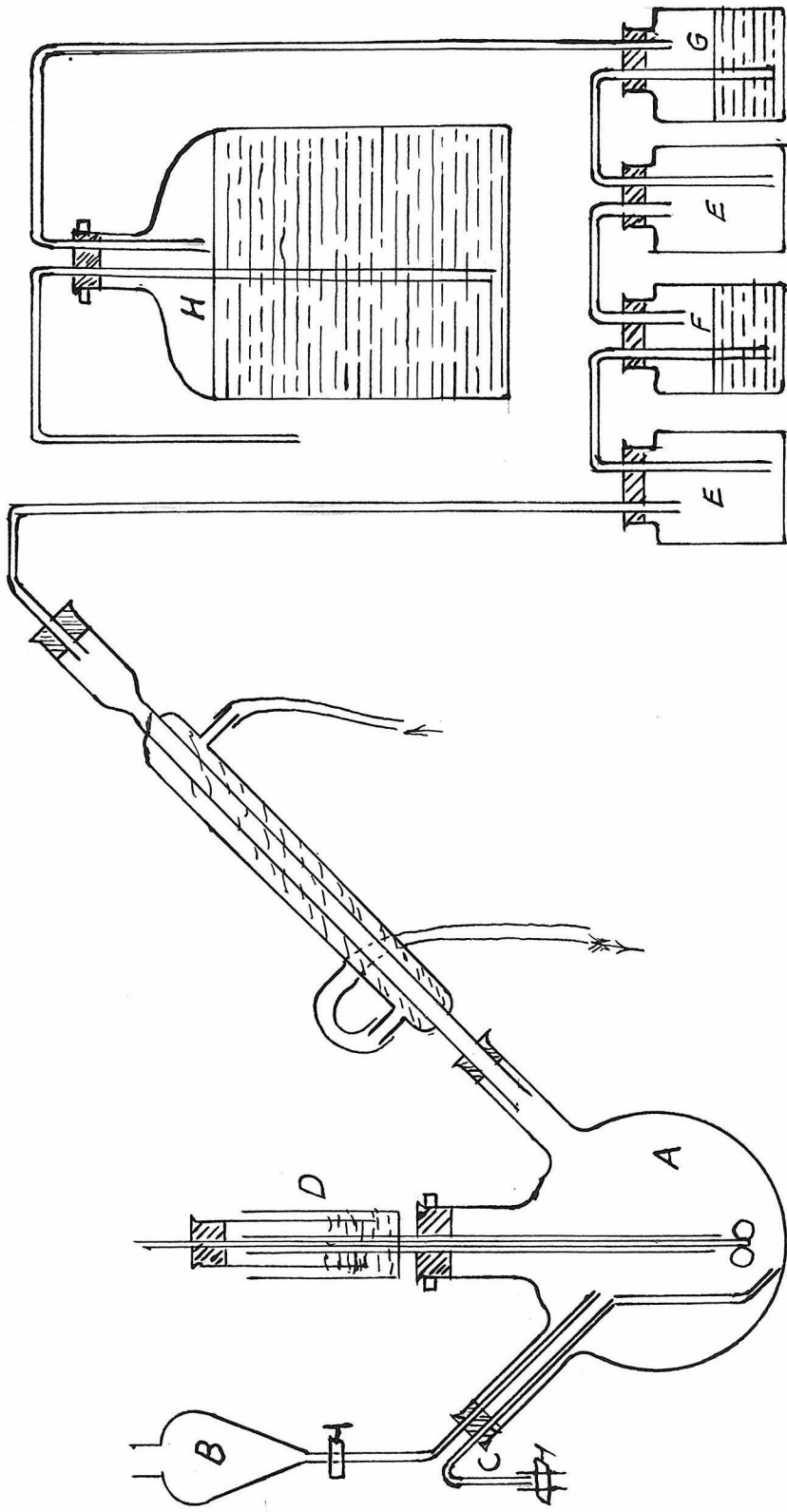
III 5.65%

Calculated for  $\text{C}_6\text{H}_3 \begin{cases} \text{CH}_3 & (1) \\ \text{SO}_3\text{H} & (3) \\ \text{CN} & (4) \end{cases}$  7.1%

Calculated for  $\text{C}_6\text{H}_3 \begin{cases} \text{CH}_3 & (1) \\ \text{SO}_3\text{Na} & (3) \\ \text{CN} & (4) \end{cases}$  6.4%

Determination No. II was not reliable since the mercury





### Apparatus used for Study of Sandmeyer Reaction

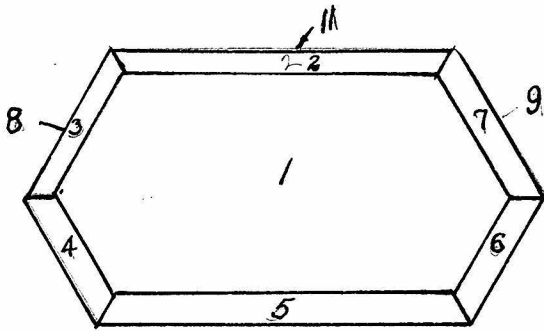
- A - Reaction Flask
- B - Separatory Funnel Reservoir
- C - Safety Tube
- D - Mercury Seal
- E, E - Safety Bottles
- F - Standard  $H_2SO_4$
- G - Strong KOH
- H - Gasometer

used as a catalyst in the oxidation process was not completely precipitated as HgS. Some of it came down on adding water to the oxidation liquid and when Na<sub>2</sub>S was added a light brown precipitate formed instead of a black one. The presence of sodium in abundant quantity was proved by the potassium pyroantimonate test. (Noyes, Qualitative Chemical Analysis 9th ed. P. 128). This analysis would indicate that the hexagonal plates were the sodium salt of the para-nitrile of meta-toluene sulfonic acid.

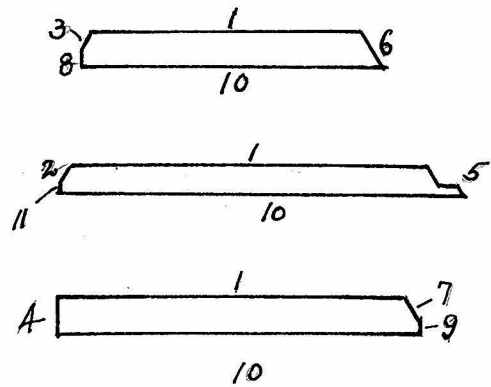
The crystals are probably triclinic although it is difficult to say definitely, since the crystal measured had very low symmetry. Measurements of the face angles are given on the following page. (The measurements were by Dr. Linus Pauling of this laboratory)

In order to discover to what extent the reaction goes to completion, a decomposition was carried out in the apparatus shown in the figure. The result of a run using fourteen grams of the sulfonic acid were as follows,

No NH<sub>3</sub> was given off. This was tested by absorption in standard H<sub>2</sub>SO<sub>4</sub> and back titrating with standard NaOH. This would not give dependable results if the amount of NH<sub>3</sub> were very small. Consequently the acid was made alkaline



Face 5 broken stepwise



Section 8,3,1,6

8- 291° 20'  
 3- 326° 57'  
 1- 26 11  
 6- 289 2  
 1- 11 14 x

Section, 9714

9- 282° 15'  
 7- 318 28  
 1- 15 11 x  
 4- 297 8  
 1- 20 47 x

Section 5,1,2,11

5- 299° 8'  
 1- 17 16  
 11- 282 29  
 2- 315 25  
 1- 23 44 x

Angle 4,5

4- 106° 40'  
 5- 49 39

Angle 4,8

4- 106 48  
 8- 166 39

Angle 5,6

5- 200 54  
 6- 140 42

Angle 6,7

6- 198 7  
 7- 137 39

Angle 7,2

7- 193 31  
 2- 140 47

x indicates a poor reflection.

The difference between two successive readings is the angle between the corresponding faces.

and distilled, - with the same results. The gas measurements were not so conclusive as the absorption system used was not completely absorptive nor were the connections completely airtight. The data obtained were as follows,

Air displaced by heating to boiling, -----3065 c.c.

Air displaced during addition of diazonium  
compound,-----1550.

During the boiling and refluxing a steady leak kept up so that the figures on the gases evolved are inconclusive beyond the point given above. The gas evolved during the addition corresponds roughly to the theoretical volume of nitrogen which should be given off during the reaction (Theoretical Nitrogen--- 1700 c.c.).

For future work on this point it might be suggested that a similar apparatus be used but with a more efficient absorption bottle and better gasometric appliances.

#### Conclusion.

From this work it may be concluded that the Sandmeyer reaction on p-toluidine-m-sulfonic acid goes nearly to completion. From the manner in which the experiments were carried out it would seem likely that Hantsch's diazo cyanide was first formed but is at once transformed into the nitrile with the loss of  $N_2$ , these conditions being brought about by heat and alkaline solution (see Hantsch, B. 28,666 et seq.)

This work was carried out at the suggestion and with the aid of Professor H.J. Lucas, to whom many thanks are due for whatever success may have been attained in it. The aid of Mr. Linus Pauling, who made the crystallographic measurements, is also much appreciated.

### Experimental Part.

#### Sulfonation of p-toluidine

One mol of  $H_2SO_4$  (as concentrated sulfuric acid) was placed in a 1500 c.c. flask equipped with a mechanical stirrer and a thermometer, and surrounded by a cold water bath. 107 gms. of p-toluidine (one mol) were melted and poured very slowly into the sulfuric acid, stirring all the while. The flask was cooled as often as necessary to prevent the reaction from becoming too violent. When all the p-toluidine had been added the water bath was removed and the flask heated to a temperature of  $210^{\circ}$  -  $230^{\circ}$  and kept there during the remainder of the reaction. (A naked flame was used in this experiment but an oil bath would probably work better especially as the reacting mass becomes more nearly solid). The heating was continued over a period of about two hours during which time the contents of the flask became gray-green in color and extremely viscous. When they became too thick to stir the stirrer was removed and the

heating cautiously continued until the mass was nearly ready to solidify in the flask. The contents were then emptied as completely as possible in to cracked ice ( about 500 c.c.). The portion that solidified in the flask was washed out when cool, using the minimum quantity of water. The whole mixture was then set aside for twenty-four hours to crystallize as completely as possible. The resulting crystal mass was separated from the spent acid by suction. ( The spent acid contains some sulfonic acid which may be removed, but the quantity is quite small and is hardly worth the trouble and material to obtain it. In case considerable quantity of p-toluidine were sulfonated it might pay to do so, in which case the same procedure can be used as for the crystallized portion.) The crystals are dissolved in 1500 c.c. of water in a three liter flask and  $\frac{1}{2}$  mol of  $Ba(OH)_2$  added plus about 20% or enough to completely precipitate the sulfuric acid remaining with the crystals. ( $BaCO_3$  may be used but the mixture requires boiling and is somewhat troublesome on account of the gases evolved.  $CaO$  forms  $CaSO_4$  which is soluble enough to remain in solution and crystallize out with the sulfonic acid.) The  $BaSO_4$  is filtered off, the precipitate washed twice by boiling with water and filtering and adding the washings to the filtrate. (Any toluidine not reacting can be recovered by distilling the Ba precipitate with steam. This

affords a good check on the completeness of the reaction. About 20 gms of toluidine were recovered in the run described.) The filtrate was now a light yellow liquid and slightly alkaline in reaction. Dilute  $H_2SO_4$  was then added until a precipitate ceased to form ( a slight excess does no harm). The barium sulfate was filtered off as before and the solution ( now about three liters) was evaporated to about 800 c.c. and set aside to crystallize.

After about twenty-four hours the dish was filled with long needles, light yellow in color. Their bulk is deceptive for they shrink tremendously on filtering. Successive crops of crystals were taken off each day until microscopic examination showed that other substances were crystallizing out in quantities comparable to that of the sulfonic acid. Recrystallizing gives a lighter colored product. Yield, 60 - 65 gms of p-toluidine-m-sulfonic acid, 33% of theoretical. ( If the final mother liquor is evaporated to dryness and saved and combined with similar residues from other runs, and recrystallized again considerable more sulfonic acid may be recovered.)

Preparation of toluene-meta-sulfonic acid para-diazonium chloride.

As the para-toluidin-meta-sulfonic acid was obtained it was a coarse crystalline powder. In the preliminary experiment, ten gms. of the acid were placed in a 600

c.c. beaker surrounded by ice water. A mechanical stirrer was provided and 100 c.c. of water were added to the acid. 3.42 gms. of anhydrous sodium carbonate were added and the mixture stirred until effervescence had ceased and the acid had gone into solution. 4.75 gms of HCl (13 c.c. of 31.5% acid) were then added slowly. A thick yellow cream resulted. The whole object of this procedure is to get the sulfonic acid into as fine a state of subdivision as possible since it is only slightly soluble in water at ordinary temperatures.) The theoretical quantity of  $\text{NaNO}_2$  was now added in the form of a dilute solution (0.075 gms per c.c.) through a dropping funnel. The reaction was considered complete when the reacting mixture gave a permanent blue color with starch and potassium iodide T.S. ( Since the reaction goes slower toward the end, the mere production of a blue color does not necessarily mean the end of the reaction. The flow of sodium nitrite should be stopped and the reacting solution stirred for a minute or two and tested again. Only when the solution contains free nitrous acid should the reaction be considered complete. Even then there may be a few yellow crystals remaining in the bottom of the beaker.)

#### Preparation of $\text{NaCu}(\text{CN})_2$ solution.

Fifty gms. of  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  ( 1/5 mol) were dissolved in 100 c.c. of water and 13 gms of NaCl added. The solution was carried out in a 600 c.c. beaker by heating



and stirring with a mechanical stirrer. 11 gms. of  $\text{NaHSO}_3$  and 7 gms. of  $\text{NaOH}$  were dissolved in 100 c.c. of water and added slowly to the boiling copper solution. When entirely added and the supernatant liquid was of a very light blue color ( if not more  $\text{NaHSO}_3$  should be added) the heating and stirring were stopped and the  $\text{CuCl}$  was washed by decantation or by suction and washing on the filter. When the wash water appeared clear the cuprous chloride was mixed with about 200 c.c. water and 26 gms. of 96 - 98%  $\text{NaCN}$  dissolved in 100 c.c. of water were added. The copper goes into solution with the evolution of heat. Some  $\text{Cu}(\text{OH})_2$  may appear in the solution but may be filtered off. The filtering should be done into a tared bottle so that the solution may be weighed out for the Sandmeyer Reaction. ( This is essentially the same method as is given in Organic Syntheses Vol. III p. 33 and Vol. IV p. 69.)

#### The Sandmeyer Reaction (nitrile)

The theoretical quantity of  $\text{NaCu}(\text{CN})_2$  ( one mol of  $\text{Cu}$  to one mol of diazonium compound) was placed in a three liter flask equipped with a mechanical stirrer. 6.8. gms. of anhydrous sodium carbonate was added (sufficient to neutralize the  $\text{HCl}$  in the diazonium chloride) and the solution boiled. When the boiling commenced the diazonium compound was run in from a separatory funnel at a rate sufficient to introduce the whole in about fifteen minutes. The cyanide solution was kept boiling during the

17  
time of addition of the diazonium compound. The stirring was stopped when the addition was complete and the dark red liquid refluxed for five hours.

When the solution had cooled dilute HCl was added carefully until precipitation had ceased ( if too much acid is added the precipitate dissolves). HCN<sup>f</sup> is evolved during the addition of the acid. The precipitate of CuCl was filtered off and H<sub>2</sub>S passed into the filtrate until it was saturated. The solution was now heated to boiling to remove H<sub>2</sub>S and the CuS precipitated was filtered off. The filtrate was evaporated until a portion of it crystallized on cooling and then set aside to crystallize.

The first crop of crystals was removed and washed once by sucking as dry as possible, removing the suction, moistening the crystals for an instant and reapplying the suction at once. The crystals are so soluble that any other treatment dissolves them almost immediately. The mother liquor and washings were set aside to crystallize by evaporation. The first crop were dissolved in water and recrystallized. The crystals separated as transparent, rose colored, hexagonal plates. The crystals can be grown larger by slow crystallization in a deep dish. Some difficulty is involved however as the solution shows a remarkable<sup>f</sup> tendency to creep over the sides of the dish.

Sandmeyer Reaction with gas absorption.

The reaction was carried out as given before but in the modified apparatus shown in the figure on page 8. The gases evolved bubbled first through .3 N sulfuric acid and then through strong KOH solution to absorb the CO<sub>2</sub> given off and were finally collected in a gasometer. The H<sub>2</sub>SO<sub>4</sub> was titrated with standar NaOH and the amount of NH<sub>3</sub> formed was calculated. This was checked by making the acid alkaline and distilling as in the Kjeldahl method. The N<sub>2</sub> was calculated from the volume of water removed from the gasometer.

Summary

1. The sulfonation and diazotization of p-toluidine has been described.
2. The Sandmeyer (nitrile) reaction on p-toluidine-*m*-sulfonic acid has been studied and a method suggested for its further study.