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I hereby recommend that the thesis prepared under my supervision by Stuart Cohen

entitled Preparation of Sulfonated Aromatic Amines and their Employment as Oxidation-Reduction Indicators. Improved Preparation of Naphthidine.

be accepted as fulfilling this part of the requirements for the degree of Doctor of Philosophy

Approved by:

Ralph E. Oesper

W. M. Burgess Chairman

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The Preparation of Sulfonated Aromatic Amines and their Employment as Oxidation-Reduction Indicators. Improved Preparation of Naphthidine.

A dissertation submitted to the
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Stuart Cohen
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Introduction

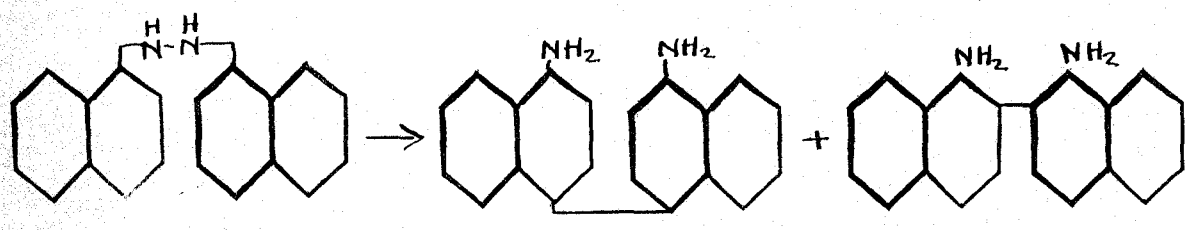
The incentive for developing an improved preparation of naphthidine was inspired by the work of Straka and Oesper (1) who found that naphthidine serves as an excellent oxidation-reduction indicator in the volumetric determination of iron and chromium. The naphthidine used in their work was prepared by reducing azoxynaphthalene with stannous chloride as recommended by Cumming and Steel (2). Only small yields were produced by this procedure. The present investigation was undertaken in an effort to develop a procedure which would be both a simple and a practical preparation of naphthidine.

Historical

Naphthidine was first prepared by Nietski and Goll (3). Their starting material was azonaphthalene prepared by diazotizing amino azonaphthalene and reducing the resulting diazonium salt with boiling ethanol. The reduction of the azo compound and the rearrangement of the hydrazonaphthalene thus obtained was carried out in two ways:

1. One part of finely divided azonaphthalene is suspended in a solution of one and one half parts of sodium hydroxide in 160-170 parts of alcohol. The suspension is heated to boiling, and zinc dust is introduced cautiously until the color disappears. The solution is filtered, and since the dissolved product oxidizes very readily in contact with air, the filtrate is delivered directly into very dilute ammonium sulfide solution. The flocculent, light red precipitate which appears is dried and then extracted with hot benzene. Upon cooling of the solution the hydrazonaphthalene separates, and after numerous recrystallizations from benzene finally is obtained in crystals melting at 275°. If the hydrazonaphthalene is warmed cautiously with the calculated quantity of dilute hydrochloric acid upon the water bath, maintaing the temperature at 70-80°, the hydrazo compound

goes almost completely into solution and upon the addition of concentrated hydrochloric acid, the difficultly soluble hydrochloride of naphthidine is precipitated. The quantity of this salt is small. The greater portion, about two-thirds, of the hydrazo compound is transformed into the isomeric dinaphthylene, whose hydrochloride remains dissolved in the mother liquor.



Hydrazonaphthalene Naphthidine Dinaphthylene

2. Naphthidine is obtained in abundant quantity by reduction of azonaphthalene with stannous chloride. The procedure is:

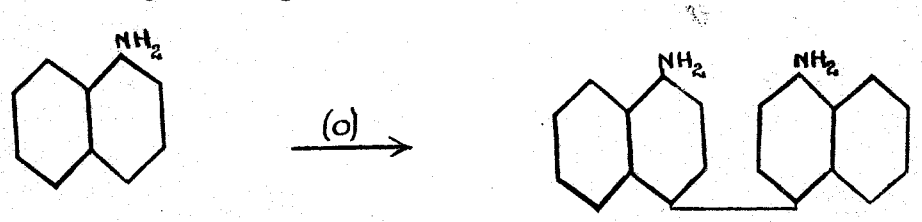
Dissolve the azo compound in 45 parts of hot acetic acid and add stannous chloride solution (one part stannous chloride, two parts of hydrochloric acid, two-three parts water) until the red mixture turns colorless. Upon addition of concentrated hydrochloric acid the difficultly soluble hydrochloride of naphthidine is precipitated and obtained pure by washing with dilute hydrochloric acid, dissolving in hot water and precipitating with concentrated hydrochloric acid.

By action of alkalies upon the hydrochloride obtained by these two methods of preparation, a base,

naphthidin, is liberated which crystallizes from dilute alcohol in silver shining leaves or as colorless tablets from benzene. Both forms melt at 198-199°.

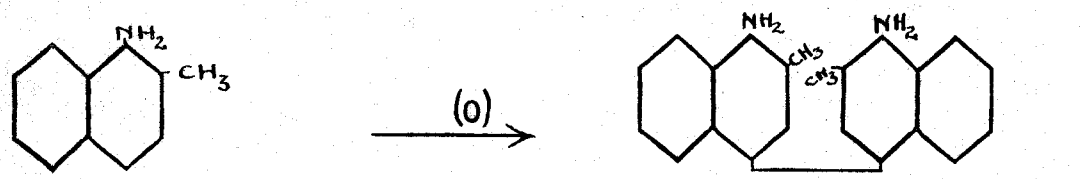
The next method of preparing naphthidin was that proposed by Reverdin and la Harps (4). One hundred grams of alpha naphthylamine is dissolved in 88% sulfuric acid (higher concentrations of acid must be avoided, to prevent sulfonation). To this solution cooled to approximately 40°, a quantity of impure ferric oxide corresponding to 55 grams of pure ferric oxide is added, and the mixture allowed to stand for 24 hours. The ferric oxide is transformed into a white powder of ferric sulfate, and the mixture becomes light grey. After heating for six or seven hours slowly to 75° and finally several hours at 100° with good stirring, the reaction mixture is poured into 5 liters of water and let stand overnight. The suspended matter, consisting of naphthidine sulfate with some naphthylamine sulfate and iron sulfate, is filtered off and washed with 2-3 liters of warm water and then treated warm with sodium hydroxide in the presence of 1 liter of water. The transformation of the naphthidin sulfate is rather slow. The solid is filtered, washed and again dissolved in dilute hydrochloric acid. After filtering 120 grams of sodium sulfate is added to the filtrate and impure naphthidin sulfate is precipitated. This is transformed into the free base by treating

filtering and washing with water. In order to completely purify the naphthidin it must then be dissolved in boiling alcohol and precipitated by the addition of a little water..The product looks much like benzidine, namely, silvery, shining leaves, which melt at 198°. Reverdin and la Harp claim to have obtained a 60% yield of naphthidine by this procedure. The equation for this reaction may be represented as follows:



alpha naphthylamine naphthidine

The next preparation concerns a naphthidine derivative prepared by the oxidation of a methyl aminonaphthalene. Fries and Hohman (5) in their research in the series of 2-methyl naphthalenes report a preparation of 3-3' dimethyl 1-1' naphthidine(4-4') from 2-methyl amino(1) naphthalene formulated as follows:



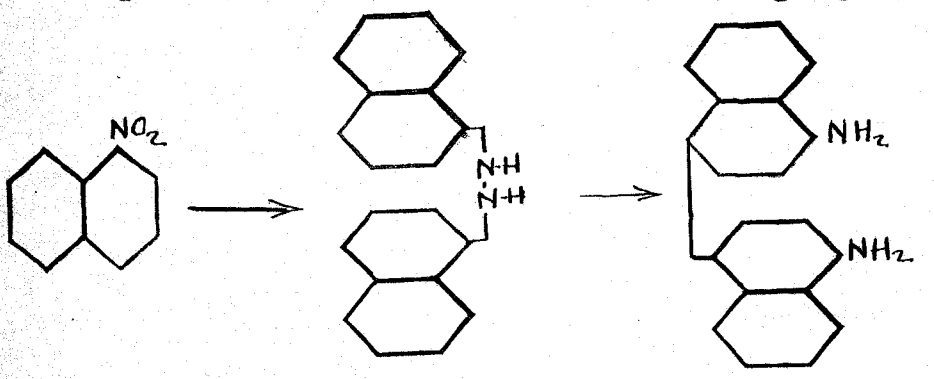
2-methyl 1-amino naphthalene

3-3' dimethyl 1-1'naphthidine(4-4')

Five grams of the sulfate of 2-methyl 1-amino naphthalene is dissolved in 25c.c. glacial acetic acid and a few drops of 30% hydrogen peroxide added to the

boiling solution. Bright shining crystals separate from the solution; these are filtered off and the filtrate again treated with 2 drops of 30% hydrogen peroxide. A further crystal separation takes place, and this procedure can be repeated. Finally no more crystal separation takes place, and only 2-methyl 1-4 naphthoquinone can be obtained. The crystals are purified through extractions with alcohol. Two grams of the sulfate salt are obtained out of which the free base may be obtained by treatment with ammonium hydroxide. Extraction with hot alcohol separates the desired reaction product from the alcohol insoluble impurity. The amino compound is precipitated from the alcoholic solution by addition of water. After recrystallization from high boiling gasoline (120-150°), crystals of 3-3' dimethyl 1-1' naphthidine(4-4') are obtained which melt at 213°.

Cumming and Steel (2) state that the work was undertaken in order to reduce, if possible, alpha nitronaphthalene to the hydrazo compound and to then convert this into naphthidine as shown in the following equation:

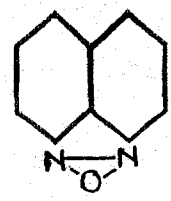


alpha nitro naphthalene — hydrazo naphthalene — naphthidine

Their attempts to reduce the nitro compound to azoxynaphthalene by means of sodium amalgam or zinc and sodium hydroxide proved unsuccessful. The azoxynaphthalene was finally isolated in the following manner:

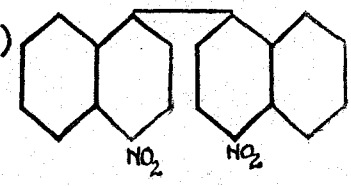
Twenty grams of alpha nitronaphthalene, 175 c.c. of water and 40 grams of ammonium chloride were heated together on the water bath at 70°, the nitronaphthalene going completely into solution, but some of the ammonium chloride remaining undissolved. To this solution was added 28 grams zinc dust at such a rate that the temperature was maintained at 70-75°; above 75° tarring took place, and below 70° a part of the nitronaphthalene was precipitated. The solution which gradually turned from yellow to red was filtered hot, the residue extracted with boiling 90% alcohol, and the combined extract and filtrate cooled. The yellow crystalline precipitate was removed, and the filtrate concentrated under diminished pressure, a further deposit being obtained. When kept for more than 12 hours, or if heated, the filtrate became dark in color and decomposition took place. The crystalline product was extracted with warm water to remove ammonium chloride and then several times with alcohol. The product obtained from the alcohol extracts was recrystallized from alcohol, and the yellow crystals

deposited melted at 127° and displayed the characteristic reactions of 1-1' azoxynaphthalene.



Naphthidine was obtained by reducing azoxy naphthalene by means of stannous chloride dissolved in hydrochloric acid, (under similar conditions alpha nitro naphthylamine is not reduced). Reduction readily took place, and no alpha naphthylamine was detected. The white compound that precipitated on the addition of concentrated hydrochloric acid was washed with dilute hydrochloric acid and then dissolved in water, and the solution treated with sodium hydroxide. The base was recrystallized from alcohol and formed silvery plates, m.p. 198°.

A rather anomalous result is recorded by Clemo, Cockburn and Spence (6).



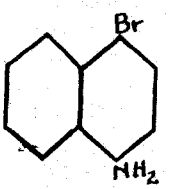
4-4' dinitro 1-1' dinaphthyl(1 gram) was dissolved in boiling glacial acetic acid (100 c.c.), and zinc dust (5 grams) added. Hydrochloric acid (5 c.c.) was added drop by drop, and after ten minutes the solution was diluted with an equal volume of water and filtered. The naphthidine was precipitated by the addition of solid potassium hydroxide in sufficient quantity to keep the zinc in solution, and the precipitate was then extracted with a little dilute hydrochloric acid to remove the zinc. The residue is again heated with sodium hydroxide, collected, dried ,

and distilled at 1 m.m.(no boiling point is given). The product when recrystallized from alcohol appeared as fan-shaped needles, melting at 191°, either alone or mixed with authentic naphthidine.

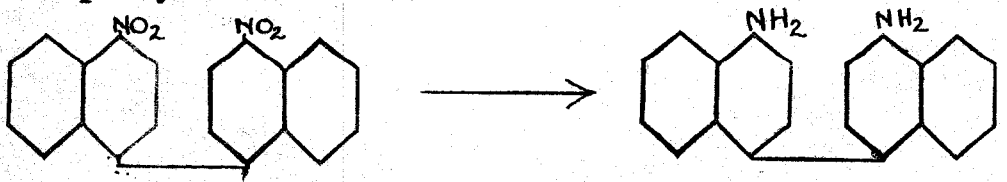
In connection with the above experiment Cumming and Howie (7) state:

'' it may be mentioned that 2-2' diamino 1-1' dinaphthyl melts at 191° (Meisenheimer and Witte (8), Cumming and Ferrier (9), Chudozilov (10) records m.p. 187°). In our hands the conditions of Clemo and co-workers did not give a product of m.p. 191°, but 196-197°; the yield from one gram being insufficient for further purification''.

Cumming and Howie observed further that attempts to prepare naphthidine and its diacetyl derivatives by condensation of 1-bromo 4-naphthylamine



and its acetyl derivatives respectively, by means of copper powder, sodium, sodium amalgam, or aluminum chloride, with or without solvents, and at temperatures up to 230° failed. Naphthidine was finally isolated from 4-4' dinitro 1-1' dinaphthyl as follows:



4-4' dinitro 1-1' dinaphthyl naphthidine

5 grams dissolved in 100 c.c. glacial acetic acid and 10 c.c. of concentrated hydrochloric acid were gently

boiled under reflux. Zinc dust was added, a little at a time, until a clear solution was obtained (1 hour). On cooling the filtrate naphthidine hydrochloride separated, and this recrystallized from boiling water several times, gave the free base on treatment with ammonia. When recrystallized several times from alcohol, 3.5 grams of naphthidine were finally obtained in silvery plates, m.p.202°. It was found that the reduction of 4-4' dinitro 1-1' dinaphthyl could be effected with zinc dust in a melt of salicylic acid, th naphthidine obtained melting at 198-199°. Boiling dilute hydrochloric acid and zinc dust or iron are incapable of reducing the dinitro compound.

Cumming and Howie (11) reviewed methods of preparation of some dinaphthyl bases, such as hydrazonaphthalene, azonaphthalene, naphthidine, etc. Their results on the preparation of azonaphthalene and naphthidine follow:

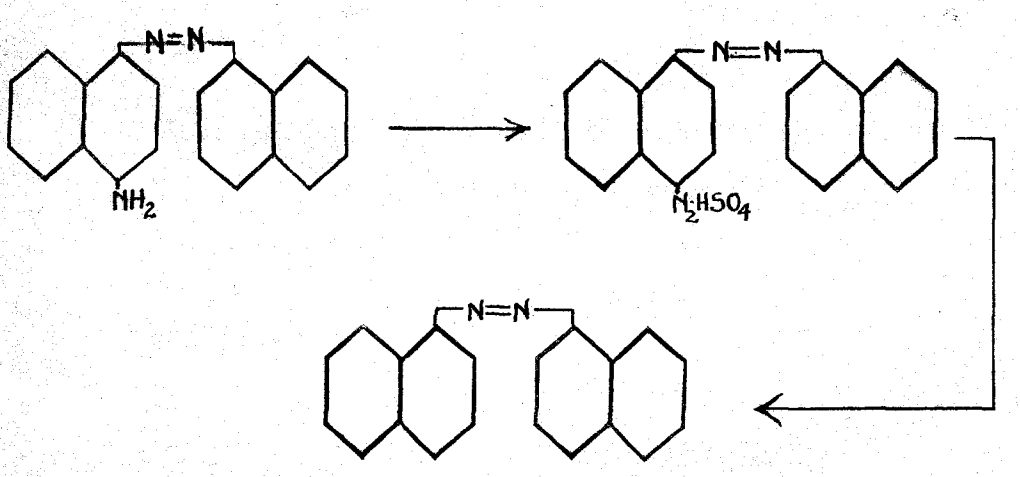
1-1' azonaphthalene

1-1' azoxynaphthalene prepared in 32% yield by the method of Cumming and Steel (2) could not be reduced to the azo stage with 5% excess zinc in neutral media.

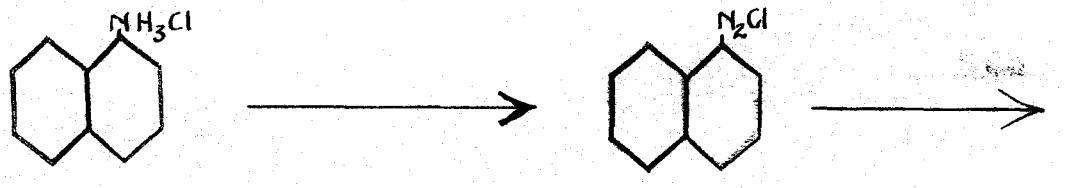
The method of Nietski and Goll (3) for the preparation of azonaphthalene was modified by Cumming and Howie as follows:

9 grams of 4-amino 1-1' azonaphthalene (prepared by coupling 1-naphthalene to diazotized 1-naphthylamine in

900 c.c. absolute ethanol and 26 c.c. concentrated sulfuric acid) was treated with an excess of amyl nitrite, and the whole refluxed until it was deep red. Addition of water precipitated a brownish mass which recrystallized from acetic acid with boneblack yielded orange-red crystals of azonaphthalene,, m.p.. 188°; a further yield was obtained by addition of water to the filtrate (total-3 grams). The equation for the reaction is::

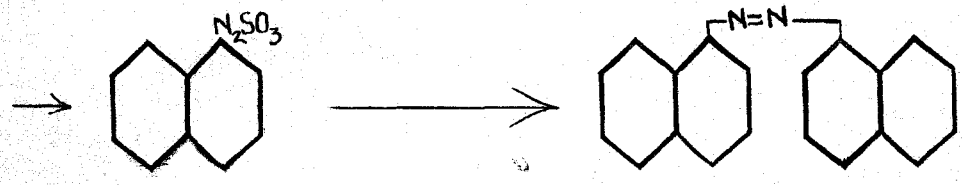


The method of Hantzsch and Schmiedel (12) via 1-naphthalene syn diazonium sulfonate yielded in the hands of Cumming and Howie (11) only 2.5 grams of azonaphthalene from 20 grams alpha naphthylamine, but is nevertheless the more convenient. The reaction may be written as follows:



alpha naphthylamine hydrochloride

alpha naphthalene diazonium chloride



alpha naphthalene syn diazonium sulfonate

azonaphthalene

Cumming and Steel record azonaphthalene as melting at 186°; Hantzsch and Schmiedel record 188-189°. The variation is explained by the fact that azonaphthalene begins to sublime at 170°.

Cumming and Howie obtained the following results in reviewing several methods of preparing naphthidine:

1. One gram of 1-1' azoxynaphthalene was reduced with zinc dust according to the directions of Cumming and Steel (loc. cit.) until the solution became colorless. The solid residue obtained by concentration of the solution almost to dryness under reduced pressure was quickly dried and extracted with benzene. After concentration to about 20 c.c., the benzene solution was cooled and deposited naphthidine in colorless plates, which after several recrystallizations from ethanol melted at 202°. Traces of hydrazonaphthalene and dinaphthylene were also obtained by further concentration of the filtrate.

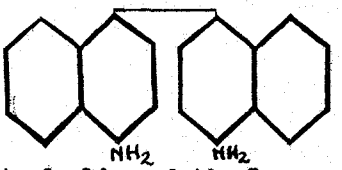
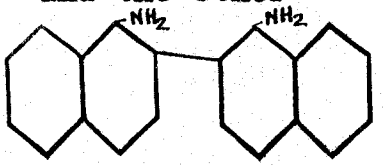
2. Reduction with stannous chloride of s. and as. azoxynaphthalene by the method of Cumming and Steel (2) gave a very poor yield of naphthidine, silvery flakes, m.p. 202°. (The s. form is more readily reduced in acid

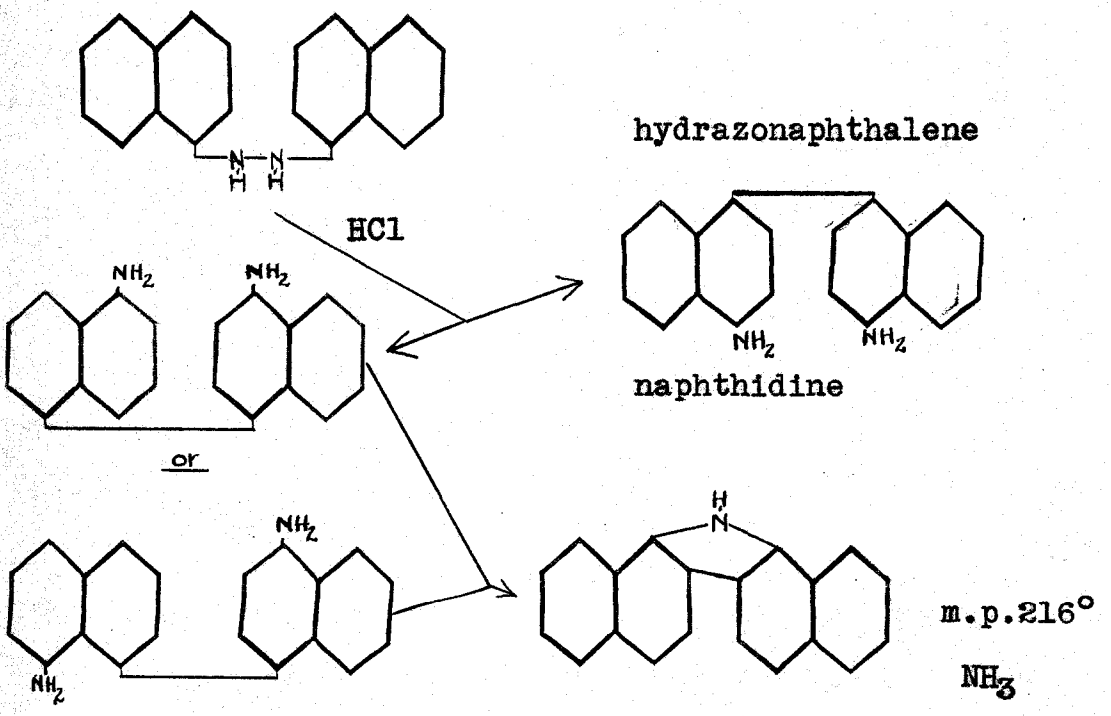
solutions than the as. form, whilst in alkaline solutions the reverse holds).

3. Reduction with stannous chloride by the method of Nietski and Goll gave a very nearly theoretical yield of naphthidine from 1-1' azonaphthalene.

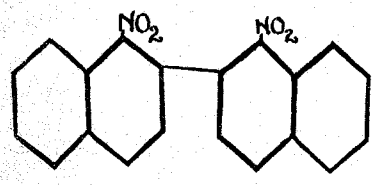
Straka and Oesper (1 and 21) in their preparation of naphthidine for use as an oxidation-reduction indicator, followed the procedure of Cumming and Steel(2). Alpha nitronaphthalene was reduced with zinc dust in alcoholic solution to form 1-1' azoxynaphthalene. Twenty grams of the nitro compound yielded five grams of the azoxynaphthalene. One part of the azoxy compound was dissolved in 45 parts of acetic acid. The red solution was treated with stannous chloride solution (one part of stannois chloride; two parts of concentrated hydrochloric acid; two parts of water) until the color was almost discharged. Concentrated hydrochloric acid was then added and a precipitate, the hydrochloride of naphthidine, appeared. The hydrochloride had a decided blue appearance and was recrystallized from hot water. It was then suspended in cold water, and a concentrated solution of sodium hydroxide added. Methyl alcohol was found to be the best medium for recrystallizing naphthidine. Accordingly, the base was dissolved in hot methyl alcohol, and water was carefully added to the cooled solution. A silvery precipitate separated which was

crystalline and quite pure, melting at 197°. One gram of azoxynaphthalene yielded 0.2 gram of naphthidine.

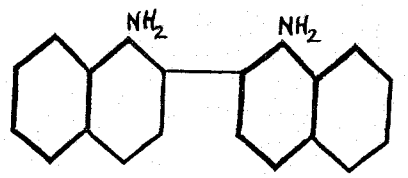
The small yield of naphthidine is due to the complications arising during the rearrangement of the hydrazo compound. Nietski and Goll showed that in this rearrangement two isomers are obtained, one which they named naphthidine,  and the other which they designated dinaphthylene,  the former having an insoluble hydrochloride, and the latter giving a very soluble hydrochloride. Upon heating of dinaphthylene, ammonia is lost and there is formed dinaphtho carbazol, as shown:



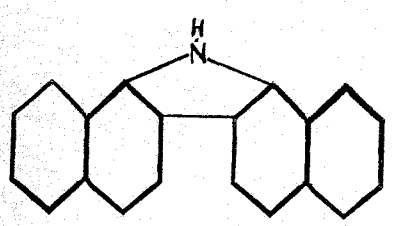
The above structures were those assigned to naphthidine and dinaphthylene by Nietski and Goll. The structure assigned to dinaphthylene was subsequently shown to be wrong. Vesely (13) corrected the error by preparing 1-1' dinitro 2-2' dinaphthyl synthetically. It gave upon reduction and removal of ammonia the same dinaphtho carbazol which the discoverer had on hand.



1-1' dinitro 2-2' dinaphthyl



1-1' diamino 2-2' dinaphthyl



+ NH_3

1-1' dinaphtho carbazol

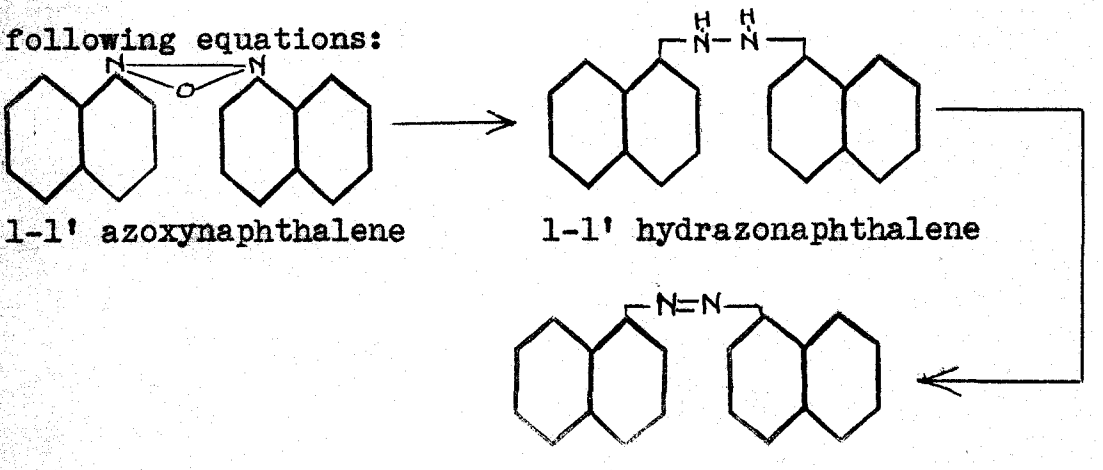
Preparation of Azonaphthalene

Inasmuch as a successful preparation of naphthidine appeared to require as its first stage a practical preparation of azonaphthalene, the present worker first set about to investigate this problem.

The original preparation of azonaphthalene by Nietski and Goll (3) involved the diazotization of amino-azonaphthalene followed by the reduction of the diazonium salt with boiling ethanol. This procedure was discarded because of low yields and because of the excessively large volumes of ethanol required in preparing azonaphthalene in any considerable quantity.

Hantzsch and Schmiedel (12) started with alpha-naphthylamine which was diazotized and the diazonium salt solution poured into an excess of potassium bisulphite solution, whereupon the alpha naphthalene diazonium sulphonate precipitated. 1-1' azonaphthalene is obtained from the diazonium sulphonate by allowing the latter to stand in a desiccator at ordinary temperature for a few days. The crude mass was then extracted with chloroform; the extract evaporated, and the residue recrystallized from acetic acid. The product, azonaphthalene, was obtained in reddish green needles, m.p. 188-189°. No yield is stated, but Cumming and Howie (7) who repeated this procedure found that 2.5 grams of the azo compound were obtained from 20 grams of alpha naphthylamine.

Wacker (14) prepared azonaphthalene by reducing azoxynaphthalene with zinc and potassium hydroxide in ethanol solution. The reaction may be represented by the following equations:



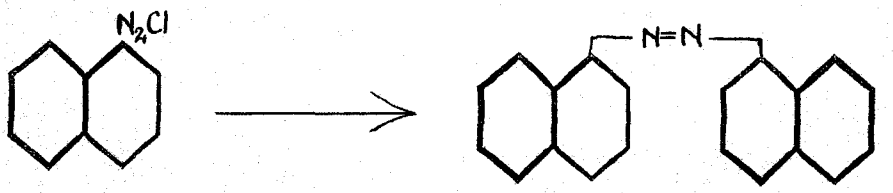
1-1' azoxynaphthalene

1-1' hydrazonaphthalene

1-1' azonaphthalene

The hydrazonaphthalene is oxidized to azonaphthalene by standing in air for several days. This procedure requires azoxynaphthalene which by even the best method, that of Cumming and Steel, can be obtained in only 32% yield.

Bornstein (15) obtained some azonaphthalene by the action of copper sulfate and sodium thiosulfate on alpha naphthalene diazonium chloride. No yield is mentioned. The equation is as follows:



alpha naphthalene diazonium chloride

azonaphthalene

Brydowna (16) obtained azonaphthalene by the reduction of the iso diazo salt of alpha naphthylamine.with alcohol at 5°. No yield is stated. The equation for this reaction is the same as that used in the preceding preparation.

Lochor (17) obtained azonaphthalene by the action of potassium ferrocyanide on the diazonium salt of alpha naphthylamine. No yield is stated. The equation for this reaction is the same as that represented for Bornstein's preparation.

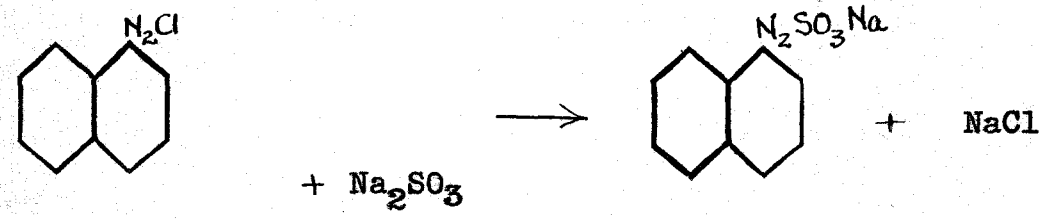
In their present form none of these preparations of azonaphthalene have any practical significance. The procedure finally employed in this study was a modification of that proposed by Lange (18).

Experimental

Preparation of Azonaphthalene

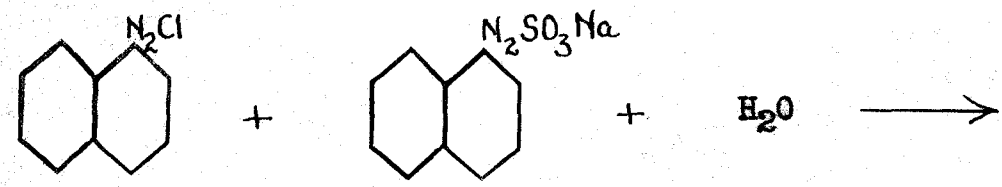
35.0 grams alpha naphthylamine hydrochloride was stirred up with about 500 c.c. water in an 800 c.c. beaker. 17.5 c.c. concentrated hydrochloric acid was added and the mixture cooled in an ice bath with mechanical stirring to about 0°, and then this is treated with 21 c.c. concentrated sulfuric acid diluted to 200 c.c. A cooled solution of 14 grams sodium nitrite, acidified slightly with very dilute, ice cold hydrochloric acid, is added slowly to the suspension of the amine salt with good stirring. When all the nitrite has been added there remains a reddish brown solution of the diazonium salt. After five minutes standing in the ice bath filter with suction, the receiving flask being placed in an ice bath to keep the filtrate cold. This is then placed in a two liter beaker, and to it is added slowly with stirring (maintaining the temperature between 0° and 5°) a solution of 66 grams fused sodium acetate in 300 c.c. water. After this addition is completed a solution of 31 grams sodium sulfite in 200 c.c. water is run in slowly. A vigorous evolution of nitrogen ensues, and 1-1' azonaphthalene separates as a brown or an orange flocculent precipitate. After all the sulfite has been added the solution is stirred for five minutes and then taken out of the ice bath and warmed on the water bath. This warming causes the precipitate of

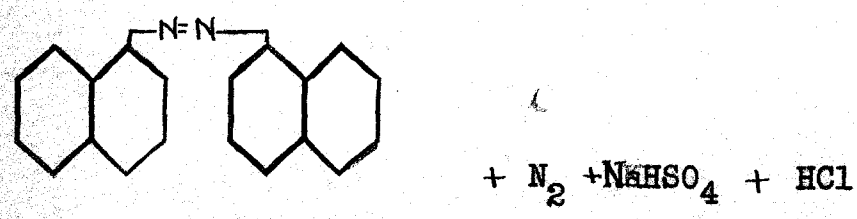
the azonaphthalene to separate in better form for filtration. Allow the mixture to cool and filter with suction. The precipitate is pressed out on a porous plate and finally dried at 100°. The average yield is 31 grams (calculated 27.5 grams) of impure azonaphthalene, melting over the range 180-184°. The melting point of pure azonaphthalene is given as 186° by Cumming and Steel, while Hantzsch and Schmiedel record 188-189°. This azonaphthalene was found quite pure enough for the preparation of naphthidine so that no attempt was made to purify it further. The equations for the reaction follow:



alpha naphthalene diazonium chloride

sodium alpha naphthalene diazonium sulphonate





1-1' azonaphthalene

Preparation of Naphthidine

The method of Nietski and Goll (3) for the preparation of naphthidine by reduction of azonaphthalene in acetic acid solution with stannous chloride was found by the present writers to give only 34% yield. In addition large volumes of acetic acid are required, 45 c.c. glacial acetic acid for every gram azonaphthalene used or about 135 c.c. for every gram of naphthidine obtained.The method described below was developed by the authors and was found to be more convenient and profitable than any previous proposals.

Twenty grams of powdered 1-1' azonaphthalene is suspended in 200 c.c. ethanol, and the mixture heated to a weak boil. To this suspension a solution of stannous chloride (40 grams stannous chloride in 100 c.c. concentrated hydrochloric acid) is added slowly until the precipitate turns to a light tan. Occasional shaking hastens the reduction of the azo compound. When the reaction is completed the boiling is discontinued immediately, since otherwise the dinaphthylene (1-1' diamino 2-2' dinaphthyl) existing in solution when boiled with hydrochloric acid loses ammonia to form dinaphtho carbazol which contaminates the naphthidine and prevents an easy purification of the latter. Concentrated hydrochloric acid is added to precipitate any naphthidine hydrochloride which is in solution. The mixture is then cooled and filtered. The

precipitate of crude naphthidine hydrochloride is suspended in water, and the base is liberated by adding sodium hydroxide solution. The suspension is kept warm, stirring occasionally. The crude naphthidine is then filtered off, washed with water and dried. Various recrystallizing media for purification of this crude naphthidine were tried. Methyl. ethyl, propyl and butyl alcohols were satisfactory for small quantities, but naphthidine is only slightly soluble in any of them. The solubility in isoamyl alcohol is greater, not sufficient for actual use, but the product melted rather low, (ca.) 190°. Ethyl, butyl and amyl acetates were tried with very little success. Xylene gives a very nice looking product, but the solubility of the naphthidine in this solvent is too small. The best method which did not entail large volumes, gave a pure product and did not require a great amount of manipulation consisted of boiling the crude naphthidine with ethanol, adding pyridine until a clear solution was obtained, filtering and allowing to cool and crystallize. Accordingly the dried precipitate of the crude base is placed in a 300 c.c. round bottom flask with 120 c.c. ethanol and the mixture heated to boiling and maintained at this temperature while pyridine is allowed to run in slowly until the material dissolves,about 40-45 c.c. of pyridine being required. The solution is filtered hot and allowed to cool slowly, preferably over-

night, whereupon light tan crystals separate, m.p. 197.5-199° (uncorrected). Cumming and Howie (7) report a melting point of 202° after several recrystallizations from ethanol. Six grans of naphthidine were obtained from 20 grams of crude azonaphthalene. This corresponds to a 33.5% yield of pure naphthidine based on pure alpha naphthylamine hydrochloride.

The method of Reverdin and la Harps (4) was reviewed in light of the fact that the authors claim a 60% yield of naphthidine. This method depends on the oxidation of alpha naphthylamine in sulphuric acid solution with ferric sulphate. They use ferric oxide and allow this to stand in contact with the sulphuric acid overnight to form ferric sulphate. It was found, however, that the ferric oxide reacts very slowly with the sulphuric acid, and we observed that it is much more convenient to start with anhydrous ferric sulphate. The mixture of alpha naphthylamine, ferric sulphate, and 88% sulphuric acid was heated 6-7 hours at 75° and 3 hours at 100° with stirring. The reaction mixture was poured into water, allowed to stand overnight, and then filtered. The mixture of naphthylamine sulphate, iron sulphates, and naphthidine sulphate was washed with warm water and then treated warm with sodium hydroxide solution to precipitate the free bases. Reverdin and la Harps claim to have purified the naphthidine by dissolving the crude base in dilute

hydrochloric acid and precipitating with sodium sulfate. We found this a well-nigh impossible task due to the insolubility of the naphthidine hydrochloride. Attempts to purify the naphthidine by extraction of this mixture with ethanol proved unsuccessful, the naphthidine obtained was contaminated with alpha naphthylamine and melted at (ca.) 180°.

Attempts were made to prepare naphthidine by oxidation of alpha naphthylamine sulphate in acetic acid. Five grams of alpha naphthylamine sulphate were dissolved in 50 c.c. hot glacial acetic acid, 2 drops of 30% hydrogen peroxide added, the mixture cooled and the precipitate filtered off. This is then suspended in water and treated with sodium hydroxide solution. Brown flocks immediately formed, and the solution smelled strongly of alpha naphthylamine. The precipitate was tested for naphthidine, but only a trace could be detected. By decreasing the original concentration of the alpha naphthylamine about 5 times no precipitate was obtained on treatment with hydrogen peroxide and no naphthidine could be detected.

Other methods of reducing the azonaphthalene were tried. Sodium amalgam did not reduce the azo compound either dissolved in acetic acid, or when suspended in dilute sulphuric acid. Stannous sulphate was tried as a reducing agent, but its use offered no advantages over

the stannous chloride reduction. Various modifications of the stannous chloride method were run, such as suspending the azo compound in cold concentrated hydrochloric acid and adding the stannous chloride solution with stirring; or suspending the azonaphthalene in cold alcohol and adding the reducing agent. The advantage of running the reduction hot is that the naphthidine hydrochloride precipitate is easier to filter, complete reduction is obtained more rapidly, and it is not necessary to grind the azonaphthalene very fine to avoid small lumps of unreduced azo compound.

The Preparation of Sulfonated Aromatic Amines and their Employment as Oxidation-Reduction Indicators

This study was a continuation of the work by Straka and Oesper (19 and 1) on sulfonated derivatives of aromatic amines, in particular, those formed by the action of ethyl sulfate on diphenylamine. These workers encountered a very queer reaction between ethyl sulphate and diphenylamine, and an investigation of this reaction was the starting point of the present study.

33.8 grams diphenylamine (0.2 mol) and 30.8 grams ethyl sulphate were heated on the water bath for 1 hour and then on the metal bath at 130° for 1 hour;the product obtained, a light colored tar, was refluxed with a solution of 7.5 grams of sodium in 275 c.c. 95% ethanol until the product became nearly white. The solid obtained was separated by filtration, suspended in water, the water insoluble portion removed by filtering, and the filtrate extracted with ether. The aqueous solution was separated and the ether removed by a current of air. Excess concentrated sodium hydroxide was added and by common ion effect caused the sodium salt of the sulfonated compound to precipitate. The gel which formed at first became crystalline after standing three days. This compound when tested as an indicator in iron and chromium analyses was found entirely satisfactory. The directions just outlined were followed in subsequent preparations, but of their

numerous attempts to repeat the preparation none proved successful. All indicators which they obtained subsequent to the original preparation gave a red oxidation product whose developement during a titration is accompanied by a yellow-red intermediate stage which is objectionable. They postulated that the difference in the products obtained might have been due to the fact that in the first preparation an old lot of ethyl sulfate was used, and this may have contained some material which served to catalyze that reaction and to direct the sulfonation along a particular line.

In reviewing the above work we were very fortunate in being able to procure a sample of ethyl sulphate, manufactured by Kahlbaum, about 15 years old. Upon repeating the above reaction between diphenylamine and the old sample of ethyl sulphate the same satisfactory indicator was obtained. The precipitate resulting from treatment with concentrated sodium hydroxide was dissolved in a minimum quantity of alcohol and then precipitated by the addition of ether. This removes a large part of the sodium hydroxide. The precipitate was filtered, redissolved in alcohol, and carbon dioxide passed into the solution until no more sodium carbonate precipitated. The filtrate from this treatment was evaporated to a small volume, filtered and allowed to stand until crystallization took place. An analysis of the compound obtained by the reaction

of diphenylamine and the old sample of ethyl sulphate, purified in the above manner, showed percentage of sodium: 8.37 and 8.49%. Calculated for diphenylamine sodium sulfonate gives: 8.49 % sodium. An analysis for sulphur showed: 11.37 % sulphur. Calculated for diphenylamine sodium sulfonate: 11.48 % sulphur.

Attempts to use fresh ethyl sulphate and alter the conditions so that we might obtain the above indicator failed. Various additions to reaction mixtures such as small quantities of sulphuric acid, butyl sulphate, ethyl hydrogen sulphate always produced a compound whose indicator action was not identical with that of the indicator obtained from old ethyl sulphate.

It was thought interesting to investigatea reaction between one of the higher homologues of ethyl sulphate and diphenylamine. A new method of preparation of primary n-alkyl sulphates had just been published by Barkenbus and Owen (20), using the reaction between the alkyl sulfite and the alkyl chlorsulphonate. Using this method, which works very well, we were able to prepare dibutyl sulfate,b.p. 97.4° at 3 m.m., in 70 % yield.

21.0 grams of dibutyl sulphate (0.1 mol) and 16.9 grams diphenylamine (0.1 mol) were heated on the water bath for 1 hour and then on the metal bath at 130-140° for 1 hour. The tar obtained was refluxed with a solution of 4.8 grams sodium in 200 c.c. ethanol, until

the tar was completely changed into a white precipitate. The alcohol was removed by evaporation, and the residue dissolved in water, the solution filtered, and the filtrate extracted thoroughly with ether. The water layer was warmed and air passed through the solution until all the ether is removed. Concentrated sodium hydroxide was then added until a faint turbidity persists, and the solution is allowed to stand for 24 hours. The precipitate was filtered and then purified as described previously. The compound analyzed for sodium showed: 8.32; 8.39 % Na. Calculated for diphenylamine mono sodium sulphonate: 8.49 % Na. A sulphur analysis of the compound showed: 11.42 % S. Calculated for diphenyl amine mono sodium sulphonate: 11.48 % S.

A 0.1 % aqueous solution of this compound was prepared, and a series of titrations were run to determine whether or not it possessed suitable indicator properties. The ratio of ferrous solution to dichromate is given in the table below.

$FeSO_4$ (c.c.)	$K_2Cr_2O_7$ (c.c.)	Conditions
20	23.0	$K_3Fe(CN)_6$ as indicator 150 c.c. H_2O
20	23.0	10.0 c.c. dil. H_2SO_4
20	23.12	1.0 c.c. indicator solution 15.0 c.c. retarder 150 c.c. H_2O
20	23.09	

In the case of the internal indicator the end-point is very sharp and unmistakable, the color changing from the green of the chromic ions to the purple color of the oxidized indicator.

In the next series of titrations mercuric, mercurous and stannic ions were introduced to determine whether or not they would interfere with the indicator action of the compound. 150 c.c. water, 15 c.c. retarder solution, 1.0 c.c. indicator solution (0.1%), 2 drops stannous chloride solution and 20.0 c.c. 0.1 N ferrous sulphate were mixed in a 250 c.c. beaker and 5 c.c. saturated mercuric chloride solution was then added and the solution titrated without delay. The results are given in the following table. In the case of the ferricyanide, 10 c.c. dilute sulfuric acid were substituted for the retarder solution.

$FeSO_4$ (c.c.)	$K_2Cr_2O_7$ (c.c.)	Indicator
20	23.0	$K_3Fe(CN)_6$
20	23.0	
20	23.10	1 c.c. internal indicator
20	23.12	

A series of iron ore analyses were run using the

compound as indicator and comparing the values with those obtained by the standard ferricyanide method. The iron values of the dichromate employing the external indicator were obtained from a standard iron ore from the Bureau of Standards (# 27 containing 69.2 % Fe).

The iron ores were analyzed by treating a 0.3 gram sample in a 100 c.c. beaker with 15 c.c. concentrated hydrochloric acid and 3 c.c. stannous chloride solution and warming to decompose the ore. If the solution became permanently yellow the color was discharged with stannous chloride. The reduced solution was rinsed into a 250 c.c. beaker containing 100 c.c. water and 5 cc. saturated mercuric chloride solution. When the internal indicator was used 1 c.c. of a 0.1 % solution was added and also 15 c.c. retarder solution. The results obtained are given in the tables below.

Iron Value from Standard Ore

Indicator	$K_2Cr_2O_7$ (c.c.)	Fe value (average)
$K_3Fe(CN)_6$	36.53 36.55	.005682
Internal Indicator	36.62 36.65	.005668

Analysis of Iron Ore (a)

Indicator	$K_2Cr_2O_7$ (c.c.)	% Fe
$K_3Fe(CN)_6$	23.31 23.32	44.17
Internal Indicator	23.39 23.40	44.20

Analysis of Iron Ore (b)

Indicator	$K_2Cr_2O_7$ (c.c.)	% Fe
$K_3Fe(CN)_6$	25.89 25.92	49.06
Internal Indicator	25.95 26.00	49.08

Analysis of Iron Ore (c)

Indicator	$K_2Cr_2O_7$ (c.c.)	% Fe
$K_3Fe(CN)_6$	22.65 22.63	42.88
Internal Indicator	22.66 22.68	42.83

From these results we may conclude that this indicator may be used in iron determinations with accurate results.

The similarity in indicator action of this compound produced by reaction of butyl sulfate with diphenylamine and that produced by reaction of old ethyl sulphate with diphenylamine raised the question as to whether they are identical. The para toluidine salts of these compounds were prepared and the melting points of the salts taken after two recrystallizations from water. Both melted over a range 196-197°. A mixed melting point showed no depression, so that this evidence coupled with the sulphur and sodium analyses proves the identity of the two sulfonated derivatives. The evidence is collected in the following table.

	butyl sulphate with diphenylamine	ethyl sulphate with diphenylamine
% Na	8.36	8.43
% S	11.42	11.37
melting point of para toluidine salt	196-197°	196-197°
color on oxidation	purple	purple
mixed m.p. of p-toluidine salts	no depression	

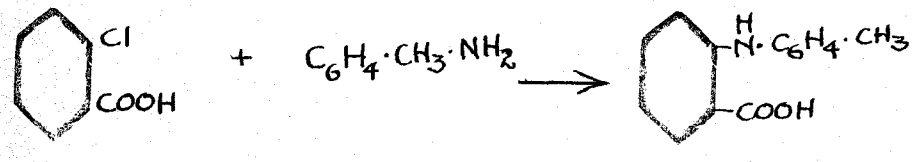
Another indicator was prepared by Straka and Oesper (1) by a reaction between ethyl sulphate and acetyldiphenylamine, but they were unable to isolate the pure compound from the reaction mixture. By an improved method of purification we were able to purify the compound and analyze it. The procedure used was the same as that desribed for the sulfonated compound obtained by reaction of the old ethyl sulphate with diphenylamine. When analyzed for sodium the compound showed: 8.42; 8.49%. Percentage sodium in diphenylamine mono sodium sulfonate: 8.49.

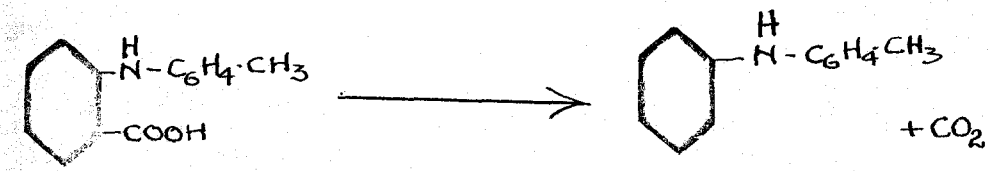
An attempt was made to condense para amino benzene sulfonic acid and brombenzene to form a sulfonated diphenylamine with the position of the sulfonic group known. 25 grams sulfanilic acid, 25 grams brombenzene, 150 grams nitrobenzene as solvent, 10 grams potassium hydroxide as condensing agent, and 0.1 gram each of cuprous iodide and iodobenzene as catalysts, were boiled on the metal bath for 20 hours. The nitrobenzene was removed by steam distillation, and the remaining liquid tested for bromide which would be present had condensation taken place, however, the test was negative. The liquid was also tested for indicator properties, but no indicator was present.

Straka and Oesper investigated the indicator properties of ortho-, meta- and para-tolyl phenyl amines.

They found that the ortho compound gave a colored oxidation product but of too little merit to warrant its use as an oxidation-reduction indicator. The meta- and para-tolyl phenylamines function satisfactorily with the exception that their action is inhibited by mercury salts. It was thought profitable to investigate the action of ethyl sulphate on these compounds and the indicator possibilities of the sulfonated compounds, if obtained.

The method of Ullman () was followed for the preparation of the tolyl phenylamines.





The ortho chlorbenzoic acid used in this synthesis was prepared by the method of Graebe (22) and purified as recommended by Straka and Oesper by dissolving in alkali and precipitating with acid. The ortho-, meta- and para-tolyl anthranilic acids were prepared by heating to boiling for 2-4 hours 12 grams of ortho chlorbenzoic acid with 12 grams potassium carbonate, 0.06 grams naturkupfer and 48 grams of the respective toluidine. The brown mass was then boiled with dilute hydrochloric acid

to remove any unchanged toluidine, filtered, the residue then dissolved in sodium carbonate solution and the acid precipitated with hydrochloric acid. These tolyl anthranilic acids were not purified further but used directly in the next step.

The acid was heated for about 2 hours to 250°, and a lively evolution of carbon dioxide took place. The temperature was then raised to or above the boiling point of the amine. The boiling points of the ortho-, meta- and para-tolyl phenylamines are respectively, 303°, 313° and 315°. The heating of the acid and the distillation of the resulting amine is preferably carried out in a 50 c.c. distilling flask and the product passed directly from the side-arm into a test tube for condensation.

Reaction mixtures consisting of 9.5 grams of the respective tolyl phenylamines and 7.5 grams ethyl sulphate were heated on the water bath for 1 hour and then on the metal bath at 130-140° for 1 hour. The reaction mixture was then refluxed with a solution of 2 grams of sodium in 100 c.c. ethanol until all the tar had been changed into a white mass. The alcohol was evaporated and water added to the mass. The solution was filtered from the solid residue, extracted thoroughly with ether, and the water layer warmed and air passed through the solution to remove the ether. Concentrated sodium hydroxide was added until a slight turbidity persisted, and the solution was allowed to stand for a day to allow

precipitation to take place. The precipitate was filtered off and purified as described for the other sulfonated derivatives. The table below gives the analyses of the products obtained.

	% Na found
o-tolyl phenylamine + ethyl sulphate	8.21
m-tolyl phenylamine + ethyl sulphate	8.19
p-tolyl phenylamine + ethyl sulphate	8.22

Calculated percent sodium for ortho-, meta- and para-tolylphenylamine mono sodium sulfonate: 8.09.

The meta-tolyl and para-tolylphenylamines formed sulfonated derivatives which gave no color change when employed in the titration of ferrous solution with dichromate. Ratios run between ferrous solution and dichromate show that ortho-tolyl phenylamine sodium sulfonate works satisfactorily in such titrations if there is no appreciable concentration of hydrochloric acid. The results are given in the table below.

Ratio of $FeSO_4$ to $K_2Cr_2O_7$

$FeSO_4$(c.c.)	$K_2Cr_2O_7$(c.c.)	Indicator	Conditions
20.0 20.0	23.10 23.12	Internal Indicator	150 c.c. H_2O 15 c.c. retarder 1c.c. indicator
20.0 20.0	23.0 23.0	$K_3Fe(CN)_6$	150 c.c. H_2O 10 c.c. dil. H_2SO_4

The indicator was also tested in the presence of mercuric, mercurous and stannic salts.150 c.c. water, 15 c.c. retarder solution, 1 c.c. 0.1 % indicator, 2 drops of stannous chloride, and 20 c.c. 0.1 N ferrous solution were placed in a 250 c.c. beaker and 5 c.c. saturated mercuric chloride solution added and the solution titrated with dichromate. The results are given in the following table.

$FeSO_4$(c.c.)	$K_2Cr_2O_7$(c.c.)	Indicator
20.0 20.0	23.0 23.0	$K_3Fe(CN)_6$
20.0 20.0	23.1 23.1	Internal Indicator

The indicator does not give a very sharp endpoint in any appreciable concentration of hydrochloric acid. It was found that erratic results were obtained, the indicator giving a colored product approximately 0.5 c.c. before the actual endpoint. Only a few c.c. of hydrochloric acid may be present in 200 c.c. of solution if a sharp endpoint is to be obtained.

In view of the sulfonating properties of ethyl sulphate it was thought of interest to investigate its action on diphenylbenzidine. The latter compound was

prepared by oxidizing diphenylamine in dilute sulfuric and acetic acids solution with potassium dichromate according to the directions of Sarver and Johnson (23). About a 50 % yield was obtained melting at 245-247°. Sarver and Johnson record melting point, 244-245°. Marqueyrol and Muraour record melting point 250-251.5°.

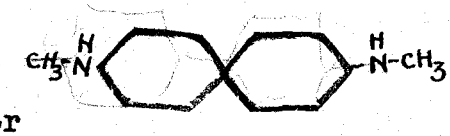
10 grams diphenyl benzidine and 24 c.c. ethyl sulphate were refluxed for 5 hours in xylene solution. A solution of 8.5 grams sodium in 300 c.c. ethanol was refluxed until the solid was light grey in color and the solvents then evaporated on the steam bath. The solid residue was ground, extracted with xylene, and then dried and washed several times with ethanol to remove gummy matter and then extracted with ethanol. The alcoholic extract was evaporated to a small volume and ether added to precipitate the sodium sulfonate which was filtered off and recrystallized from ethanol. The material obtained is very sensitive toward oxidation, turning to a brown color in the presence of air. It was analyzed for sodium, percent obtained being 5.40. Calculated for diphenyl benzidine mono sodium sulfonate: 5.25 %.

The indicator properties of this compound were investigated, and it was found to work satisfactorily with the exception that the endpoint is indistinct in the presence of hydrochloric acid, in this respect,

resembling the sulfonic acid of ortho tolyl phenylamine. The results given in the following tables show its reliability in the absence of an appreciable concentration of hydrochloric acid.

Ratio of $FeSO_4$ to $K_2Cr_2O_7$

Indicator	$FeSO_4$	K_2CrO_7	Conditions
Internal	20.0	23.07	150 c.c. water 15 c.c. retarder 1 c.c. 0.1% indicator
Indicator	20.0	23.10	
$K_3Fe(CN)_6$	20.0	23.0	150 c.c. water 10 c.c. dil H_2SO_4
	20.0	23.0	
Internal	20.0	23.08	Same as above, only that Hg^{+}, Hg^{++}, and Sn^{++++}, were present
Indicator	20.0	23.08	
$K_3Fe(CN)_6$	20.0	23.0	
	20.0	23.0	

N-N' Dimethyl benzidine  was tried as a possible indicator in view of its relation to benzidine and diphenyl benzidine. This compound was prepared as recommended by Willstätter and Kalb (24). When employed as an indicator it was found that the change at the endpoint is not very distinct, the change from the green of the chromic ions

to the yellow of the oxidized indicator being insufficient for practical use.

Benzidine mono-sulfonic acid was prepared by sulfonation with concentrated sulfuric acid at 170°, according to directions given in a patent to the Friedrich Bayer Co. (26). When employed as an indicator it was found that the endpoint change from green to yellow was too faint to be of any practical value.

The indicator properties of the compound obtained by reaction of diacetyl benzidine with ethyl sulphate was next investigated. Diacetyl benzidine was prepared by refluxing benzidine with glacial acetic acid according to the directions of Strakosch (27). 20 grams of this compound was refluxed with 16 grams of ethyl sulphate in the presence of 100 c.c. chloroform for about 10 hours. The resultant mixture was refluxed with a solution of 5.6 grams of potassium hydroxide in 150 cc. ethanol until a grey-white precipitate was obtained, the mixture then being evaporated to dryness. The residue was taken up in water, filtered, and the benzidine sulfonic acid precipitated by the addition of sulfuric acid. When this precipitate was tested for indicator properties it was found that only a slight color change was obtained at the endpoint.

Dinaphtho carbazol was next investigated. This compound is obtained as a by-product in the preparation of naphthidine by reduction of azonaphthalene with stannous chloride. The filtrate from which the naphthidine hydrochloride has been separated is boiled for 2 hours during which time all the dinaphtho carbazol will have precipitated. This precipitate is recrystallized from dilute alcohol, m.p. 214°. recorded m.p. 216°. When tested for indicator properties, however, only a slight purple color was given by the oxidized compound.

Summary

(1) An improved preparation of naphthidine has been devised..

(2) The compound produced by the reaction of old ethyl sulphate with diphenylamine has been isolated and its composition established, as the sodium salt of a mono-sulphonated derivative.

(3) A satisfactory indicator has been produced by the reaction of butyl sulphate with diphenylamine. This compound has been shown to be the sodium salt of a mono-sulphonated derivative of diphenylamine.

(4) The identity of the indicator produced by reaction of old ethyl sulphate with diphenylamine with that produced by reaction of butyl sulphate with diphenylamine was proved by means of sulphur and sodium determinations and by the identical melting points of the para-toluidine salts of these products, both individually and in mixture.

(5) The pure indicator from the reaction of ethyl sulphate with acetyldiphenylamine was isolated and analyzed and found to be the sodium salt of a mono-sulphonated derivative of diphenylamine.

(6) The following new compounds were prepared and analyzed. They gave no color changes when employed

as oxidation-reduction indicators.

meta-tolyl phenylamine mono-sodium sulphonate

para-tolyl phenylamine mono-sodium sulphonate

(7) The following compounds were prepared and found to give color changes, but these color changes are of too little merit to warrant the use of these compounds as oxidation-reduction indicators.

benzidine mono-sulphonic acid

dinaphtho carbazol

dimethyl benzidine

(8) The following new indicators function satisfactorily in the absence of appreciable concentrations of hydrochloric acid.

diphenyl benzidine mono-sodium sulphonate

ortho-tolyl phenylamine mono-sodium sulphonate

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