"EXPERIMENTS ON THE PREPARATION OF AMINOHYDROXYNAPHTHOIC ACIDS"

by

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Abbreviations employed in the references.

Abbreviated title.	Full title.
Abs.	British Chemical Abstracts.
Ann.	Justus Liebig's Annalen der Chemie.
Ann. Reports	Annual Reports of the Progress of Chemistry.
B.	Berichte der deutschen chemischen Gesellschaft.
Bull. Soc. Chim.	Bulletin de la Societe Chimique de France.
C.	Chemisches Zentralblatt.
Chem. Fabs.	Die Chemische Fabrik.
Compt. rendus.	Comptes rendus hebdomadaires des Seances de l'Acadamie des Sciences.
D.R.P.	Patentschrift des Deutschen Reiches.
E.P.	English patent.
F.P.	French patent.
Frdl.	Friedlanders Fortschritte der Teerfarbenfabrikation.
Helv. Chim. Acta.	Helvetica Chimica Acta.
I.G.	I.G. Farbenindustrie Aktiengesellshaft.
J. Amer. C. S.	Journal of the American Chemical Society.
J.C.S.	Journal of the Chemical Society.
J. Ind,E.C.	Journal of Industrial & Engineering Chemistry.
J.S.C.I.	Journal of the Society of Chemistry & Industry.
J.Gen.Chem.Russ.	Journal of General Chemistry. (U.S.S.R.).
J. pr. Chem.	Journal fur praktische Chemie.
Monatsch.	Monatshefte fur Chemie und verwandte Teile anderer Wissenschaften.
Rec. trav. chim.	Recueil des Fravaux chimiques des Pays-Bas et de la Belgique.

OBJECT OF THE RESEARCH.

The main object of this research was to find a method for the preparation of aminohydroxynaphthoic acids, corresponding to the aminohydroxynaphthalene sulphonic acids, which have wide commercial importance as intermediates in the manufacture of synthetic dye-stuffs.

Only a few of the aminohydroxynaphthoic acids are known and these do not include those corresponding to the important aminohydroxynaphthalene sulphonic acids, J-acid (2-amino-5-hydroxy-7-sulphonic acid), γ-acid (2-amino-8-hydroxy-6-sulphonic acid) and S-acid (I-amino-8-hydroxy-4-sulphonic acid).

A method of preparation of an aminohydroxynaphthoic acid (corresponding to one or all of the above-mentioned sulphonic acids) was sought therefore, with the object that a comparison of their properties might be made, and with the hope that they might be commercially important.

INTRODUCTION.

Of the fifty-six possible aminohydroxynaphthoic acids, eight have been prepared (for complete list see p. 9), and of these only three contain the substituents distributed throughout both nuclei. I.G.(F.P.620,718, 1927), Abs.(B. 1927, 808) claim to have prepared 1-amino-6-hydroxy-8-naphthoic acid. Details as to its method of preparation are not given and in the above abstracts it is simply mentioned. The re:action is not at all clear, but evidently the starting material is 1:8-cyanonaphthalene sulphonic acid, which, on treatment with acid and alkali under certain conditions, not specified, yields the above acid.

It is claimed too, by I.G.(F.P.670,462, 1928) that 2-amino-6-hydroxy-7-naphthoic acid is obtained when the corresponding dihydroxy acid is treated with ammonia under certain conditions. Earlier Froelicher & Cohen (J.C.S. 1922, 121, 1655) state that they prepared the above acid by nitrating 6-methoxy-7-naphthoic acid and reducing the product. The aminomethoxy acid thus formed, was treated with hydriodic acid, and yielded the aminohydroxy acid. Proof that the nitro group entered the <u>2</u> position was obtained by boiling this acid for some time, when 2:6-dihydroxy-7-naphthoic acid (prepared by Schmidt (B.1893, <u>26</u>, 1118,) by action of solid caustic potash on the 2-sulpho-6-dihydroxy-7-naphthoic acid) separated out. Groves (I.G. B.P. 445,278, 2.10. 34) by eliminating the azo group from the diazo oxide

oxide/ of 5-amino-6-hydroxy-2-nitro-7-naphthoic acid, and reducing the product obtained 2-amino-6-hydro-7-naphthoic acid, whilst the same author (I.G. B.P. 462,699, 14.9.35) claims the preparation of the same acid by the action of aqueous ammonia and copper bronze or copper salt on 2-bromo-6-hydroxy-7-naphthoic acid.

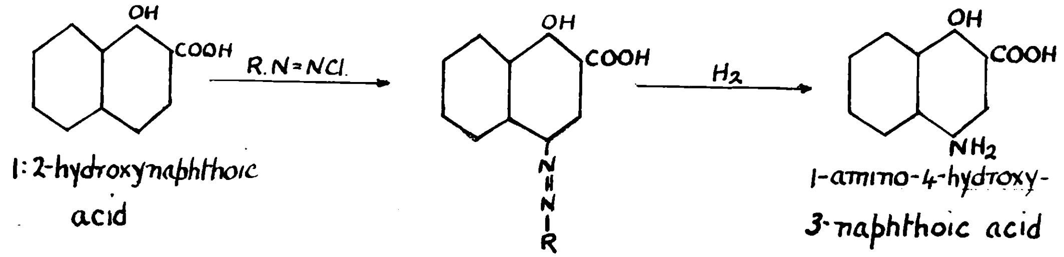
Willstatter, Ulbrich, Pogany & Maimeri (Ann. 1929, 477 , 161; Abs.A. 1930, 214) isolated the I-amino-4-hydroxy-8-naphthoic acid. They condensed I: 4-naphthaquinone with α - carbomethoxy- α - phenylhydrazine, and on treating the condensation product, methyl I: 4- naphthaquinone-phenylhydrazine-N-carboxylate, with barium hydroxide, they obtained, among others, a rearrangement product, in which the carbalkoxy group migrated to the naphthalene ring. Thus methyl-I-benzeneazo-4-hydroxy-8-naphthoate was obtained which, on reduction, gave I-amino-4-hydroxy-8-naphthoic acid.

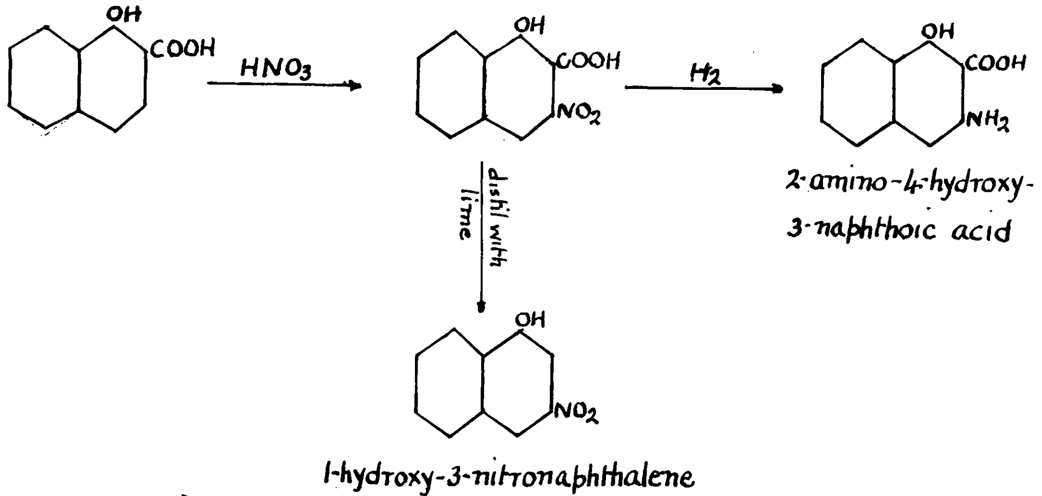
A recent patent by I.G. (B.P. 492,987, 2.6.37) claims that as patent agent Carpmael (Abs.(P)B. 1390) prepared the I-amino-4-hydroxy-8-naphthoic acid by coupling I:5-hydroxynaphthoic acid with diazotised *p* - toluidine in strongly alkaline solution, and reducing the azo compound formed, by the method first introduced by Grandmougin (B. 1906, 39, 3609). Under these conditions, coupling, it is said, takes place in the 8-position, and on reduction, the I-amino-4-hydroxy- 8-naphthoic acid is obtained. This, on heating with aqueous acids forms 4-hydroxy-naphthostyril.

The remaining five known aminohydroxynaphthoic acids all have the three substituents in the same nucleus in the naphthalene molecule, and the general method of preparation was the coupling of a hydroxynaphthoic acid of known constitution with a diazotised aromatic amine, generally aniline or sulphanilic acid, and reduction of the azo product so formed.

In this manner Nietzki & Guitermann (B.1887, <u>20</u>, 1275) claimed to have prepared the I-amino-4-hydroxy-3-naphthoic acid by coupling I:2-hydroxynaphthoic acid with diazobenzene chloride, and reducing the red azo product with tin, stannous chloride and hydrochloric acid, but the actual structure was open to doubt as no definite proof was offered, till Schmidt & Burkard (B. 1887, <u>20</u>, 2700) prepared the above acid by coupling the same hydroxynaphthoic acid with diazotised naphthionic acid and reduced the azo dyestuff with the same reducing agents. To establish the constitution, they nitrated the I: 2-hydroxynaphthoic acid, and obtained a derivative, which on distillation with lime, yielded I-hydroxy-3-nitronaphthalene. This established the position of the entering nitro group. Subsequent reduction of the nitrated hydroxy acid gave an animo acid, which differed from that obtained by coupling the I:2-hydroxy-naphthoic, and subsequently reducing. This, then, proved, that coupling had taken place in the <u>I</u> position, otherwise the products of the two experiments would have been identical.

The following equations illustrate the reasoning.





Further confirmation of the constitution of the 1-amino-4-hydroxy-3-naphthoic acid was afforded by Grandmougin (B.1906, 39, 3609) who used sodium hyposulphite ($Na_2S_2O_4$) to reduce the benzeneazo-α-hydroxynaphthoic acid in alcoholic solution, and obtained a product identical with that of Nietzki & Guitermann (loc.cit.). This, on long boiling with hydrochloric acid yielded 1:4-amino-hydroxy-naphthalene. Hence, the constitution of the two acids was definitely

definitely/ established. Some time later Froelicher & Cohen (loc. cit.) by nitrating I-methoxy-2-naphthoic acid obtained a mononitro derivative, which, when boiled with hydriodic acid, yielded the I-amino-4-hydroxy-3-naphthoic acid. This acid was also formed by the reduction of the nitro compound with stannous chloride. Later Weil & Heerdt (B. 1922, 55, 224) prepared the same acid by coupling the I:2-hydroxy- naphthoic acid with sulphanilic acid and reducing the azo dyestuff formed, with zinc dust and acetic acid. The authors also showed that the product actually isolated by Nietzki & Guitermann was not the free acid, as had been claimed, but a mixture of the free acid and the hydrochloride.

The next aminohydroxynaphthoic acid to be prepared was the I: 2: 3- acid, first isolated by Mohlau & Kriebel (B.1895, 28, 3091) who coupled the 2: 3-hydroxynaphthoic acid with diazotised α - naphthylamine, and after reduction of the azo-dyestuff with stannous chloride, they separated an aminohydroxynaphthoic acid which differed from those obtained by Nietzki & Guitermann, and Schmidt & Burkard. No definite and detailed proof is given that coupling took place in the I-position, but it is now well known and accepted, that with β-naphthol and its derivatives, coupling takes place in the I-position only. Thus it follows that the acid formed and separated by Mohlau & Kriebel was the I-amino-2-hydroxy-3-naphthoic acid.

This acid was also prepared by Weil & Heerdt (B. 1922, 55, 226) in a manner analogous to that by which they isolated the I-amino-4-hydroxy-3naphthoic acid; by Robertson (J. prak. chem. (2) 48, 535) who nitrated the 2: 3-hydroxynaphthoic acid and on reducing the product, obtained an acid identical with that of Mohlau & Kriebel (loc. cit.); and finally by Lasser & Gad (B. 1925, 25, 2554) who utilised the method introduced by Grandmougin (loc. cit.).

In 1912, Heller (B. 1912, 45, 674) claimed to have prepared the 2-amino-I-hydroxy-4-naphthoic acid. He treated the I: 4-hydroxynaphthoic acid with 66% nitric acid, and reduced the nitro compound obtained with sodium hyposulphite ($Na_2S_2O_4$) in alkaline solution. The amino acid was precipitated by addition of acetic acid. Proof of the structure is not given, but it is assumed that the nitro group entered the ortho and meta positions to the hydroxyl and carboxyl groups respectively, in accordance with the general rule for the benzene series.

Lasser & Gad (loc. cit.) utilising the same method by which they prepared the I-amino-2-hydroxy-3-naphthoic, prepared the I-amino-2-hydroxy-4-naphthoic acid, by coupling the 2: 4-hydroxynaphthoic acid with *p* - diazobenzene sulphonic acid and reducing the azo dyestuff. The nitrile of this acid is claimed to have been prepared by Bradley & Robinson by what appears to be a new reaction (I.C.I. B.P. 381, 602: B. 1933, 66, 101; cf. J.C.S. 1934,

J.C.S. 1934, 1484)./
The process consists of the interaction between a cyanide (not definitely specified but it would appear to mean a metallic alkali cyanide) and a nitroso-β-naphthol, or an azo compound derived from a naphthol, either in aqueous or alcoholic suspension, and heating if necessary. Thus, it is claimed, that when I-nitroso-2-naphthol or I-benzene-azo-2-naphthol is suitably treated with potassium cyanide, the former in aqueous and the latter in alcoholic suspension, it is converted to a substituted I-amino-2-naphthol which is believed to carry a cyano group in the 4 position. This, on hydrolysis, would be expected to yield the I-amino-2-hydroxy-4-naphthoic acid. No direct proof of the structure is given.

By using 4-benzene azo-I-naphthol and treating with potassium cyanide, the ultimate product, it is claimed, is apparently a substituted 4-amino-I-naphthol, with a carboxyl in the 2 or 3 position. Again no definite proof is given of the structure.

List of known Aminohydroxynaphthoic Acids.

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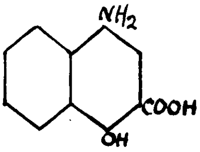
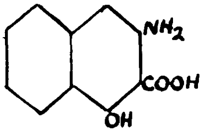
I) 

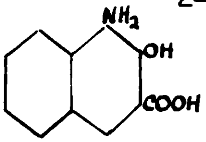
Nietzki & Guitermann (B. 1887, 20, 1275).

I-amino-4-hydroxy-3-naphthoic acid.

2) 

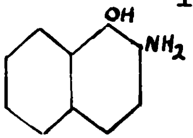
Schmidt & Burkard (B. 1887, 20, 2700).

2-amino-4-hydroxy-3-naphthoic acid.

3) 

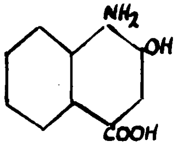
Mohlau & Kriebel (B. 1895, 28, 3091).

I-amino-2-hydroxy-3-naphthoic acid.

4) 

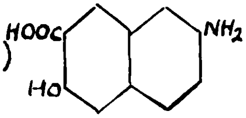
Heller (B.1912, 45, 674).

2-amino-I-hydroxy-4-naphthoic acid.

5) 

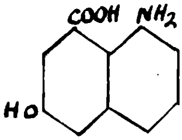
Lasser & Gad (B. 1925, 25, 2554).

I-amino-2-hydroxy-4-naphthoic acid.

6) 

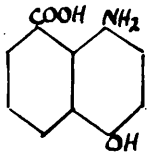
Froelicher & Cohen (J.C.S. 1922, 121, 1655).

2-amino-6-hydroxy-7-naphthoic acid.

7) 

I.G. (F.P. 620,718, 1927).

I-amino-6-hydroxy-8-naphthoic acid.

8) 

Willstatter, Ulbrich, Pogany & Maimeri
(Ann. 1929, 477, 161-194).

I-amino-4-hydroxy-8-naphthoic acid.

Methods of Approach.

For the preparation of aminohydroxynaphthoic acids, there are several methods of approach, and an examination of these, showed that there are five, which appeared to offer the best opportunities of success, each, with its apparent limitations, but capable of application, once the necessary conditions have been established.

These are

1) coupling of a hydroxynaphthoic acid of known constitution with a diazo compound, and reduction of the azo compound produced.

2) the nitration of a hydroxynaphthoic acid of known constitution, and subsequent reduction of the nitro compound formed.

3) the sulphonation of an aminonaphthoic acid of known constitution, and the conversion by alkali fusion, of the sulphonic group to hydroxyl.

4) the nitrosation of a hydroxynaphthoic acid and reduction of the product.

5) the introduction of a carboxyl group into an aminonaphthol.

Now it is highly probable that methods I, 2 & 4 have a very limited application. With regard to I) coupling generally takes place in the α - position, ortho to the hydroxyl if this is in the β - position, and para if the hydroxyl is in the α - position. It is almost certain, too, that coupling

coupling/ will take place in that part of the naphthalene nucleus occupied by the hydroxyl group. (cf. Carpmael, loc. cit.) This is borne out by a study of the aminohydroxynaphthoic acids prepared by the earlier workers using this method. Each one contains the amino-group in an α - position.

Similarly with 2). Mononitration of a naphthalene compound in the β - position is rare, (cf. Schmidt & Burkard B. 1887, 20, 2700), and it may be deduced that mononitration, owing to the activity of the α -hydrogen atom, may be expected to occur in the α -position, and in that nucleus occupied by the hydroxyl group (cf. Heller B. 1912, 43, 674; and Froelicher & Cohen J.C.S. 1922, 121, 1655).

The same reasoning may be applied to 4). The nitroso group would replace the α -hydrogen atom and an α -amino compound would result, after reduction.

With regard to 5) the carboxyl group could be introduced in one of several ways, e.g. by the modification of the Friedel-Craft's reaction using trichloracetonitrile utilised by Houben & Fischer, (J. pr. Chem. 1929 (2), 123,313; Houben B. 1920, 63, 2455; Houben & Fischer, ibid. 2464; ibid. 1933, 66, 339) to prepare carboxy & cyano derivitives of hydrocarbons, or by that method used by Willstatter etc. (loc. cit.) to prepare I-amino-4-hydroxy-8-naphthoic acid, but again, it would appear that an α - aminocarboxylic acid would result.

Thus these methods, though apparently simple in in/ execution, could be expected to give a product where the amino group was in the I position only. On the other hand preparation by 3) offered the best prospects of success, since, the amino-naphthoic acid could be chosen with the amino group either in the I or 2 position as desired; and by varying the conditions during sulphonation, it could be hoped to obtain, after fusing each product with alkali, a variety of aminohydroxynaphthoic acids, especially those corresponding to the well-known J, S, γ- acids. It was decided, therefore, to attempt the preparation of the 2-amino-5-hydroxy-7-naphthoic acid, which would correspond to the sulphonic acid, J-acid.

Part I.

Attempts to prepare 2:7-cyanonaphthol by diazotisation of 2:7-aminonaphthol, followed by Sandmeyer reaction.

Part I.

PROPOSED METHOD OF PREPARATION.

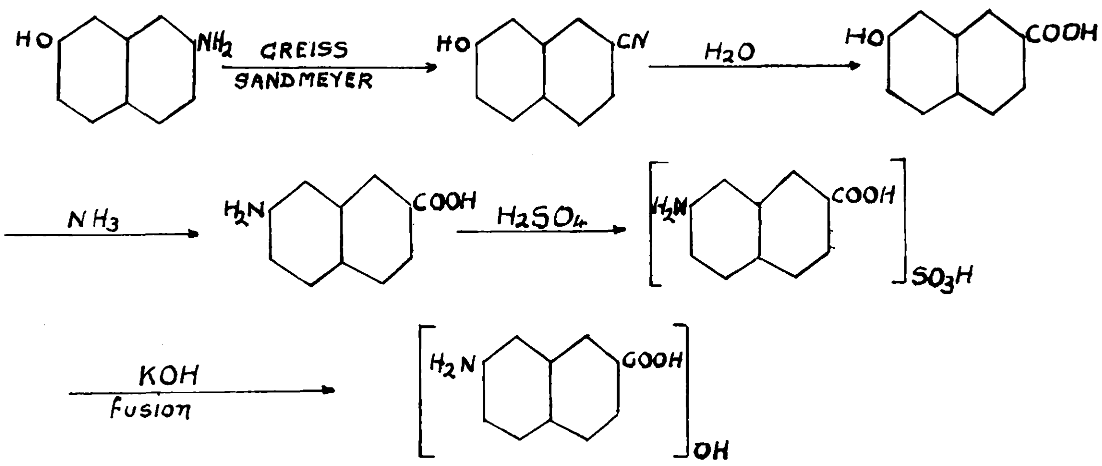
To synthesise 2-amino-5-hydroxy-7-naphthoic acid, the first essential, it was decided, was the preparation of 2:7-aminonaphthoic acid. For the first attempt it was decided to start with 2:7-aminonaphthol, and proceed according to the following scheme.

The amine would be diazotised, and the amino group replaced by the cyano group (Sandmeyer). The 2:7- cyanonaphthol obtained would, on hydrolysis, give the corresponding carboxylic acid, which, on amidation would yield the required aminonaphthoic acid. This on sulphonation followed by alkali fusion, might be expected to give an aminohydroxynaphthoic acid, in which the positions of the amino and carboxyl groups were known. To complete the orientation of the acid, all that would be required would be to fix the position of the hydroxyl group, and it was proposed to do this in one or other of the following ways.

Firstly, by elimination of the amino-group in the aminosulphonaphthoic acid by diazotisation and replacement of the diazo group by hydrogen, a sulphonaphthoic acid would be isolated and this on alkali fusion, would yield a hydroxy acid, readily identifiable, since all the hydroxynaphthoic are known. Hence the position of the sulphonic group in the molecule would be established.

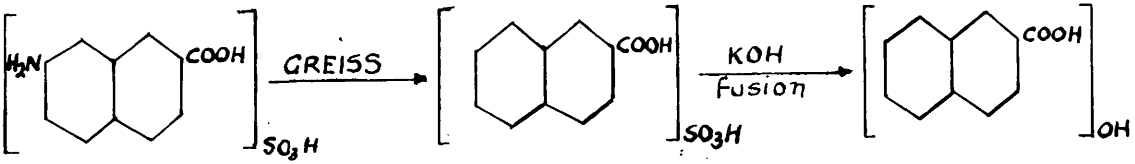
Alternatively, the amino-group of the aminohydroxynaphthoic acid would be eliminated by the same method as above and a hydroxynaphthoic acid of known constitution obtained.

The complete scheme is outlined below.



Schemes for orientation.

1)



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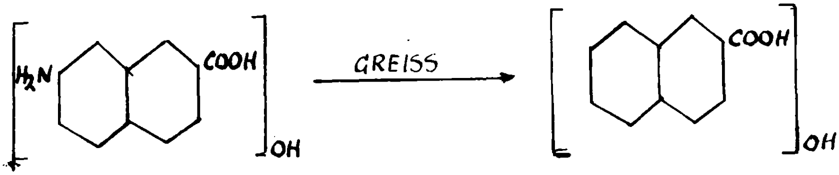


In considering the scheme for the complete synthesis it was appreciated that the product of sulphonation would, in all probability, consist of a mixture of two and possibly three isomers, but it was hoped that these would be readily separated by fractional crystallisation either of the free acids or of one of the many possible salts.

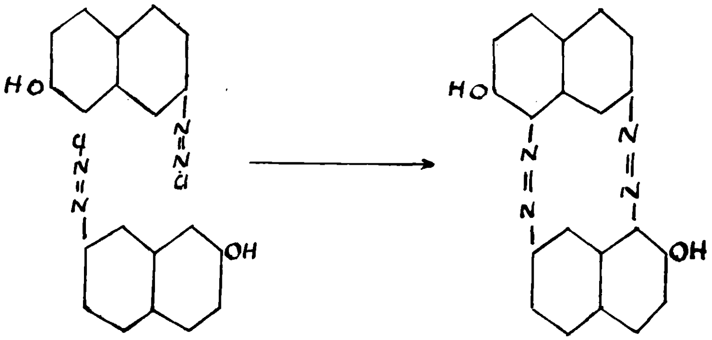
Diazotisation of Aminonaphthols.

In the literature very little is given regarding the diazotisation of the aminonaphthols. Grandmougin & Michel (B. 1892, 25, 997) state that I-amino-2-naphthol is diazotised by nitrous acid forming a yellow solution which couples with alkaline phenol to form a red azo body. Friedlander (B.1895, 28, 1952) says that the diazo compound of I-amino-3-naphthol is very unstable as on addition of nitrous acid, the bright yellow solution formed initially quickly turns dark brownish violet and a solid separates in a short time. This it would seem, is due to oxidation or possibly coupling with the formation of an azo body. The same author, in conjunction with Kilbasinski (B.1896, 29, 1979) says that 5-amino-2-naphthol is easily diazotised, but gives no details as to procedure. Sachs (B.1906, 39, 3016) mentions the 6-amino-2-naphthol and the 5-amino-2-naphthol and says the latter is easily diazotised, while the former in acetic acid solution gives with potassium nitrite a green solution and in sulphuric acid a yellowish green solution which couples with alkaline β -naphthol.

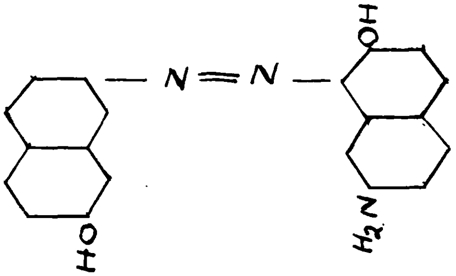
The diazotisation of 8-amino-I-naphthol is described by Fichter & Gageur (B.1906, 39, 3337). They say that nitrous acid can act in two ways. In one, the amino group is diazotised and in the other the hydroxyl group forms a quinone oxime. Diazotisation proceeds smoothly in dilute solution. It is advantageous to add the hydrochloride of of/ the aminonaphthol to the calculated quantity of nitrite solution, in order to avoid as much as possible the formation of a dark byeproduct, formed by the interaction of a diazotised molecule with an undiazotised molecule.

Geigy (E.P. 10, 235/04: D.R.P. 171,024; 172,446; (Frdl. 8, 640,656); U.S.P. 793,743; F.P. 349,989) success:fully diazotised the 2:I- and I:2 -aminonaphthols. The difficulty arises because of the possibility of nitrous acid acting as an oxidising agent. In the presence of copper sulphate its oxidising influence is diminished. In this way, by the action of sodium nitrite on the acid salts of the 2:I- and I:2-aminonaphthols in the presence of copper sulphate, Geigy (loc.cit.) successfully diazotised them.

The difficulty, due to oxidation, has arisen often, e.g. the diazotisation of some of the aminodiphenylamines, and it would appear that the influence of copper sulphate and other salts depends on the fact that they control the p_H value of the diazotisation medium, maintaining this value between the limits necessary for successful diazotisation. Kaufler & Karrer (B.1907, 40, 3267) claim to have diazotised 2:7-aminonaphthol in absolute alcohol and concentrated hydrochloric acid, using amyl nitrite as the source of nitrous acid. They say:-I) that the diazonium chloride is insoluble in alcohol and hence it is precip:itated, whilst it is characterised by a coupling with dimethylaniline in alcoholic solution on addition of of/ glacial acetic acid:- 2) that there is the possibility of the diazonium chloride coupling with itself to form a red-brown dyestuff according to the following equation.



3) that the diazonium hydrochloride may couple with unchanged aminonaphthol in alkaline solution to give a compound having the following structure:-



The author in an attempt to isolate the solid diazonium chloride, did not find that the reaction proceeded as above described. When the amyl nitrite was slowly added, a red solution was obtained which gradually became more highly coloured. In fact, on making the solution alkaline with dilute ammonia solution, a red precipitate was obtained which on washing with ether, left an insoluble residue, identified as unchanged 2:7-aminonaphthol hydrochloride. From the ethereal washings on evaporation, a reddish brown solid separated,

separated,/ which was shown to be an azo body, probably identical with that described above.

In connection with the above, it is interesting to note, with regard to Knoevenagel's statement (B.1890, 23, 2995) that the diazotisation of amines by amyl nitrite depends on the extraordinary rapidity with which the alkyl nitrite breaks up in the presence of acid (cf. vgl. Hausser & Muller, Bull. (3), 9, 353, 1893), that Bamberger in a private communication (vide Meyer & Jacobsen 11, 279, footnote) states that the diazonium compound is always obtained contaminated with unchanged amine salt.

A further important point in making diazonium salts of analytical purity by Knoevenagel's method was disclosed by Hirsch (B.1897, 30, 1148) that the amine salt must be free from any excess acid, because diazonium salts have a strong tendency to form additive compounds, which, once formed, are eliminated with difficulty. Since Kaufler & Karrer (loc.cit.) used a large excess of acid, namely 6.5 mols. the above disclosure possibly explains why the diazotisation did not go to completion.

As regards the use of absolute alcohol in diazotisation and the fact that unchanged amine was found, Mohr (Ann.221, 200) states that absolute alcohol frequently hinders diazotisation. For example, he found that p-diazobenzene sulphonic acid was not formed by the action of nitrous acid on the amino acid in alcoholic solution.

Diazotisation of 2:7-aminonaphthol and the attempts to form 2:7-cyanonaphthol.

Diazotisation of the 2:7-aminonaphthol caused a little difficulty. When attempted in the usual manner using an excess of two to three mols. over the calculated quantity of hydrochloric acid, there was formed, possibly due to the coupling of an undiazotised molecule with a diazotised molecule, a red aminoazo body. This tendency to form such a product is no doubt due to the negative hydroxyl group, whose presence in the molecule lowers the basicity of the amine and makes an increased amount of acid necessary, to prevent the formation of the azo compound. It was found by experiment that an excess of five to six mols. of acid was sufficient, but that it was necessary to add the sodium nitrite all at once, otherwise the red azo body separated. The solution of the diazonium salt formed in this way was dark in colour. It could be diluted and coupled with alkaline β -naphthol, or alkaline H-acid, and if heated evolved nitrogen with the formation of an insoluble dark coloured substance. Hence it was concluded that diazotis:ation had taken place, and the preparation of the 2:7-hydroxy-naphthoic acid, by means of the Sandmeyer reaction and subsequent hydrolysis was proceeded with.

On adding the diazonium solution to the cuprous cyanide-potassium cyanide solution in which excess alkali was reduced to a minimum by addition of hydrochloric acid according to the recommendation of Rayle & Schoedler (J.C.S. 1923, (I), Rayle & Schoedler (J.C.S. 1923, (I),/ 1643 T), some frothing took place, there was a strong smell of HCN and a brownish red solid separated. Attempts to isolate the nitrile by means of various solvents failed. (p. 27).

Diazotisation after the method of Hodgson & Walker (J.C.S. 1933, 124, 1620) where the base, dissolved in glacial acetic acid, is poured into the calculated quantity of nitrosylsulphuric acid, was next tried and was successful, but on adding the diazonium solution to the cuprous cyanide-potassium cyanide solution, heat was again evolved, there was little or no evolution of nitrogen, and a brownish red solid, similar to the one obtained in the previous experiment, separated.

Failure to obtain the nitrile in these two experiments led to the opinion that such a large excess of acid, necessarily present for diazotisation, might be interfering with the interaction of the diazonium salt and the cuprous cyanide solution. To reduce the excess of acid to a minimum, finely powdered anhydrous sodium carbonate was added to the diazonium solution at 0°C. (cf. Clarke and Reid J. Amer. C.S. 1924, 1001). A finely divided solid separated, even on very slow addition of the carbonate. This solid when filtered off and examined, was shown to be, not a diazo compound, but a highly coloured azo body, probably formed by the interaction of two diazotised molecules, as suggested by Kaufler & Karrer

Kaufler & Karrer/ (B.1907, 40, 3267). It is interesting to note that the filtrate from the azo body was perfectly clear from colouring matter, which seems to indicate quantitative coupling. The same result was obtained when an attempt was made to reduce the acidity by adding, in small quantities at a time, finely pulverised anhydrous sodium acetate.

Diazotisation of the 2:7-aminonaphthol was also successfully accomplished by a modification of the method introduced by Schoutissen (J.Amer.C.S.1933, 55, 4531) for the diazotisation of p-aminobenzaldehyde. This method, it is claimed is eminently suitable for the diazotisation of difficultly diazotisable amines. Schoutissen was of the opinion that the nitrosylsulphuric acid did not readily give up its nitrogen, so to weaken the attachment he diluted the solution with syrupy phosphoric acid. The original method of Schoutissen was to dissolve the base in conc. H_2SO_4 (sp.gr. 1.84), cool to 0°, and add the nitrosyl sulphuric acid, followed by syrupy phosphoric acid (sp.1.70°) at 0°C. In this case the 2:7-aminonaphthol was dissolved in syrupy phosphoric acid, cooled by external cooling to -3°, and to this was added, drop by drop, the calculated quantity of nitrosylsulphuric acid. Great care was taken that the temperature was not allowed to rise above 0°C. A dark viscous solution resulted, which, on dilution with ice water, gave a pale yellow solution, having all the reactions of a diazonium salt.

Accordingly it was run into a cold solution of cuprous cyanide-potassium cyanide, and subsequently warmed. HCN was evolved with frothing, and a dark reddish brown solid separated. This resembled in every respect the product obtained in the other attempts to form the nitrile. Nevertheless it was boiled with 66% H_2SO_4 in an effort to hydrolyse any nitrile which might be present, but nothing was obtained.

As is well known a factor which has a dominating influence on the coupling of any diazo compound with any particular second component is the acidity of the solution. Goldschmidt (B. 1895, 28, 2020) showed that it is the diazohydroxide, formed by hydrolysis of the metallic diazotate of the diazo salt, which is the active power in coupling and hence, in the absence of strong mineral acid, the coupling takes place, since acids prevent the conversion of the diazonium salt into diazohydroxide or diazotate.

From the foregoing experiments then, it was concluded that the diazonium salt of 2:7-aminonaphthol, once formed, is stable only in strong acid solution. Any diminution of the acidity, the lowering of the p_H value below a certain level by the addition of sodium bicarbonate or sodium acetate, sets up a condition of instability of the diazo compound, favourable for the formation of an azo body.

Again, from the failure of the Sandmeyer reaction under ordinary conditions, it would appear that the activity with which internal coupling takes place, is such that the formation of diazo cyanide is impossible.

When the aforementioned behaviour of the diazo body had been established, it was realised that the ordinary application of the Sandmeyer reaction using cuprous cyanide-potassium cyanide solution was useless, and various modifications were tried, but, unfortunately, these also proved fruitless.

Treatment of the diazonium solution with solid cuprous cyanide both in suspension and/or in the finely pulverised state, over a period of hours, always maintaining the temperature at 0°-5°C, merely reduced the acidity of the solution by formation of cuprous chloride and HCN, and, consequently, coupling, to give an azo body, took place slowly.

Heller (J. pr. Chem.1908, 11, 77, 190) mentions the beneficial effect of quinoline on the tris coupling of resorcinol, but says that pyridine has no effect. Fischer & Bauer (ibid. 190) say they tried pyridine to improve the coupling of I:5-dihydroxynaphthalene with no perceptible result.

An attempt to form the nitrile using the additive compound of cuprous cyanide and pyridine even more readily gave the azo compound. This is more or less to be expected since it is known that pyridine brings about an exaltation

exaltation/ of the "coupling energy" of many long chain diazo compounds, but it was thought that because pyridine appears to stabilise the diazo compound (I.G.,E.P.248,230: D.R.P.450,998 (Frdl. 15, 521); D.R.P.453,133 (Frdl.15,522); E.P.287,232; 298,518; J.S.C.I., E.P. 347,742), it might be sufficiently stabilised to allow the formation of the diazocyanide, before coupling took place.

How or in what manner pyridine and quinoline brings about this increase in coupling energy is not stated or published, but it would hardly appear to be simply either a mere buffering of pH, or a loose combination of the diazonium compound and pyridine, sufficiently stable during the time necessary for the coupling to take place. It is possibly a combination of these two factors.

From the foregoing it would appear that the formation of 2:7-cyanonaphthol by diazotisation of 2:7-amino-naphthol and subsequent treatment according to the Sandmeyer reaction is not possible, because the tendency for coupling with formation of an azo compound is greater than that for the formation of the nitrile. Accordingly attempts to form an aminohydroxynaphthoic acid, by the process outlined on p. 13 were abandoned.

Part 1.

EXPERIMENTAL.

1. Purification of 2:7-aminonaphthol.

The 2:7-aminonaphthol, supplied by I.C.I. Ltd. in the form of dark grey crystals, was purified by crystallisation from water using decolourising carbon. A pale grey crystalline sold M.P.201°was obtained.

2. Preparation of Cuprous cyanide solution.

12.5 gms. (1 mol.) of crystalline copper sulphate were dissolved in 40 c.c.s., hot water, and 3.25 gms. (1.1 mols) sodium chloride added, and the mixture stirred until all had dissolved, when a solution, containing 2.65 gms. (1 mol.) sodium bisulphate, 1.75 gms. (1 mol.) NaOH, and 20.0 c.c.s. water, was added with brisk stirring. The precipitated cuprous chloride was filtered off, washed first with SO_2 solution, then with distilled water, suspended in 20 c.c. cold water as quickly as possible, and 17.5 gms. (12.7-13 mols.) commercial KCN., in 10 c.c.s. water, added gradually, until the cuprous chloride dissolved and formed an almost colourless solution of potassium cuprocyanide. The amount of KCN was reduced to a minimum by very careful addition of concentrated HCl solution, until a faint milkiness was discernible.

3. Attempted diazotisation of 2:7-aminonaphthol.

6.36gms. (1 mol.) purified 2:7-aminonaphthol were dissolved in 100c.c.s. water containing 10ccs., (2.5 mols.) concentrated HCl, and to the solution, cooled to 0°C, both by addition of some crushed ice, and external cooling, was added with good mechanical agitation, a cold solution of 2.8 gms. (1 mol.) sodium nitrite dissolved in 8ccs. of water. The addition of the nitrite was slow and below the surface. A reddish brown solid, soluble in alkali to form a red solution, separated out.

This seems to indicate that diazotisation had taken place but that under the conditions and concentration of the experiment any diazonium salt formed immediately coupled with undiazotised aminonaphthol. However, the mixture was poured into the cuprocyanide solution with constant stirring, and the whole allowed to rise slowly to room temperature, after which it was warmed up to 90°C., and maintained at that temperature for two hours. There was at no time evolution of nitrogen, but the addition was accompanied by a strong smell of HCN. On cooling, a product separated out which was soluble in caustic soda solution and ether, with formation of a dark red solution. This colour could be discharged by treating the alkaline solution with sodium hyposulphite ($Na_2S_2O_4$).

4. Diazotisation of 2:7-aminonaphthol.

6.36 gms. (1 mol.) 2:7-aminonaphthol were dissolved in 100ccs. water containing 7.3gms. (5/6 mols.) HCl and the solution cooled to 0°C. as before. To this a solution of sodium nitrite containing 2.8gms. (1 mol.) in 8.0ccs. water was added all at once. The temperature rose to 3°C., but no solid separated, and the solution was dark yellow in colour. On warming, it gave off nitrogen; it also coupled with acidified dimethylaniline and alkaline β -naphthol solution.

5. Attempted preparation of 2:7-cyanonaphthol.

The above solution of naphthol diazonium chloride was poured slowly, with good brisk mechanical stirring, into a solution of potassium cuprocyanide solution, prepared as before. Some effervescence took place and frothing, accompanied with evolution of HCN. The mixture was stirred for two hours and left to rise to room temperature overnight. By next morning, a finely divided brown precipitate had separated out. This was filtered off, and washed with cold water until the washings showed no trace of anything soluble, and were not acid to litmus.

The solid was dried under a vacuum over concentrated H_2SO_4, and extracted on a Soxhlet with alcohol. A red solution was obtained and a dark red solid was left in the thimble.

H_2S was passed through the alcoholic solution, the precipitated CuS filtered off, and from the alcoholic solution a dark coloured solid was obtained by concentrating, cooling, and filtering. Further concentration yielded a black tar.

The dark coloured solid was soluble in glacial acetic acid, dilute caustic soda solution, and alcohol, giving a red solution in each case. It was slightly soluble in chloroform, and insoluble in benzene, petroleum ether, and dilute HCl.

Attempts to crystallise it from any of the above organic solvents failed.

The red colour of the alkaline solution was discharged on addition of solid sodium hyposulphite ($Na_2S_2O_4$), pointing to the product being an azo body.

The solid left in the thimble was examined and shown to be mainly $Cu_2(CN)_2$.

6. Diazotisation of 2:7-aminonaphthol.

(after the example of Hodgson & Walker J.C.S. 1933, 124, 1620).

6.36gms. (1 mol.) 2:7-aminonaphthol were dissolved in glacial acetic acid (10ccs.acid/1gm.) and the solution cooled rapidly to 10°C. by external cooling. It was then poured slowly with good stirring into a solution of sodium nitrite in concentrated H_2SO_4 (1gm.$NaNO_2$/7ccs.acid) prepared as follows.

3.1gms. (1 mol.) finely powdered sodium nitrite were gradually added to 21.7ccs. concentrated H_2SO_4, cooled to 0/3°C., with brisk stirring. After addition was complete, the temperature was raised to 70°C., until the nitrite was all dissolved. The resulting solution was cooled to room temperature, and filtered on a sintered glass filter, from sodium bisulphite.

The solution obtained by the interaction of the 2:7-aminonaphthol and the nitrosylsulphuric acid was dark in colour, but could be diluted with water without any signs of decomposition. On warming a portion, nitrogen was given off, and a tar was formed. Addition of powdered anhydrous Na_2CO_3 to a portion, precipitated a dark red solid, pointing to the probable formation of an azo body by the coupling of two molecules.

7. a) Attempted preparation of 2:7-cyanonaphthol. (Sandmeyer).

The diazonium solution prepared above was poured into a potassium cuprocyanide solution at 5°C., prepared as before. HCN was given off but no evolution of nitrogen was observed, whilst the solution became dark red in colour. The whole was allowed to rise to room temperature and heated on the water bath to 70°C. Some frothing took place during warming. The solution was allowed to cool, and poured into much water, when a precipitate settled out. This was filtered off, washed well, dried over concentrated H_2SO_4 under a vacuum, and extracted with alcohol (Soxhlet). The alcoholic extract was dark red in colour and on examination and treatment as in experiment 5,, yielded a dark red solid, which had the same properties as that obtained in that experiment.

b) Reduction of acidity by addition of solid sodium carbonate. (after the example of Clarke & Reid J. Amer.C.S.1924, 1001).

6.36gms. (1 mol.) 2:7-aminonaphthol were diazotised as in experiment 4. The solution was dark yellow and no solid had separated. The volume of the solution was 125ccs.

To 63ccs. of the diazonium solution was added, a little at a time, finely powdered Na_2CO_3 until the solution was slightly acid to litmus, care being taken that the temperature did not rise above 0°C. A very finely divided dark coloured solid appeared to separate,

separate,/ but stirring was continued until the froth had subsided, and then the liquid was carefully neutralised, when it was slowly added to a potassium cuprocyanide solution. No smell of HCN was noticeable, nor was there any evolution of nitrogen. The mixture was allowed to rise to room temperature, warmed to 70°C., cooled and filtered. (The precipitate was exceptionally finely divided and the filtration/took a long time - the filtrate was clear and colourless). It was washed well with cold water and dried on a porous plate.

To all appearances it resembled the azo body obtained in the previous experiments.

c) <u>Reduction of acidity by addition of sodium acetate</u>.

The remaining volume (62ccs.) of the diazo solution prepared in experiment b), was taken and cooled to 0°C. and to this was added with constant stirring solid pulverised sodium acetate. A reddish finely divided precipitate gradually separated out. After two hours, stirring was stopped and the precipitate filtered off, washed with water and dried as before. It exhibited the same properties as those solids obtained in the previous experiments and again the filtrate was clear and colourless.

8. Diazotisation of 2:7-aminonaphthol. (after the method of Schoutissen J.Amer. C.S.1933, 55, 4531)

1.0gm. (1 mol.) 2:7-aminonaphthol was dissolved in 15 ccs. (excess) syrupy phosphoric acid and cooled to -3°C. by external cooling using a mixture of ice and conc. HCl. To this was added drop by drop, 7.0ccs. of nitrosyl-sulphuric acid, prepared as in experiment 6. The addition was carried out very slowly with brisk stirring taking care that the temperature did not rise above 0°C. To assist in keeping down the temperature the nitrosylsulphuric acid was cooled to -5°C. before addition. After some time, as an excess of nitrite was indicated, some urea was added. Effervescence took place, and stirring was continued until this had subsided. The temperature at this time was 0°C., and the solution was dark yellowish brown in colour. It was diluted with ice cold water, and tested for diazotisation by adding portions to

1) alkaline β -naphthol solution
2) acidified dimethylaniline solution
3) alkaline H-acid solution

Coupling took place in each case, with the formation of a red precipitate, a red solution, and a reddish violet precipitate respectively.

Again, a dilute solution on warming on the water bath gave off a gas with the characteristic effervescence of a diazonium solution. Further, on adding a portion to a potassium cuprocyanide solution, effervescence

effervescence/ took place with separation of a solid.

Accordingly diazotisation had taken place.

9. Attempted preparation of 2:7-cyanonaphthol.

5.0gms. 2:7-aminonaphthol were diazotised as in experiment 8, using proportional quantities, and the diazonium solution was slowly run into a slight excess of potassium-cuprocyanide solution, prepared as described in experiment 2. Some little effervescence took place, accompanied with frothing, and a reddish brown solid separated. The mixture was treated as in experiment 5 et sequa, and a solid similar in properties and appearance obtained.

10. Attempted diazotisation of 2:7-aminonaphthol, to isolate the solid diazonium bromide.

Kaufler & Karrer B. 1907, 40, 3267.)

1.0gm. (1 mol.) 2:7-aminonaphthol was dissolved in 100 ccs. absolute alcohol, treated with 2gms. (8.5 mols.) freshly distilled HBr, and cooled to 0°C. by external cooling, 4.5gms. (6 mols.) amyl nitrite were slowly added, drop by drop, with brisk mechanical stirring, and the reaction continued for three hours. Nothing separated but the solution became red, and the intensity of the colour increased with time. The solution was tested for diazotisation by adding test portions to alkaline

alkaline/ β -naphthol solution, dimethylaniline dissolved in dilute hydrochloric acid, and alkaline "H-acid" solution, but in no case did coupling take place, even on standing.

Hence the solution was made just alkaline with NH_4OH solution, the resulting precipitate filtered off, washed with water, dried in a vacuum oven at 70°C. and finally washed with dry ether. The solid obtained had a M.P. of 205-206°, and a mixed M.P. with some of original showed no depression.

From the ethereal washings a dark-reddish brown solid was left on evaporating off the ether. This solid had properties similar to those obtained in previous experiments.

Part II

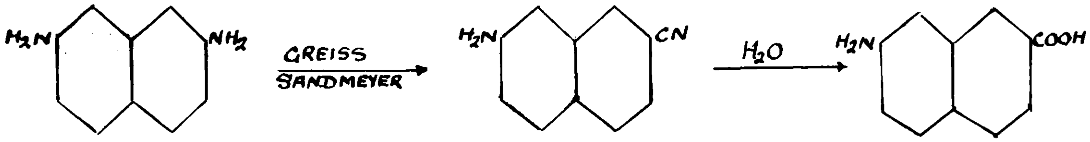
Attempts to prepare 2:7-aminonaphthonitrile by diazotisation of 2:7-diaminonaphthalene, followed by Sandmeyer reaction.

Part II.

Proposed method of preparation.

It was now proposed to attempt the preparation of the 2-amino-5-hydroxy-7-naphthoic acid starting with the 2:7-diaminonaphthalene.

The method it was proposed to adopt was as follows. One amino group of the diamine would be diazotised, replaced (Sandmeyer) by CN and the aminonaphthonitrile formed, on hydrolysis would yield an aminonaphthoic acid and then the procedure would be identical to that outlined before.



Review of known Aminonaphthonitriles.

An examination of the literature showed that though the fourteen aminonaphthonitriles were known only one of them had been prepared by application of the Greiss and Sandmeyer reactions. Bamberger & Philip (B.1887, 20, 243) prepared 1:8-aminonaphthonitrile from the corresponding diaminonaphthalene in this manner. The other known aminonaphthonitriles were made by Friedlander, Heilpern & Spielfogel (Frdl. 4, 611, & Casella & Co., D.R.P.92995) by distilling the anhydrous sodium salts of the

the/ corresponding aminonaphthalene sulphonic acids with finely pulverised and thoroughly dried potassium cyanide or ferrocyanide.

Action of nitrous acid on, and diazotisation of, diaminonaphthalenes.

The action of nitrous acid on the diaminonaphthalene salts has been the subject of wide study.

It has long been recognised that when two or more primary amino groups are attached to different parts of aromatic nuclei forming one molecular unit, then for the purpose of diazotisation, these amino groups may be considered as entirely different units, and so it follows that the diazotisation of one will not affect the reactivity of the other. When however, the two amino groups are in the same part of the molecule tetrazotisation is not likely unless careful attention is given to conditions and it has been shown that if the two amino groups are in the ortho position, there results, except under very special conditions, not a tetrazo compound but an extremely stable azimine, an internal diazoamino compound. (Ladenburg B. 1876, 9, 221, Greiss B. 1872, 5, 200; 1882, 15, 1878; Zinoke & Lawson, Ann. 1887, 240, 119; Zincke & Arzberger Ann. 1888, 249, 350). Since this is a general reaction, it follows that it takes place with the diaminonaphthalenes, where the amino groups are adjacent to one another.

In this way, the 1:2-, 2:3-, and 1:8-diaminonaphthalenes give azimines. Thus, de Aguiar (B.1874,7,316), Friedlander & Zakrewaski (B.1894,27,764) and more recently

recently/ Morgan & Godden (J.C.S.1910, 97, 1702) and Morgan & Micklethwait (ibid., 2557), showed that when these diamines were treated in dilute acid solution with nitrous acid, using either sodium and potassium nitrite or ethyl and amyl nitrite, there resulted not a tetrazo compound but a diazoimide. Again, Morgan, and his co-workers, in investigations into the structure of these azimines, showed that the 1:2-diamonaphthalene differed from the 2:3- and 1:8-diamonaphthalenes by forming a mixture of two isomeric diazoimides.

His earlier experiments were made with the sparingly soluble sulphate of the 1:2-diamonaphthalene suspended in glacial acetic acid, and when excess sodium nitrite was added, a brownish yellow solution was formed. This, on pouring into ice-cold water and partly neutralising with ammonia, gave a compound which sintered at 158°C. and melted at 174°C. When, however, the sulphate was intimately mixed with 20% aqueous sodium nitrite, and added to glacial acetic acid, the product obtained sintered at 260°C. and melted at 285°C. Analysis of both these compounds were identical and hence, since their properties were the same, he concluded they were isomers.

The remaining seven diamines give diazonium salts of varying degrees of stability (Ewer & Pick D.R.P. 45549, 45788; Badische Anilin & Soda Fabrik. D.R.P. 130475).

The 1:4-diamine, however, belongs to that class of substances which suffers destructive oxidation with nitrous acid, with the formation of 1:4-naphthaquinone. Diazotisation, however, of one amino group is accomplished by acetylating one amino group, and treating in the usual manner with sodium nitrite (E.P.18783 & 2496).

Kaufler & Karrer (B.1907, 40, 3262), claim to have diazotised the 2:7-diaminonaphthalene, They state too, that only "monodiazotisation" takes place and that by diazotisation in aqueous solution there always results an azo body due to coupling of a diazotised molecule with an undiazotised molecule or with a decomposition product of the diazonium salt, since evolution of nitrogen occurs. On the other hand, diazotisation is successful in glacial acetic acid or alcoholic solution and especially if the hydrobromide of the base is used.

By dissolving the diamine in glacial acetic acid or absolute alcohol, adding the necessary quantity of 50% hydrobromic acid and using amyl nitrite as the source of nitrous acid, they claim to have obtained yellow lustrous needles of the diazonium compound.

Experiments on the diazotisation of 2:7-diaminonaphthalene, and the attempted preparation of 2:7-aminonaphthonitrile.

In an attempt to obtain the solid diazonium salt of the 2:7-diaminonaphthalene the author repeated the experiment of Kaufler & Karrer (loc.cit) but he did not find the reaction to proceed as stated. On treating the 2:7-diamine dissolved in glacial acetic acid, with 50% hydrobromic acid and subsequently dropping into the solution, cooled to 0°C., the quantity of amyl nitrite stated by them, a red solution was obtained, and, even after five hours stirring during which the temperature was maintained at 0°C., a solid remained suspended in the solution. This solid, on examination, was found to be the hydrobromide of 2:7-diaminonaphthalene. The same result was obtained using absolute alcohol as the solvent. On warming the suspension of the solid in the red solution an intensely red colour developed without evolution of gas.

It would appear then that diazotisation under the above conditions only takes place to a very limited extent, possibly due to a condition of equilibrium being set up. On warming, coupling, probably of the diazo compound with itself or unchanged diaminonaphthalene takes place, upsetting the equilibrium and allowing more of the amine to be diazotised.

Even when concentrated sulphuric acid was added to the amine in glacial acetic acid solution with sodium bromide, either before or after addition of amyl nitrite, diazotisation was incomplete. When, however, pulverised sodium nitrite was used as the source of nitrous acid and concentrated sulphuric acid was present, the solution blackened and a tarry resinous mass, soluble in caustic alkali was formed. The same result was obtained using absolute alcohol as a solvent and diluent.

This, then, seemed to indicate that diazotisation was actually taking place, but, that under the conditions of the experiment, the diazonium salt was very unstable and immediately it was formed it decomposed or that the nitrous acid acted as an oxidising agent.

Accordingly an attempt was made to diazotise the diamine by the ordinary direct method using a large excess of concentrated hydrochloric acid, which was so successful for the diazotisation of the 2:7-aminonaphthol, but a tarry mess was all that was obtained. It will be seen therefore, that to diazotise the 2:7-diaminonaphthalene was even more difficult than in the case of the 2:7-aminonaphthol.

The presence of copper sulphate (Geigy-see page 16) failed to give a diazonium solution, and an attempt using a modification of the method used by Hodgson & Walker (J.C.S.1933,1620) also failed. In this attempt the solution turned dark and finally was black, whilst there was evolution of a gas, though this may be accounted for by the fact that on addition of glacial acetic acid to nitrosylsulphuric acid, brisk evolution of gas takes place. Phosphoric acid, on the other hand, does not cause the evolution of a gas from nitrosylsulphuric acid, and it was found that diazotisation of the 2:7-diaminonaphthalene was successfully accomplished on applying a modification of the method introduced by Schoutissen (J.Amer.C.S.1933, 55, 4531) (cf.diazotisation of 2:7-aminonaphthol). The strongly acid solution obtained after addition of the calculated quantity of nitrosylsulphuric acid for monodiazotisation, was dark coloured. On dilution with ice water it gave a clear yellowish solution, which coupled with alkaline β -naphthol and H-acid.

Now Morgan & Micklewaite (J.C.S.1910, 97, 2557) succeeded in tetrazotising the diamine by dissolving it in concentrated sulphuric acid adding a little ice, followed by nitrosylsulphuric acid in excess and the solid which separated on addition of an ether alcohol mixture was stable, appreciably soluble in alcohol, and

and/ dissolved in water to form a yellow solution. Now, on adding alcohol to the syrupy phosphorous acid diazo solution, the author obtained a yellow solid which was very unstable, and dissolved in water with decomposition to form a bright red solution.

Since the quantity of nitrosylsulphuric acid necessary to diazotise one amino group only was used, it follows that monodiazotisation had taken place.

Having succeeded in diazotising the 2:7-diaminonaphthalene, attempts were made to prepare the nitrile by the same methods used for the 2:7-aminonaphthol.

In all these attempts, and more rapidly with alkaline reagents, a yellowish-brown solid was obtained but in no case was the nitrile isolated.

Part II.

EXPERIMENTAL.

1. Purification of 2:7-diaminonaphthalene.

The 2:7-diaminonaphthalene, supplied by I.C.I.Ltd., as a brown crystalline solid, was purified by recrystallisation from aqueous alcohol, using decolourising carbon and was obtained as almost white plates M.P.160°C.

2. Attempted diazotisation of 2:7-diaminonaphthalene.

a) method of Kaufler & Karrer (B.1907,40,3262).

1gm. (1 mol.) 2:7-diaminonaphthalene was dissolved in 30ccs. (80mols.) glacial acetic acid, treated with 10.3ccs. hydrobromic acid of 40.5% strength (3.37gms.= 3.3 mols.) the solution cooled to 0°C, and 3gms. (2.5mols.) amyl nitrite added drop by drop, with brisk mechanical stirring, which was continued for five hours. The solution was then pale pink. The following tests for diazotisation were carried out .

A little of the solution was added to
1) cold water 2) NaOH solution 3) NH_4OH solution
4) cuprocyanide solution. A red solution was formed in each case and, on warming, there was no evolution of nitrogen, but a red solid separated in tests 2), 3), and 4).

Hence it was concluded that little or no diazotisation had taken place, so caustic soda solution was added to the solution till it was alkaline and the precipitate filtered off, washed with water until the washings showed no alkalinity to litmus paper, then with a little absolute alcohol, and finally with a little ether. It was then recrystallised from aqueous alcohol. Almost white crystals (0.7gms.) were obtained which melted at 150°C. A mixed M.P. with some original substance showed no depression.

b) Using absolute alcohol (Kaufler & Karrer loc.cit.) and attempted conversion to the nitrile.

1gm. (mol.) 2:7-diamine was dissolved in 50ccs. absolute alcohol and treated with 3 gms. (3mols.) freshly distilled hydrobromic acid of 50% strength. The solution was cooled to 0°C by external cooling, and 3gms. (2.5mols.) amyl nitrite were added drop by drop, and with brisk mechanical stirring, which was continued for five hours. The solution was red and colourless crystals had separated. The mixture was well stirred and treated with 3gms. (excess) pulverised CuCN. No evolution of nitrogen took place. The whole was stirred and heated to 80°C and allowed to stand overnight. Colourless crystals (A) separated. These were filtered off and an attempt made to crystallise them from water. No crystals separated, only a white precipitate. A portion of this on examination, showed

showed/ the presence of copper, so hydrobromic acid was added to the suspension, H_2S passed, the CuS filtered off, and the filtrate made alkaline with NH_4OH. Crystals separated which on recrystallising from water, melted at 159°C. A mixed M.P. with the original gave no depression. The amount recovered was 2.6gms.

The crystals (A) were thus probably a complex of CuCN and the hydrobromide of the base.

c) <u>Method of Greiss</u>.

1gm. (1mol.) was dissolved in 18ccs. water containing 3ccs. (=3mols.) concentrated HCl. The solution was cooled to 0°C. by external cooling and a solution of sodium nitrite containing 0.6gms. (1 mol.) in 1cc. water added all at once. A tarry mess resulted.

d) <u>Using glacial acetic acid and sodium bromide</u>.

1gm. (1mol.) was dissolved in 30ccs. glacial acetic acid and 4gms. finally powdered sodium bromide added with constant stirring. A precipitate - the hydrobromide of the base - separated. The mixture was cooled to 0°C. by external cooling, and 1.5gms. (1.2mols.) amyl nitrite added, followed by 2ccs. concentrated H_2SO_4. The whole was stirred for some time. The solution was blueish-red and a solid was in suspension. This solid was filtered off, washed well with ether, and then added to a few ccs. water. Ammonia was added and the mixture boiled and then cooled. Crystals separated which were

were/ recrystallised from water, and had M.P.161°C. A mixed M.P. with original gave no depression.

e) as for d) with addition of concentrated H_2SO_4.

1gm. (mol.) was dissolved in 30ccs. glacial acetic acid and 4 gms. finely powdered sodium bromide added, followed by 2ccs. concentrated H_2SO_4. The mixture was cooled to 0°C. by external cooling. (It turned very thick and viscous making stirring very difficult). 0.5gms. (1mol.) pulverised sodium nitrite was added a little at a time when the solution blackened and finally formed a black tarry mess.

f) as for d) with addition of absolute alcohol.

1gm. (1mol.) was dissolved in 30ccs. glacial acetic acid, 10gms. finely powdered sodium bromide gradually stirred in, 10ccs. absolute alcohol added, followed by 2ccs. concentrated H_2SO_4. The mixture was cooled to 0°C. as before, stirred well, and a solution of 0.5gm. (1mol.) sodium nitrite in 1cc. water added all at once. The solution turned dark red, and there was evolution of a gas on standing. On addition of ether to the solution, a dark precipitate came down. This was filtered off, washed with ether until the washings were colourless. Only a black amorphous powder, soluble in caustic soda solution and acetone, giving a red coloured solution, was obtained. The alkaline red colour could be discharged on addition of sodium hyposulphite ($Na_2S_2O_4$.)

g) after the example of Hodgson & Walker (loc.cit.)

1gm. (1mol.) was dissolved in 20ccs. glacial acetic acid and the solution cooled rapidly to 10°C. with external cooling and poured slowly on to a solution of 10ccs. nitrosylsulphuric acid, cooled to 0°C.

The solution turned dark, there was evolution of a gas and a black solid separated. This solid had the same properties as that obtained in f).

3. Monodiazotisation of 2:7diaminonaphthalene. (modification of method of Schoutissen J. Amer. C.S.1933,55,4531).

1gm. (mol.) dissolved in 20ccs. (excess) syrupy phosphoric acid and cooled to - 3°C., by external cooling, was treated, with constant stirring, with 0.7cc. nitrosylsulphuric acid (1gm. $NaNO_2$/10ccs. H_2SO_4) also cooled to 0°C. The addition was carried out very slowly, and drop by drop, care being taken that the temperature did not rise above 0°C. Stirring was continued for 2 hours, when the reaction was deemed completed. The solution was dark brown. Crushed ice was added, and iced water, the temperature being controlled at 0°C. The solution was now pale yellow and clear.

The following tests for diazotisation were made. A little was added to:-

a) Alkaline β -naphthol b) acidified dimethylaniline
c) alkaline H-acid. In each case coupling took place with formation of azo dyes.

The aqueous solution on warming evolved nitrogen. Thus diazotisation had been accomplished.

Addition of alcohol to the syrupy phosphoric acid solution after addition of nitrosylsulphuric acid gave a pale yellow solid which was very unstable, and on standing, or on addition of water formed a red solution. Since the tetrazotisation product isolated by Morgan &

Morgan &/ Micklethwait (J.C.S. 1905,87, 1302; B.1906, 39, 2867) using a similar method and excess nitrous acid, was stable, it was considered that, since the theoretical amount of nitrous acid had been used, monodiazotisation had been accomplished.

4. Attempts to prepare 2:7-aminonaphthonitrile.

a) Sandmeyer at 20°C.

5.0gms. (1mol.) 2:7-diaminonaphthalene were diazotised as in previous experiment using proportional quantities. The strongly acid solution of the diazonium compound was diluted with about 10 times its volume of ice cold water, and then slowly run, with mechanical stirring, into 25ccs. of a cold cuprous cyanide-potassium cyanide solution prepared as before, diluted with water to 7 times its volume. Effervescence and frothing took place, and a brown precipitate appeared. After the addition was complete, the mixture was slowly heated to 70°C., stirring all the time, and maintaining at that temperature until evolution of gas had ceased. It was allowed to cool, filtered, and the brown solid washed well with water, warmed with dilute caustic soda solution to free it from any naphthols formed during the reaction, filtered, washed with water, boiled with HCl,to free it from copper, and filtered. A brown powder was obtained which could not be crystallised from any of the usual solvents.

H_2S was passed through the dilute HCl filtrate, the CuS filtered off, and the filtrate evaporated to dryness, but nothing was isolated. H_2S was also passed through the original filtrate from the brown solid, the CuS filtered off and the filtrate concentrated, but on making neutral nothing came down.

b) Sandmeyer at 50/60°C.

b) Sandmeyer at 50/60°C. (followed by attempted hydrolysis of the product obtained).

5 gms. (1 mol.) diamine were diazotised as before and added to a solution of cuprocyanide at 50/60°C. A precipitate separated, accompanied by effervescence and frothing. The brown solid was filtered off, washed well with water, and then refluxed for 24 hours with 66% H_2SO_4, when the precipitate was filtered off, washed, and examined for carboxylic acid, but none was found. H_2S was passed through the filtrate for a few minutes. the CuS filtered off, and the filtrate evaporated to dryness; only a few crystals of NaCl were obtained.

c) Sandmeyer at 90°C.

5gms. (1mol.) diamine diazotised as above and run into a cuprocyanide solution kept at 90°C. Effervescence took place, and again a brownish solid separated. It was treated as above, but results were the same.

d) as for c) and using Guitermann's modification.

5gms. (1mol.) diamine were diazotised as before, and the resulting solution poured slowly with good stirring into a cold solution of 15gms. KCN dissolved in 50ccs. water and in which 5 gms. copper powder were suspended. The resulting mixture was well stirred and allowed to rise slowly to room temperature, and then heated to 85/90°C. There was some effervescence and frothing,

frothing,/ and a yellowish brown solid separated. After 15 minutes, the mixture was allowed to cool, the solid filtered off and examined as in previous experiments. No nitrile was isolated.

e) <u>using solid CuCN</u>.

1gm. (1mol.) diamine was diazotised as above, and 3gms. finely powdered CuCN was added. No apparent reaction took place in the cold. On warming, a yellowish brown solid, similar in properties to the above, was obtained.

f) <u>using complex of pyridine & CuCN</u>.

1gm. (1mol.) diamine diazotised as before, and to it was added a solution of 3gms. (excess) CuCN, dissolved in 10ccs. pyridine. No apparent reaction took place in the cold. On warming, a yellowish brown solid, similar to that obtained in e) was precipitated.

Part III

Preparation of 2:7-aminonaphthonitrile by the dry distillation of the sodium salt of 2:7-aminonaphthalene sulphonic acid with KCN and $K_4Fe(CN)_6$.

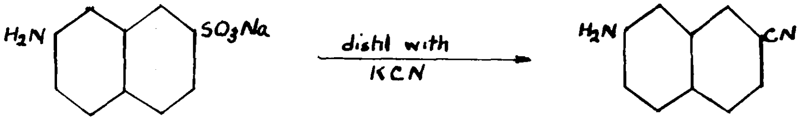
Part III.

Proposed method of preparation.

It was now proposed to prepare the 2:7-aminonaphthonitrile by utilising the general reaction

$$R.SO_3H \ + \ KCN \rightarrow R.CN \ + \ KHSO_3$$

By distilling the perfectly dry mixture of the sodium or potassium salt of 2:7-aminonaphthalene sulphonic acid and potassium cyanide or ferrocyanide, the sulphonic group would be replaced by cyano, and the desired substance would be obtained. Subsequent procedure would be as outlined before



Review of the distillation of sulphonic acids with potassium cyanide and potassium ferrocyanide.

According to D.R.P. 92995, (Frdl. 4, 611, 612.) the conversion of aminonaphthalene sulphonic acids to amino:naphthonitriles is best carried out by mixing carefully Ipt. of the finely powdered anhydrous sodium salt of the sulphonic acid with 1.2 pts. finely pulverised potassium cyanide and distilling the mixture in an iron retort. Thereby, it is said, the nitrile passes over as a yellow oil, easily congealed and yellow in colour. By recrystal:lisation from alcohol, it is obtained completely pure. No details as to yields are given but the properties of the various aminonaphthonitriles are fairly fully described.

Merz & Muhlauser (B. 1870, 3, 709) in a study on the preparation of the naphthalene nitriles by distilling the naphthalene sulphonic acids with potassium cyanide showed that the yield was greatest when the proportion of potassium cyanide to sulphonic acid was 2:3, and an increase in the amount of cyanide to I:I, had no beneficial effect.

Later, Witt (B1873, 6, 448) on the advice of Prof. Kopp, replaced potassium cyanide with ferrocyanide and improved the yield of nitrile. This, according to Etard & Bünont (Compt.rendus. 1885, 100, 108) is possible because dry anhydrous ferrocyanide heated to incipient

incipient/ fusion in a vacuum emits no gas, but, forms only potassium cyanide and $FeK_2Fe(CN)_6$.
At a red heat this is decomposed according to the equation

$$FeK_2Fe(CN)_6 \rightarrow 2Fe + 2KCN + 2C_2N_2$$

It follows, therefore, that the amount of alkali present at any time, is reduced to a minimum.

According to Vieth (B.1875, 8, 1278) when the β -sulphonic acid of α -naphthylamine was distilled with potassium cyanide and potassium ferrocyanide in a "binformigen" distillation vessel, besides gaseous and solid products, in greater or less proportion, a yellow oil of impure naphthalene nitrile was obtained.

In a study on the preparation of quinoline nitriles by distilling the sulphonic acids of quinoline with potassium cyanide, Fischer & Korner (B.1884, 18, 765; ibid. 1889, 22, 1391) state that if the distillation is done under reduced pressure, a pure product is obtained. They also report that Bedall & Fischer (B.1882, 15, 684), though they describe the preparation of the ortho nitrile, failed to observe that a molecular rearrangement took place to an appreciable extent, with the formation of the ana-isomer.

Ebert & Mertz (B.1876, 9, 604) distilled the potassium salt of 2:7-cyanonaphthalene sulphonic acid with potassium ferricyanide and KCN, forming the dicyanonaphthalene. Later Weissgerber & Kruber (B.1919, 52, 345) prepared the prepared the/ 1:6-dicyanonaphthalane, and Bradbrook & Linstead (J.C.S.1936, 1739) completed the synthesis of the dicyanonaphthalenes by the same method. These workers concluded that there appears to be no difference in the ease of displacement of an α -, or β -sulphonic group by a cyano group.

Distillation of 2:7-aminonaphthalene sulphonic acid (sodium salt) with potassium cyanide, (D.R.P. 92,995, Frdl.4,611,612)

The sodium salt of the 2:7-aminonaphthalene sulphonic acid and the potassium cyanide were thoroughly dried, the former at 70°C under a vacuum, and the latter in an electric oven at 110°C. They were mixed, completely pulverised and placed in an iron crucible in an iron retort, containing a lead bath. This ensured that when the lead melted, the iron crucible was pressed flush against the lid of the retort, and so any volatile matter driven off, passed into the neck of the retort.

The retort was heated until a gaseous product and distillate appeared in the receiver, and then the temperature was regulated about that point. Only a few crystals were obtained as distillate, and when the apparatus had cooled, an examination of the contents revealed only a charred mass. Extraction of this with benzene and then alcohol gave no product.

It appeared then that the reaction did not proceed as smoothly as indicated, so a series of small scale experiments was conducted to find out, if possible, the conditions necessary for success.

Action of heat on dry anhydrous sodium and potassium salts of 2:7-aminonaphthalene sulphonic acids and mixtures with KCN & $K_4Fe(CN)_6$.

When the anhydrous sodium salt of the acid was heated in a hard glass test-tube immersed in a lead bath, the colour darkened about 300°C, and above 300°C, a few white crystals condensed at the top of the tube, while the contents became solid and stirring was impossible. The potassium salt behaved similarly, although on the whole the corresponding temperatures were slightly lower.

When Ipt. of the potassium salt was mixed and heated with Ipt. of potassium cyanide, there took place in succession, darkening, fusing and charring and yellow vapours were evolved. Similar results were obtained with the sodium salt, the mixture fusing about 260°C, a few crystals subliming about 300°C, and at 400°C an oil appearing on the sides of the cooler part of the tube. This, when dissolved in benzene, gave a few crystals. The residue in the test tube was a charred mass, and nothing was obtained on extracting it with benzene.

It would appear then that a fairly high temperature-- somewhere in the region of 400°C is required-- before any oil distils over. An addition of copper powder or iron powder to conduct heat into the mass, was detrimental

detrimental/ to the reaction. Fusion took place at a high temperature, there was no oily distillate, and extraction of the fused mass with benzene on each occasion gave only a little tarry matter.

On distillation of the mixture under reduced pressure in glass, the mixture turned brown at 300°C, and at 400°C fused and bubbled, whilst a white sublimate appeared at top of the tube, and a yellow one lower down. A somewhat similar result was obtained when the potassium cyanide was replaced by an equivalent amount of potassium ferrocyanide. In this case fusion took place at 370° - 380°C, and about 420°C, a few white crystals appeared in the leading tube, and a few yellow crystals at the top. Nothing further distilled over above 440°C. The white sublimates were possibly the same as those obtained when the sodium salt of the sulphonic acid was heated alone.

From these experiments it appeared that if charring of the distillation mixture could be reduced to a minimum, the chances for the formation of the nitrile would be considerably increased. Further the presence of as small a quantity of oxygen as possible would reduce oxidation, so it was decided to carry out the distillation in a vacuum (cf. Fischer & Korner B.1889, <u>22</u>, 391), and since potassium cyanide fuses, froths and oxidises to potassium cyanide, it was considered advisable to use potassium ferrocyanide, according to the proposition of Prof. Kopp.

Prof. Kopp/ (cf. Witt B.1873, 6, 448; Vieth B.1875, 8, 1278).

Since carbon is such a poor conductor of heat, any carbon formed during the initial stages of the reaction would be deposited at the surface, and this deposition would prevent the heat from reaching the other particles of the mixture. However, it has been shown that addition of copper or iron as a heat conductor was detrimental to the reaction. In view of all this, it was decided to place the mixture in a thin layer in a long combustion tube, and to use a circular electric furnace, in order to expose the maximum surface to the heat, and to conduct the distillation under reduced pressure. About 370° - 380°C fusion took place with evolution of HCN, and only a few drops of a yellow deposit appeared at the end of the tube. The residue inside the tube was a charred, carbonaceous mass.

To reduce, further, the chance of oxidation, distillation was done in a current of nitrogen, (6cc/min). A yellow deposit was collected in the receivers, and on purification by recrystallisation, yielded a pale yellow crystalline solid M.P.194° - 196°C. (Friedlander loc.cit. gives 170° - 171°C; Frdl. 4, 612 gives 186°C: cf. Friedlander, Hielpern & Spielfogel C.1899, I, 289).

Since the inert atmosphere seemed to give better results, distillation was next carried out in an atmosphere of nitrogen and under reduced pressure, but again the yield was very poor, sufficient only for a few tests.

Evidently the dry distillation method for the preparation of the nitriles offered little prospects of success. and in this connection it is interesting to note that Bradbrook & Linstead (J.C.S. 1936, 1739) when preparing the dicyanonaphthalenes, obtained a yield of 6% with the 2:7-cyanonaphthalene sulphonic acid.

Fusion of sodium salt of 2:7-aminonaphthalene sulphonic acid with KCN, under pressure

It was now proposed to attempt the formation of the aminonaphthonitrile by fusing the sodium salt of the 2:7-aminonaphthalene sulphonic acid with KCN in a sealed tube, with the addition of a few ccs. benzene, to act as a solvent when cold, and to give a pressure sufficient just not break the tube. (The amount which could be added with safety was found by trial and error to be 2.0ccs.)

The series of experiments conducted showed that below 400°C, unchanged sulphonic acid was always recovered. Above 400°C, the mixture fused, there was a strong smell of ammonia on opening the tube, and β -naphthylamine was obtained in quantities sufficient to show that the replacement of the sulphonic group was the main reaction. Exactly similar results were obtained when the air in the tube was replaced by nitrogen.

From the results of those experiments in which a reaction occurred, it would appear that the sulphonic group in the 7 position is comparatively easily displaced (cf. Friedlander & Sacht B.1893, 23, (3), 3029) who state, when discussing aminonaphtholsulphonic acids, that the sulphonic group in position 7, is less firmly bound than that in 3, and this less than that in 6.

Distillation of sodium salt of 2:7-benzoylaminonaphthalene sulphonic acid with KCN.

An examination of the results of all dry distillation and fusion experiments showed that, in those where a reaction took place, there was considerable charring, no doubt due to the presence of such a large proportion of alkali.

Consequently, if the relative amount of alkali present in the mixture was reduced, increased nitrile formation might result. With this object in view, an attempt was made to form the aniline salt of the aminonaphthalene sulphonic acid, by adding together equimolecular proportions of aniline hydrochloride and the sodium salt of the acid, but the free sulphonic acid was precipitated. This was due, possibly, to the basicity of the amino group being partially neutralised by the acidity of the sulphonic group. To strengthen the acidity of the sulphonic group, the amino group was benzoylated by the Schotten-Baumann method, and the benzoylamino derivative used in a series of distillation experiments, using the same apparatus described before. At 300°C, the mass fused, was quite fluid at 320°C, and HCN was evolved. Distillation under reduced pressure yielded a few crystals and the mass charred about 400°C. If, however, the experiment was carried out for one hour maintaining the temperature at 350°C, the mass fused,

fused,/ HCN was given off, and nothing was obtained on extraction with benzene.
However, extraction with water yielded unchanged benzoyl derivative in quantities sufficient to indicate that little reaction had taken place.

The results of this investigation were so discouraging that the plan of attack was recast to investigate the scheme outlined on page 82.

Part III.

EXPERIMENTAL.

1. Preparation and purification of the sodium salt of 2:7-aminonaphthalene sulphonic acid (amino-F-acid).

The 2:7-aminonaphthalene sulphonic acid was supplied as the free acid in the form of a dark grey powder, containing 90% - 93% free acid as estimated by nitrite. (I.C.I. Ltd.)

A large quantity (approx. 200gms.) of the crude acid was suspended in about 400ccs. hot water, and a concentrated solution of caustic soda slowly added with stirring, until the solution was just alkaline to litmus. A further 10gms. of the free acid were added and the whole stirred for ten minutes, after which, the solution now acid to litmus, was carefully neutralised by addition of finely powdered sodium bicarbonate. When evolution of CO_2 had ceased, the solution was diluted to 800ccs. by addition of boiling water, boiled with animal charcoal for a few minutes, and then filtered hot through a Buchner. Filtration at this stage was exceedingly difficult, due to a very finely divided insoluble impurity choking the filter, and frequent changing of the filter paper was necessary. The filtrate was allowed to cool to room temperature, and finally in ice. The greyish white solid was filtered off and recrystallised three or four times from water until the sodium salt was obtained as beautiful white plates with a waxy touch. They contained

contained/ $5H_2O$ of crystallisation.

It was found that the original mother liquour contained so much tarry matter that it was discarded.

2. Preparation of 2:7-aminonaphthonitrile.

(Friedlander, Hielpern & Spielfogel C.1899,I,289 Frdl.4,612, Cassella & Co., D.R.P. 92995).

26.0gms. (1mol.) sodium salt of 2:7-aminonaphthalene sulphonic acid were dehydrated at 70°C under a vacuum (30"), finely powdered and intimately mixed with 31.2gms. (4.5mols.) pulverised potassium cyanide, dried at 110°C. The mixture was placed in an iron retort (for description see p. 58), and distilled. A very small quantity of a yellow oil, which quickly solidified to form a yellow crystalline mass, came over. The neck of the retort was heated to drive over any solid deposited there. After the apparatus had cooled, the neck of the retort was washed out with alcohol, but nothing was obtained on evaporating the solvent.

The contents of the retort was a blackened charred mass. This was taken out, pulverised and extracted with benzene and then alcohol on a Soxhlet, but nothing was obtained on evaporating off the solvents.

3. Fusion tests on the potassium and sodium salts of 2:7-aminonaphthalene sulphonic acid.

a) 0.5gm. (1mol.) of the finely pulverised anhydrous potassium salt of the acid was intimately mixed with the same weight (3.7mols.) of dry powdered KCN, and heated in a test-tube very carefully and slowly with a naked flame. There took place in succession, darkening, fusing, and charring and yellow vapours were evolved.

b) 0.5gm. (1mol.) of the finely pulverised anhydrous soldium salt were treated with 0.5gm. (3.7mols.) of KCN as above. Less darkening and fusing took place and a yellow vapour was evolved.

c) 0.5gm. of the sodium salt was heated alone in a test-tube immersed in a lead bath. About 300°C the mixture darkened, and above 300°C a few white crystals condensed at the top of the tube. The contents of the tube thickened and stirring became impossible.

d) 0.5gm. (1mol.) sodium salt + 0.5gm. (3.7mols.) KCN were intimately mixed and heated as in 3). About 260°C the mixture fused, and about 300°C a few crystals sublimed to the top of the tube (cf.c). Above 400°C, an oil appeared on the sides of the tube, and condensed near the top. Extraction of the sublimate and residue in the tube with alcohol yielded a few yellow crystals M.P.165° - 175°C.

e) Same charge as in d) with the addition of a little copper powder (about 1gm.) to conduct the heat. It fused at a high temperature, but yielded no sublimate. The contents were extracted twice by boiling with benzene, but on evaporating to dryness, only a little tarry matter was obtained.

f) Same charge as in d) with the addition of 1gm. iron filings to act as a heat conductor. Fusion occurred at 350°C but again there was no sublimate. The contents treated as in e) yielded no solid.

g) Same charge as in d) and the pressure reduced to 22mms. About 300°C the mixture turned brown, and fused about 400°C, with bubbling and charring. A white sublimate appeared in the top of the tube (cf. expts. c & d), with a yellowish oil, which solidified to a yellow solid on cooling.

h) 1.0gm. (1mol.) anhydrous sodium salt + 1.2gm. (1mol.) dehydrated potassium ferrocyanide were intimately mixed and distilled as in g). Fusion occurred about 370° - 380°C, accompanied by a considerable amount of charring. On increasing the temperature to 420°C, white crystals appeared in the leading tube, and yellowish crystals at the top. At 440°C nothing further volatilised over.

4. Attempted preparation of 2:7-aminonaphthonitrile.

5.0gms. (1mol.) of the dehydrated sodium salt of the 2:7-aminonaphthalene sulphonic acid were intimately mixed with 6gms. (5mols.) potassium ferrocyanide, previously dried at 110°C and cooled in a desiccator. The mixture was pulverised and placed in a thin layer in a combustion tube, closed at one end. A 500°C thermometer was placed inside the tube with the mercury bulb covered with the mixture. The combustion tube was then placed in a circular horizontal electric furnace, and connected to two 300cc Buchner flasks, connected in series, to act as a receiver. In the second flask was placed 50ccs. water to act as a trap. The second Buchner was attached to an electric vacuum pump. The pressure was reduced to 5mms., and the heating switched on. About 370° - 380°C, fusion and evolution of a gas, recognised as HCN by its smell, took place, and a small quantity of a yellow solid was deposited at the end of the tube, and as a very fine film in the first Buchner flask. After evolution of the gas had ceased, the apparatus was allowed to cool, when the contents were examined. A blackened, charred mass was all that remained. It was removed from the tube, powdered in a mortar, extracted with hot benzene, and then water, and the solvents evaporated, but no product was isolated.

5. Preparation of 2:7-aminonaphthonitrile, using a current of nitrogen.

5.0gms. (1mol.) sodium salt + 6.0gms. (3mols.) potassium ferrocyanide, $K_4Fe(CN)_6$, mixed as in previous experiment, and placed in the same way in a combustion tube open at both ends. One end was attached to two Buchner flasks, arranged in series, the second one containing 50ccs. H_2O, and the other end to a cylinder of nitrogen.

A current of nitrogen was passed through for 20 minutes, to drive out all the oxygen and then the pressure of nitrogen was fixed to allow a flow of 6cc/min. The current was then turned on, and about 440° - 460° C, a yellow distillate appeared, and was collected in the first flask. The current of nitrogen carried the finely divided distillate along the connecting tube into the second flask, where it was collected on bubbling through the water. The product in each flask was yellow. HCN was also given off. The product in the second flask was filtered,&dissolved on the filter paper by the addition of hot alcohol. That in the first flask, was dissolved by washing out the flask with alcohol, and the two alcoholic solutions combined, and poured into a dilute solution of caustic soda, to free it from any naphthols, acids, etc., and the insoluble portion, after washing with cold water, treated with dilute HCl and filtered. Cold ammonia solution was added to the solution until

until/ it was just alkaline, and the yellowish precipitate recrystallised from water. After six treatments with alkali, acid, and recrystallisation from water, yellowish crystals M.P. 194° - 196° C were obtained. Yield 0.1gm (= 4%).

These crystals were soluble in alcohol, benzene, and in a large volume of hot water. They contained nitrogen, and were soluble in dilute acids.

(Friedlander, Hielpern & Spielfogel C.1899, I, 289. Frdl. 4, 612, give M.P. 170° - 171° C; Cassella & Co., Frdl. 4, 612, give 186°C.)

6. Preparation using a current of nitrogen and reduced pressure.

Same charge as in previous experiment and same arrangement of apparatus with the addition of a vacuum pump attached to the exit end. The air was driven out by a current of nitrogen as before, the pressure reduced to 16mm. by means of the pump and the current switched on. When the temperature reached 460° - 480°C, a yellowish vapour appeared, but it was sucked too quickly through the apparatus to condense, so the vacuum pump was turned off, and the vapour bubbled through 50ccs. dilute hydrochloric acid in the second flask. When nothing further distilled over, the contents of the first flask were dissolved in hot alcohol. The acid solution in the second flask was made alkaline with dilute caustic soda solution, to remove naphthols, acid etc., the yellowish precipitate filtered off, washed with water and combined with the alcoholic solution from the first flask. The combined solutions were treated as in previous experiment. 0.15gms. of yellowish plates M.P. 192° - 195° C were obtained. A mixed melting point with the crystals obtained in experiment 5 gave no depression.

Yield 6%.

7. Attempted preparation by fusion of sulphonic acid and KCN under pressure,

1) Temperature 220°C.

5.0gms. (1mol.) anhydrous sodium salt were intimately mixed with 6.0gms. (4.5mols.) KCN finely powdered, and placed with 4.0ccs. benzene in a Carius tube of 125cc. capacity and sealed. The tube was placed in an iron container and heated in the furnace to 220°C for two hours. After cooling the tube was opened and there appeared to be no fusing or charring of the contents which were scraped out and dissolved in as little hot water as possible. The tube was washed out with hot water and the washings added to the solution, which was then filtered and cooled on ice. A crystalline product (4.6gms.) (= 93%.) was obtained. Examination of their crystalline structure through the microscope suggested they were unchanged salt of sulphonic acid, so they were dissolved in hot water, and dilute HCl added. The free acid was precipitated and these on crystallisation from water, showed the same crystalline structure as 2:7-amino-:naphthalene sulphonic acid, and besides a qualitative analysis showed the presence of sulphur.

2) Temperature 320°C.

Same charge as above, but the temperature was raised to 320°C. The tube fractured.

3) 5gms. (1mol.) anhydrous sodium salt + 6.0gms. (4.5mols.) KCN, + 3ccs. benzene heated to 320°C for 2 hours. On examination of the tube after cooling, there had been no reaction, so the temperature was increased to 350°C, when the tube fractured.

4) 5gms. sodium salt + 6 gms. KCN + 2.0ccs. benzene were heated to 350°C for 2 hours. On opening the tube and treating as in experiment 1), 4.0gms. sodium salt were recovered. There was no fusing or charring.

5) Same charge as above, but temperature taken to 380°C. On cooling, the contents were darker in colour, but there had been no fusing. After treatment as in previous experiment, 3.5gms. sodium salt were recovered. (70%).

6) Charge as above, but temperature to 400° - 420°C for two hours. The mixture had fused, and while opening the tube there was a strong smell of ammonia. The fused mass was taken out, powdered in a mortar, and extracted with boiling benzene. The yellow coloured extract was filtered, the benzene evaporated off, and an almost white solid was left. This was washed with dilute NaOH solution, some cold water, taken up in dilute HCl, reprecipitated with alkali and recrystallised from water. White plates M.P. 109°C, were obtained. Benzoyl derivative M.P. 159°C. This corresponds to β -Naphthylamine M.P.111°C. Qualitative analysis gave no S. Hence the sulphonic group had been eliminated.

7. Same charge as in above experiment, but the air in the Carius tube was replaced by nitrogen. The tube was sealed carefully, and heated to 400°C for two hours. On opening the tube there was a strong smell of NH_3. The mixture was fused and charred, and yielded β -naphthylamine on treatment with benzene and subsequent purification.

8) Attempted preparation of aniline salt of 2:7-aminonaphthalene sulphonic acid.

10gms. (1mol.) sodium salt of the acid were dissolved in hot water (200ccs.) and a solution containing 5.3gms. (1mol.) aniline hydrochloride dissolved in 50ccs. H_2O, run in slowly with good agitation. The product came down suddenly as fine prisms ~~was~~ viewed through the microscope. They were filtered off, and washed well with water, and dried at 120°C in an electric oven. Examination showed the substance was 2:7-aminonaphthalene sulphonic acid.

9) Preparation of 2:7-benzoylaminonaphthalene sulphonic acid.

6.0gms. sodium salt of 2:7-aminonaphthalene sulphonic acid were benzoylated according to the usual Schotten-Baumaun method, for benzoylation of aromatic primary amines. A white crystalline substance was obtained which was filtered off, and recrystallised from aqueous alcohol by dissolving in hot water and adding alcohol.

Analysis (micro)

	Fd.	Req. for $C_{17}H_{12}O_4 . N.S\ Na.4H_2O$
Na =	5.3	5.5
N =	3.7	3.3

10. Fusion tests on mixture of above benzoyl derivative and KCN.

a) 1.0gm. (1mol.) anhydrous sodium salt of 2:7-benzoylaminonaphthalene sulphonic acid and 2.0gms. (10.8mols.) potassium cyanide, dried at 110°C, were finely powdered and intimately mixed, and heated in a hard glass test-tube immersed in a lead bath as before. About 300°C. the mass began to fuse, and at 320°C. it was quite fluid. Bubbles of a gas (HCN) were given off. When the temperature was increased to 400°C. a little oil collected at the top of the tube. The contents charred.

b) Same charge as above, but tube connected to a manometer attached to a vacuum pump, by which the pressure was reduced to 6mms. About 350°C, bubbles of gas (HCN) were given off and at 400°C a few crystals appeared at the top of the tube.

c) 1.0gms. (1mol.) anhydrous sodium salt of 2:7-benzoylaminonaphthalene sulphonic acid and 3.0gms. (1.6mols.) potassium ferrocyanide dried at 110°C, were treated as in a). Above 330°C mass fused, and bubbles of HCN were given off. When the temperature was increased to 400°C, a little oil collected at the top of the tube. The contents of the tube on cooling were seen to be charred. This was powdered in a mortar and extracted two or three times with hot benzene, but on evaporating the benzene, nothing was obtained.

10. d) Same charge as in c), but the tube connected as in b). About 320° - 430°C, bubbles of gas (HCN) were given off and the mixture fused; at 400° - 420°C, a few crystals appeared at the top of the tube. The mass was charred, and this on extraction with benzene, yielded nothing.

11. <u>Attempted preparation of 2:7-aminonaphthonitrile using anhydrous sodium salt of 2:7-benzoylaminonaphthalene sulphonic acid</u>.

2.5gms. (1mol.) anhydrous sodium salt of 2:7-benzoylaminonaphthalene sulphonic acid and 7.0gms. (15mols.) potassium cyanide, dried at 120°C, were finely powdered and intimately mixed, and placed in a long combustion tube as in expt. 6. At 350°C the mass fused and HCN was given off. Above 400°C the charge charred, and a little yellow deposit appeared at the end of the tube. The charred mass was ground up on cooling, and extracted in a Soxhlet with benzene, but only a very small quantity of a yellow product was obtained.

12. Same charge as above, but the pressure was reduced to 4mms., and the temperature was maintained for <u>one</u> hour at 350°C and in an inert atmosphere of nitrogen. The mass fused as in expt.11, at 350°C, became yellow, and HCN was given off, but nothing distilled over. The fused mass was extracted as

12. (contd.)

as/ before, but on evaporating the solvent, no product was obtained. The mass was then boiled up with 20ccs. water, filtered from insoluble carbonaceous matter, and cooled in ice. 1.6gms. sodium salt were recovered.

Part IV

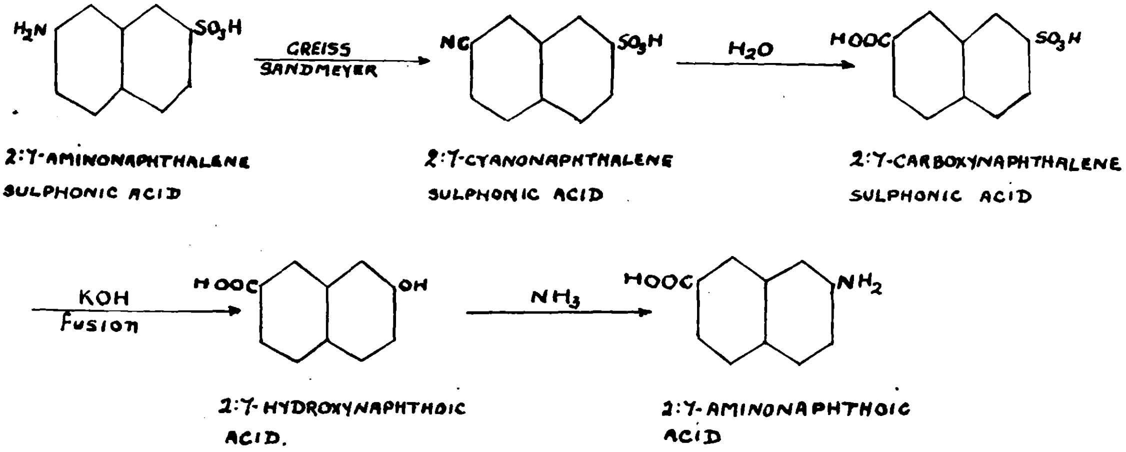
Synthesis of 2:7-aminonaphthoic followed by attempted preparation of aminohydroxynaphthoic acids.

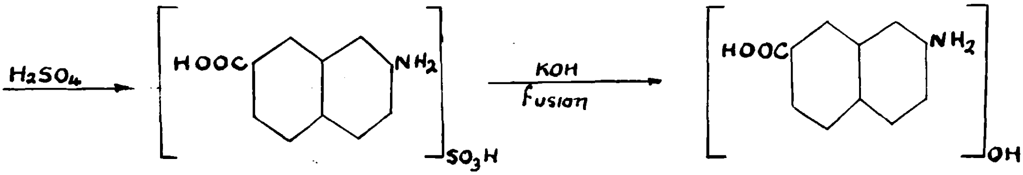
Part lV.

Proposed method of preparation.

It was now decided to endeavour to form the amino-hydroxynaphthoic acids, starting from the aminonaphthalene sulphonic acids. The aim was still to prepare an amino-naphthoic acid of known constitution. The proposed method involves a much longer synthesis, so experiments were conducted to find out the conditions necessary for optimum yield.

The scheme is outlined below. Since the compound desired is the aminohydroxynaphthoic acid corresponding to J-acid, then the starting material is the 2:7-amino-naphthalene sulphonic acid. This would be diazotised and converted to the nitrile by the Sandmeyer reaction. Hydrolysis, would yield the sulphonaphthoic acid, and this, on alkali fusion, a hydroxynaphthoic acid, The rest of the synthesis would be the same as outlined on p. 14, part I. It is illustrated below.





2-AMINO-?-SULPHO-7-NAPHTHOIC ACID.

2-AMINO-?-SULPHO-7-NAPHTHOIC ACID

The proposed method of orientation would be that outlined on p. 14, part I.

Preparation of Diazonaphthalene sulphonic acids.

A survey of the literature showed that the fourteen aminonaphthalene sulphonic acids were all more or less easily diazotised.

The general methods employed were:

1) to suspend the free acid in alcohol or water and pass nitrous acid gas into the suspension when the diazo compound either separated out or remained in solution (Forsling B.1887, 20, 80).

2) to suspend the free acid in water, add HCl, and run in a solution of sodium nitrite (Bayer B.1887, 20, 1419)

3) to mix together solutions of the sodium salt and sodium nitrite and pour on to a cooled solution of dilute HCl or dilute H_2SO_4. (Bucherer & Schmidt J.pr.chem. (2), 79, 396; Cleve B.1891, 24, 3474).

Various modifications of the above methods were used with success. A summarised list of the diazonaphthalene sulphonic acids is given below, together with the methods used for their preparation, by various investigators.

7:2-diazonaphthalene sulphonic acid: by suspending the free acid in water, adding HCl, then running in sodium nitrite solution. (Bayer & Duisberg B.1887, 20, 1419; Weimberg B.1887, 20, 2910; Erdmann ibid. 21,638; Butler & Royle J.C.S. 1923, 1651T). It separated as yellow crystals.

<u>1:2-diazonaphthalene sulphonic acid:</u> by pouring a cooled solution of the sodium salt and potassium nitrite into cooled dilute HCl (Cleve B.1891, <u>24</u>, 3474, Gattermann ibid. <u>32</u>, 1146).

<u>4:2-diazonaphthalene sulphonic acid</u>: by suspending the free acid in alcohol and passing in nitrous acid gas. (Cleve B. 1888, <u>21</u>, 3272), Royle & Schedler J.C.S.1923, 1643T) add sodium nitrite to a suspension of the free acid in dilute HCl.

<u>5:2-diazonaphthalene sulphonic acid</u>: by treating the suspension of the free acid in dilute HCl with a solution of sodium nitrite (Erdmann Ann.275,213; Royle & Schedler loc.cit.). Also by Weissgerber & Kruber (B.1919, <u>52</u>, 354), by dropping a solution of the sodium salt and the calculated quantity of sodium nitrite on to ice cooled dilute H_2SO_4.

<u>6:2-diazonaphthalene sulphonic acid</u>: by suspending the free acid in alcohol and passing in nitrous acid gas generated from arsenious acid and sodium nitrate (Forsling B.1887,<u>20</u>, 80): by treating the sodium salt and sodium nitrite solution with HCl (Bucherer & Schmidt J.pr.chem. (2) <u>79</u>, 396): and by Butler & Royle (loc.cit.) as for 5:2-acid.

<u>8:2-diazonaphthalene sulphonic acid</u>: by Cleve (loc. cit.) as for 4:2-acid, and by Royle & Schedler (loc.cit.) as for 5:2-acid.

2:1-diazonaphthalene sulphonic acid: by acting on a suspension of the free acid with HCl & $NaNO_2$ solution (Friedlander & Woroshzon Ann. 388, 7): also by Kaeker (Ann.414,245) who adopted the method used by Cleve for the 1:2-acid.

3:1-diazonaphthalene sulphonic acid: by acting on the free acid suspended in water and HCl with $NaNO_2$ (Kall & Co., D.R.P.78605; Frdl.4, 535; also Royle & Schedler (loc.cit.)

4:1-diazonaphthalene sulphonic acid: by treating the free acid in alcohol with HCl and $NaNO_2$ solution. Blcomstrand (B.1877, 10, 1723): by Winther (B.1880, 13, 1949) & Cleve (B.1893, 26, 241) as for 4:2-acid.

5:1-diazonaphthalene sulphonic acid: prepared by Cleve (B. 1891, 24, 512) as for the 4:1-acid; and by Erdmann (Ann. 247, 331) by introducing simultaneously solutions of the sodium salt and $NaNO_2$ into HCl or H_2SO_4.

6:1-diazonaphthalene sulphonic acid: prepared by Forsling (B.1887, 20, 2105)as for 6:2-acid; by Erdmann (loc.cit.) as for 5:1-acid; and by Butler & Royle (loc.cit.) who used the method of Erdmann with a slight modification.

7:1-diazonaphthalene sulphonic acid: by Forsling and Butler & Royle as for 6:1-acid.

8:1-diazonaphthalene sulphonic acid: by treatment of the free acid in HCl with $NaNO_2$ in as strong a solution as possible (Erdmann Ann. 247,331) and by Butler & Royle (loc.cit.) as for 7:1-acid.

Preparation of 2:7-carboxynaphthalene Sulphonic acid.

The preparation of the above takes place in three stages and embraces

1) the diazotisation of the aminonaphthalene sulphonic acid

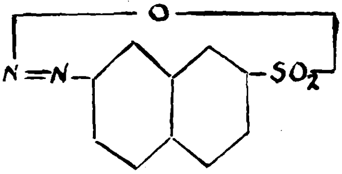
2) conversion of the diazo compound to the nitrile (Sandmeyer).

3) hydrolysis of the nitrile to the carboxylic acid.

It was found, by experiment, that it was advantageous not to isolate the nitrile, but to proceed directly with the hydrolysis.

The diazotisation of the amino sulphonic acid, and the method ultimately employed by the author was a modification of that used by Weissgerber & Kruber (B.1919, 52, 354), Erdmann (Ann.275,279), and later by Royle & Schedler (loc.cit.) For details see page 130. An excess of at least $\frac{1}{3}$ mol. of hydrochloric acid prevented the formation of a red coloured impurity, which was always formed if the theoretical quantity was used. Further, if the sodium nitrite was added slowly and beneath the surface, coupling was considerable and a red azo dyestuff, discoloured and contaminated the diazo compound. Addition of the nitrite all at once with brisk mechanical stirring, prevented this and the diazo compound was obtained as a finely divided crystalline solid, pale yellow in colour and free from any trace of colouring matter.

It is interesting to note that Royle & Schedler (loc.cit.) say that the diazonium chloride separates, but a qualitive analysis revealed no chlorine present, and it would appear therefore, that the compound, hereafter called the diazo compound, is of the inner anhydride type and has the formula



The diazo compound in the acid solution could then be used for the Sandmeyer reaction but once its stability had been established it was filtered off, washed with a cold saturated NaCl solution, and then suspended in cold water, sufficient to form an easy flowing paste. An even better yield of carboxynaphthalene sulphonic acid was obtained if solid sodium chloride was added, after destruction by urea of the excess nitrite, as the diazo compound is less soluble in a saturated solution of sodium chloride.

To prepare the nitrile, the suspension of the diazo compound was slowly run into a solution of potassium cuprocyanide, prepared as described on page 139 part IV. Brisk evolution of nitrogen took place and the solution gradually turned red, due no doubt, to secondary reactions. It was noticed that if the diazo compound came into contact with alkali, then a red azo compound was formed instantaneously. Hence to reduce the alkalinity to a alkalinity to a/ minimum, dilute hydrochloric acid was added to the potassium cupro-cyanide, until a faint opalescence was obtained. After all the diazo compound had been added the solution, now reddish coloured, was heated for some time, concentrated HCl carefully added to precipitate the CuCN, which was filtered off, and the cyanonaphthalene sulphonic acid isolated by evaporating to dryness and extracting the mass several times with 90/95% alcohol (Butler & Royle loc.cit.) However it was found by experiment, that complete extraction of the nitrile was long, laborious and unnecessary. A yellowish brown solid was obtained on concentrating the alcoholic solution, which represented, if it is taken as composed entirely of cyanonaphthalene sulphonic acid, a yield of 28%. It was refluxed with caustic potash and on acidification and recrystallisation from water, gave beautiful pinkish needles of the sulphonaphthoic acid. These were fused in a glue pot with caustic potash, and yielded the 2:7-hydroxynaphthoic acid (24% calculated on the sodium salt of amino-F-acid). M.P. 273° - 274°C. Butler & Royle (J.C.S. 1923, 1654) give M.P. 269° - 270°C; Friedlander, Heilpern & Spielfogel (Mitt. des Tech. Gewerbe Museums in Wein 1898, 8, 316-323, and J.S.C.I. Abs. 1898, 17, 836) give 262°C.

An experiment was next conducted to find out if the extraction with alcohol was complete. The amino F-acid was treated as above, and after completion of the Sandmeyer reaction, the solid was extracted, after evaporation to dryness as before, with alcohol. The extracted solid was then refluxed with alkali, and the solution treated with HCl and H_2S to precipitate the copper. The CuS was filtered off and from the filtrate yellowish needles were obtained which were sulphonaphthoic acid. (Equivalent to 59.5% calculated on the sodium salt of amino-F-acid). From the alcoholic solution only an amount equivalent to ~28% was obtained. This then showed that extraction was far from complete and the above sequence of reactions was carried out with variation in the experimental details. The amino-F-acid was diazo:tised as before and treated with the cuprous-cyanide as before. The excess cuprous cyanide was precipitated with concentrated HCl and the filtrate treated in the following way, which differs from the procedure previously described in that the alcoholic extraction of the nitrile is omitted. Solid KOH was added to the filtrate until just alkaline, and then an amount sufficient to give an alkaline strength of from 10/15% added, and the solution refluxed until no more ammonia was given off, stirring being maintained all the time. HCl was then added and the copper precipitated as sulphide, and filtered off. On concentration and

and/ cooling of the filtrate an amount of sulphonaphthoic acid equivalent to 64.5% calculated as before was obtained. This on alkali fusion yielded hydroxynaphthoic acid.

Hydroxynaphthoic acids and the method of preparation of 2:7-hydroxynaphthoic acid

All the fourteen hydroxynaphthoic acids are now known and identified, and there appears to be two methods for their preparation, namely:

1) by the action of CO_2 under pressure on the naphthols
2) fusion of the carboxynaphthalene sulphonic acids.

It would appear that method 1) is only available for the preparation of hydroxynaphthoic acids where the substituents are in the ortho positions to one another. In this way Kauffmann (B.1882, 15, 506) and Schmidt & Burkard (B.1887, 20, 2699); Schmidt (D.R.P. 31240; Chem. Fabs. V. Heyden (D.R.P. 38052; Frdl. 1, 236; vgl. Schaeffer Ann. 152, 192) prepared the 2:1-, 1:2-, & 2:3-hydroxynaphthoic acids. The method first employed (Schaeffer loc.cit., Eller Ann. 152, 277), was to lead CO_2 into α -naphthol in the presence of metallic sodium at water bath temperature. In this way the 1:2-acid was prepared but the yield was low, and it was not until the reaction was carried out under pressure that good yields were obtained. The sodium salt of the naphtholate was treated with CO_2 in an autoclave (Schmidt loc.cit.) When the reaction was carried out at 120/145°C. using β -naphtholate, the 2:1-hydroxynaphthoic acid was formed, but by altering the temperature to 280/290°C, the important 2:3-acid was formed in almost 100% yield (cf. Mohlau & Kriebel B.1895, 28, 3089). Using α -naphtholate and the

the/ temperature at 120/140° C, the 1:2-acid was isolated. A great deal of research has been done on the preparation of the 2:3-acid and various modifications of experimental procedure have been suggested, but the essentials remain the same.

Battershall (Ann.168,144) and later Stumpf (Ann.188, 1) in experiments on the sulphonation of α -, and β -naphthoic acids, isolated isomeric monosulphonic acids, and by fusing these with KOH the corresponding hydroxy acids, but did not establish their constitutions by proof. Friedlander, Hielpern & Spielfogel (C.1899, I,289; Mitt. tech. Gew. 1898, 8 (11 & 12), 316; also J.S.C.I. 1898, 17, 836), prepared the 5:1-hydroxynaphthoic acid and the 7:2-acid from the corresponding aminonaphthoic acids by Greiss and Sandmeyer reactions and hydrolysis, while Ekstrand (J.pr.chem. 188 (2), 28,278) claimed to have prepared the 8:1-acid, by forming the lactone from the amino acid by diazotising, warming and then boiling the lactone with alkali and acidifying with dilute acid.

The 1:4-acid was prepared by Heller (B.1912,45, 675) by melting the 1:4-hydroxynaphthaldehyde with alkali and a little water, and also by the alkali fusion of 2-(4-chlornaphthoyl-(1)-) benzoic acid.

Later Royle & Schedler (J.C.S.1923,1641T) and Butler & Royle (ibid. 1649T) completed the preparation of the hydroxynaphthoic acids and established the constitution of those prepared but not identified by Battershall &

Battershall &/ Stumpf. The method employed was that of Weissgerber & Kruber (B.1919,52,354) for the preparation of the 2:7-hydroxy acid derivatives. The sulphonaphthoic acid, prepared from the aminosulphonic acid, was fused with KOH and on acidifying with dilute HCl, the hydroxynaphthoic acid separated and was recrystallised from aqueous alcohol.

The method employed by the author was the usual one for replacement of $-SO_3H$ by $-OH$. It was found that it was not essential to prepare the sodium or potassium salts of the sulphonaphthoic acid, as the free acid gave excellent results, though some frothing occurred after each addition of the sulphonic acid, and care was necessary. The fusion was carried out in an open iron gluepot. After the fusion was complete, the melt was dissolved in hot water, almost neutralised with 50/50 aqueous sulphuric acid, filtered from insoluble matter and the hydroxy acid precipitated with concentrated HCl. It was cooled and filtered and recrystallised from aqueous alcohol and was obtained as white crystalline flakes, M.P. 273-274° C. (Butler & Royle loc. cit.269-270° C; Friedlander, Hielspern, & Spielfogel loc. cit. 262° C).

It was converted into the sodium salt by suspending in a few ccs. hot water, adding sodium bicarbonate until no more CO_2 was given off, filtering and evaporating until crystals began to separate. The sodium salt was obtained as almost white plates.

Aminonaphthoic acids and the preparation of the 2:7-aminonaphthoic acid.

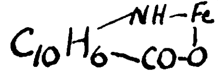
All the fourteen possible isomeric aminonaphthoic acids have now been prepared, but prior to 1926, only four amino derivatives of α -naphthoic acid (the 2:1-, 4:1-, 5:1-, and 8:1-aminonaphthoic acids) and five amino derivatives of β -naphthoic acid (the 1:2-, 3:2-, 5:2-, 7:2-, and 8:2-acid) had been prepared and their constitutions established. Thus Ekstrand (J.pr.chem.1890 (2), **38**, 244) claim to have prepared the 5:1-, and 8:1-, 5:2-, and 8:2-aminonaphthoic acids by reducing the corresponding nitronaphthoic acids in ammoniacal solution with ferrous sulphate. These nitro acids were prepared by the direct nitration of the α -, and β - naphthoic acids. Friedlander, Heilspern & Spielfogel (C.1899, I, 289; Cassella & Co., D.R.P.92995; Frdl. **4**, 611) formed the 5:1-, 5:2-, 7:2-, and 8:2-amino acids by the hydrolysis of the nitriles, prepared by the distillation of the sodium and/or potassium salts of the corresponding aminonaphthalene sulphonic acids with potassium cyanide or ferrocyanide (see p.58), thereby establishing their constitution; while Bamberger & Philip (B.1887, **20**, 243) formed the 8:1-aminonaphthoic acid by heating naphthostyril with caustic soda, and treating the mass with hydrochloric acid. In a further paper, Friedlander and his co-worker Weisberg (B.1895, **28**, 1842) formed the 4:1-aminonaphthoic acid. They state that it is formed along with

with/ α -naphthylamine by the reduction of 4:1-nitro:naphthoic acid with ferrous sulphate or ammonium sulphide. Its method of preparation established its constitution. They started with 4:1-nitronaphthylamine and by the Greiss & Sandmeyer reactions formed the 4:1-nitronitrile, which on hydrolysis, and subsequent reduction gave the 4:1-aminonaphthoic acid.

Mohlau (B. 1893, 26, 3067) and later Mohlau & Kriebel (B. 1895, 28, 3096) claimed to have prepared the 3:2-aminonaphthoic acid by heating the 3:2-hydroxy acid with 35% ammonia under pressure, but this is contradicted by Harrison & Royle (J.C.S.1926, 86T?) who state that they repeated their experiments and obtained no appreciable conversion either with the 3:2-acid or any other isomeride when no bisulphite was present. By heating the 1:2-aminonaphthonitrile with KOH at 180°-190°C, Friedlander & Littner (B. 1915, 48, 331) formed the 1:2-aminonaphthoic acid. They formed the 1:2-amino:naphthonitrile from the 1:2-nitronaphthylamine in the same way that Friedlander & Weisberg (loc.cit.) prepared the 4:1-nitrile. The same authors prepared the 2:1-acid by warming β -naphthisatin with excess caustic soda, and treating the hot melt with lead dioxide on the water bath.

Later Harrison & Royle (J.C.S. 1926, 87T?) prepared the remaining aminonaphthoic acids by the amidation of the corresponding hydroxy acids.

As stated before, they repeated the experiments of Mohlau & Kriebel but could obtain no amidated product when ammonia was present only. When bisulphite was present in the reaction mixture, as recommended by Bucherer (C.1904, 11, 811) for the amidation of aromatic hydroxy compounds, the reaction went very smoothly and the aminonaphthoic acids were obtained in almost theoretical yields.

Tobler (E.P.259598;B. 1926, 39, 736) used aqueous ammonia in the presence of an ammonium double salt of zinc or calcium eg. the double chlorides, for the amidation of the 3:2-hydroxynaphthoic acid, while Imray (I.G. B.P. 282450) used ferrous sulphate as a catalyst and obtained a compound of the formula  $C_{10}H_6\begin{matrix}\diagup NH-Fe \\ \diagdown CO-O\end{matrix}$, which on decomposition of alkalis, yielded the 3:2-amino-:naphthoic acid; and Carpmael (I.G.B.P. 339941, 1929) describes the use of zinc oxide and zinc carbonate in combination with ammonium chloride. He heated 3:2-hydroxy-:naphthoic acid with these substances in a current of dry air or ammonia gas and obtained the amino acid in good yield.

Preparation of 2:7-aminonaphthoic acid.

The method adopted by the author for the amidation of the 2:7-hydroxynaphthoic acid was essentially that recommended by Bucherer (J. pr. chem. (2), 71, 445), for the amidation of aromatic hydroxy compounds and used by Harrison & Royle (loc.cit.) The sodium salt of the 2:7-hydroxy acid was heated in an autoclave with an excess of 0.88 ammonia and a quantity of ammonium bisulphite solution, prepared by passing SO_2 into aqueous ammonia until it was saturated. After boiling off the excess ammonia, solid caustic soda was added to the contents of the autoclave dissolved in water, and in this way, the sodium salt of the 2:7-amino naphthoic acid separated as golden flakes. They were filtered through a sintered glass filter, recrystallised from caustic soda solution, filtered, and washed with dilute alcoholic caustic soda, and finally with 80% aqueous alcohol, and then dried in a vacuum over concentrated sulphuric acid.

The free acid was obtained by dissolving the sodium salt in hot water and adding dilute acetic acid. After cooling it was recrystallised from aqueous alcohol. It melted at 244° - 245° C. in long prismatic needles. (Harrison & Royle give 245°C.)

It forms an almost insoluble hydrochloride, and sulphate. It is soluble in hot alcohol and glacial acetic acid, almost insoluble in benzene, and chloroform.

It diazotises and couples with alkaline naphthols.

The acetyl derivative was prepared by refluxing the free acid with acetic anhydride and glacial acetic acid, in the presence of a little fused sodium acetate until it was all dissolved. On pouring into cold water, and on cooling the 2:7-acetylaminonaphthoic acid separated and was recrystallised from alcohol. It crystallised in pale yellow plates M.P. 287° - 289°C. Harrison & Royle (loc.cit.) give 200° - 201°C, so analyses were done to confirm the identity of the product.

<u>Fd.</u>		Req. for $C_{13}H_{11}O_3N$
C = 68.1, 67.4, 68.1, 68.3	)hemi-macro	C = 68.1
H = 4.8, 4.4, 4.8, 4.8		H = 4.8
N = 6.32 & 6.09	(micro	N = 6.11

This proved that the compound isolated was the 2:7-acetlyaminonaphthoic acid, and hence the sulphonation of the aminonaphthoic acid was attempted.

In the first series of experiments the free acid was used, and it was dried by heating in a vacuum at 70°C for two hours, but later the finely powdered anhydrous sodium salt (cf. Witt B.1886,19,578). When it was established that the sulphonation of the free acid was not proceeding smoothly (see page 144), the sodium salt of the acetyl derivative was formed as for that of the free acid and used.

It separated as a mass of rectangular crystals containing two molecules of water of crystallisation. By heating at 70°C. under a vacuum of 5mms. it was converted into the anhydrous salt and after pulverisation was used for the sulphonation.

Notes on the Sulphonation of Substituted Naphthalenes.

Though the degree of developement and expansion of naphthalene chemistry has been wide, no comprehensive theory of its sulphonation is as yet possible, due to the difficulties of separating the mixtures of acids obtained, and of recognising the presence or absence of small amounts of isomerides in the sulphonation mixture, recognition of which is necessary to establish the validity of any theory. In this connection, there are, as yet, no orientation rules for disubstitution etc., corresponding to those of Armstrong, Crum Brown and Gibson, and Vorlander, though Veseley & Jakes (Bull. Soc. Chim. 1929, (V), 33, 955) proposed the division of directive substituents into two types:- quinonoid (o- & p-directing) and non-quinonoid (meta-directing). Later Ufimtzev (J. Gen. Chem. Russ. 1935, 5, 653-660; Abs. P. 1938, 62) in a paper regarding substitution in the naphthalene series, came to the conclusion that substitution takes place according to the same laws as for the benzene series on the assumption that the naphthalene molecule exists in three tautomeric forms, containing two aromatic nuclei and one aromatic and one hydrocarbon nucleus.

Consequently, it is impossible to predict with accuracy the probable orientation of the isomerides formed by sulphonation of substituted naphthalenes. For disubstitution Watters (Physical Aspects of Organic Chemistry) states "as a general empirical rule, if the first substituent is an activating polar character, such as -OH & $-NH_2$ then the second substituent will enter the same ring, and that within a single ring, the ordinary o- & p- directive influence of an activating grouping" seems to be exerted, but whereas an -OH or $-NH_2$ group in the α -position appears to favour substitution in the 4- & 2-positions, the same group in the β -position promotes substitution in the adjacent α , and not the β. Again, polar activation is capable of transference from one ring to another, since, when an ortho or para directive substituent occupies a β -position, the diametrically opposite 6-position may be the point of substitution. This is well known in the sulphonation of β -naphthylamine (Erdmann Ann. 1893, 275, 192; Fierz-David Helv.Chim. Acta, 1923, <u>6</u>, 1133, and numerous other workers).

Now it has long been recognised that sulphonation is a reversible reaction, with the reversibility in the α -series more easily accomplished, and Noelting (B.1875, <u>8</u>, 1095) to explain this, suggested that the naphthalene, regenerated by the hydrolysis of the α -sulphonic acid,

acid,/ is resulphonated in the β -position. Erdmann (Ann.1893, 275, 192) modified this view, accepted by Weinberg (B.1887, 20, 3354) and Bender (B. 1899, 22, 994) and postulated that the sulphonic acids with the $-So_3H$ group in the 4-, 5-, & 6-positions, obtained by sulphonating α -naphthylamine, were produced simultaneously but in different amounts (cf. Euwes Rec. trav. chim. 1909, 28, 298) and by a process of hydrolysis and resulphonation the most stable one is formed in greatest amount. Confirmation of this view seems to have been obtained by Amblers & Scanlon (Ind. Eng. Chem. 1927, 12, 417) and Lynch & Scanlon (ibid. 1010) who showed that naphthalene was the only product of hydrolysis and that desulphonation of both $- SO_3H$ groups occurs simultaneously since in no case was a β -monosulphonic acid obtained. Recently Lantz (Bull. Soc. Chim. 1935 (V) 2, 2092 - 2108) showed that hydrolysis of the α -acid is about 50 times as fast as the β -acid.

Now Holleman (Die direkte Einfurhung von Substituenten in den Benzolkern; see Watson's Modern Theories of Organic Chemistry pp 46-47) showed that when a second substituent enters the nucleus, all three derivatives are formed, and he showed further, that while factors such as concentration of the acid, temperature of mixture, the duration of the reaction and catalysts exert a considerable effect on the proportions of the isomerides, it is the directive

directive/ influence of the substituent already present which is the prime factor. From a series of experiments he measured the relative directive powers of various groups and concluded that the

o.p - directive influence of OH > NH_2 > Halogen > CH_3
m - " of COOH > SO_3H > NO_2

But Fusch (Monatsh. 1917, 38, 331) says that though a number of groups give rise to almost exclusive ortho and para derivatives, marked differences in the relative effectiveness is noted on pitting one against the other in the same molecule and that in a molecule containing both an $-NH_2$ group & a $-CH_3$ group, though both are o & p- directing, it is the $-NH_2$ group which controls. He also says that the relative directive influence of NH_2 > OH > OCH_3 > NHAc > OAc. (cf Holleman).

Again it is of considerable significance that ortho and para directing groups facilitate substitution in the ring whilst meta directing, retard, and Ingold (Ann. Reports 1926, 23, 134; Rec. trav. chim 1929, 48, 805) attributes this to a selective activation and deactivation of the o- & p- positions, hence in naphthalene, the presence of an op- directive group normally leads to homonucleal substitution, while a m -directive group causes heteronucleal substitution.

When β -naphthylamine is sulphonated, four monosulphonic acids, all heteronucleal are formed, and six disulphonic acids by sulphonation of these mono-acids, but it is worthy of note that sulphonation in the 1-position occurs only when at least one sulphonic group is already present and that that group is the first to be removed by hydrolysis (Lantz loc.cit.). Thus Dahl & Co. (D.R.P. 32276, Frdl. 1 425) and Erdmann (1893, 275, 277) Green (J.C.S. 55, 35 B. 1889, 22, 722) on sulphonating β -naphthylamine obtained the 6-, & 8-, acids. Later Green & Vakil (J.C.S. 1918, 113, 35) showed that the four heteronucleal acids (5-, 6-, 7-, & 8-,) were present.

Now when we come to consider the sulphonation of the 2:7-aminonaphthoic acid, it is reasonable to assume that, since the substituents present have the same directive influences as those in 2:7-aminonaphthalene sulphonic acid, the products obtained would be comparable to those obtained by the sulphonation of the latter acid. According to Armstrong & Wynne (J.C.S. 1890, 6, 129); Bayer (D.R.P. 79243 of 1894); and Dressel & Kothe (B. 1894, 27, 1194) when 2:7-aminonaphthalene sulphonic acid is sulphonated the products obtained are the 1:7-disulphonic acid (25%), 4:7-acid (25%) and 5:7-acid (50%). Thus it was anticipated that the corresponding aminosulphonaphthoic acids would be obtained by sulphonation of 2:7-aminonaphthoic acid.

It is, of course, possible that since the directive influence of COOH > SO_3H, and that meta directing groups favour heteronucleal substitution, that the yield of 5:7-diacid, would be considerably lowered, with a corresponding increase in the 1:7-, & 4:7-acids.

Nevertheless, separation of the isomers by one or more of the available salts should give three aminosulpho:naphthoic acids, one of which would correspond to the acid desired, namely the 2-amino-5-sulpho-7-naphthoic acid.

Experiments on the sulphonation of 2:7-aminonaphthoic acid.

The sulphonation of the 2:7-aminonaphthoic acid was first attempted with concentrated sulphuric acid of 93% strength, using 7mols. excess, and maintaining the temperature at 15° - 20° C, but no sulphonation took place, even after 72 hours continual stirring. After each experiment the strongly acid liquor was discoloured, as if carbonisation and oxidation had taken place, and it appeared that there was a gradual increase in the intensity of the discolouration with increase in duration of the experiment. The temperature was then increased to 40° - 45° C, the other conditions being maintained, but still there was no sulphonation. In fact, even when the temperature was 100° C, no reaction had taken place, and it was not until the temperature of the solution was 140° - 145° C, that a product containing nitrogen and sulphur was isolated, and appeared to be a sulphonic acid. The yield, however, was very poor, amounting to 0.8gms. (8%). The mother liquor was very black, indicating a high degree of charring or oxidation, caused, no doubt, by the high temperature. So a series of experiments was undertaken, using 10% oleum, the other conditions such as temperature and proportions of reagents, remaining as before, but sulphonation did not even take place at 40° - 45° C. Besides, the acid liquor was very black in colour.

Hence, it appeared that the lower the temperature at which the reaction was carried out, the less would be the chance of oxidation, so the strength of the acid was increased to 20% oleum. Again no reaction took place at 15° - 20° C, but at 40° - 45° C, on working up as described on p.141 , a white crystalline substance was isolated, but in very poor yield. (Analysis gave S = 11.6 (micro). Req. for $C_{10}H_5(NH_2)(COOH)SO_3H.H_2O$, S = 11.23). Hence it appeared that the product was a monosulphonic acid.

The above experiment was repeated and about 0.8gms. white feathery needles or prisms as viewed from the microscope were obtained. These were soluble in sodium bicarbonate solution with evolution of carbon dioxide, slightly soluble in water, with an acid reaction towards litmus, and insoluble in most organic solvents. They could be diazotised and coupled with alkaline β -naphthol solution, showing the presence of an amino group.

Analysis (micro) gave

C = 47.92 H = 3.48 N = 4.66 S = 11.32

Req.for $C_{11}H_{11}NSO_6$ C = 46.3 H = 3.86 N = 4.93 S = 11.23

Though the analysis figures do not show the necessary agreement, nevertheless the combined reactions and analysis indicate a monosulphonic acid. Besides, on warming at 120°C, loss of weight occurs, due to the loss of water, because on recrystallisation from water, the original

original/ substance is regenerated.

Obviously then, sulphonation was taking place under the conditions of the experiment, but the greater part of the amino-naphthoic acid was lost or unaccounted for, so the method of isolating the sulphonic acid was altered and the salting out process of Gatterman (B.1891, 24, (2), 121) was tried, but the result was even worse. Hence the method of sulphonation was altered and chlorosulphonic acid was used, with dichloroethylene as a diluent. This has a B.P. of 55° C., so the temperature of the reaction was about the same as before. According to Limpricht (B.1885, <u>18</u>, 172) the reactions with chlorosulphonic acid go very smoothly with little or no byeproducts, and as a rule the same products are obtained. From amines however sulphaminic acids are obtained (Traube B. 1890, <u>23</u>, 1654). After <u>four</u> hours, a dark viscous solid, suspended in a clear liquid (probably the diluent), was in the flask. After working up (see pp.146) a few crystals similar in structure to those obtained before were isolated.

Oxidation and charring even with chlorosulphonic acid were taking place, probably due to the activating influence of the easily oxidisable amino group, so it was decided to protect the amino group either by acetylating or benzoylating it, and to attempt the sulphonation of the derivative , after which operation the free amino group could be regenerated by hydrolysis.

The choice of derivative fell on the acetyl as it was thought possible that the sulphonic group might enter the benzoyl part of the molecule in preference to the naphthalene part, if the benzoyl derivative was used.

Acetylation of 2:7-aminonaphthoic acid.

The 2:7-aminonaphthoic acid was acetylated in the usual manner, using glacial acetic acid, acetic anhydride, and a little fused sodium acetate. Difficulty was experienced in obtaining a pure derivative. This was due partly to incomplete acetylation, and partly to the difficulty of separating the original from its acetyl derivative by crystallisation. By using a large excess of acetic anhydride in the process a pure product was obtained. This was recrystallised from aqueous alcohol and formed pale yellow plates M.P. 287° - 289° C. (Harrison & Royle J.C.S.1923,82(T) give 200° - 201° C.)

In view of the discrepancy between the melting points, analyses were carried out to prove or disprove that the above compound was 2:7-acetylaminonaphthoic acid.

Fd. (hemi-macro)	Req. for $C_{13}H_{11}O_3N$
C = 68.1, 67.4, 68.1, 68.3	C = 68.1
H = 4.8, 4.4, 4.8, 4.8	H = 4.8
N = 6.32, 6.09 (micro)	N = 6.11

These results showed that the compound was the 2:7-acetylaminonaphthoic acid. No explanation of the above difference in the melting points can be put forward, since the range given is only over 1°C.

Experiments on the sulphonation of 2:7-acetylaminonaphthoic acid.

The conditions of the experiments were exactly the same as for those carried out on the free amino acid. The 2:7-acetylaminonaphthoic acid was converted into the sodium salt which was thoroughly dried in a vacuum oven at 70°C and finely powdered (Note:- a higher temperature causes the product to be very dark in colour), and as a fine white powder, added a little at a time to 20% oleum at 20°C, with brisk stirring. As in the case of the amino acid, there was an increase in temperature after each addition, so the temperature was allowed to return to 20°C, before further addition. The acetyl derivative gradually dissolved forming a clear solution with a slightly yellowish tint.

After three hours a sample was extracted, run on to crushed ice, and the solid which separated, examined. It was found to be unchanged original. A similar procedure was adopted after six hours, and again after twelve hours, but in no case was sulphonation found to be accomplished, and in each case there was no evidence of charring or oxidation as shown by the acid mixture turning black. Accordingly the temperature was raised to 40° - 45° C., and after three hours the solution, still only slightly yellowish in colour, was poured, very slowly and carefully and with brisk mechanical stirring, on to crushed ice, when a very finely divided white solid separated. The

The/ temperature was kept as low as possible by continued addition of crushed ice, in order to minimise the possible hydrolysis of the acetyl compound. Nevertheless, in spite of these precautions, there was a distinct smell of acetic acid, indicating that the acetylaminosulphonaphthoic acid was easily hydrolysed under these conditions.

The product, was filtered off, washed well with ice-cold water, and suspended in warm water. (The filtrate - the strongly acid liquor - was worked up with milk of lime, but only a few crystals were obtained, so in all subsequent sulphonations, it was stored for future reference if required). Solid sodium bicarbonate was added until no more carbon dioxide was evolved, and the solution filtered from a small amount of insoluble matter. Dilute hydrochloric acid was now added and the whole cooled in ice. This treatment eliminated the possibility of sulphates of amino acids being present. The white precipitate was filtered, boiled with glacial acetic acid to remove any 2:7-aminonaphthoic acid and recrystallised from water in which it was fairly soluble in hot, almost insoluble in cold. The substance contained N and S, and had no melting point.

Analysis.

Fd.(micro)	Req.for $C_{13}H_{11}O_6NS$	Req.for $C_{11}H_9O_5NS.H_2O$
C = 48.55	C = 50.5	C = 46.3
H = 3.63	H = 3.6	H = 3.86
N = 4.55	N = 4.5	N = 4.93
S = 11.43	S = 10.4	S = 11.23

The analysis suggested that partial hydrolysis had taken place. Examination, by action of HNO_2, showed the presence of free amino group, so the product was hydrolysed.

Removal of Acetyl Group by Hydrolysis.

The product from above was neutralised by addition of sodium bicarbonate to its suspension in water, and solid caustic soda, sufficient to give a 10 - 15 % solution added, and the solution refluxed for some time, the free acid liberated by dilute hydrochloric acid, and recrystallised from water. Qualitative analysis gave C, H, N, S.

Analysis

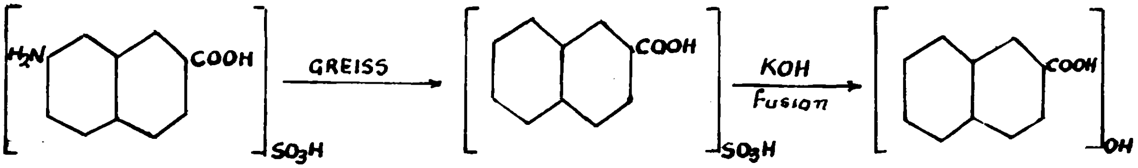
Fd.	Req. for $C_{11}H_9O_5NS.H_2O$
C = 46.0	46.3
H = 4.2	3.86
N = 4.6	4.93
S = 11.3 & 11.6	11.23

They were insoluble in cold water, fairly soluble in hot, and insoluble in organic solvents. Examination through the microscope showed prismatic needles, which appeared homogeneous in structure, and this, combined with the above analysis, lead to the conclusion that a mono-sulphonic group had been isolated. Consequently the position of the sulphonic group was the next consideration.

A slightly different procedure for the separation of any unsulphonated 2:7-aminonaphthoic acid was ultimately evolved, as it was considered possible that any 2-amino-1-sulpho-7-naphthoic acid formed and in solution in the oleum might lose its sulphonic group by hydrolysis on pouring the strongly acid solution on solution on/ to crushed ice, for according to Erdmann (Ann.1893,19,417; cf. Lynch & Scanlon ibid. 1010, and Lantz, Bull.Soc.Chim. 1935, V, 12, 2092-2108) the sulphonic group in the I-position in the naphthalene molecule is sometimes easily hydrolysed off. The method depends on the fact that the sodium salt of the 2:7-aminonaphthoic acid is almost insoluble in strong caustic soda solution. After the sulphonation product had been hydrolysed, solid caustic soda was added until a solid began to separate, and the whole cooled on ice. The sodium salt of the 2:7-aminonaphthoic acid separated as well defined yellow flakes, and were filtered off through a sintered glass filter. Acidification of the filtrate with concentrated hydrochloric acid liberated the sulphonic acids.

Proposed method to determinate the orientation of the amino-sulpho-naphthoic acid.

It was proposed to attempt the orientation by the elimination of the NH_2 group by diazotisation and subsequent replacement of the resultant diazo group by hydrogen, by one or other of the available methods. This would probably give a sulpho-naphthoic acid of known constitution, which could be easily identified by conversion to the hydroxy-naphthoic acid by alkali fusion. The following scheme illustrates:-



Diazotisation of the aminosulphonaphthoic acids.

This was smoothly accomplished by the method so successful for the diazotisation of the 2:7-diamino-:naphthalene. The sulphonated acid was dissolved in syrupy phosphoric acid, nitrosylsulphuric acid added at 0°C, and the resulting solution diluted with ice cold water or addition of crushed ice was even better. The diazo compound separated as a creamy crystalline solid, in a very fine state of division. It was stable. To obtain it in the dry state for the first experiment on replacement, it was filtered off, washed with water, then aqueous alcohol, followed by absolute alcohol, and then dry ether. Air was sucked through until the compound

compound/ was quite dry. The solid diazo compound consisted of creamy prisms.

Replacement of the diazo-group by hydrogen.

It is well known that the diazo group is replaced by hydrogen by a process of reduction, the reducing agent itself being oxidised during the process.

According to Greiss (B. 1864, 164, 863; Ann. 1866, 137, 67; J.C.S. 1867, 20, 54) reduction of diazo compounds may be brought about by boiling the diazo compound in absolute alcohol, and in this manner, the diazo group is replaced by hydrogen. But it was soon recognised that the alcohol tended to form with the diazo compound, a greater or lesser quantity of the mixed ether, (Greiss B. 1888, 21, 978) and Hantzsch (B. 1901, 34, 3337; 1903, 36, 2061) and later Hantzsch & Thomson (B. 1908, 41, 3519) go so far as to say that replacement as above occurs as a bye-product. It soon became apparent, however, that the presence of substituents in the molecule had a marked effect on the product obtained, and it is now generally agreed that negative groups particularly, in the ortho position to the diazo group, favour replacement by hydrogen. Greiss (Ann. 1866, 137, 39) also noticed the formation of diaryls when absolute alcohol was used.

The method of Greiss often fails, and because of the uncertainity of the reducing action, and the necessity of employing dry diazo compounds, other reagents were employed by other workers. Thus Friedlander (B.1889, 22, 587) found that reduction of the diazo compounds is best accomplished

accomplished/ by an alkaline solution of stannous hydroxide, his method taking advantage of the fact that most diazo derivatives are soluble without decomposition in cold caustic soda solution, and that this alkaline is usually as stable as the acid solution, although this does not appear to be the case with aminonaphthalene sulphonic acids, and naphthols. When, however, an alkaline reducing agent is added, a vigorous reaction ensues with brisk evolution of nitrogen, even in the cold.

Again the addition of alkali, sodium alkoxides, or zinc dust to the alcoholic solution of the diazonium salt favours the replacement of the diazo group by hydrogen, although this reaction appears also to yield quite a noticeable proportion of diaryl (Beeson J. Amer. C.S. 1894, 16, 235).

Wohmann (Ann. 259, 283) made use of an alkaline solution, using ammonia as the alkali, and zinc dust as the metal reducing agent, but a hydrazine derivative was obtained.

Hypophosphorous acid was first employed by Mai (B. 1902, 35, 162; cf. Bertheim 1908, 41, 1855; Stoermer & Heymann 1912, 45, 3103) and has been utilised by Raiford & Oberst (Ann. J. Pharm. 1935, 107, 242). In this way Mai prepared toluene from p-toluidine, diphenyl from benzidine, by diazotising and tetrazotising respectively these two compounds and treating with hypophosphorous acid

acid/ at 0° C. The yields were quite good.

Finely divided metals in conjunction with absolute alcohol have been used with varying degrees of success. Morgan & Evans (J.C.S. 1919, 115, 1132) used aluminium to eliminate the diazo group from 1-diazo-4-nitro-2-naphthol, and Parsons & Bailar (J.C.S. 1935, 58, 269) made use of copper bronze to remove the diazo group from 4-methyl-4'-diazo-azobenzene chloride.

In a recent paper Hodgson & Marsden (J.C.S. 1940, 207) describe a method which consists in first of all stabilising the diazotised amine by means of a naphthalene disulphonic acid or an oxy-acid such as a Tobias acid, and treating the dry stabilised salt in alcohol suspension with finely divided metals. The most effective agent is zinc dust, but precipitated copper powder can be used where zinc dust might act with other groups. e.g. $-NO_2$.

According to them, decomposition appears to be a simple exchange of hydrogen from one of the sulphonic groups via the agency, catalytic or otherwise, of the metal, since no aldehyde was detected when alcohol was used (cf. Saunder's "The Aromatic Diazo Compounds and their Technical Application" p.146, who states that it is the alcohol which is activated, the metals not reacting).

It would appear, then, that each "diazo" compound has certain conditions which must be satisfied before replacement by hydrogen can take place, and these seem to depend greatly on the stability of the "diazo" compound.

Replacement of the diazo group of Hydrogen.

The creamy diazo compound obtained by diazotisation of the sulphonated aminonaphthoic acid was suspended in absolute alcohol, and an attempt made to replace the diazo group by hydrogen by the method of Greiss (loc.cit.). Even after boiling for one hour, the diazo compound was quite unchanged and no discoloration of the alcohol was seen. In boiling absolute alcohol, therefore, the compound is stable. It was filtered off, and used for the next attempt using alkaline stannite solution (Friedlander B. 1889, 22, 587). The diazo compound was suspended in water, and, since it was very stable, poured into a solution of stannous chloride dissolved in caustic soda, the temperature being maintained at 70°C. Little or no nitrogen was given off, the solution turned red, indicating that coupling had taken place, but the solution was warmed on the water bath for one hour, and then cooled. Nothing separated, but on addition of common salt to the solution, a reddish product was obtained, which contained nitrogen. It was reduced by zinc and hydrochloric acid, and 2.9gms. original compound obtained, thus showing it was in all probability an azo body.

A somewhat similar result was obtained when an ammoniacal suspension of stannous hydroxide was used as the reducing agent, but the product was reddish yellow in colour.

Success was ultimately achieved using hypophosphorous acid (Mai B. 1902, 35, 162; cf. Bertheim B1908, 41, 1855; Stoermer & Heyman B. 1912, 45, 3103). In the first successful attempt the hypophosphorous acid was liberated from the barium salt by sulphuric acid, but great difficulty was experienced in getting rid of the barium sulphate precipitated - it was so finely divided that it passed through the finest of filters - so in all subsequent experiments the hypophosphorous acid was liberated from the sodium salt by addition of the calculated quantity of hydrochloric acid.

The diazo compound was suspended in water, sufficient to form a smooth flowing paste and slowly added to a solution of hypophosphorous acid prepared as above, heated to 50°C. No perceptible reaction took place, so the whole was warmed to 80°C. when nitrogen was evolved and the diazo compound slowly and evenly dissolved with the formation of a clear solution, only slightly coloured. After heating on the water bath for <u>one</u> hour, the solution was evaporated down, and cooled, when almost colourless crystals separated out. These were filtered off, and recrystallised from dilute hydrochloric acid. Examination through the microscope showed the presence of at least two crystalline structures. A qualitative analysis gave the presence of C,H, & S but no nitrogen.

Analysis (micro)

Found	Reqd. for $C_{11}H_8O_5S$.
C = 51.5	C = 52.4
H = 3.9	H = 3.2
S = 13.1	S = 12.7

From the above then, it would appear that the reaction had proceeded smoothly and that the product was a carboxynaphthalene sulphonic acid. This was converted into the hydroxynaphthoic acid by fusing with alkali in the ordinary manner (pp. 134), The product so obtained was an almost white crystalline solid, with M.P.205° - 220°C, which after recrystallisation three times from aqueous alcohol, melted over a range of ten degrees 210° - 220°C. This then would seem to indicate that the product was a mixture of hydroxynaphthoic acids.

Analysis

Fd. (hemi-macro)	Reqd. for $C_{11}H_8O_3$
C = 69.9	70.2
H = 4.8	4.3

This analysis would seem to prove this assumption.

Now if we accept the principle that a pure substance almost invariably melts at a higher temperature than an impure one, it is possible to eliminate, from the list of probables, those hydroxynaphthoic acids, having a melting point less than 210°C.

Perusal of the literature showed that the 1:2-, 1:3-, 2:3- acids could be thus eliminated, and since the 2:7-acid was the starting material, this leaves only the 1:6-, 2:6-, and the 1:7- hydroxynaphthoic acids.

This was very disappointing as it would appear that a hydroxyaminonaphthoic acid, corresponding to J-acid, could not be prepared by these means.

Attempts to separate the isomers.

However, various attempts were made to separate the isomeric sulphonic acids (see p. 156). First a fractional crystallisation of the free acids, in which six fractions were obtained, failed. An attempt using the disodium salts formed a thick syrupy liquor, from which seeding and scratching failed to cause crystallisation. Even spontaneous evaporation under a vacuum yielded a viscous liquor. Addition of alcohol both to this liquor and after dilution caused the separation of a sticky mass.

The normal barium salt, formed by addition of solid $BaCO_3$(A.R.) to the aqueous suspension of the free acid, failed to separate, but on addition of alcohol to the solution, a whitish precipitate came down, which on standing, or more quickly on warming, changed to a yellow crystalline compound composed of microscopic needles (Fd. Ba = 31.1, 31.2 (micro). Req.for $C_{11}H_7O_5NS.Ba.2H_2O$. Ba = 31.22). From the mother liquor a small quantity of buff coloured crystals was obtained by addition of more alcohol (Fd. Ba = 29.9 (micro) Reqd.for $C_{11}H_7O_5NS.Ba.H_2O$ Ba = 30.3). By dissolving in a little water and adding alcohol these were converted to the yellow salt.

The yellow salt was then converted into the hydroxynaphthoic acid, but again the melting point was not

not/ sharp, though the analysis agreed with that of a hydroxynaphthoic acid. Consequently it was assumed that separation of the isomers had not been accomplished.

Attempts to form the acid sodium and barium salts failed, as the free acids only were precipitated, and these, after elimination of NH_2 and alkali fusion yielded a product having no definite melting point.

Similar results were obtained when attempting to form arylamine salts e.g. aniline and p-toluidine, whilst, in trying to form the salts of the acids with benzylthiourea (cf. Chambers & Scherer J. Ind.E.C.1924, **16**, 1272). in order to identify the sulphonic acids, a reaction did take place, but, if the salt was formed, it was decomposed under the conditions tried, as mercaptan always resulted, and the free acid was ultimately recovered.

Hence, since the separation of the sulphonic acids isomers was unsuccessful, they were fused with alkali to form aminohydroxynaphthoic acids. It was hoped that they might be easily or readily separated and distinguished, since they should have definite melting points.

Fusion of the sulphonated aminonaphthoic acids with caustic potash.

The mixture of the sulphonic acids was fused in an open glass vessel with caustic potash. Charring occurred about 260° and frothing about 280°C, indicating the possibility of oxidation. Addition of acid to the melt, dissolved in water, separated a dark coloured solid, which contained N but no S. It dissolved in caustic alkali solution, acetone and alcohol to form a red coloured solution. Attempts to crystallise it from various organic solvents failed, and it exhibited the properties of some resinous oxidation product. So a series of experiments was conducted in an autoclave, in an atmosphere of nitrogen, to reduce the chances of oxidation to a minimum.

With 33% and 50% KOH, unchanged acid was recovered even at 250°C, but with 70% KOH and the temperature increased to 280°C, an oxidation product which contained neither N nor S was isolated. Attempts to crystallise this substance failed. It dissolved in caustic alkali, alcohol, acetone and ether to form a red solution. Acid appeared to reprecipitate it from alkaline solution. Obviously oxidation was taking place, so in an endeavour to restrain the oxidising effect, iron filings were introduced to the charge, and a series of experiments conducted, but again no crystalline product was isolated.

Below 220° - 230° C unchanged sulphonic acid was recovered, but above 240° C a dark coloured oxidation product, containing N but no S, soluble in alkalis, acetone, alcohol and ether, and insoluble in sodium bicarbonate solution, was obtained.

It would appear from these experiments, that the replacement of $-SO_3H$ by $-OH$ in the aminosulphonaphthoic by alkali fusion is too drastic a treatment, probably due to the ease with which the aminohydroxynaphthoic acids are oxidised, especially in alkaline solution.

Part IV.

EXPERIMENTAL.

1. Preparation of potassium cupro-cyanide solution.

50gms. (1mol.) blue copper sulphate were dissolved in 200ccs. hot water, and a solution of 35gms. KCN in 100ccs. water, slowly run in with brisk and efficient stirring. After all the cyanide had been added, a pale yellow solution was obtained. To reduce the excess alkali to a minimum, dilute HCl was added until a faint opalescenc was detected. This solution was kept at 50° - 60° C. and the diazo compound run slowly in.

2. Preparation of the sodium salt of 2:7-aminonaphthalene sulphonic acid.

This is described in experimental section Part III. The crystals so obtained contain five molecules of water of crystallisation.

3. Diazotisation of 2:7-aminonaphthalene sulphonic acid (Amino-F-acid)

31.7gms. (1mol.) of the crystalline sodium salt of amino-F-acid were dissolved in 300ccs. hot water and 3.65gms. (1mol.) HCl (= 9ccs.concentrated HCl) in three times its volume of water, run in with good mechanical stirring. In this way, the free acid was precipitated in a very fine state of division.

A further 3.65gms. HCl plus 3ccs. (= $\frac{1}{3}$mol.) to prevent the formation of aminoazo compounds, were added and the whole cooled to 10°C, when 7.2gms.(1mol.) sodium nitrite dissolved in 15ccs. water were added all at once, and diazotisation continued for about three hours, stirring all the time. On addition of the nitrite the diazo compound separated as a bulky yellow crystalline solid and was not contaminated with any red coloured matter. The excess nitrite was destroyed with urea, and common salt was then added to complete the separation of the diazo compound, which was filtered off, washed with saturated NaCl solution, and suspended in a volume of cold water, sufficient to give an easily running suspension.

4. Preparation of 2:7-cyanonaphthalene sulphonic acid. (Butler & Royle J.C.S.1923,1644, extracting with 95% alcohol)

The aqueous suspension of the 2:7-diazo compound was poured, very slowly, with very brisk stirring, into the potassium cupro-cyanide solution. Evolution of nitrogen occurred, and the solution turned red. After addition was complete, the whole was warmed on the water bath for one hour, heated to boiling, and concentrated HCl, sufficient to precipitate the CuCN, added. This was filtered off, washed with hot water, and the combined filtrate and washings evaporated to dryness. The solid obtained was then extracted three times with 100ccs. 90 - 95% alcohol.

A yellowish brown solid was obtained. Weight 6.3gms. =~28%.

The extracted residue was then placed in a flask with 250ccs. water containing 20gms KOH, and the mixture refluxed for three hours. Ammonia was given off. When evolution ceased, the solution was acidified with HCl, and the remaining copper precipitated by passing H_2S through the hot solution. The CuS was filtered off, and the filtrate on cooling deposited yellowish needles which were recrystallised and dried. Weight 13.5gms. These proved to be 2:7-carboxynaphthalene sulphonic acid. (59.5% calculated on aminosulphonic acid.)

Hence extraction with alcohol is incomplete.

5. Preparation of 2:7-carboxynaphthalene sulphonic acid, without separation of the intermediate product, 2:7-cyanonaphthalene sulphonic acid.

62.5gms. of the sodium salt of amino F acid were diazotised, and treated with the cuprous-cyanide solution as before. After precipitation of the CuCN with conc.HCl, it was filtered off, washed with hot water, and the combined washings and filtrate just neutralised by addition of solid KOH, and then a quantity of solid KOH added, sufficient to give a solution of 15% strength. This solution was boiled, with constant stirring till no more ammonia was given off, made acid by addition of conc.HCl, and H_2S passed to precipitate the remaining copper, the

the/ CuS filtered off, and the filtrate left to stand. Crystals of 2:7-carboxynaphthalene sulphonic acid separated out on cooling. They were filtered off and dried. The mother liquor was concentrated and cooled, but only a tarry mass was obtained on cooling.

Wt. 30.8gms. (64.5% calculated on aminosulphonic acid.)

The above was the method adopted for all subsequent preparations.

Preparation of 2:7-hydroxynaphthoic acid.

(Conversion of 2:7-carboxynaphthalene sulphonic acid. Butler & Royle J.C.S. 1923, 1654.)

9gms. (1mol.) 2:7carboxynaphthalene sulphonic acid were fused with 12 gms. (6mols.) potassium hydroxide dissolved in 3ccs. water. The finely divided sulphonic acid was added, a little at a time to the caustic potash melt at 240° - 260° C, and the mass stirred. After all the acid had been added, the temperature was raised to 280° C for five minutes, and the mass allowed to cool, when it was dissolved in hot water, almost neutralised with 50% H_2SO_4, filtered from some insoluble impurities, and the hydroxynaphthoic acid precipitated by addition of conc. HCl. The SO_2 was partially driven off by boiling, and after cooling in ice, the free acid was filtered off, and washed with ice cold water. It was purified by converting to the sodium salt in the usual way, using sodium bicarbonate, filtering from insoluble, and reprecipitating with conc. HCl.

Recrystallisation from aqueous alcohol gave a product with M.P. 273° - 274° C (Butler & Royle J.C.S. 1923, 1654 give 269° - 270° C; Friedlander, Hielpern & Spielfogel, Mitt. tech. G.M.W. 1989, 8, (11 and 12); J.S.C. I, 1898, 17, 836 give 262° C).

Weight was 4.5gms., hence yield is 67%.

Analysis.

Fd.	Req. for $C_{11}H_8O_3$
C = 70.1	70.2
H = 4.7	4.3

Preparation of 2:7-acetylhydroxynaphthoic acid.

The acetyl derivative, prepared by dissolving the acid in glacial acetic acid, and adding the solution to acetic anhydride in crushed ice, filtering and recrystal-:lising from aqueous alcohol gave M.P. 211° - 212° C. (Butler & Royle loc.cit. gave 209° - 210° C).

Preparation of sodium salt of 2:7-hydroxynaphthoic acid.

The 2:7-hydroxynaphthoic acid was converted into its sodium salt by suspending the free acid in aqueous alcohol (50/50,) warming till dissolved and adding solid sodium bicarbonate till no more CO_2 was evolved. On cooling the sodium salt recrystallised out in shining plate.

Conversion of 2:7-hydroxynaphthoic acid into 2:7-aminonaphthoic acid.

(After the method of Harrison & Royle J.C.S. 1926, 87)

10gms. (1mol.) sodium salt of 2:7-hydroxynaphthoic acid were dissolved in 10ccs. water in a monel metal crucible, 70ccs. 0.88 ammonia, followed by 20ccs. of a solution of NH_4OH saturated with sulphur dioxide were added, and the whole diluted with 70ccs. water. On the addition of the SO_2 solution, the free hydroxy acid was precipitated in a very fine state of division. The crucible was put into an autoclave and heated to 200° - 220° C for 10 hours. After cooling, the contents of the crucible containing a pale yellow crystalline solid, were emptied into a beaker, and the excess ammonia boiled off, water added, and the solution filtered from a little insoluble. On addition of solid caustic soda, the sodium salt separated out in beautiful yellow flakes. These were filtered, washed with a little alcohol, and dried in a desiccator.

Addition of acetic acid to the solution of the sodium salt precipitated the free acid, which, on recrystallisation from alcohol, gave yellow rectangular crystals. M.P. 244° - 245° C (Harrison & Royle J.C.S. 1923, 82T, give 245° C).

The acetyl derivative gave M.P. 287° - 289° C (for preparation see p. 148.) Harrison & Royle give 200° - 201°C

Analysis.

	Fd.		Req. for $C_{13}H_{11}O_3N$
hemi-macro	(C = 68.2	Av. of 4.	C = 68.1
	(H = 4.7		H = 4.8
micro	N = 6.09, 6.32.		N = 6.11

Attempted Sulphonation of 2:7-Aminonaphthoic Acid.

II

Using 93% H_2SO_4.

1. The apparatus consisted of an ordinary wide-mouthed, round-bottomed, glass flask, attached by means of a mercury-sealed stirrer to an electric motor. The amino-naphthoic acid was added to the acid, and cooled to 0° C.

5.0gms. (1mol.) anhydrous and finely powdered 2:7-amino-naphthoic acid were added gradually to 25ccs. (8mols.) 93% sulphuric acid, with constant stirring. After all the amino acid had been added, the apparatus was sealed with a mercury seal, immersed in an oil bath at 15° - 20° C, and stirring continued for six hours. At the end of that time, the strongly acid liquor, which contained some dark solid in suspension, was diluted by pouring into 250gms. crushed ice, and the resulting liquor heated almost to boiling, filtered from an insoluble product (0.4gm.) and cooled in ice. A crystalline solid separated. This was filtered off, suspended in a few ccs. warm water, and $NaHCO_3$ added till the solution was alkaline to phenolphthalein. Effervescence took place, the solid dissolved, forming a pale yellow solution. It was filtered, the filtrate made just acid with dilute acetic acid, when a crystalline solid separated, which was filtered off, washed with water and dried.

Weight 3.0gms. M.P. 248° C.

The crystals were yellow, and a mixed melting point with 2:7-aminonaphthoic acid gave no depression. Hence it was unchanged original. Evaporation of the mother liquor gave only sulphate and acetate.

The filtrate from the acid liquor was diluted with water till its bulk was about 1 litre. (This dilution is necessary in order to have sufficient liquid present to keep the mixture stirred during the precipitation of the H_2SO_4 as $CaSO_4$.) The solution was boiled and milk of lime, in the form of a fairly stiff paste, run in slowly till the liquor was just alkaline to phenolphthalein. The $CaSO_4$ formed was filtered off, washed with boiling water several times, and the combined filtrate and washings concentrated to 100ccs., when 15ccs. of a solution of Glauber's salt, containing 5gm./200ccs. solution, were added. The $CaSO_4$ was filtered off, the filtrate evaporated to dryness on the water bath, and the residue extracted with aqueous alcohol (50/50). The alcohol was then distilled off, the solution concentrated, and made just acid with dilute acetic acid, and cooled in ice. A few crystals were obtained with M.P. 248° C. and a mixed M.P. with 2:7-aminonaphthoic acid gave no depression.

The filtrate from the separation of these crystals was concentrated, and acidified with dilute HCl, and cooled in ice, but nothing appreciable separated.

N.B. If less sulphuric acid is used in the sulphonation the mixture forms a paste, and efficient stirring and mixing is difficult. Diluents were used later (cf. page 146.).

2. 5gms. (1mol.) 2:7-aminonaphthoic acid + 25cc. (8mols.) 93% H_2SO_4 treated as in Expt. I, Temp. 15° - 20° C, time 12 hours.

The acid liquor was worked up as in Expt. I, 3.0gms. unchanged amino acid recovered. No sulphonation product was obtained.

3. Same charge as above -----temp. 15° - 20° C. Time 72 hours. Acid liquor treated as in Expts. 1 and 2.

2.8gms. unchanged amino acid recovered.

No sulphonation product was obtained.

4. Same charge as above-----temp. 40° - 45° C for 6 hours.

Acid liquor treated as above.

2.1gms. unchanged acid recovered. No other product isolated.

5. Same charge as above-----temp. 40° - 45° C, for 12 hours.

Acid liquor treated as above.

2.1gms. unchanged acid recovered. No other product isolated.

6. Same charge as above-----temp. 90° - 100° C for 6 hours.

Acid liquor treated as above.

2.2gms. unchanged acid recovered. No other product isolated.

Sulphonation of 2:7-aminonaphthoic acid using 93% H_2SO_4.

7. 5gms. (1mol.) amino acid)
\+) temp. 145°-150° C for 12 hours.
25cc. (8mols.) 93% H_2SO_4.)

The strongly acid liquor was black as if considerable charring had taken place. On pouring the acid liquor into crushed ice, and cooling, a solid separated. This was filtered off, dissolved in $NaHCO_3$ till just alkaline, filtered, and dilute HCl added. A pale yellowish crystalline solid separated. The whole was cooled in ice, the solid filtered off, and recrystallised from water using animal charcoal. 0.4gm. feathery white needles were obtained. These had no M.P. and contained S and N.

The acid filtrate was worked up with milk of lime as before. 0.2gm. white feathery needles were obtained, which appeared to have the same crystalline structure as above. Contained S and N and did not melt.

Yield 8.5%.

Attempted Sulphonation using 10% oleum and 20% oleum.

III

1. 5gms. (1mol.) 2:7-aminonaphthoic acid + 25ccs. (10mols. SO_3) 10% oleum) 15°-20°C for 6hrs.

Acid liquor was black as if considerable charring had taken place. It was worked up as in previous experiments. 2.2gms. unchanged amino acid were recovered. No other product was isolated.

2. Same charge as in expt. 1-----temp. 15°-20°C for 12 hours. Acid liquor black as above. Worked up as before, and 2.0gms. unchanged amino acid were recovered. No other product was isolated.

3. Same charge as in expts. 1 & 2-----temp. 45°-50° C for 12 hours. Acid liquor, black in colour, was treated as before. 3.0gms. unchanged amino acid were recovered. No other product isolated.

4. Same charge using 20% oleum at 15°-20° C for 6 hours. Acid liquor black in colour, treated as before. 2.0gms. unchanged amino acid recovered, but no other product isolated.

IV

Sulphonation of 2:7-aminonaphthoic acid using 20% oleum.

1. 5gms. (1mol.) 2:7-aminonaphthoic acid) + 25ccs. 20% oleum) 40°-45°C. for 3 hrs.

The strongly acid liquor was very black, probably with charring of the organic acid. On pouring it into ice cold water as before, heating to the boil, filtering and allowing to cool on ice, a dirty looking solid separated. This was filtered off, suspended in a few ccs. warm water, and $NaHCO_3$ added till just alkaline to litmus. Effervescence took place. The solution was filtered and made just acid with dilute acetic acid, but nothing separated on cooling in ice. It was acidified with dilute HCl, and a solid separated in a dark liquor. This solid, on filtering off, and recrystallising from water using animal charcoal, gave 0.7gms. white feathery needles. They contained N and S but did not melt. Viewed through the microscope they appeared similar to those obtained in expt. 7, I. Yield 9.8%.

Analysis. (micro)

Fd.	Req. for $C_{10}H_5(NH_2).(COOH).SO_3H.H_2O$.
S = 11.6%	11.23%.

The filtrate from the strongly acid liquor was treated with milk of lime as before, and yielded 0.2gms. white feathery needles, which through the microscope appeared to be identical to those obtained above. Contain N and S, and do not melt.

2. Repeated expt. II, and obtained 1.0gms. white feathery needles.

Analysis. (micro)

	Fd.	Req. for $C_{11}H_{11}O_6NS$.
C	= 47.92	46.3
H	= 3.48	3.86
N	= 4.66	4.93
S	= 11.32	11.23

They are soluble in $NaHCO_3$ solution with evolution of CO_2. Fairly soluble in water, and aqueous solution acid to litmus. Insoluble in organic solvents.

3. Sulphonation of 2:7-aminonaphthoic acid---separation of product by "salting out process"---(Gattermann B.24, 2, 121.)

5.0gms. amino acid)
+) 40° - 50° C for 12 hours.
25ccs. 20% oleum.)

The dark coloured acid liquor was cooled and finely ground NaCl added carefully, until no more fumes were given off, and then allowed to stand. A white solid, which was shown to be $NaHSO_4$ separated. This was filtered off, and extracted with aqueous alcohol, but only a few crystals were obtained on evaporating down. These contained N and S, and on examination, through the microscope appeared identical with those obtained in previous experiments.

The filtrate from above, which was dark in colour, was concentrated and cooled, when a dark greyish solid separated. This was separated, and extracted with alcohol (90%) and the extract evaporated to dryness. A white solid

solid/ was obtained, which was dissolved in water, the resulting solution acidified with dilute acetic acid, when a brownish crystalline solid separated, which was recrystallised from aqueous alcohol. The M.P. was very indefinite, and there was not sufficient to identify them. The filtrate from the acetic acid solution was acidified with dilute HCl, and a small dirty precipitate, with which nothing could be done, was obtained.

V.

Sulphonation using Chlorosulphuric acid and dichlorethylene as a diluent.

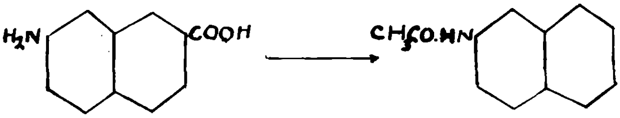
5.0gms. (1mol.) amino acid were dissolved in 20ccs. dichlorethylene (B.P.55°C) and 9.3gm. (3 mols.) chlorosulphuric acid slowly added, with cooling, and the whole refluxed on a bath for 4 hours. A dark viscous solid, suspended in a clear liquid (probably the dichlorethylene) was in the flask, and HCl issued from the top condenser. The dichlorethylene was distilled off on the water bath, and the contents of the flask poured on to 100ccs. ice cold water. The resulting solution was very dark in colour. It was cooled in ice but when no product separated, solid $NaHCO_3$ was added carefully till the solution was alkaline to litmus. It was then warmed, filtered from insoluble matter and allowed to stand for 2 days, by which time a dark tarry solid had separated. This tarry solid was discarded, and the filtrate, a dark liquid, was acidified with HCl, and after standing, filtered from a dark solid, which was treated with water and organic high boiling solvents, but nothing crystalline was obtained. The filtrate, however, was pale yellow in colour, and, on standing, deposited white feathery crystals. After cooling on ice, these were filtered off, They contained N and S, and had the same crystalline appearance as those obtained before. The weight was 0.4gms. The yellow filtrate was evaporated almost to dryness, but nothing separated. Yield 5.6%.

Yield 5.6%./

(calculated on amino-naphthoic acid and assuming product a monosulphonic acid.)

VI

1. Preparation of 2:7-acetylaminonaphthoic acid.



15gms. (1mol.) 2:7-aminonaphthoic acid sodium salt were gradually added to 400ccs. glacial acetic acid containing 50gms. (12mols.) acetic anhydride and a little anhydrous sodium acetate and the mixture refluxed for 2 hours until all the amino acid had dissolved. The solution was poured into water, allowed to cool to room temperature, cooled in ice, and the pale yellow crystalline solid which had separated, filtered off, and recrystallised from glacial acetic acid or alcohol using decolorising carbon. Pale yellow crystalline plates were obtained, slightly soluble in alcohol, almost insoluble in ether, benzene and chloroform. M.P. 287° - 289° C. (Harrison and Royle give 200° - 201° C.)

Analysis. (hemi-macro)

	Fd.	Req. for $C_{13}H_{11}O_3N$.
C =	68.1, 67.4, 68.1, 68.3	68.1
H =	4.8, 4.4, 4.8, 4.8	4.8
N =	(micro) 6.32, 6.09	6.11

2. Attempted Sulphonation of 2:7-acetylaminonaphthoic acid-----temp. 20° C.

5.0gms. (1mol.) 2:7-acetylaminonaphthoic acid were dried in a vacuum oven at 70° C, and 5 mms. pressure,

2. (contd.)

pressure,/ pulverised and cautiously added, a little at a time to 60gms. (10mols.) 22% oleum, the temperature not being allowed to rise above 20° C, and good mechanical agitation being maintained all the time. After 3 and 6 hours no sulphonation had taken place so the solution was maintained at 20° C for 12 hours. with stirring. The solution, now only slightly discoloured, was poured on to crushed ice, and the pale yellow solid filtered off. It was dissolved in $NaHCO_3$ and dilute acetic acid added. A yellow precipitate was obtained, which was recrystallised from glacial acetic acid M.P. 287° - 289° C. A mixed M.P. with original gave no depression.

Wt. recovered = 4.6gms.

3. <u>Sulphonation of 2:7-Acetylaminonaphthoic acid</u>.

15gms. (1mol.) 2:7-aminonaphthoic acid + 60gms. (10mols.) 22% oleum, were mixed as before and maintained at 45° - 50° C, for 3 hours with good stirring, when the solution, only slightly discoloured, was poured on to crushed ice. A pale yellow solid separated out, at first, but as the temperature rose, this changed to a white finely divided solid, definitely of a crystalline structure. After all the mixture had been added, the whole was cooled on ice, and the crystals so obtained, filtered off and recrystallised from water.

3(contd.)

Examination of these crystals through the microscope showed them to be composed of white or colourless rectangular needles (x40) with a few yellowish crystals as focal points. As these appeared to be unchanged acetylaminonaphthoic acid, the crystals were first dried under a vacuum and boiled three times with glacial acetic acid, and recrystallised from water. This time, on examination through the microscope, they appeared to be uniform in structure. They were filtered off, and dried in a vacuum over concentrated sulphuric acid.

Analysis.

Fd.	Req.for $C_{13}H_{11}O_6NS$	Req.for $C_{11}H_9O_5.NS.H_2O$
C = 48.5	50.5	46.3
H = 3.63	3.6	3.86
N = 4.55	4.5	4.93
S = 11.43	10.4	11.23

4. Hydrolysis of Sulphonated Product.

The product from the above experiment was mixed with 200ccs. water, and sodium bicarbonate added until carbon dioxide ceased to be evolved. 20-25gms. solid caustic potash were added, and the solution refluxed for two hours, cooled, and then carefully acidified with excess hydrochloric acid. An almost white solid separated, which was filtered off, and recrystallised from water, in which it is fairly soluble in hot, and almost insoluble in cold.

4. (contd.)

The product, prisms or needles, appeared identical with those obtained by direct sulphonation of the amino-:naphthoic acid. The yield was 14.7gms. (84%, theory.)

<u>Analysis</u> (micro.)

	Fd.	Req. for $C_{11}H_9O_5NS.H_2O$
C =	46.0	46.3
H =	4.2	3.86
N =	4.6	4.93
S =	11.3	11.23

VII

Orientation of product obtained by Sulphonation of 2:7-aminonaphthoic acid.

Elimination of NH_2 group.

1. Diazotisation of sulphonic acid.

5gms. (1mol.) sulphonic acid were dissolved in 10ccs. syrupy phosphoric acid, cooled to -3° C by external cooling, and nitrosylsulphuric added drop by drop, till a drop taken out and diluted with water showed a positive on starch iodide paper. The solution was diluted by pouring into 30cc. ice cold water, when, on standing, the diazo compound separated as creamy crystalline, and finely divided. It was filtered off and washed with ice cold water.

2. Attempted Replacement of "diazo" group by hydrogen using absolute alcohol. Greiss B. 1864, 164, 683; Ann. 1866, 137, 67; J.C.S. 1865, 18, 315T; 1867, 20, 54).

The diazo compound obtained from above, was washed with absolute alcohol, then ether and dried, suspended in 100ccs. absolute alcohol, and the whole gradually heated till the alcohol boiled, and boiling continued for one hour under a reflux. No reaction took place, so the mixture was cooled and the diazo compound filtered off and used for the next attempt.

3. Attempted replacement using alkaline stannite solution (Friedlander B. 1889, 22, 587)

The diazo compound recovered from expt. 2, was suspended in 100ccs. water, and since it was very stable poured into a solution of 10gms. stannous chloride dissolved in caustic soda solution at 70° C. The solution turned red and little or no nitrogen was given off, but it was warmed on the water-bath for one hour, and then cooled. Nothing separated, but on salting out, a reddish product was obtained which contained nitrogen. It was reduced by Zn and HCl and 2gms. acid recovered.

4. Attempted replacement using a suspension of $Sn(OH)_2$ in ammoniacal solution.

5gms. amino acid were diazotised as before and the diazo compound poured into a suspension of stannous hydroxide made by dissolving 10gms. $SnCl_2$ in 20ccs. water, and adding excess 0.88 ammonia. Slight frothing occurred and the solution turned red. After warming on the water-bath for one hour, the solution was cooled and when nothing separated it was salted out. A reddish yellow substance separated which contained N. It was probably an azo body, as it was reduced by Zn and HCl to a colourless substance.

5. Replacement using hypophosphorous acid. (Mai. B.1902, 35, 162; cf. Bertheim 1908, 41, 1855; Stoermer & Heymann 1912, 45, 3105).

In the first attempt the hypophosphorous acid was generated from Barium hypophosphite by addition of dilute sulphuric acid, but in all subsequent experiments the sodium salt was used.

27.8gms. $NaH_2PO_2.H_2O$ were dissolved in cold water, and 19.7gms. HCl (= 22cc.conc.HCl) diluted with 20cc. H_2O poured slowly in. A clear solution was formed which was heated to 50° C.

5 gms. (1mol.) of the amino acid were diazotised as before, and the aqueous suspension of the diazo compound poured with good mechanical stirring into the solution of hypophosphorous acid. Nothing happened at 50° C., so the whole was warmed to 80° C. when nitrogen was evolved and the solution became clear though slightly coloured. After heating on the water bath for one hour, the solution was evaporated till crystals became to separate when it was cooled. These crystals were filtered off, and recrystallised from H_2O. Examination through the microscope, showed two crystalline structures. Qualitative analysis showed presence of C, H & S, but not N.

Analysis.

Found	Reqd. for $C_{11}H_8O_5S$
C = 51.5	52.4
H = 3.9	3.17
S = 13.1	12.7

Fusion of product of previous experiment with caustic alkali.

The crystals from previous experiment (about 2gms.) were fused with alkali as before (see p. 134)

The product was recrystallised from aqueous alcohol

Analysis (hemi-macro)

Found	Reqd. for $C_{11}H_8O_3$
C = 69.9	C = 70.2
H = 4.8	H = 4.26

M.P. 205° - 220°. After three recrystallisations M.P. 210° - 220°.

Attempted Separation of Isomers.

2:7-acetylaminonaphthoic acid was sulphonated as before and an attempt to separate the isomers formed was made by fractional crystallisation of the Barium salt.

Formation of Barium salt and attempted separation.

A quantity (approx. 10 gms.) of the dried free acid was suspended in cold water and solid barium carbonate (A.R. reagent) added till excess carbonate remained. The whole was warmed, filtered hot and allowed to stand. Nothing separated even after concentration of the solution, so some alcohol was added when a white solid separated, which, on warming in the solution turned yellow. The whole was cooled in ice, and the yellow solid filtered off. These were recrystallised from water containing a little alcohol, and gave the following analysis:-

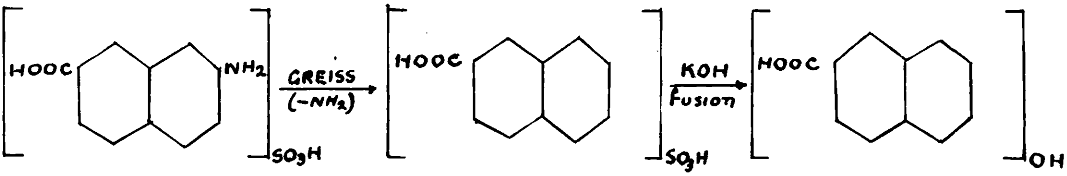
Fd. (micro)		Req. for $C_{11}H_7O_5NSBa.2H_2O$
Ba = 30.98)	31.11	31.22
31.02)	31.2	

From the mother liquor a small quantity of crystals (buff coloured) containing 29.9% (micro) was obtained. Req. for $C_{11}H_7O_5NS.Ba.H_2O$. Ba = 30.3%.

These buff coloured crystals were easily converted to the yellow by dissolving in water and adding alcohol as before.

Examination of yellow salt to ascertain if separation had been effected.

The yellow barium salt was dissolved in hot water and excess of dilute hydrochloric acid added and the whole cooled, by external cooling. The free acid separated immediately. Examination through the microscope led to the belief that a pure acid had been obtained and so orientation of the $-SO_3H$ group was attempted as before.



The product (c) again did not have a definite M.P. Therefore it was concluded it was not pure, and hence that the separation of the isomers produced by sulphonation had not been accomplished. Otherwise, to explain the fact that (c) was a mixture it would be necessary to assume that an intromolecular change had taken place either during the elimination of the $-NH_2$ group, or during the replacement of the $-SO_3H$ group by $-OH$.

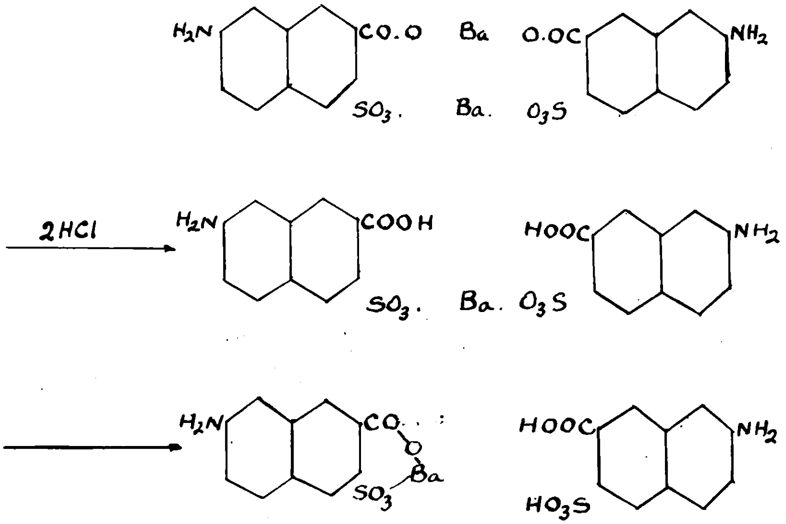
Analysis of (c) gave results corresponding with the requirements of a hydroxynaphthoic acid.

Fd. (micro)	Req. for $C_{11}H_8O_3$
C = 69.9	70.2
H = 4.45	4.26

Attempted formation of acid barium salt of Sulphonic Acids.

12gms. free acid (dried under a vacuum at 60°C, and finally over P_2O_5) were titrated with standard baryta and back titrated with standard HCl (2-3N) till half the equivalent of the baryta had been added. A white solid separated, which on recrystallisation from water was found to contain no barium, and was the free acid.

This could be explained thus.



Analysis gave.	Req. for $C_{11}H_9O_5NS. H_2O$
C = 46.76	46.3
H = 3.72	3.86
N = 4.89	4.93
S = 11.37	11.28

Elimination of the NH_2 group and subsequent fusion with alkali gave a product containing no N or S, but it had not a definite M.P. So it was concluded it was not a pure product, and hence that separation had not been complete.

Attempted formation of acid sodium salt.

A quantity (approx. 20gms.) free acid was titrated with standard sodium carbonate solution, using phenolphthalein as indicator, and then back titrated with standard hydrochloric acid till half the equivalent of the sodium carbonate had been added. The white crystalline solid, which separated, was again the free acid. Concentration of the mother liquor yielded a solid which, on recrystallisation from water, was again the free acid.

Production of the hydroxynaphthoic acids as before, had no definite M.P.

Attempted preparation of Arylamine salts.

Since the attempts to separate the isomers by means of the metallic salts had failed, attempts were made to form the salts of the arylamines; aniline and p-toluidine.

Equimolecular quantities of aniline hydrochloride and the sodium salts of the sulphonic acids were dissolved in water. The first solution was gradually added to the second, and a white crystalline precipitate separated. It was shown to be the free acid.

The same procedure was carried out with p-toluidine, and again the free acid separated.

Attempted preparation of Aminohydroxynaphthoic acids by alkali fusion of the sulphonated aminonaphthoic acids.

1) Fusion with caustic potash in an open vessel temperature 260° C

(see fusion of 2-sulpho-7-naphthoic acid p.134), 5gms. (1mol.) of the product obtained by sulphonation of the 2:7-aminonaphthoic acid were fused with 10.5gms. (12 mols.) caustic potash in an open glass vessel. The temperature was raised to 250° - 280° C., when the melt turned dark in colour and frothing took place. After two minutes the melt was cooled, dissolved in hot water, and almost neutralised by 50% H_2SO_4. It was filtered from a dirty precipitate and acidified with dilute acetic acid. A dark solid separated. This was filtered off.

It was soluble in caustic soda solution to form a red coloured solution, and was reprecipitated by acids; it was insoluble in water, neutral to litmus, and insoluble to $NaHCO_3$ solution, soluble in acetone, and the usual organic solvents. Attempts to form a crystalline product and an acetyl derivative failed.

Obviously it is an oxidation product.

2) Fusion in an Autoclave with 33% KOH, in an atmosphere of nitrogen - temp. 220° - 250° C.

10gms. (1mol.) sulphonic acids were fused in an autoclave in an atmosphere of nitrogen with 8mols. 33% KOH solution, The temperature was maintained at at/ 220° - 250° C for ten hours, during which the pressure varied from 40-69 atmospheres.

The resulting solution was dark in colour. It was washed out with hot water, almost neutralised with 50% H_2SO_4, filtered from a little insoluble matter, acidified with conc. HCl, cooled in ice, and the dark coloured solid filtered off. This product was found to contain K, so it was boiled with fairly concentrated HCl, cooled in ice and filtered.

It was partly soluble in alcohol, so it was boiled with alcohol and filtered. The insoluble in alcohol portion contained S & N, and examination showed it to be unchanged sulphonic acid (3gms. were recovered).

The soluble in alcohol portion was evaporated to dryness, and a black powder (0.5gms.) obtained. This had the same properties as that obtained in expt. I.

3). With 50% KOH at 220° - 250° C. in atmosphere of nitrogen.

10 gms. (1mol.) acid + 8 mols. 50% KOH as in 2).

Pressure was 50-55 atmospheres. The melt, on examination as in 2), gave 2 gms. unchanged sulphonic acid; and a black product having the same properties as that obtained in expts. 1 & 2.

4). With 70% KOH at 250° - 280° C. in atmosphere of nitrogen.

10gms. (1mol.) acid + 50 ccs. (8.5mols.) 70% KOH heated in autoclave as in 3), but temperature was

was/ 250° - 280° C; pressure 55-60 atmospheres. The melt was washed out with hot water, and filtered from a little insoluble matter, composed mainly of iron. The filtrate was acidified with concentrated HCl, boiled to expel SO_2, cooled in ice, and the solid filtered off.

It contained no N nor S, and was partially soluble in ether, so it was extracted with ether, and the ether evaporated off under vacuum. A black solid was obtained which had the same properties as that obtained in expts. 1, 2 & 3. Attempts to crystallise from various solvents failed.

The insoluble in ether portion was NaCl.

A notable point is that the fusion has eliminated the NH_2 group.

5) as for 3) with addition of iron filings.

Same charge as in expt. 3) with addition of 1 gm. iron filings. The melt on working up as before yielded 7gms. unchanged sulphonic acid.

6) as for 5) temperature 250° - 280° C.

Same charge as in expt. 5), but temperature was 250° - 280° C. The product was composed of a black powder soluble in caustic alkalic and organic solvents to form a red solution. It contained N but no S.

Attempts to crystallise failed.

Estimation of percentage of sulphonic acid containing the $-SO_3H$ group in o & p. positions with respect to NH_2.

The displacement of α $-SO_3H$ groups by halogens, especially by bromine is well known and established. Thus Blanksma (Rec. trav. chim. 1910, 29, 377) utilised the readiness with which $-SO_3H$ and - COOH groups in the ortho and para positions, with respect to an animo group can be displaced by bromine, to elucidate the constitution of certain aminosulphobenzoic acids.

Sudborough & Lakhumalain (J.C.S. 1917, 41) describe the action of halogen on various aminosulphonic and aminocarboxylic acids, including some in the naphthalene series. They indicate that when bromine is employed, an almost quantitative displacement of sulphonic group, as sulphuric acid, takes place. Later Friedlander, Karamensis & Schenk (B. 1922, 55, 45) showed that substitution of $-SO_3H$ group by halogens is not applicable to β-sulphonic acids (see Angabon von Rudolf D.R.P. 101349, 103893. Frdl. 5, 162).

From these observations it was thought possible to estimate the percentage of aminosulphonaphthoic acid , containing the $-SO_3H$ group in the α -position, most probably that in the o.p. positions to the $-NH_2$ group.

The method employed was to take a known weight of sulphonated product, convert it to the soluble sodium salt by addition of the calculated amount of solid $NaHCO_3$ in H_2O, add excess $NaBrO_3$ and NaBr, followed

followed/ by excess N/5 HCl. The free acid was first precipitated, then reaction took place and the substance slowly dissolved, while excess bromine coloured the solution, which was boiled and $BaCl_2$ solution added in slight excess. The precipitated $BaSO_4$ was filtered off, ignited and weighed.

Result:-1.7gms. sulphonated acid yielded 0.16gms. $BaSO_4$.

$\therefore$ % α $-SO_3H = 65.6\%$.

Part V.

Preparation of the 1: 2: 7-, and 1: 2: 6-aminohydroxynaphthoic acids.

Part V.

Proposed method of preparation.

It was proposed to attempt the preparation of the 1: 2: 7-, and 1: 2: 6-aminohydroxynaphthoic acids by the method first used by Nietzki & Guitermann (B.1887,20, 1275) for the preparation of aminohydroxynaphthoic acids (see Part I page 14).

The hydroxynaphthoic acid would be coupled with diazobenzene chloride, and the red azo compound formed would, on reduction, give an aminohydroxynaphthoic acid. Now, as stated on page 6, it is well known and established that with β-naphthol and its derivatives, coupling only takes place in the 1-, position. It follows, therefore, that the product obtained by coupling 2:7-hydroxynaphthoic acid with a diazonium compound, would be an azo compound with the azo group in the 1-position. Hence reduction would give 1-amino-2-hydroxy-7-naphthoic acid.

Similarly, the product obtained by coupling 2:6-hydroxynaphthoic acid with a diazonium compound followed by reduction would be 1-amino-2-hydroxy-6-naphthoic acid.

Preparation of 1-amino-2-hydroxy-7-naphthoic acid hydrochloride.

Preparation of 1-benzeneazo-2-hydroxy-7-naphthoic acid.

The 2:7-hydroxynaphthoic acid prepared as described in Part IV, was coupled with diazobenzene chloride at 0°C. and after acidifying with dilute HCl, the bright red azo compound was recrystallised from aqueous dioxan. It crystallised in shining, bright red microscopic needles.

m.p. ?

Reduction of 1-benzeneazo-2-hydroxy-7-naphthoic acid.

This was first attempted in alkaline solution using $Na_2S_2O_4$ (Grandmougin B.1906,39,3609). The red 1-benzeneazo-2-hydroxy-7-naphthoic acid was dissolved in alkali and solid $Na_2S_2O_4$ added, till the red solution changed to pale yellow, Addition of acid precipitated a yellow solid, which was extracted with ether, but on evaporating off the solvent, under a vacuum, a black resinous solid was obtained which had all the properties of an oxidation compound.

An attempt to reduce the azo compound using stannous chloride and conc. HCl. was also unsuccessful, due probably to its complete insolubility in acid.

Success, however, was achieved by taking advantage of the solubility in galcial acetic acid and using anhydrous stannous chloride which is also soluble in that acid.

The red azo compound was dissolved in the minimum quantity of glacial acetic acid and a slight excess of anhydrous stannous chloride, prepared according to the

the/ method of Stephen (J.C.S. 1930,2786) added in small quantities. The red solution was warmed and it quickly turned to pale yellow, when it was diluted with water, a few drops conc. HCl added, the tin precipitated by H_2S, filtered off, and on addition of conc. HCl to the filtrate, the hydrochloride was precipitated as very pure small white needles.

The hydrochloride of the base is fairly soluble in water, soluble in alkali, and ammonia, insoluble in alcohol. Addition of sodium acetate to the solution or suspension of the hydrochloride in water precipitates the free base, which rapidly discolours on exposure to the air, more quickly on warming. Attempts to crystallise the free base from various organic solvents failed to give a pure compound due to the ease with which the base oxidises.

Attempts to diazotise and couple the base with alkaline naphthols failed. Addition of a solution of sodium nitrite to the aqueous suspension of the hydrochloride formed a yellow solution which deposited a yellow solid. Attempts to diazotise by the methods so successful for the aminonaphthol also failed and the presence of copper sulphate utilised by Geigy (see page 16) for the successful diazotisation of 1:2-, & 2:1-aminonaphthol also gave a yellow precipitate , which failed to couple.

Preparation of 1-amino-2-hydroxy-6-naphthoic acid.

The procedure was exactly the same as for the preparation of the 1: 2: 7-acid. The 2:6-hydroxynaphthoic acid, prepared from the 2:6-aminonaphthalene sulphonic acid by the same series of reactions utilised to prepare the 2:7-isomer, was coupled with diazonium chloride. The red 1-benzeneazo-2-hydroxy-6-naphthoic acid crystallised from dioxan as very minute clusters of needles. It is not as red as the 1: 2: 7-isomer, and it darkens on exposure to the air, especially if damp.

It was reduced by anhydrous stannous chloride in glacial acetic acid solution, and after removal of the tin as sulphide, the hydrochloride of 1-amino-2-hydroxy-6-naphthoic acid was obtained on addition of concentrated HCl. It separated as white needles closely resembling the hydrochloride of the 1: 2: 7-acid.

EXPERIMENTAL.

Preparation of 1-amino-2-hydroxy-7-naphthoic acid.

1) Preparation of 1-benzeneazo-2-hydroxy-7-naphthoic acid.

4.45gms. (1mol.) aniline were dissolved in 8.75gms. (5mol.) HCl (= 32.2ccs. conc.HCl) containing 10ccs.water, and cooled to 0° C, with addition of crushed ice. To this was added slowly, with brisk stirring, 3.45gms. (1.2mols.) sodium nitrite dissolved in 5ccs. water, and diazotisation continued for thirty minutes, when it was deemed complete and the excess nitrous acid destroyed by addition of urea.

This solution was added, drop by drop, with brisk agitation, to a solution, cooled to 0°C, of 10gms. (1mol.) 2:7-hydroxynaphthoic acid sodium salt dissolved in 50ccs. water containing 15gms. (excess) NaOH. Coupling took place immediately, and during addition of the diazonium solution, crushed ice was added to keep the temperature at 0° C. After addition was complete, the whole was allowed to rise slowly to room temperature, stirring all the time. Concentrated HCl was added, the mixture stirred, and the precipitated red azo product filtered off, washed well with water, and dried in a vacuum over conc. H_2SO_4. It was recrystallised from dioxan, and was obtained as microscopic red needles. M.P. 273° - 275° C.

Analysis.

	Fd. (hemi-macro)	Req. for $C_{17}H_{12}O_3N_2$
C	69.6, 69.8	69.9
H	4.6, 4.5	4.1
N	9.8, 9.9	9.6

It is slightly soluble in acetone, alcohol, and chloroform, from each of which it crystallises in very small needles.

2) Reduction of 1-benzeneazo-2-hydroxy-7-naphthoic acid. (by the method of Grandmougin B. 1906, 39, 3609.)

2.0gms. (1mol.) red azo compound were dissolved in 2.7gms. caustic soda (10mols.) in 20ccs. water, and 0.5gms. sodium hyposulphite ($Na_2S_2O_4$) added, a little at a time, with good stirring, until the red colour had disappeared. The solution, now pale yellow, was acidified with hydrochloric acid, extracted with ether. On evaporation of the ether, all that was obtained, was a black resinous substance, pointing to oxidation.

3) Reduction using anhydrous stannous chloride.

a) Preparation of anhydrous stannous chloride. (Stephen J.C.S. 1930, 2786; cf. 1925, 1874).

22.8gms. (1mol.) $SnCl_2 . 2H_2O$ were treated with 20.4gms. (2mols.) acetic anhydride. The reaction was almost instantaneous, and exothermic. The anhydrous salt separated, and after cooling, was filtered off, washed free from acetic acid with dry ether, and kept in a desiccator.

b) 2gms. (1mol.) 1-benzeneazo-2-hydroxy-7-naphthoic acid were refluxed with 30ccs. glacial acetic acid and 2.4gms. (1mol.) anhydrous stannous chloride, until the solution was pale yellow.

It was then diluted with water, a few ccs. dilute HCl added, and H_2S passed, to precipitate the tin. The whole was then warmed on the water bath, the sulphide filtered off, washed well with hot water, and the combined filtrate and washings evaporated till the volume was about 50ccs., when addition of conc. HCl, precipitated the hydrochloride of the base. This was filtered off, and dried in a vacuum desiccator over caustic soda, washed with dry ether and dried in a vacuum.

Analysis. (hemi-macro)

	Fd.	Req. for $C_{11}H_{10}O_3N.Cl$.
C =	54.6	55.1
H =	4.3	4.2
N =	5.9	5.8
Cl =	13.9	14.8

Preparation of 1-amino-2-hydroxy-6-naphthoic acid.

1) Preparation of 1-benzeneazo-2-hydroxy-6-naphthoic acid.

10gms. (1mol.) 2:6-hydroxynaphthoic acid were coupled with 4.45gms. (1mol.) aniline. The procedure and subsequent treatment to isolate the red azo compound was exactly the same as that used for the preparation of the 1: 2: 7-compound. It crystallised from dioxan as clusters of minute needles. M.P. 283° - 285° C.

Analysis.

	Fd.		Req.for $C_{17}H_{12}O_3N_2$
C =	69.7,	70.3	69.9
H =	4.8	4.6	4.1
N =	9.9	9.7	9.6

2) Reduction of 1-benzeneazo-2-hydroxy-6-napthoic acid.

2gms. (1mol.) of the above azo compound were reduced by treating in exactly the same manner as described for the 1: 2: 7-compound. The hydrochloride of the 1-amino-2-hydroxy-6-naphthoic acid was obtained as white needles, closely resembling the hydrochloride of the 1: 2: 7-acid.

Analysis.

	Fd.		Req.for $C_{11}H_{10}O_3NCl$
C =	54.6	54.5	55.1
H =	4.2	4.5	4.2
N =	5.3	5.4	5.8
Cl =	13.9	14.0	14.8

Comparison of the properties of 1:2:7- and 1:2:6-aminohydroxynaphthoic and aminohydroxynaphthalene sulphonic acids.

The 1:2:7- and the 1:2:6-aminohydroxynaphthoic acids resemble the corresponding aminohydroxynaphthalene sulphonic acids in not being diazotised in the usual way with sodium nitrite in the presence of free mineral acid (Witt. B.1888,21,3476). Even treatment with sodium nitrite in the presence of copper chloride or sulphate and in the absence of free mineral acid (Geigy & Co. D.R.P.171024; C.1906, IV, 474), successful in the case of the sulphonic acids, failed to convert them into the 1-diazo-2-hydroxy-7-naphthoic and the 1-diazo-2-hydroxy-6-naphthoic acids, but yellow solutions were formed.

The alkaline solutions of the 1;2;7- and 1:2:6-aminohydroxynaphthoic acids are easily coloured brown on exposure to the air and in this respect they again resemble the corresponding sulphonic acids (Meldola B.1881,14,532; Greiss ibid. 2042; Witt B.1888,21,3475; Reverdin de la Harpe B.1892,25,1405).

The free bases, liberated by addition of sodium acetate to solutions of the hydrochlorides, rapidly darken on exposure to the air.

Like the sulphonic acids, they do not react readily with diazo compounds (Witt loc.cit., Nietzki & Becker B.1907,40,3400).

Part VI.

The action of Nitrous Acid on 2:6- and 2:7-hydroxynaphthoic acids.

Part VI.

The action of Nitrous Acid on 2:6- and 2:7-hydroxynaphthoic acids.

The 2:6- and 2:7-hydroxynaphthoic acids were treated with nitrous acid with the object of forming nitroso compounds, which, on reduction, with bisulphite, would be expected to give aminohydroxynaphthoic acids, and, since in the naphthalene series, if the -OH group is in the β-position, a 1-nitroso compound would result (Hodgson & Kershaw J.C.S. 1930, 1969), then the 1: 2: 6-, and the 1: 2: 7-acids were ~~be~~ the products expected.

Kostanecki (B. 1895, 28, 2898) reports the preparation of 1-nitroso-2-hydroxy-3-naphthoic acid, and Lasser & Gad (B. 1925, 58, 2551) the 1-nitroso-3-hydroxy-4-naphthoic acid by the action of nitrous acid on the 2:3-, and 2:1-hydroxy-naphthoic acids respectively, while Grandmougin (B.1906, 39, 3609) states that the 1:2-hydroxynaphthoic acid loses CO_2 on treatment with nitrous acid, and forms β -nitroso-α-naphthol.

When the 2:7-hydroxynaphthoic acid was treated with nitrous acid according to the method given in a private communication from I.C.I., Ltd., for the preparation of nitroso-β-naphthol, a pale yellow precipitate was obtained, which on recrystallisation from dioxan, yielded brown prismatic crystals. Investigation, both by Lassaigne's test and by Dumas for the estimation of nitrogen, showed the complete absence of this element.

The product dissolved in alkali to form a greenish yellow solution, which exhibited a bright green fluorescence

fluorescence/ in ultra-violet light, and coupled with diazo solutions, forming soluble red azo dyestuffs, and pointing to the probable phenolic character of the molecule.

When an aqueous suspension of the substance was treated in the cold with sodium bisulphite (37%), no change was observed, but on warming, the yellow precipitate, changed to buff, and after recrystallising from alcohol, almost white crystals were obtained (M.P. 268-272° C). These dissolved in alkali, and the solution coupled to form azo dyestuffs. When boiled with glacial acetic acid and acetic anhydride, white needles were obtained (M.P. 209-211° C), and these on hydrolysis yielded a white crystalline product M.P. 269° C with decomposition.

Since the product dissolves in $NaHCO_3$ solution with evolution of CO_2 and in NH_4OH, it obviously contains at least one carboxyl group, and various decarboxylation experiments were attempted with the object that a similar compound, probably more easily recognised, might be obtained. Distillation with soda lime, yielded a very small amount of a substance smelling strongly of naphthalene, but the main bulk simply charred. The process, often advantageous, of eliminating CO_2 by boiling with dry quinoline in presence of copper bronze (Shepherd, Winslow, & Johnson J.Amer.C.S. 1930, 2084; Davies, Heilbron & Irving J.C.S. 1932, 2715) yielded a black substance with which nothing could be done. Similar results were obtained using copper chromite, prepared according to to/ the method of Adkins & Connor (J.Amer.C.S. 1931, 53, 1092), as the catalyst (Kinney & Langlois J.Amer.C.S. 1931, 53, 2189: Reichstein, Grussner & Zschokke, Helv.Chim.Acta, 1932, 15, 1067: cf. Taylor & Crawford J.C.S. 1934,1130).

The molecular weight of the compound, as estimated by Rast's method was 207. Using the freezing point method and dioxan as the solvent, the figure obtained was 205. The constant for dioxan was first obtained by using pure 2:7-hydroxynaphthoic acid, since it was thought that it had a structure similar to that of the product obtained from it.

The action of HNO_2 on 2:7-acetylhydroxynaphthoic acid gave a product identical with that obtained from the 2:7-hydroxy-naphthoic acid. This would seem to indicate that, since the acetyl group was removed, the hydroxyl group had something to do with the reaction.

To ascertain if the product and the 2:7-hydroxy-naphthoic acid were polymorphous or tautomeric, advantage was taken of the method mentioned by Sidgwick (J.C.S. 1915, 672). If the substances are polymorphic, the differences between them will disappear in solution; if they are tautomeric, the differences will persist in solution. Hence, according to Sidgwick, by measuring the depression of the freezing point of a solvent, saturated with one substance, then addition of the second substance will cause a further depression if different or tautomeric but

but/ no further depression if polymorphic.

The results obtained indicated that the molecules in the solution, derived from the two forms, were different.

With regard to the 2:6-hydroxynaphthoic acid, a yellow product separated which on crystallisation from dioxan formed orange coloured flakes. These also showed the complete absence of nitrogen.

The product dissolved in alkali to form a greenish solution which had a bluish fluorescence in ultra-violet light and coupled with diazonium solutions to form red azo dyestuffs. It showed properties exactly similar to those of the product from the 2:7-hydroxy acid and it was examined in the same way. Treatment in the cold with bisulphite showed no change but on warming the yellow solution became paler and after recrystallising from alcohol showed white crystals M.P. 242-247° C. When boiled with glacial acetic acid and acetic anhydride almost white needles were obtained M.P. 217-220° C. Hydrolysis of this derivative yielded a white crystalline product M.P. 240-245° C. Since the product dissolved in $NaHCO_3$ solution with evolution of CO_2 and in ammonia, it contains at least one carboxyl group, but various decarboxylation experiments yielded only a black powder with which nothing could be done.

The molecular weight as estimated by Rast's method was 202, by the freezing point method using dioxan, the figure was 207.

Part VI

EXPERIMENTAL.

Action of nitrous acid on 2:7-hydroxynaphthoic acid.

9gms. (1mol.) 2:7-hydroxynaphthoic acid sodium salt, 18.5gms. (excess) 35% NaOH, and 100ccs. water were stirred together until a clear solution was obtained, when the solution was alkaline to Clayton Yellow (oxydiamine paper). Ice was added to cool the solution to 0°C, and then 3.4gms. (1mol.) $NaNO_2$ dissolved in a few ccs. water, added. 40% H_2SO_4 was then added drop by drop, until HNO_2 was indicated on starch iodide paper. The temperature was kept at 0°C. by addition of crushed ice. Stirring was continued for 2 hours, and the excess HNO_2 was destroyed by urea. A pale yellow precipitate separated. This was filtered off, washed with ice cold water, and recrystallised from aqueous dioxan. Weight?

Brown prismatic crystals were obtained. These did not contain N. They dissolved in alkali to form a yellow solution, which had a green fluorescence in ultra-violet light. It was precipitated by acid, and the alkaline solution coupled with diazo benzene chloride solution. M.P. 260 - 270°C.d.

Analysis.

Fd.

C = 68.3, 68.3,

H = 4.3, 4.4, 4.6.

Preparation of Acetyl derivative.

1gm. of brown crystals were refluxed with 3ccs. glacial acetic acid and 3ccs. acetic anhydride, and poured into water. A white solid separated which recrystallised from aqueous alcohol as white plates which softened at 205° C and melted at 212° - 215° C.

Hydrolysis of above derivative.

The above acetyl derivative was refluxed with 5ccs. 8% KOH solution. On acidification a white solid separated which recrystallised from aqueous alcohol as white plates M.P. 260° - 270° C.

Estimation of Molecular Weight.

By freezing point method (using dioxan) = 205.

By Rast's method = 207.

Preparation of 2:7-acetylhydroxynaphthoic acid.

This is described in Part IV, page 134.

It was converted to the sodium salt as described before.

Action of Nitrous acid on 2:7-acetylhydroxynaphthoic acid.

3gms. (1mol.) sodium salt of 2:7-acetylhydroxynaphthoic acid were treated with HNO_2 in exactly the same manner as the 2:7-hydroxynaphthoic acid. A yellow precipitate was obtained which on recrystallisation from alcohol gave yellow needles M.P. 255-270° C.

Analysis (micro)

Fd.

C = 68.54

H = 4.23

M.W. = 209
(Rast's)

The product dissolved in alkali forming a yellow solution with a green fluorescence in ultra-violet light. It coupled with diazobenzene chloride solution and when treated with glacial acetic acid and acetic anhydride gave a product M.P. 209-211° C. The yellow solution in alkali, on treatment with $Na_2S_2O_4$ turns pale yellow and after acidification gave a product which on recrystallisation from alcohol gave white plates M.P. 269-270° C.

Experiment to determine if the brown compound and the 2:7-hydroxynaphthoic acid are tautomeric or dimorphous.
(Sidgwick J.C.S. 1915, 672).

Glacial acetic acid was used as a solvent.

A = white 2:7-hydroxynaphthoic acid.

B = brown product.

1) Freezing point of HAc			=	3.99		3.94
-do-	+	A	=	3.70	+ B =	3.69
depression			=	0.29		0.25
	+	B	=	3.61	+ A =	3.58
depression	A	+ B	=	0.38	B + A =	0.36

Attempted decarboxylation.

(Shepherd, Winslow & Johnson J. Amer. C.S. 1930, 2084; Davies, Heilbron & Irving J.C.S. 1932, 2715).

1) 0.5gms. brown crystals were refluxed for 15 minutes with 20ccs. pure redistilled quinoline and 0.25gms. copper bronze powder added. The liquid turned very black. It was poured into dilute HCl and extracted with ether. On evaporating off the ether, a black solid with which nothing could be done was obtained. It dissolved in alkali and acetone forming dark coloured solutions.

2) (Taylor & Crawford J.C.S. 1934, 1130).

9.5gms. brown crystals + 9.25gms. copper chromite were refluxed for one minute with 20ccs. pure redistilled quinoline. The liquid was again very black. It was treated as in 1) and again a black solid was obtained.

Action of nitrous acid on 2:6-hydroxynaphthoic acid.

9gms. (1mol.) 2:6-hydroxynaphthoic acid were treated with nitrous acid in exactly the same way as its isomer the 2:7-acid. A yellow solid separated and was filtered off. An attempt to crystallise from aqueous alcohol (50/50) yielded a product consisting of needles and amorphous nodules, so tests were made with various solvents. Dioxan was used and a well formed crystalline product obtained. This was in the form of orange coloured plates M.P. 238-242°C. and contain no N.

They were slightly soluble in water, and acid to litmus; soluble in NaOH to form a greenish solution which had a blue fluorescence in ultra violet light, and couples with benzene diazonium chloride solution.

Analysis

Fd.

C = 66.3, 66.3

H = 5.1, 5.5

Preparation of Acetyl derivative.

1gm. of the orange crystals were refluxed with 5ccs. glacial acetic acid and 3ccs. anhydride and poured into water. A white solid separated which was filtered off and recrystallised from aqueous alcohol. Almost white needles M.P. 217-220°C.

Hydrolysis of acetyl derivative.

The above acetyl was hydrolysed with 8% KOH solution. On acidification a white solid separated, which crystallised as white needles from aqueous alcohol. M.P. 240-245°C.

Treatment with $Na_2S_2O_4$.

0.5gms. of orange crystals taken and dissolved in in/ 5ccs. 8% NaOH solution. A greenish solution was formed, which showed a blue fluorescence in ultra violet light. A little sodium hyposulphite ($Na_2S_2O_4$) was added and the colour of the solution changed to pale yellow. It was allowed to stand for 15 minutes, acidified with dilute HCl, and the white product crystallised from aqueous alcohol. Rectangular needles M.P. 242-247°C.

Analysis.

Fd.

C = 65.7 66.5
H = 4.6 4.7

Treatment with NaOH followed by dilute HCl.

0.5gms. orange crystals were dissolved in NaOH, allowed to stand, reprecipitated with dilute HCl, and crystallised from aqueous alcohol.
Pale yellow plates M.P. 239-240°C.

Analysis.

Fd.

C = 66.5 66.2
H = 5.1 5.1

Estimation of Molecular Weight.

By freezing point method (using dioxan) = 207
By Rast's method = 202 & 214

Table, comparing 2:7-hydroxynaphthoic acid with the products obtained by treatment with nitrous acid.

	2:7-hydroxynaphthoic acid	Product from 2:7-hydroxynaphthoic acid by action of HNO_2.
Appearance	white needles	brown prisms or clusters
M.P.	269 - 270°C.	260 - 270°C d.
Analysis	C = 70.2 H = 4.26	C = 68.3 H = 4.4
M.P. of acetyl deriv.	209 - 210°C	softens 205°C melts 212 - 215°C
M.W.	188	205 (Rast's) 207 (Freezing point)

Table, comparing 2:6-hydroxynaphthoic acid with the product obtained by treatment with nitrous acid.

	2:6-hydroxynaphthoic acid	Product from 2:6-hydroxynaphthoic acid by action of HNO_2.
Appearance	white needles	orange plates
M.P.	241 - 242°C.	238 - 242°C.
Analysis	C = 70.2 H = 4.26	C = 66.3 H = 5.1
M.P. of acetyl. deriv.	221 - 223°C	217 - 220°C
M.W.	188	202 (Rast's) 204 (Freezing point)

Calculation of empirical formula of product from 2:7-hydroxy acid.

C = 68.3	9.96
H = 4.4	7.77
O = 27.3	3

$C_{10}H_8O_3$

Calculation of empirical formula of product from 2:6-hydroxy acid.

C = 66.3	9.33
H = 5.1	8.58
O = 28.6	3

$C_9H_9O_3$

Conclusion.

This reaction was most unexpected but very interesting. Unfortunately, lack of material and pressure of time, prohibits the investigation being completed at present, but further work will be done.

No definite conclusions can be drawn at this stage, but the colour of the substances and their reduction by sodium hyposulphite ($Na_2S_2O_4$) to form colourless products, suggest the possibility of at least, a quininoid structure.

Summary.

Some suggested methods for the preparation of aminohydroxynaphthoic acids have been investigated.

The main part of the research was devoted to the preparation of those having the $-NH_2$ group in the 2-position, and the particular one desired was the 2-amino-5-hydroxy-7-naphthoic acid. The scheme, outlined on pages 13 and 14, shows that the -OH group was to be introduced by sulphonation and subsequent alkali fusion of 2:7-aminonaphthoic acid. Consequently the first consideration was the preparation of 2:7-aminonaphthoic acid.

The formation of 2:7-aminonaphthonitrile by replacement of $-SO_3H$ by -CN by the dry distillation of 2:7-aminonaphthalene sulphonic acid with KCN and $K_4Fe(CN)_6$ (pp. 67-73) gave very poor yields, insufficient for the subsequent series of reactions, while fusion with KCN under pressure (p. 75) eliminated the $-SO_3H$ group.

The diazotisation of 2:7-aminonaphthol was successfully accomplished by the usual Greiss reaction in the presence of a large excess of HCl (p. 27); also after the method of Hodgson & Walker (J.C.S. 1933,124,1620) (p.28), and that of Schoutissen (J.Amer.C.S. 1933,55,4511) (p.32), but attempts to form the 2:7-cyanonaphthol by the Sandmeyer reaction and various modifications of same (pp. 27,30,31,33) failed due to the preference of the diazo compound to couple with itself.

The diazotisation of 2:7-diaminonaphthalene was accomplished using a modification of the method of Schoutissen (loc. cit.) (p. 49), but attempts to form the 2:7-aminonaphthonitrile failed (pp. 51-53).

2:7-Aminonaphthoic acid was synthesised from 2:7-aminonaphthalene sulphonic acid by the series of reactions outlined on page 82 and described on pages 120-136, and successfully sulphonated (pp. 141,143,144)

(pp. 141,143,144)/
but the yield of sulphonic acid was poor. The same result was obtained with chlorosulphuric acid (page 146). Sulphonation of the acetyl derivative (p. 149) gave excellent yields, but isomers were present and various attempts to separate them were unsuccessful (pp. 156-159), while conversion to the aminohydroxynaphthoic acids by alkali fusion yielded oxidation products (p.160).

Estimation of the α-SO_3H groups in the sulphonation mixture gave 60% (p.164). It would appear, judging from results on page 125, that about 40% of the sulphonic mixture contains the -SO_3H group in the 6-position.

The preparation of 1:2:7- and 1:2:6-aminohydroxynaphthoic acids was accomplished (p.170) by method i (see page 10). They were obtained as the hydrochlorides since the free bases oxidise very rapidly in the air.

The action of nitrous acid on 2:7- and 2:6-hydroxynaphthoic acids (p. 176) gave highly coloured products containing no nitrogen. A table of properties is given on page 189.