This is to certify that Miss NANCY McLEISH successfully sustained an oral examination on the subject matter of her thesis by a committee of the Department. The examination was held in January of this year.

Members of
Committee.

5 May, 1937.

THE STRUCTURE OF NAPHTHALENE.

By

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Thesis for the Degree of Doctor of Philosophy.

May, 1937.

University of Edinburgh.

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PREPARATIONS

INTRODUCTION.

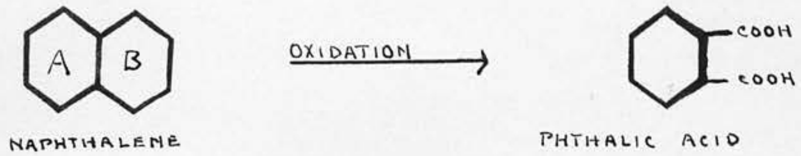
The Structure of Naphthalene.

To the problem of determining the structure of naphthalene have been applied many methods, physical and chemical. Among the physical methods may be mentioned, measurement of dipole moments, refractivities, and X-ray spectra. It is intended in this thesis, to deal with the subject chiefly from the evidence obtained from chemical reactions. In spite of innumerable researches the structure of naphthalene still remains indefinite.

That the naphthalene molecule is built up from two benzene rings having two carbon atoms in common has been shown both by degradation and by synthesis. Gräbe (Ann., 1866, 149, 20) described some of the earliest experiments on the oxidation of naphthalene derivatives.

On oxidation, naphthalene itself gave phthalic acid, α-nitro-naphthalene gave a nitro-phthalic acid, but if the nitro group were first reduced to give α-amino-naphthalene then the amine gave phthalic acid.

a.



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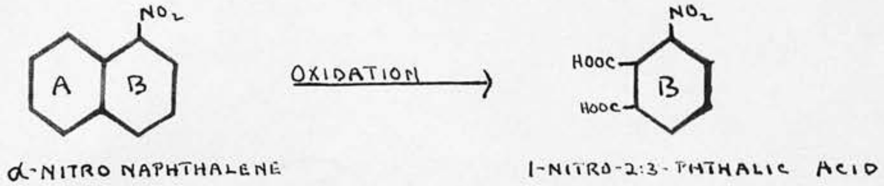
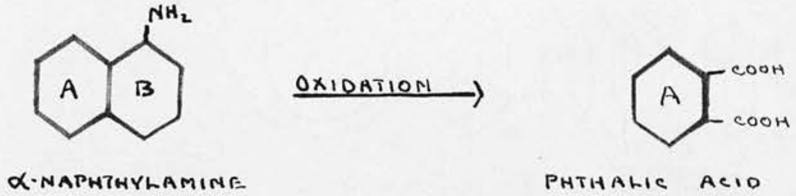
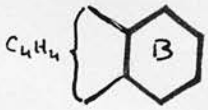


c.

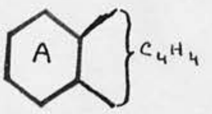


Therefore, depending upon the nature of the substituent on ring B, A or B was oxidised away to give the carboxyl groups of phthalic acid.

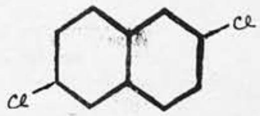
By (b) naphthalene was shown to contain:-



and by (c):-

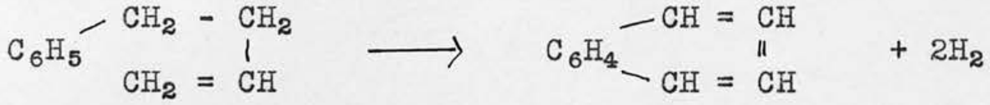


i.e. naphthalene contains two symmetrically placed benzene rings. This conclusion is in agreement with the results of work on dipole moments. Weissberger, Sangewald and Hampson (Trans. Far. Soc., 1934, 30, 884) prepared the different dichloro-naphthalenes and found that the 2: 6-compound had zero dipole moment as would be expected in a plane symmetrical molecule.



2:6-DICHLORO NAPHTHALENE

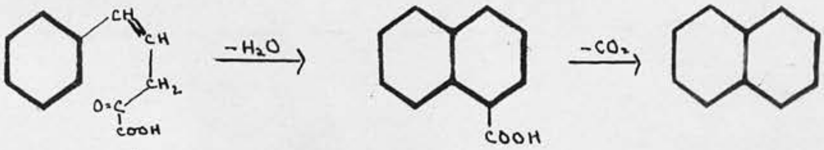
The presence of two benzene rings is confirmed by synthesis. If the vapour of phenyl butylene is led over red hot lime, naphthalene is formed with the splitting off of two molecules of hydrogen.



$$C_6H_5\begin{array}{l} CH_2 - CH_2 \\ \qquad\quad | \\ CH_2 = CH \end{array} \longrightarrow C_6H_4\begin{array}{l} CH = CH \\ \qquad\quad \| \\ CH = CH \end{array} + 2H_2$$

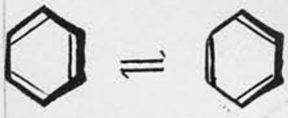
Phenyl butylene Naphthalene

Again, if cinnamyl-pyruvic acid is heated with concentrated hydrochloric acid, naphthoic acid and finally naphthalene are formed (Erlenmeyer and Kunlin, Ber., 1902, 35, 384).



CINNAMYL-PYRUVIC ACID NAPHTHOIC ACID NAPHTHALENE

If naphthalene consists of two "benzene rings", the structure of these units is worth considering. In the development of chemical knowledge various formulae were suggested for benzene, and the most important of these were :-



KEKULÉ

CLAUS

ARMSTRONG-BAEYER

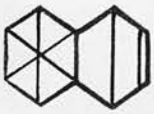
DEWAR

LADENBURG

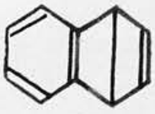
Pauling and Wheland (J. Chem. Physics, 1933, 1, 362) dismissed all of these except Kekule's which they retained as giving the best possible representation of the chemical behaviour of benzene, but they suggested that probably a small proportion of the total number of molecules exist in the state represented by Dewar's formula.

The Claus formula with its para bonds would represent a very unsaturated molecule and the exact meaning of the central valencies in the Armstrong-Baeyer formula is unspecified.

In this connection it is interesting to note that Sir Wm. Pope has recently referred to the Armstrong-Baeyer formula as the most suitable for benzene. At one time or another each of these formulae was used in an attempt to represent the chemical properties of naphthalene graphically. Claus proposed I, Wreden II and Bamberger III.



I



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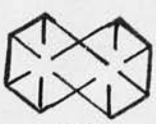
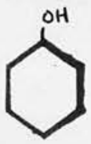
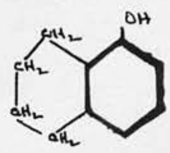


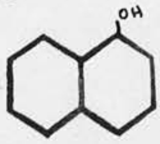
III

The Claus and Wreden formulae can be dismissed on the same grounds as the parent formulae for benzene but the formula of Bamberger is worthy of consideration if only because he claimed it to be the logical deduction from a vast amount of experimental work. (Ann., 1890, 257, 1) Bamberger carried out many experiments on the reduction of naphthalene derivatives. From the fact that he always obtained a tetrahydro naphthalene he concluded that one ring was not a benzene ring and since the molecule was symmetrical neither ring could be a benzene ring. Later preparations of octahydro and decahydro naphthalenes showed the foundation of his argument to be faulty.

Bamberger claimed that by reduction of naphthalene compounds to give "aromatic" tetrahydro-compounds he could destroy the peculiar properties which distinguish derivatives of naphthalene from those of benzene and the compounds he obtained by reduction behaved like benzene derivatives, e.g. phenol and ar. tetrahydro-α-naphthol were easily alkylated by means of methyl alcohol and hydrochloric acid whereas α-naphthol was not.



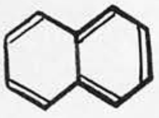




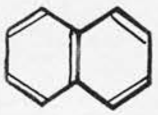
But in this example, as in all others quoted by Bamberger, he was trying to discriminate between degrees of activity since all three can be alkylated by dimethyl sulphate, and to find a formula which would express the difference. This was almost sure to meet with failure as formulae are only somewhat crude expressions of the properties of compounds. Thus a formula containing a double bond indicates that bromine will add on at this, but no indication is given as to the rate at which the addition will take place.

The Bamberger formula may therefore be discarded.

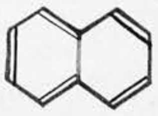
Therefore the Kekule benzene formula is applied to naphthalene giving three possible arrangements of bonds :-



A



B



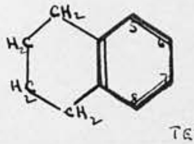
C

Naphthalene may be represented by one of these or by an equilibrium mixture of all three. An equilibrium mixture was suggested first by Erdmann (Ann., 1893, 275, 191).

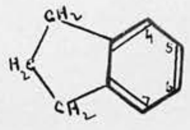
In recent work on resonance by Pauling and Wheland (J. Chem. Physics, 1933, 1, 362) it was indicated that naphthalene molecules probably exist at some time in all of these states as well as in many others, but from observation of chemical reactions there would appear to be grounds for an assumption that the bonds are fixed, or tend to be fixed in position B, and this is the formula proposed for naphthalene by Erlenmeyer in 1866. This is the only formula in which both rings are truly aromatic.

Fixation of bonds.

The evidence for the existence of this phenomenon is chiefly drawn from examination of semi-reduced compounds. Mills and Nixon (J.C.S., 1930, 2510) argued from a purely theoretical basis, by consideration of the relative sizes of the angles between two single bonds and a double and a single bond, that the most stable states, in which there would be least strain in the molecules of tetralin and hydrindene, could be represented by the following arrangements of double and single bonds.



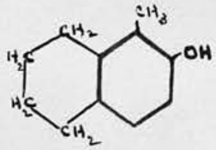
TETRALIN

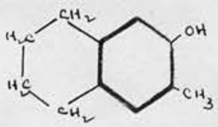


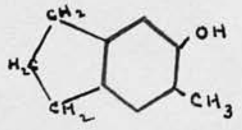
HYDRINDENE

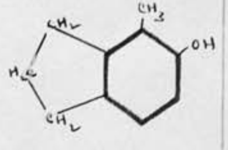
As experimental confirmation they quoted the bromination of 5-hydroxy-hydrindene when bromine attacked position 6 whereas in 6-hydroxy-tetralin bromine entered position 5. Coupling reactions with diazonium salts occur at the same positions.

Recently Fieser and Lothrop (J.A.C.S., 1926, 58, 2050) investigated the so-called Mills-Nixon effect with very interesting results. They prepared 5-hydroxy-4-methyl and 5-hydroxy-6-methyl hydrindenes and found the former coupled easily with diazo residues while the latter did not couple at all.



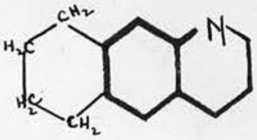


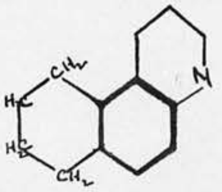




Whatever the actual mechanism involved in the substitution of a diazo residue it seems certain that a double bond is involved (Gattermann, Laboratory Methods of Organic Chemistry, 2nd Edition p. 295), and, therefore, the inability of 5-hydroxy-6-methyl hydrindene to couple showed the absence of a double bond between C_4 and C_5 and indicated that the relative positions of the double and single bonds were fixed. Examination of 6-hydroxy-7-methyl and 6-hydroxy-5-methyl tetralin showed that both compounds gave azo derivatives indicating that the relative positions of the bonds in tetralin were not fixed.

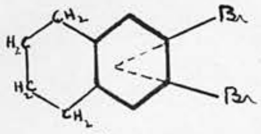
J. von Braun and H. Gruber (Ber., 1922, 55, 1710) performed a Skraup reaction on ar.β-amino-tetralin and found that two different quinolines were obtained. These they separated, by forming the picrates, and identified the two quinolines as :-



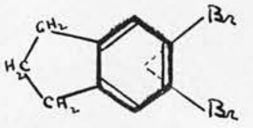


It is interesting to note that although two quinolines were formed indicating the presence of a double bond sometimes between C_5 and C_6 and sometimes between C_6 and C_7 the tetrahydro-anthrapyridene compound was formed in greater quantity.

Further evidence for the fixed positions of the bonds in substituted hydrindene molecules has recently been supplied by Sidgwick (J.C.S., 1936, 1534) who prepared 6:7-dibromo tetralin and 5:6-dibromo hydrindene, then compared the dipole moments of these compounds with these of o'-dibromo benzene and 2:3-dibromo-5:6-xylene.



I



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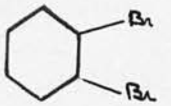
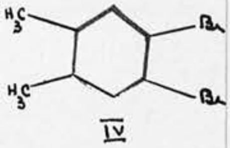


III



IV

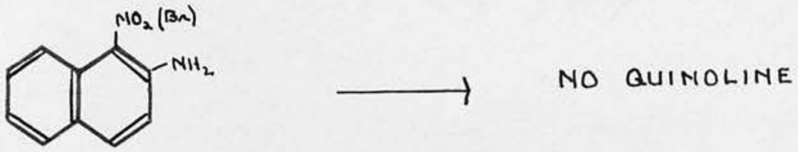
Sidgwick found the value of the dipole moment attributable to the bromine atoms was the same in I, III and IV but quite different to that in II. Further the value in II corresponded exactly to the calculated value for an arrangement of bonds and resultant angles as shown in the figure. III and IV are definitely compounds in which there can be no fixation of bonds therefore Sidgwick concluded that there must be no fixation in I since the value of the dipole is the same in the three cases. Since the phenomenon of fixed positions of double bonds in a benzene ring does exist it may or may not exist in the naphthalene series.

Evidence for Erlenmeyer Formula.

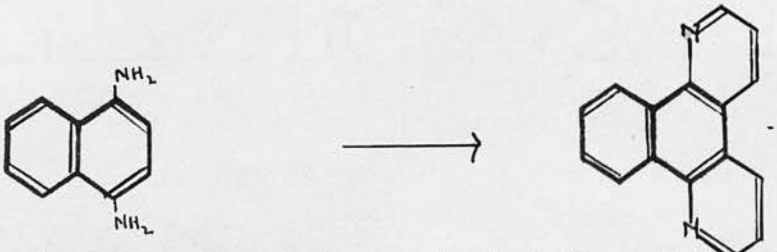
(1) Marckwald (Ann., 1894, 279, 1) subjected β-naphthylamine, α-nitro-β-naphthylamine, α-bromo-β-naphthylamine to a Skraup reaction also $\alpha_1\alpha_2$-diamino-naphthalene. He found that a group in the α-position, which could not easily be split off, prevented quinoline formation.

a.

b.



c.

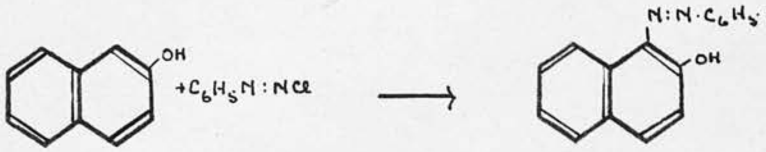


By (c.) Marckwald demonstrated C_2 and C_3 could be involved simultaneously in the formation of pyridene rings but, it would appear from (b.), they never form two units in the same pyridene ring.

(2) When the combination of α and β-naphthols with diazonium salts was examined it was found that in β-naphthol a substituent such as a methyl group in the α-position effectively prevented any coupling, whereas with a substituent like Cl, coupling took place with

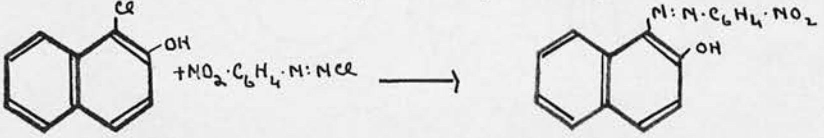
displacement of halogen. α-naphthol, substituted in the α_2 position, unites with a diazonium salt through C_2.

a.

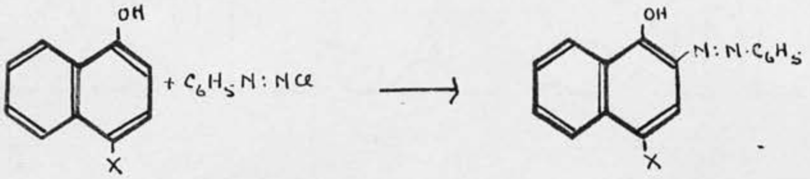


b. Fries and Hubner (Ber., 1906, 39, 442).

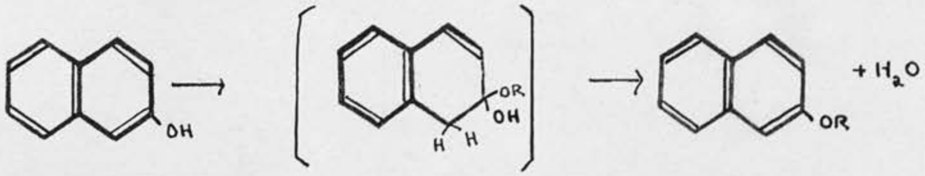
c. Hewitt and Mitchell (J.C.S., 1912, 89, 1172).



d.

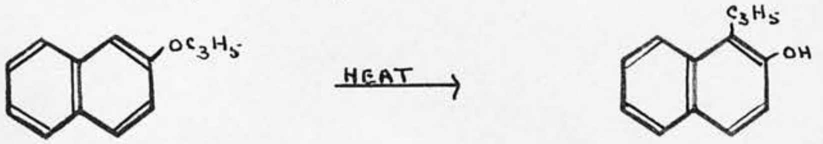


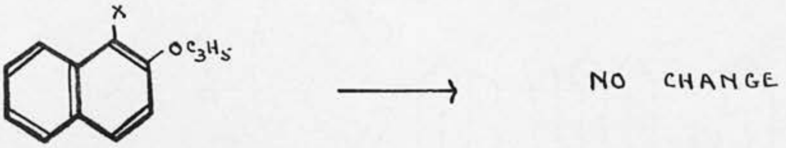
(3) Henry (Ber., 1877. 10, 2041) and Wegscheider (Monatshefte, 1895, 16, 140) suggested a mechanism for the etherification of β-naphthol with an alcohol and mineral acid, as follows :-



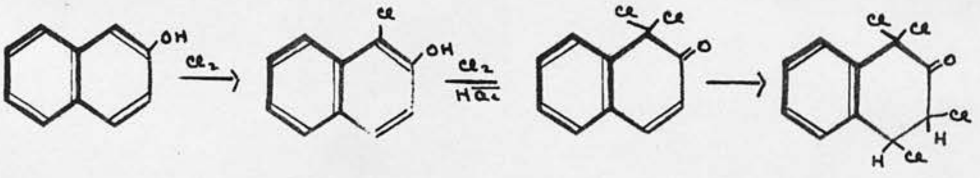
Davis (J.C.S., 1900, 77, 33) showed that Cl-, NO_2-, CH_3- substituted at C_1 practically stopped the etherification.

(4) Claisen (Ber., 1912, 45, 3157) prepared the alkyl ethers of β-naphthol and β-naphthol with a substituent at C_1. He examined the effect of heat on these ethers and found that the former suffered an intramolecular rearrangement giving rise to α-alkyl-β-naphthol, whereas the latter were perfectly stable.

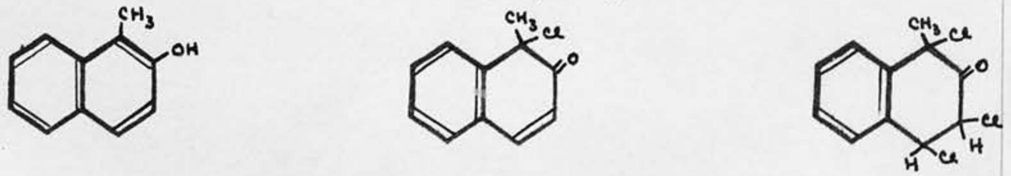




(5a) Zincke (Ber., 1888, 21, 3379) performed experiments on the chlorination of β-naphthol. One molecular equivalent of chlorine gave α-chloro-β-naphthol. Further chlorination in acetic acid or chloroform solution gave a dichloro-ketone and then a tetrachloro-ketone.

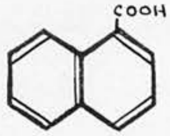
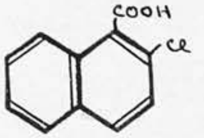
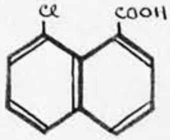
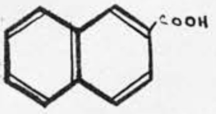
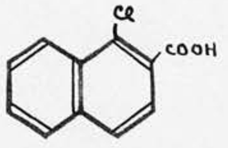
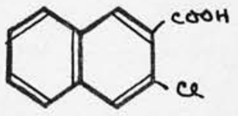


(5b) Fries (Ber., 1908, 41, 2614) performed a similar set of reactions with α-methyl-β-naphthol.



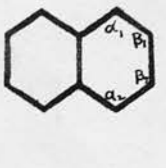
(6) Bergman and Hirshberg (J.C.S., 1936, 331) examined the dissociation constants of naphthoic and chloro-

naphthoic acids. Their results were as follows :-

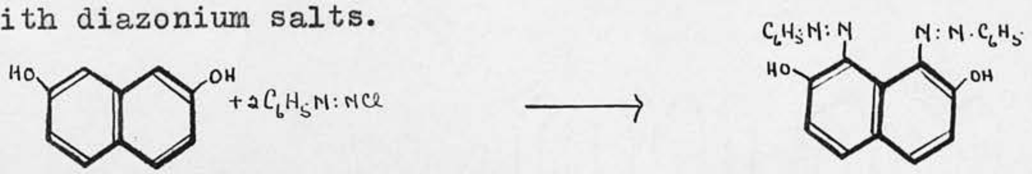
Compound:-			
Dissociation Constant:-	4·8	3·9	4·05
Compound:-			
Dissociation Constant:-	4·67	3·8	4·37

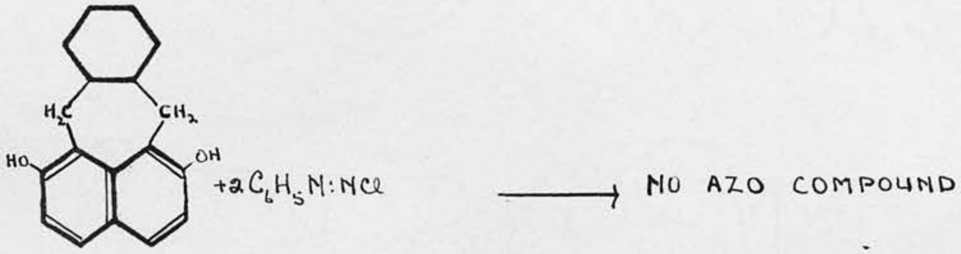
As was expected from the Erlenmeyer formula the lowering of the value of the dissociation constant by Cl- at C_2 in α-naphthoic acid was in the same proportion as that produced by Cl- at C_1 in β-naphthoic acid. The comparatively great effect of Cl- at C_8 in α-naphthoic acid cannot be explained by transmission of effect through double bonds.

These results show that β-substituted naphthalenes are further substituted in the α-position but not in the β_2-position i.e. the ortho positions in β-substituted naphthalenes are shown not to be equivalent and for some reason a second substituent tends to attach itself to C_1 rather than to C_3.



Double bonds between C_1C_2 and C_3C_4 might account for all the reactions quoted above. The above five points are all compatible with the unsymmetrical formulae A and C, therefore Fieser (J.A.C.S., 1935, 57, 1459) set out to show that the naphthalene molecule is symmetrical. He prepared 2:7-dihydroxy naphthalene and showed that diazo residues attached themselves to C_1 and C_8. Next he prepared a compound in which C_1 and C_8 were involved in a seven membered ring; this compound would not unite with diazonium salts.





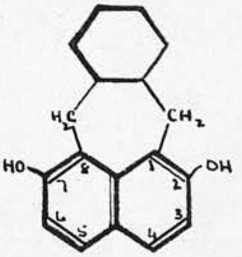
The alkyl ethers of this substituted compound were prepared and were found to be stable towards heat. The more conclusive of these two tests is the coupling with diazonium salts for this process almost certainly involves a double bond in some manner or other, since it has been shown that diazo residues will unite with the enolic form of acetoacetic ester as well as with compounds of the butadiene type.

$CH_3.CO.CH_2.COOH$ $CH_3.C.(OH)=CH.COOEt.$

Keto form of aceto-acetic ester Enol form.

$CH_2=CH.CH=CH_2$

Butadiene



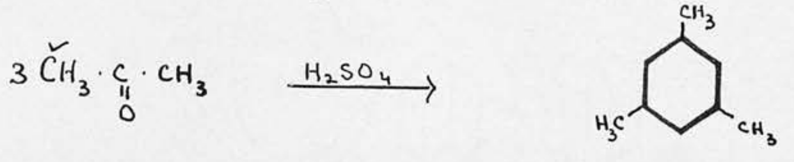
Had there been a double bond between C_2C_3 or C_6C_7 one diazo residue would presumably still have entered the molecule. The lack of a double bond in these positions is further evidence that the double bonds in a substituted naphthalene molecule do not oscillate.

Fieser concluded that herein lay the reason for the differences between naphthalene and benzene - why naphthalene is more unsaturated than benzene and generally less aromatic.

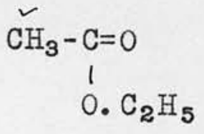
The above reactions also show that when the β_1 position of naphthalene is substituted it is almost impossible to substitute the β_2 position, but Marckwald's experiment with $\alpha_1\alpha_2$ diamino-naphthalene showed that the $\beta_1\beta_2$ positions could be substituted simultaneously, and are therefore not dissimilar.

Phenomenon of Activation by Unsaturated Groups.

The experimental evidence in this thesis is based on the assumption that a bromine atom substituted in the naphthalene molecule can be activated under certain positional conditions by a nitro group. It has long been known that a nitro group substituted in methane activates the methyl group so that it will readily enter into chemical reactions. Carboxyl, nitrile and all similar unsaturated groups have the same effect.

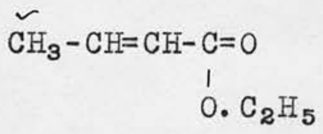


Further this activating effect can be transmitted through a double bond and through a conjugated system of double bonds, e.g. the methyl groups in ethyl acetate and ethyl crotonate are similarly activated.



$$\overset{\checkmark}{C}H_3-\underset{\displaystyle O.C_2H_5}{\underset{|}{C}}=O$$

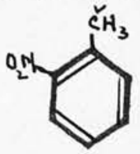
Ethyl acetate



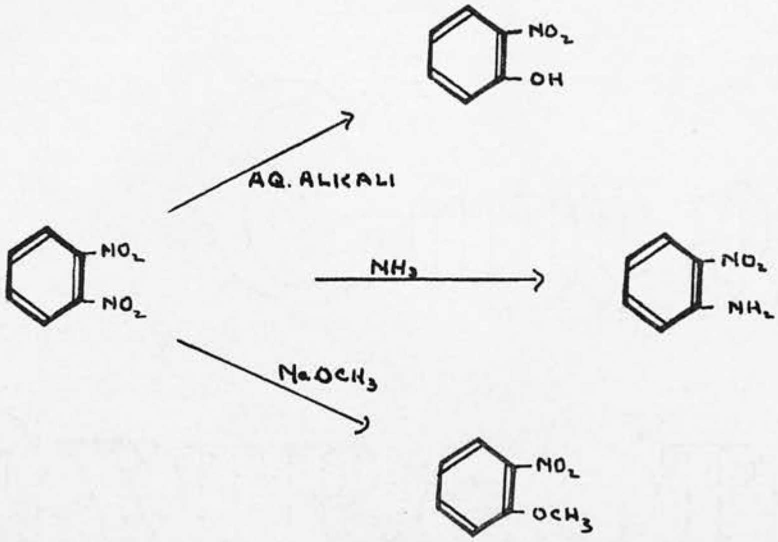
$$\overset{\checkmark}{C}H_3-CH=CH-\underset{\displaystyle O.C_2H_5}{\underset{|}{C}}=O$$

Ethyl crotonate

The evidence collected by Fuson (Chem. Reviews, 1935, 16, 1) showed this effect to be of general application. He quoted applications of the principle to o' and p'-disubstituted benzenes by Angeli in work on the nitro-toluenes. The benzene ring (Kekule formula) is a conjugated system of double bonds, and as expected Angeli found the methyl group in o' and p' nitro-toluenes to be reactive but not that in m nitro-toluene.



Also he found that in o' dinitro benzene one nitro group could be replaced by amino, hydroxyl or methoxyl by means of ammonia, aqueous alkali and sodium methoxide.

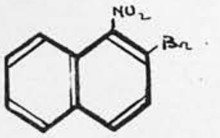


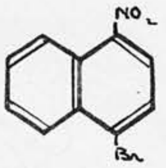
Angeli's work demonstrated the effect which one substituent in a benzene ring might have on another. If this principle of activation be applied to compounds in the naphthalene series further evidence will be obtained of the positions of double bonds and whether these bonds are mobile or tend to be fixed.

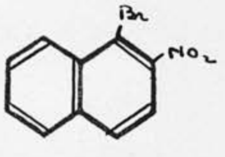
Subject of Research.

The principle of activation outlined above forecasts the results of experiments on the mobility of the halogen atom in nitro-bromo and nitro-chloro-naphthalenes.

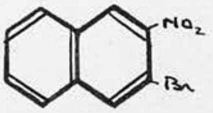
The following compounds should have reactive halogen:-

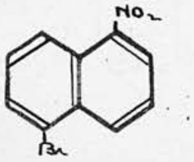


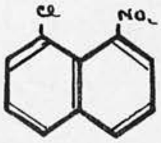


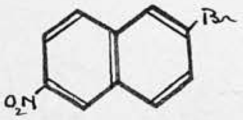


And the following inactive halogen:-



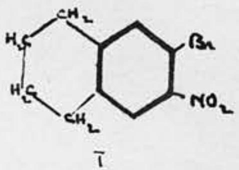




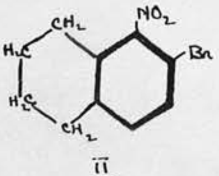


Activity of the halogen in this compound would depend on the ability of the double bond common to the two rings to transmit the effect.

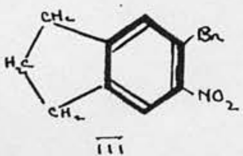
As a means of testing the applicability of the theory of activation to the determination of the positions of double bonds it was decided to prepare bromonitro compounds of the tetralin and hydrindene series, e. g.



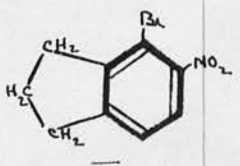
I



II



III



IV

Since there is no fixation of bonds in the tetralin series the bromine atoms in I and II should be reactive but since in hydrindene there is a double bond permanently situated between C_5 and C_6 the bromine atom should be reactive in III but not in IV.

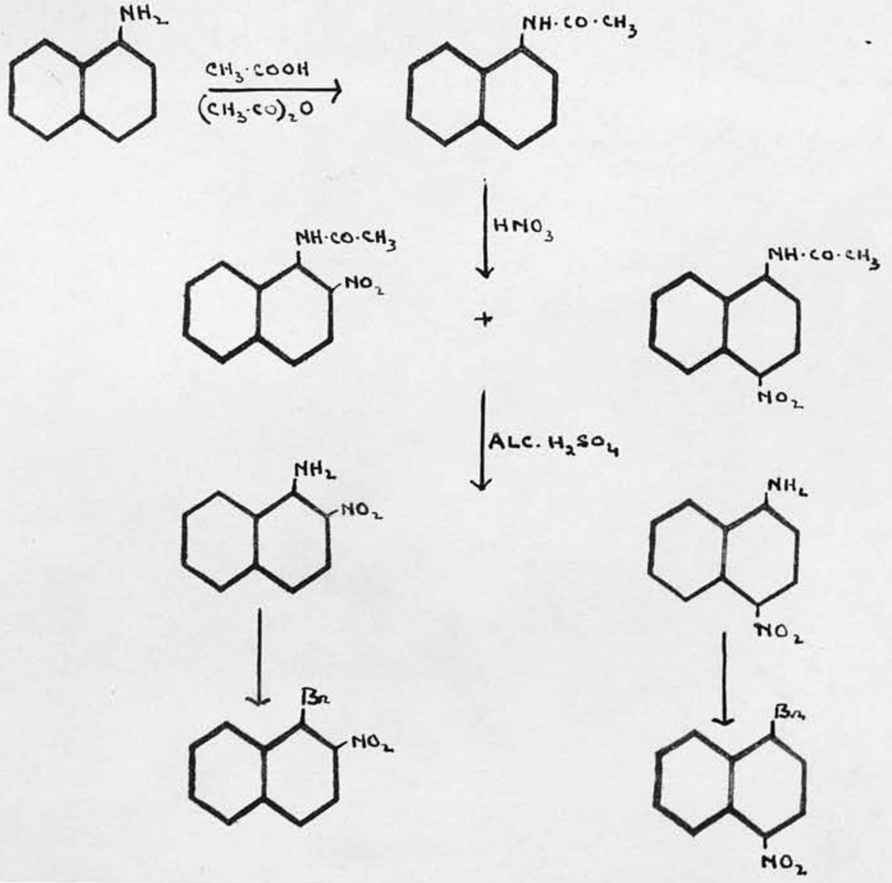
In the literature there are several references to methods of determining the reactivity of halogen in bromo-nitro benzenes. A. H. Rheinlander (J.C.S., 1923, 3099) investigated the activity towards aniline, methylaniline, aniline hydrochloride and sodium ethoxide but the most convenient reagent for our purpose seemed to be piperidine. Brewin and Turner (J.C.S., 1928, 332) heated the bromo-nitro compounds with piperidine in boiling benzene for several hours, then weighed, in a Gooch crucible, the precipitated piperidine hydrobromide. Salkind (Ber., 1931, <u>64</u>, 289) on the other hand determined the amount of piperidine hydrobromide formed by titration in aqueous solution with silver nitrate and potassium thiocyanate. This method can be applied to smaller quantities of the bromo-nitro compound and was therefore selected by us. Salkind found that in 1:4-bromo-nitro-naphthalene 58% of the bromine was removed after heating with piperidine at 50°C for 24 hours. Under similar conditions 7% of bromine was removed from the 1:5 compound. These results are not in agreement with the results of our experiments to be described later.

PREPARATIONS - NAPHTHALENE SERIES.

Preparation of Bromonitronaphthalenes.

Those methods of preparation which have been described in detail in the literature have been given in outline only in this thesis while methods which have been modified in any way have been described in full.

Preparation of 1:2- and 1:4-bromonitronaphthalenes.



The corresponding nitro-amines were prepared and isolated by the method of Hodgson and Walker (J.C.S., 1933, 1205) i.e. the α-aceto-naphthalide was nitrated in glacial acetic acid containing acetic anhydride and the mixture of nitro-amines, obtained by hydrolysis was separated from nitrobenzene solution by precipitation as 4-nitro-1-naphthylamine hydrochloride and 2-nitro-1-naphthylamine sulphate respectively.

The diazotisation and subsequent Sandmeyer Reaction were adapted from the work of Hodgson and Walker (J.C.S., 1933, 1621) on 4:4'-dichloro-3:3'-dinitrodiphenyl and the same procedure found application in performing all later preparations of the same type. The low solubility of some amines in cold glacial acetic acid necessitated this procedure. The calculated quantity of sodium nitrite, finely powdered, was added slowly to the concentrated sulphuric acid, contained in a beaker which was cooled in iced water. When all the sodium nitrite had been added the beaker was heated slowly and the contents stirred until their temperature reached 70°C. When solution was complete, the mixture was cooled to room temperature. The weighed amount of nitroaminonaphthalene was stirred into the solution slowly while the temperature was kept below 20°C, by cooling the beaker in iced water. An equal volume of glacial acetic acid was then added slowly while the temperature remained below 30°C. This diazo solution was run gradually, with stirring, into a solution of cuprous bromide in concentrated hydrobromic acid. When evolution of nitrogen had ceased, water was added, the resultant precipitate filtered off, and worked up.

Experimental Data.

a. Acetylation and nitration.

240 gms. α-naphthylamine
220 cc. acetic anhydride
1600 cc. glacial acetic acid
40 cc. + 76 cc. conc. nitric acid.

Yield:- 255 gms. of mixture of 2 and 4-nitronaphthylamines,
82 gms. 4-nitro-1-naphthylamine,
25 gms. 2-nitro-1-naphthylamine.

Properties of 2-nitro-1-naphthylamine:-

Crystallised from alcohol M.P. 143°C. (Quoted 144°C by Hodgson and Walker)

Attempted benzoylation gave back the original amine.

Properties of 4-nitro-1-naphthylamine:-

Crystallised from alcohol M.P. 195°C (Quoted 194-5°C by Hodgson and Walker)

Benzoyl derivative M.P. 222°C (Quoted 224°C)

b. Diazotisation of 2-nitro-1-naphthylamine.

24 gms. 2-nitro-1-naphthylamine
7.5 gms. sodium nitrite
75 cc. conc. sulphuric acid
75 cc. glacial acetic acid

19 gms. cuprous bromide

130 ccs. conc. hydrobromic acid.

Yield: - 7.5 gms.

Properties of 2-nitro-1-bromo-naphthalene: -

Crystallisation from alcohol gave yellow needles, M.P. 99°C (Quoted 97°C).

c. Diazotisation of 4-nitro-1-naphthylamine.

25 gms. 4-nitro-1-naphthylamine

7.5 gms. sodium nitrite

75 ccs. conc. sulphuric acid

75 ccs. glacial acetic acid

19 gms. cuprous bromide

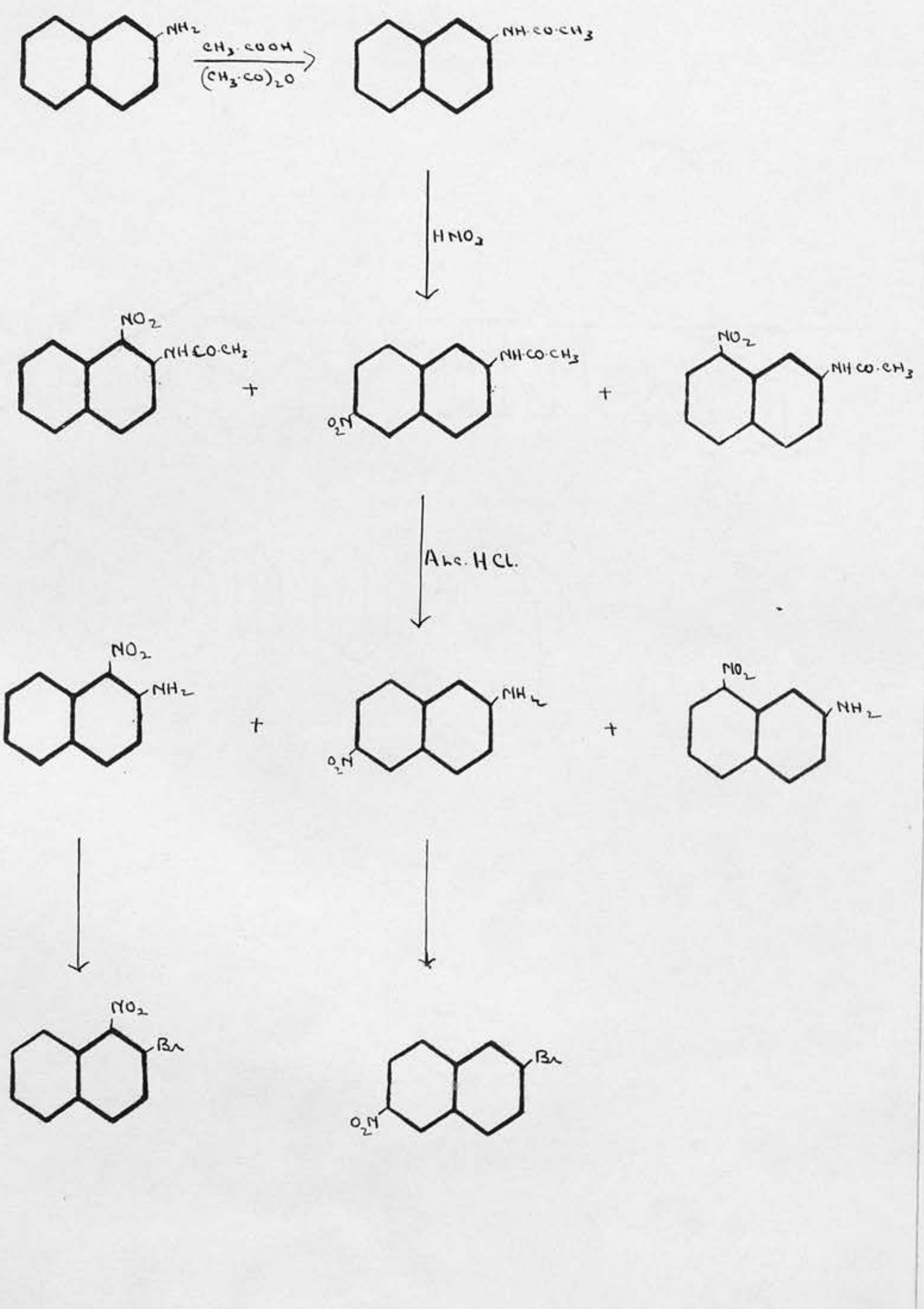
130 ccs. conc. hydrobromic acid.

Properties of 1-bromo-4-nitro-naphthalene: -

Crystallisation from alcohol gave yellow needles, M.P. 86°C (Quoted 85°C).

Note. The substance seemed to soften at 84° but two further recrystallisations did not sharpen the melting point.

Preparation of 2:1- and 2:6-bromonitro-naphthalenes.



The corresponding nitro-amines were prepared by the method of Saunders and Hamilton (J. A. C. S., 1932, 54, 638). The diazotisations and Sandmeyer Reactions were carried out exactly as before.

Experimental Data.

a. Acetylation and nitration of β-naphthylamine.

400 gms.	β-naphthylamine
600 cc.	glacial acetic acid
300 cc.	acetic anhydride
320 cc.	conc. nitric acid

b. Hydrolysis, and separation of isomers.

420 gms.	mixture of nitro-naphthalides
1680 cc.	alcohol
420 cc.	conc. hydrochloric acid.

Yield:- 140 gms. 1-nitro-2-naphthylamine
24 gms. 6-nitro-2-naphthylamine
7.5 gms. 8-nitro-2-naphthylamine.

Properties of 1-nitro-2-naphthylamine:-

Crystallisation from alcohol gave orange-yellow prisms M.P. 127°C (Quoted 127°C).

Sym.-trinitrobenzene derivative M.P. 115°C (Quoted 115-6°C).

Properties of 6-nitro-2-naphthylamine:-

Crystallisation from glacial acetic acid gave golden plates M.P. 206-7°C. Saunders and Hamilton quoted the melting point as 203°C; the sample prepared softened at 203°C and finally melted at 206-7°C.

Acetyl derivative M.P. 222°C.

Properties of 8-nitro-2-naphthylamine:-

Crystallisation from alcohol gave red prisms M.P. 104°C (Quoted 103.5°C).

Acetyl derivative M.P. 198°C.

c. Diazotisation of 1-nitro-2-naphthylamine.

25 gms. 1-nitro-2-naphthylamine
7.5 gms. sodium nitrite
75 cc. conc. sulphuric acid
75 cc. glacial acetic acid

19 gms. cuprous bromide
130 cc. conc. hydrobromic acid.

Yield:- 10 gms. 2-bromo-1-nitro-naphthalene.

Properties of 2-bromo-1-nitro-naphthalene:-

Crystallisation from alcohol gave reddish yellow needles M.P. 103°C (Quoted 102-3°C).

d. Diazotisation of 6-nitro-2-naphthylamine.

25 gms. 6-nitro-2-naphthylamine
7.5 gms. sodium nitrite
75 cc. conc. sulphuric acid
75 cc. glacial acetic acid

19 gms. cuprous bromide
130 cc. conc. hydrobromic acid.

Yield: - 9 gms.

Properties of 2-bromo-6-nitro-naphthalene.

Crystallisation from glacial acetic acid gave brownish-yellow needles M.P. 190°C. Further recrystallisation did not raise the melting point.

Analysis by Weiler, Oxford.

Found: N, 5.6% ; Br, 31.3%.

Calculated: N, 5.56%; Br, 31.7%.

An attempt to prepare the sym-trinitrobenzene derivative was unsuccessful.

Preparation of 1-bromo-5-nitro-naphthalene.

1-Bromo-5-nitro-naphthalene was obtained in an experiment which was primarily carried out in an attempt to prepare 1-bromo-8-nitro-naphthalene by an analogy with the method given by Ferrero and Caflisch (Hel. Chim. Acta, 1928, 11, 806) for the preparation of 1-chloro-8-nitro-naphthalene.

20 gms. α-nitronaphthalene was well mixed with .5 gm. ferric chloride, and placed in a flask which was heated to 60-70°C on a water bath. The mixture became liquid and a good stream of bromine vapour was passed in for an hour and hydrobromic acid was evolved. The product was washed with water and sodium carbonate solution, then dissolved in alcohol and the solution boiled with animal charcoal. Repeated crystallisation from

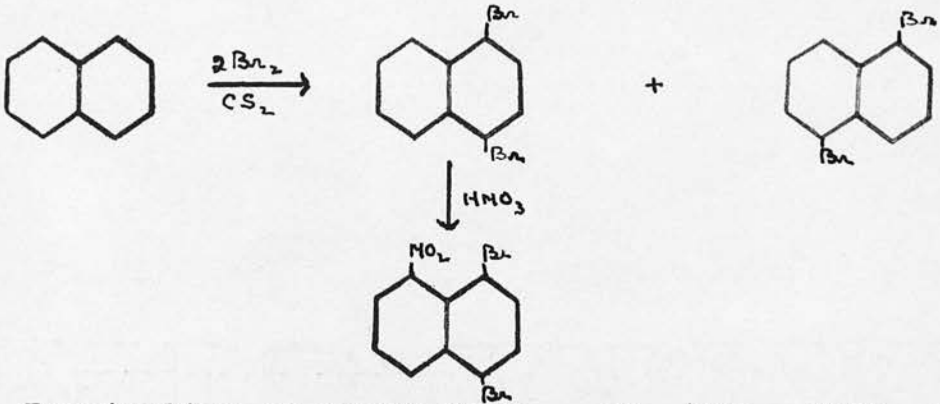
alcohol gave yellow needles M.P. 121°C (Quoted 122.5°C). Yield:- 4 gms.

Analysis by Weiler:

Found: N, 5.3%; Br. 31.5%.

Calc. N, 5.6%; Br, 31.7%.

Preparation of 1:4-dibromo-8-nitro-naphthalene.



a. Bromination of naphthalene. Cf. (Ber., 1931, 64, 953. Chem. Abstracts, 1931, 25, 2714)

100 gms. naphthalene

350 ccs. carbon disulphide

95 ccs. bromine

150 ccs. carbon disulphide.

The solution of naphthalene in carbon disulphide was cooled in an ice bath and the solution of bromine in carbon disulphide added fairly rapidly. The mixture was allowed to stand overnight (21 hrs.) before the carbon disulphide was evaporated on a steam bath. Excess bromine was removed by washing the oily product with sodium hydroxide. The oil was dissolved in ether and the solution dried over calcium chloride. The ether was removed and the resulting oil stirred with petrol ether

(B.P. 40-60°), when a solid separated. This was filtered off. Fractional crystallisation from petrol ether (B.P. 40-60°) raised the melting point of a portion from 55° to 75°C (approx.). One more crystallisation, this time from alcohol gave long white needles M.P. 81-83°C.

From two experiments with the above quantities 30 gms. 1:4-dibromonaphthalene was obtained.

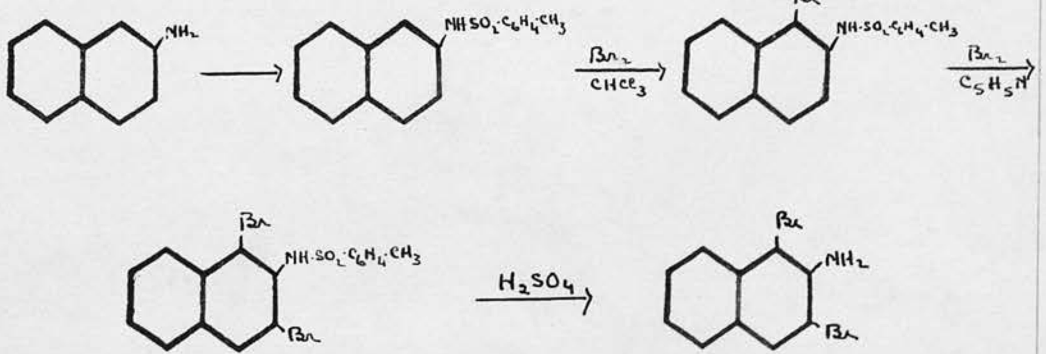
b. Nitration. Cf. Salkind (Ber., 1931, 64, 958).

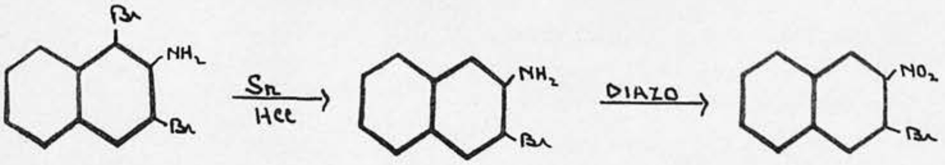
19 gms. 1:4-dibromonaphthalene
110 ccs. conc. nitric acid.

These were stirred in a flask at approximately 54°C for 4 hours. After cooling, the precipitate was filtered off in a sinter glass crucible - no water being added to the nitration mixture. The precipitate was crystallised repeatedly from glacial acetic acid giving pale yellow needles of 1:4-dibromo-8-nitro-naphthalene. M.P. 118°C (Quoted 116-7°C).

Yield:- 6.5 gms.

Preparation of 2-bromo-3-nitro-naphthalene.





a. Toluene p-sulphonyl-β-naphthalide.

Morgan and Micklethwait (J.C.S., 1912, 101, 148).

100 gms. β-naphthylamine

136 gms. p-toluene sulphonyl chloride

300 ccs. pyridene.

The β-naphthylamine was dissolved in pyridene and the p-toluene sulphonyl chloride added; the solution became bright red in colour. The mixture was boiled gently under reflux for 1 hour to complete the condensation and the solution became brown and clear. The mixture was poured into excess dilute hydrochloric acid with stirring. An oily layer formed from which the aqueous layer was decanted. Alcohol was added to the oil giving first solution, but after a few minutes the toluene p-sulphonyl-β-naphthalide separated. The precipitate was filtered off and recrystallised from glacial acetic acid until the melting point remained constant at 133°C (Quoted 134°C).

Yield:- 190 gms.

b. 1-bromo-2-p-toluenesulphon-naphthalide.

Consden and Kenyon (J.C.S., 1935, 1595).

190 gms. toluene-p-sulphon-β-naphthalide
630 ccs. chloroform
34.2 ccs. bromine in 126 ccs. chloroform.

The naphthalide was dissolved in chloroform and the bromine solution added fairly rapidly. When evolution of hydrobromic acid had ceased and the solution was clear the mixture was heated under reflux for 1½ hours. On warming, copious fumes of hydrobromic acid were first evolved and some white needles separated from the solution (hydrobromide of free base produced by partial hydrolysis). On cooling, the precipitate was filtered off and the filtrate evaporated to small volume on the steam bath. Ligroin was added to the residue, giving an oil which solidified on stirring. The precipitate was filtered off and crystallised from aqueous alcohol, giving 1-bromo-2-p-toluenesulphon-naphthalide M.P. 100°C (Quoted 99°C).

c. 1:3 dibromo-2-p-toluenesulphon-naphthalide.

153 gms. 1-bromo-2-p-toluenesulphon-naphthalide
460 ccs. pyridene
21.35 ccs. bromine.

The monobromo compound was dissolved in pyridene and the bromine added slowly. The mixture was allowed to stand overnight and the solution remained clear. The whole was poured into dilute hydrochloric acid and stirred; the aqueous layer was decanted and the oily layer stirred with alcohol. At first the oil went into solution but on rubbing and standing a solid separated which was filtered off.

d. Hydrolysis to 1:3-dibromo-2-naphthylamine.

The precipitate from (c) was dissolved in excess warm concentrated sulphuric acid and the solution poured into a large volume of water. A pinky-white precipitate of 1:3 dibromo-2-naphthylamine separated, which was filtered off and crystallised once from alcohol giving a product M.P. 117°C (Quoted 119°C).

Yield:- 40 gms.

Note:- An attempt was made to prepare the dibromo-p-toluene-sulphon-naphthalide directly without preparing the monobromo (J.C.S., 1932, 2733) but in spite of precautions to prevent charring a sticky product was always obtained which could not be crystallised.

e. 2-amino-3-bromo-naphthalene.

Consden and Kenyon (J.C.S., 1935, 1595).

40 gms. dibromonaphthylamine
320 ccs. R.S.
40 gms. granulated tin
320 ccs. conc. hydrochloric acid.

The mixture was refluxed for 3 hours when the solution became clear except for inorganic material. The solution was filtered hot. On cooling, shining plates of the hydrochloride of 2-amino-3-bromo-naphthalene separated; these were filtered off and the free base obtained by treatment with excess bench sodium hydroxide solution. 2-amino-3-bromo-naphthalene was obtained with a melting point of 171°C (Quoted 173°) by recrystallisation from alcohol.

Yield:- 10 gms.

f. 3-bromo-2-nitro-naphthalene.

Several attempts were made to find a method of oxidising an amino group to a nitro group using potassium persulphate and sulphuric acid, followed by perhydrol as oxidising agents. No definite results were obtained.

Hantzsch and Blagden (Ber., 1900, 33, 2554) described a method by which they replaced an amino group attached to an aromatic nucleus by a nitro group e.g. from p-chloraniline they prepared p-chloronitrobenzene. First the p-chloraniline was diazotised to give p-chlorobenzene diazonium sulphate which in the presence of cupri-cupro-sulphite ($CuSO_3, Cu_2SO_3, 2H_2O$) and sodium nitrite reacted to give p-chloronitrobenzene.

We decided to perform a similar reaction on 2-bromo-3-nitro-naphthalene.

(1) Preparation of cupro-cupri-sulphite.

Abegg, Anorganische Chemie Vol.II, Part I Page 556.

10 gms. copper sulphate crystals were dissolved in 100 ccs. water and 2N sodium hydroxide added until all

the copper had been precipitated as hydroxide. Sulphur dioxide gas was passed into the suspension, cooled in iced water, yielding finally a dark green solution. On warming, a red precipitate of cupro-cupri-sulphite was obtained weighing 5 gms.

(2) Preparation of diazo solution.

6 gms.	3-bromo-2-naphthylamine
3 ccs.	conc. sulphuric acid
26 ccs.	water
2 gms.	sodium nitrite in solution.

The amine was converted to its sulphate by addition of sulphuric acid. A paste of the sulphate in 26 ccs. water was transferred to a small flask, cooled in iced water. The sodium nitrite solution was added slowly with stirring and the mixture became red in colour.

(3) Introduction of nitro group.

10 gms.	cupro-cupri-sulphite
32 gms.	sodium nitrite
120 ccs.	water.

This mixture was stirred mechanically in a flask and the diazo solution from (2) added fairly slowly. There was brisk evolution of gas and until this had ceased the mixture was stirred at room temperature. Distillation with super-heated steam was used to separate the bromonitro-compound, but the method was not very satisfactory due, probably, to the low volatility of the compound. The product was crystallised from alcohol giving pale yellow needles M.P. 84°C (Quoted 83°C by Vesely, Chem. Abstracts, 1925, 19, 3486).

Yield:- .5 gm.

The product was examined by an elements test for nitrogen and bromine. By heating an aqueous-alcoholic solution with zinc and calcium chloride a solution was obtained which reduced ammoniacal silver nitrate. These tests gave confirmation of the presence of bromine and nitro groups.

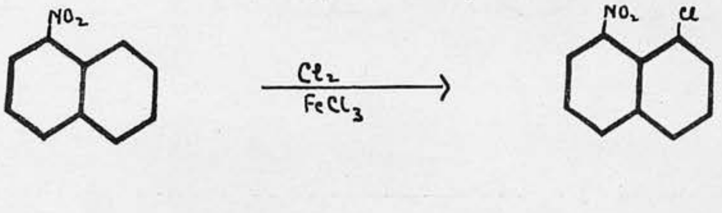
Analysis by Weiler.

Found: N, 5.7% ; Br, 33.4.

Calc. N, 5.6% ; Br, 31.7%.

Preparation of 1-chloro-8-nitro-naphthalene

Ferrero and Caflisch (Hel. Chim. Acta, 1928, 11, 806).



20 gms. α-nitro-naphthalene and .5 gm ferric chloride were well mixed in a flask. The flask was kept at a temperature between 65° and 70°C while a good stream of chlorine was passed into the mixture for three hours. The product was washed with water and sodium carbonate solution and dissolved in hot alcohol. The alcoholic solution was boiled twice with animal charcoal, filtered and allowed to cool. This process raised the melting point from 65-83°C (approx.). White needles separated,

which after repeated crystallisation from alcohol, melted at 97°C (Quoted 94°).

Yield: - 2 gms.

Preparation of 1-Chloro-2-nitro-naphthalene.

10 gms. 1-amino-2-nitro-naphthalene
3 gms. sodium nitrite
30 ccs. conc. sulphuric acid
30 ccs. glacial acetic acid

5.2 gms. cuprous chloride
52 ccs. conc. hydrochloric acid.

The usual procedure for diazotisation and Sandmeyer reaction was adopted.

The product, crystallised from alcohol, melted at 77°C (Quoted 76°C).

Yield: - 4 gms.

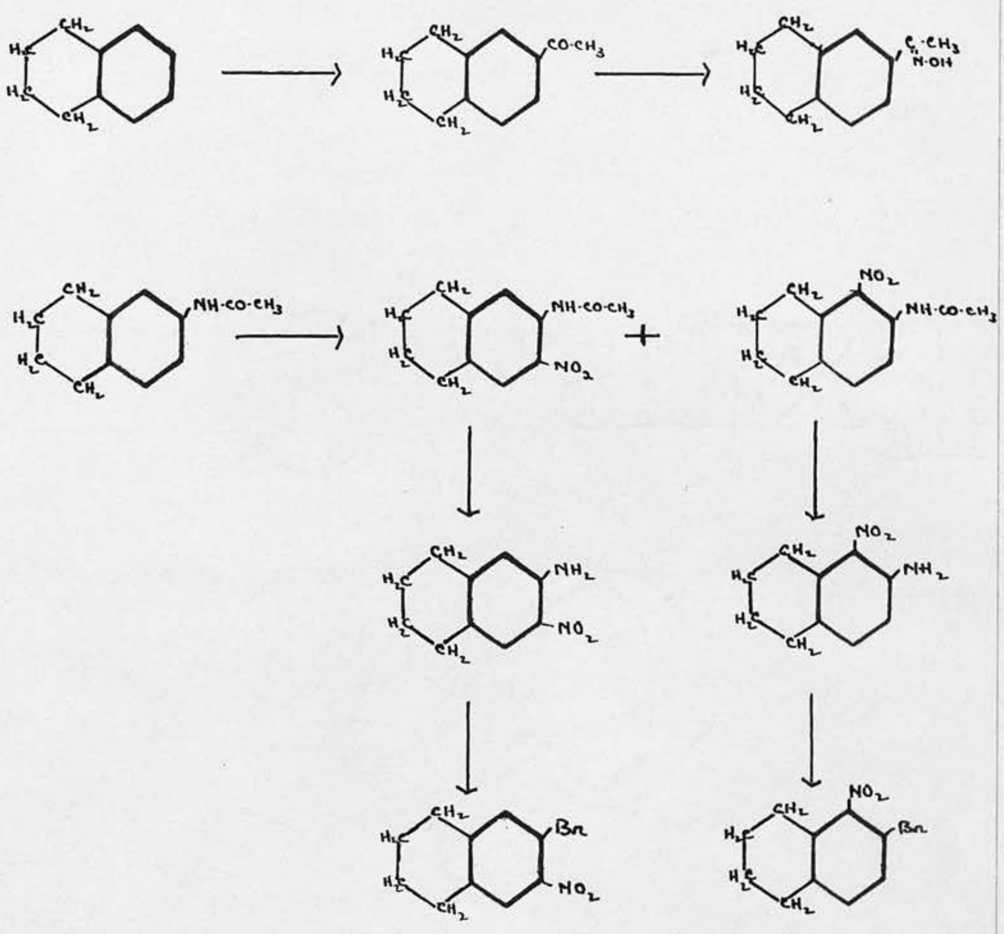
Preparation of 2-Chloro-1-nitro-naphthalene.

Method: - Exactly as above.

Product crystallised from alcohol melted at 98°C (Quoted 95°C).

PREPARATIONS - TETRALIN SERIES.

Preparation of Bromonitrotetralins.



a. 6-Aceto-tetralin.

Cf. W. Scharwin (Ber., 1902, 35, 2511)

50 gms. powdered aluminium chloride

A

200 gms. carbon disulphide

40 gms. tetralin
34 gms. acetic anhydride B
100 gms. carbon disulphide.

A was placed in a flask fitted with a cork bearing a condenser, a dropping funnel and a stirrer. B was added to A over a period of one hour and the temperature rose to about 30°C. Copious fumes of hydrochloric acid were evolved. The temperature was raised to about 60°C by heating on a water bath and after one hour evolution of hydrochloric acid had practically ceased. The mixture was poured into iced water in a separating funnel. Concentrated hydrochloric acid was added to dissolve the aluminium hydroxide produced and the whole shaken vigorously. The carbon disulphide layer was run off and dried over calcium chloride. The carbon disulphide was evaporated on the steam bath, and the residual oil distilled in vacuo. The fraction B.P. 150-1°C at 11-12 mms. was collected as 6-acetotetralin.

Yield:- 24 gms.

N.B. 10 gms. tetralin were recovered.

By several repetitions of this experiment a quantity of 6-acetotetralin was obtained.

b. 6-Acetotetralin oxime.

Cf. "Gattermann Laboratory Methods of Organic Chemistry" p. 334, and Ber., 1902, <u>35</u>, 2511.

75 gms. 6-acetotetralin
400 ccs. alcohol. A

57 gms. hydroxylamine hydrochloride
114 ccs. water.
B

95 gms. potassium hydroxide
95 ccs. water
C

B and C were cooled in ice and added fairly slowly to A with cooling. A precipitate of potassium chloride was formed. The whole was refluxed for 3 hours on a water bath and poured into a litre of water. An oily precipitate separated. The solution was made acid by addition of glacial acetic acid and a crystalline precipitate soon separated. This was filtered off and dissolved in alcohol; to the hot alcoholic solution was added half its volume of water and the solution reheated. On cooling slowly colourless prisms of 6-acetotetralin oxime appeared which melted at 104°C (Scharwin quoted needles M.P. 106°C).

Yield:- 65 gms.

c. Beckmann Rearrangement to 6-acetamino-tetralin.

Several unsuccessful attempts were made to carry out the Beckmann Change using phosphorus pentachloride, and concentrated sulphuric acid as reagents. Reference was made to the work of Blatt and Barnes (J.A.C.S., 1934, <u>56</u>, 1150) on methyl benzoin oxime, in which they used benzene sulphonyl chloride as reagent. We found by experience that the best results were obtained when the transformation was performed on small quantities; with larger quantities charring became very noticeable and a considerable amount of material was lost. 5 gm. portions of oxime were therefore treated separately.

5 gms. 6-acetotetralin oxime
50 ccs. pyridene
6 ccs. benzene sulphonyl chloride.

The oxime was dissolved in pyridene and the solution cooled in iced water. The benzene sulphonyl chloride was added slowly with stirring so that the temperature remained below 20°C, and the liquid remained clear although coloured brown. After standing for 3 hours at room temperature, the solution was poured into excess iced hydrochloric acid with stirring. In a well-manipulated experiment there was no charring and crystals separated from the solution on standing for some hours. The precipitate was recrystallised from ligroin giving colourless needles of 6-acetamino-tetralin melting at 107°C (Scharwin quoted 107°C).

Yield:- 3 gms.

d. Nitration of 6-Acetamino-tetralin.

(Schroeter, Ann., 1921, <u>426</u>, 66)

72 gms. 6-acetamino-tetralin were treated in six portions.

A
12 gms. 6-acetamino-tetralin
48 ccs. glacial acetic acid.

B
5.6 ccs. conc. nitric acid
4 ccs. conc. sulphuric acid.

B was added drop by drop to A with stirring. The temperature rose slowly and care was taken to keep it below 45°C, particularly during the first ten minutes after the acid had been added. The mixture was allowed to stand for ½ hour, and was then poured into iced water, with stirring, to give a rather sticky yellow precipitate.

The precipitates from the six experiments were subsequently treated together. The solid was shaken first with 150 ccs. cold alcohol and then with two portions of 50 ccs. The solid was no longer gummy, and was dissolved in 125 ccs. of hot alcohol. On cooling, fine yellow needles of 6-acetamino-7-nitro-tetralin, M.P. 132-3°C, separated and were filtered off. Crystallisation from 110 ccs. alcohol raised the melting point to 134-5°C. Further crystallisation of a sample from benzene did not change the melting point. (Schroeter quoted M.P. 134-5°C)

Yield:- 23 gms. 6-acetamino-7-nitro-tetralin.

The filtrate from the first crystallisation (125 ccs.) was evaporated until all the alcohol had been removed. To the residue 25 ccs. of alcohol were added, and a solution obtained which on cooling deposited impure 6-acetamino-5-nitro-tetralin. The filtrate from this precipitate was evaporated and the residue treated with 5 ccs. of alcohol. On cooling a further quantity of impure 6-acetamino-5-nitro-tetralin was obtained. 6-acetamino-5-nitro-tetralin was purified by crystallisation from a benzene-ligroin solution and was obtained as colourless plates M.P. 127-8°C (Schroeter quoted needles M.P. 128-9°C).

Yield: - 7 gms.

e. Hydrolysis of 6-Acetamino-7-nitro-tetralin and 6-Acetamino-5-nitro-tetralin.

Each acetyl compound was boiled for 10 minutes with four times its weight of alcohol and twice its weight of concentrated hydrochloric acid.

6-acetamino-7-nitro-tetralin gave red needles, which, after crystallisation from alcohol, melted at 125-6°C. (Quoted 126-7°C)

6-acetamino-5-nitro-tetralin gave red needles, which, after crystallisation from alcohol melted at 94°C. (Quoted 96°C)

f. 6-Bromo-7-nitro-tetralin.

4 gms.	6-amino-7-nitro-tetralin
1.2 gms.	sodium nitrite
12 ccs.	conc. sulphuric acid
12 ccs.	glacial acetic acid

3 gms.	cuprous bromide
21 ccs.	conc. hydrobromic acid.

The diazotisation and Sandmeyer reaction were carried out exactly as the corresponding reactions in the naphthalene series. Crystallisation of the product from methyl alcohol gave pink-red prisms which melted at 53-54°C. (Vesely and Chudozilov quoted 50-51°C. Chem. Soc. Abstracts, 1925, <u>128</u>, 1056)

Yield:- 1.2 gms.

Analysis by Weiler:

Found: N, 5.3% ; Br, 31.3%.

Calc.: N, 5.5% ; Br, 31.3%.

g. 6-Bromo-5-nitro-tetralin.

3	gms.	6-amino-5-nitro-tetralin
1	gm.	sodium nitrite
10	ccs.	conc. sulphuric acid
10	ccs.	glacial acetic acid
3	gms.	cuprous bromide
21	ccs.	conc. hydrobromic acid.

The product was very soluble in hot alcohol, and practically insoluble in the cold, crystallising in golden plates melting at 103-4°C (quoted 101-2°C).

Yield:- 1.3 gms.

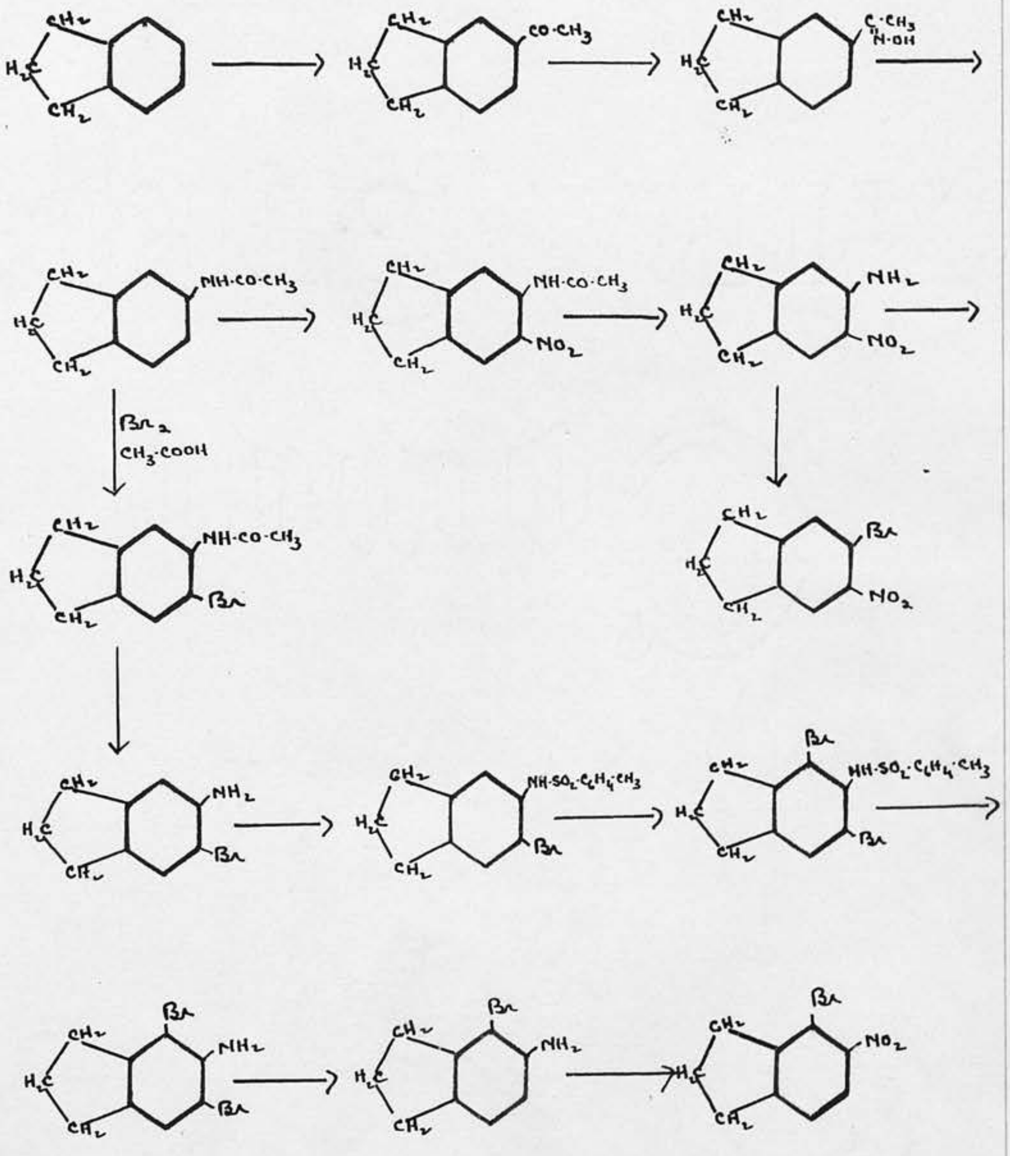
Analysis by Weiler:

Found: N, 5.7% ; Br, 30.6%.

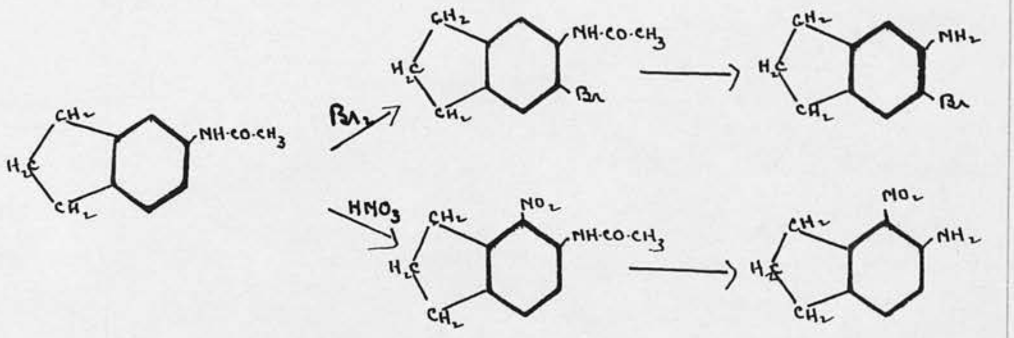
Calc.: N, 5.5% ; Br, 31.3%.

PREPARATIONS - HYDRINDENE SERIES.

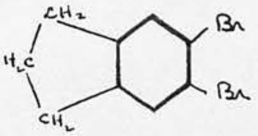
Preparation of Bromonitro-hydrindenes.



This work was originally modelled on a paper by Borsche and Bodenstein (Ber., 1926, 59, 1909), who claimed to obtain from 5-acetamino-hydrindene by bromination and nitration 5-acetamino-6-bromo-hydrindene, and 5-acetamino-4-nitro-hydrindene respectively.



The instructions of Borsche and Bodenstein were followed exactly to the point at which the above amino-bromo and amino-nitro compounds were supposed to be obtained. By methods of diazotisation previously described in this thesis the amino group was replaced by an -NO_2 group in the first case and by a -Br atom in the second. The products of the two experiments were shown to be identical by the method of mixed melting points. That 5:6 compounds were obtained in each case and not 5:4 was suggested by the evidence which has been collected for the presence of a double bond between C_5 and C_6 in hydrindene and confirmed by the work of Sidgwick and Springal (J.C.S., 1936, 1534) who used the method of Borsche and Bodenstein to prepare 5:6 amino-bromo-hydrindene and so the 5:6-dibromo-hydrindene. The dipole moment of this compound agreed with the moment calculated for a compound of formula: -



a. 5-Aceto-hydrindene.

35 gms. hydrindene
34 gms. acetic anhydride
100 gms. carbon disulphide

50 gms. aluminium chloride
200 gms. carbon disulphide.

The procedure was exactly as in the preparation of 6-aceto-tetralin. An attempt was made to perform the preparation on a large scale but the percentage yield decreased rapidly as the quantities were increased; therefore, it was necessary to repeat the preparation many times on a small scale. In the vacuum distillation the fraction boiling at 134-5°C under 11 mms. pressure was collected as 5-aceto-hydrindene.

Yield: - 20 gms.

b. 5-Aceto-hydrindene oxime.

110 gms. 5-aceto-hydrindene
800 ccs. alcohol

97 gms. hydroxylamine hydrochloride
194 ccs. water

162 gms. potassium hydroxide
162 ccs. water.

The method of preparation was the same as that used in the preparation of 6-aceto-tetralin oxime. The product was crystallised twice from aqueous alcohol, giving colourless prisms (or plates) melting at 113-4°C. Two further crystallisations only raised the melting point to 115-6°C although Borsche and Bodenstein quoted 119°C as the melting point of the pure compound.

Yield: - 108 gms.

c. Beckmann Transformation to 5-Acetamino-hydrindene.

5 gms. 5-aceto-hydrindene oxime
5 ccs. benzene sulphonyl chloride
50 ccs. pyridene.

In all, 105 gms. aceto-hydrindene oxime were treated in 5 gm. portions.

The hydrindene compound was dissolved in pyridene and the solution cooled in iced water to a temperature below 5°C. The benzene sulphonyl chloride was added in a fairly rapid series of drops with stirring. The temperature was observed to rise, and the best results were obtained when it was kept below 20°C.

About ¼ hr. after the addition of benzene sulphonyl chloride some samples were removed from the cooling bath; on standing for 4 hours these became very dark coloured and charred slightly, as was discovered on pouring into iced dilute hydrochloric acid. Other samples were clear although brown in colour, and were quite clean when poured into hydrochloric acid; from these, large needles (or prisms) separated overnight while the charred samples required treatment to remove a black oil and induce crystallisation.

The crystals were purified by crystallisation from petrol ether (B.P. 100-120°C) and a colourless product melting at 106-7°C was obtained (Quoted 108°).

Yield:- 25 gm.

d. 5-Acetamino-6-nitro-hydrindene.

11 gms. 5-acetamino-hydrindene
100 gms. conc. nitric acid.

Acetamino-hydrindene was added slowly to nitric acid, contained in a flask cooled in iced water, so that the temperature did not rise above 20°C - there was not much tendency for the temperature to rise. The solution was set aside for 2 hours, and then poured into iced water with stirring. A clean yellow precipitate was filtered off. A sample, twice crystallised from aqueous alcohol gave yellow needles melting at 108-9°C. Borsche quoted the product of nitration melting at 107°C.

e. 5-Amino-6-nitro-hydrindene.

The main portion of the product from (d) was boiled for 20 minutes with 44 gms. alcohol and 22 gms. conc.

hydrochloric acid; the colour of the solution became dark brown. The solution was poured into 300 ccs. of water and a red precipitate appeared which on crystallisation from alcohol gave red prisms melting at 126-7°C. (Borsche quoted 128°C as the melting point of the compound he called 5-amino-4-nitro-hydrindene.)

Yield:- 7 gms.

f. 5-Bromo-6-nitro-hydrindene.

6.5	gms.	6-nitro-5-amino-hydrindene
3.4	gms.	sodium nitrite
34	ccs.	conc. sulphuric acid
34	ccs.	glacial acetic acid.

9 gms. cuprous bromide
90 ccs. conc. hydrobromic acid.

The method was that described for similar compounds of the naphthalene series. The product was dissolved in methyl alcohol, and the solution boiled with animal charcoal. 6-nitro-5-bromo-hydrindene was obtained as golden-yellow needles, melting at 44°C by low temperature crystallisation from methyl alcohol.

Yield:- 2.2 gms.

Analysis by Weiler:

Found: N, 6.0% ; Br, 32.8%.

Calc.: N, 6.0% ; Br, 33.0%.

g. 5-Acetamino-6-bromo-hydrindene.

25 gms. 5-acetamino-hydrindene
125 ccs. glacial acetic acid
8 ccs. bromine.

As bromine was added to the solution of acetamino-hydrindene in acetic acid with shaking a precipitate soon separated which increased in quantity when the mixture was allowed to stand. After half an hour the whole was poured into iced water, and the precipitate filtered off. Crystallisation from alcohol gave colourless needles melting at 143°C (Quoted 143°C).

Yield:- 40 gms. (damp).

h. 5-Amino-6-bromo-hydrindene.

The product from (g) was boiled for 1½ hours with 250 ccs. of 20% hydrochloric acid. A hydrochloride separated from the solution during the hydrolysis. After being cooled the solution was filtered and the hydrochloride decomposed with concentrated ammonia solution diluted with half its volume of water. An oil separated which soon became solid, and on crystallisation from methyl alcohol gave nearly colourless needles melting at 46°C (Quoted 43°C).

Yield:- 18 gms.

i. 5-p-Toluenesulphon-amino-4:6-dibromo-hydrindene.

18 gms. 5-amino-6-bromo-hydrindene
16.5 gms. p-toluene sulphonyl chloride
50 ccs. pyridene
4.5 ccs. bromine.

The amine was dissolved in pyridene, and p-toluene sulphonyl chloride added. The condensation was completed by boiling for 20 minutes; the solution was cooled to room temperature. Bromine was added slowly and the mixture allowed to stand overnight. Large crystals separated, but the whole was poured into dilute hydrochloric acid with stirring giving a sticky solid which could be filtered off. A clean product was obtained by treating the sticky mass with 100 ccs. hot alcohol. The precipitate was filtered off, and recrystallised from a large volume of alcohol giving colourless prisms melting at 199-200°C.

Yield:- 12 gms.

Analysis by Weiler:

Found: Br, 36.7% ; S, 7.1%.

Calc.: Br, 35.9% ; S, 7.1%.

j. 5-Amino-4:6-dibromo-hydrindene.

11 gms. 5-p-toluenesulphon-amino-4:6-dibromo-hydrindene was dissolved in approximately 110 ccs. warm concentrated sulphuric acid. The solution was poured into a large volume of water giving a colourless precipitate melting at 70°C. Crystallisation of a sample from alcohol raised the melting point to 71°C.

Analysis by Weiler:

Found: Br, 53.8%.

Calc.: Br, 54.9%.

k. 5-Amino-4-bromo-hydrindene.

The product from the above was heated for 1 hour with 40 ccs. alcohol, 40 ccs. concentrated hydrochloric acid and 8 gms. tin. After 40 minutes the solution became clear of organic material. The solution was filtered hot, and poured into 250 ccs. 2N sodium hydroxide. A bulky white precipitate was obtained with a very high melting point or decomposition point (215°C). Since this was precipitated from alkaline solution it could not be a hydrochloride, and was presumed to be a compound of the amine and stannous chloride. For its decomposition hot concentrated caustic potash was used giving a grey precipitate which was extracted repeatedly with alcohol. A fine grey precipitate remained insoluble and was removed with difficulty by filtration. The filtrate was diluted with approximately its own volume of water; the solution became milky and overnight long white needles separated which melted at 50-51°C.

Yield:- 2 gms.

On mixing some of this product with 5-amino-6-bromo-hydrindene on porous tile the mixture became oily and disappeared into the tile.

Analysis by Weiler:

Found: N, 6.4% ; Br, 39.8%.

Calc.: N, 6.6% ; Br, 37.6%.

Note.- The decomposition of the tin compound was unsatisfactory, and at this stage a quantity of material was believed to be lost.

1. 4-Bromo-5-nitro-hydrindene.

2 gms. 5-amino-4-bromo-hydrindene
1.5 ccs. conc. sulphuric acid
.8 gms. sodium nitrite in 5 ccs. water
10 ccs. water.

The amine was converted to its sulphate and a paste of the sulphate in 10 ccs. of water placed in a small flask when it was cooled and stirred mechanically. Sodium nitrite solution was added slowly giving a green solution which was added with cooling and stirring to a mixture of 3.7 gms. cupro-cupri-sulphite, 11 gms. sodium nitrite and 45 ccs. water. There was brisk evolution of gas and the mixture was allowed to stand for ½ hour before being steam distilled. A pale yellow oil appeared in the distillate and was isolated by extraction with ether, and subsequent evaporation of the ether. An attempt was made to crystallise the oil by dissolving in .5 cc. methyl alcohol and freezing out. This was followed by attempted precipitation by petrol ether (B.P. 40-60°) and freezing in ice-salt mixture and in carbon dioxide snow. This merely gave three layers with perhaps a trace of solid; the solution became homogeneous as the temperature rose to normal. The solvents were removed on the steam bath and in a vacuum desiccator. It was found possible to solidify a small quantity of the oil in carbon dioxide snow but it could be melted at the temperature of tap water.

Yield:- .3 gm. (approx.)

An attempt to determine the boiling point by a micro-method was not very satisfactory and it is only possible to say that it was above 230°C. The oil became very dark coloured at this high temperature, and decomposed.

Analysis by Weiler:

Found: N, 4.25% ; Br, 35.2%.

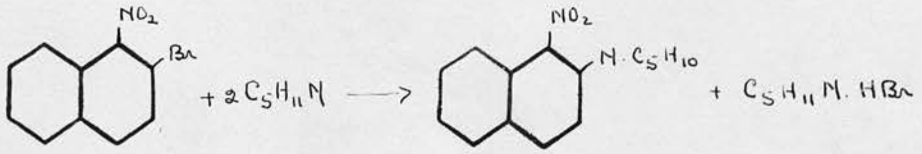
Calc.: N, 6.0% ; Br, 33%.

Semi-quantitative Experiments.

(J. Salkind, Ber., 1931, 64, 289)

Approximately 0.15 gm. of halogeno-nitro-compound was weighed accurately in a test tube provided with a ground glass stopper. 1 cc. of piperidine was added from a pipette, and the tube immersed in a thermostat at 40-50°C. After a definite interval of time the contents of the tube were washed into a separating funnel with distilled water (about 50 ccs.) and shaken up with pure benzene. The benzene removed organic material from the aqueous layer while the halogen was left behind. In most cases a good separation was obtained, and the aqueous layer was left almost or completely colourless. The halogen in the solution was determined by Volhard's Method, by titration with silver nitrate and potassium thiocyanate, ferric alum being used as indicator.

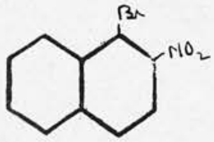
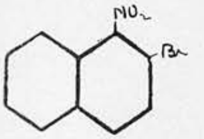
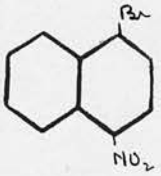
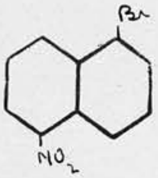
In reactive halogeno-nitro-compounds of the benzene, naphthalene, tetralin and hydrindene series the halogen was removed by piperidine giving piperidine hydrochloride or hydrobromide and a compound of piperidine and the nitro hydrocarbon e.g.

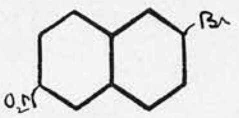
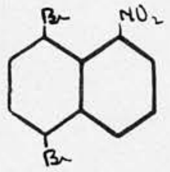
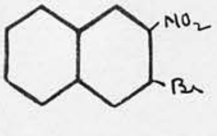
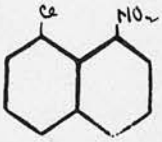
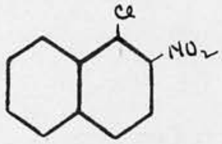
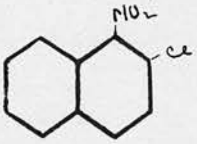
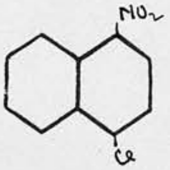


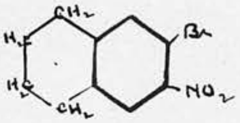
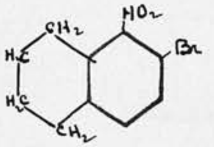
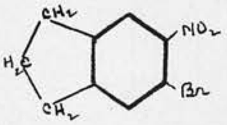
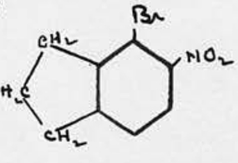
On mixing with water the piperidine hydrochloride or hydrobromide went into solution with decomposition into piperidine and free acid while the other organic material remained in suspension colouring the solution yellow. Before the amount of hydrochloric or hydrobromic acid formed could be determined volumetrically the colour had to be removed - extraction with pure benzene served.

For the titration, standard solutions of silver nitrate and potassium thiocyanate of approximately N/50 concentration were prepared and standardised accurately. The normality of the silver nitrate was determined by titration against weighed quantities of potassium bromide, and the volume of silver nitrate solution equivalent to 1 cc. of potassium thiocyanate solution was determined by titration using ferric indicator.

Results.

Compound	Weight (gms.)	Vol. piperidine	Time (hrs.)	Temp. (°C)	% bromine removed
	.1466	1	20	47	101
	.1506	1	3.5	47	101
	.1506	1	.5	47	90.6
	.1526	1	20	47	99.8
	.1454	1	3.5	47	99.5
	.1536	1	.5	47	69.8
	.1522	1	.5	47	65.0
	.1515	1	.5	42	45.8
	.1473	1	.5	42	49.9
	.1488	1	.5	42	54.2
	.1494	1	.5	42	46.2
	.1466	1	26	47	97.5
	.1420	1	20	47	98.1
	.1542	1	3.5	47	97.4
	.1517	1	.5	47	65.0
	.1515	1	.5	42	53.0
	.1516	1	.5	42	53.6
	.3066	.6	.5	44	79.2
	.1432	1	26	47	0
	.1460	1	168	47	0

Compound	Weight (gms.)	Vol. piperidine	Time (hrs.)	Temp. (°C)	% bromine removed
	.1515	1	.5	42	1
	.1494	1	22	42	0
	.1589	1	.5	42	0
	.1613	1	24	42	0
	.0646	.5	.5	42	0
		1	24	45	0
	.1512	1	22	45	0
	.1492	1	.5	45	50.6
	.1489	1	.5	45	45.6
	.1478	1	.5	45	ca. 43

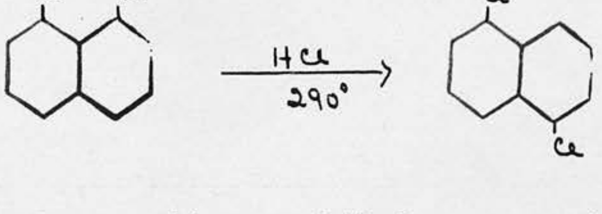
Compound	Weight (gms.)	Vol. piperidine	Time (hrs.)	Temp. (°C)	% bromine removed
	.1505	1	22	45	50.9
	.1008	1	2	45	7.9
	.1037	1	.5	45	5.1
	.0780	1	2	45	1.3
	.1498	1	22	45	2.6
	:0997	1	2	45	13.0
	.0929	1	2	45	11.8
	.1515	1	22	45	71.7
* 	.0964	.7	22	45	8.8(?)

* The amount of halogen apparently removed from this compound might easily be attributed to impurity. Analysis gave a high result for halogen content.

It was found that the figures were not absolutely reproducible, and therefore the experiments were termed semi-quantitative. However, the essential point was activity or non-activity of the halogen in the halogeno-nitro-compounds rather than variation in degree of activity.

DISCUSSION.

The bromo-nitro-compounds of the naphthalene series were on the whole easily obtained. An interesting and surprising result was obtained in the bromination and chlorination of α-nitro-naphthalene, when the 1:8-chloronitro-compound and the 1:5-bromo-nitro-compound were formed by the same procedure. Perhaps there is something analogous here to the phenomenon quoted by Meyer-Jacobson 2, 2, 335 of a transformation from 1:8-dichloronaphthalene to 1:5-dichloronaphthalene by heating with conc. hydrochloric acid.



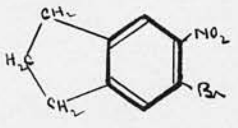
If the 8:1-bromo-nitro-naphthalene were less stable than the 5:1-bromo-nitro-compound the former might change immediately into its isomer.

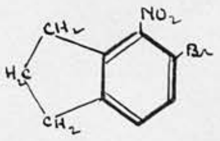
1:8-bromo-nitro-naphthalene seemed to be difficult to obtain, and after it had been discovered that the bromine atom in 1: 5-bromo-nitro-naphthalene was inactive it was decided to substitute 1: 4-dibromo-8-nitro-naphthalene for the former since this had bromine and nitro groups in the required relative positions. The preparation of the 2: 3-bromo-nitro-naphthalene promised to provide some difficulty since it was known to be difficult to substitute the β_2 position in a β_1 substituted naphthalene molecule. However by reference to Bell's work (J. C. S., 1932, 2732) on the powerful ortho directing action of the p. toluene-sulphonamido-group it was possible to obtain first a 1: 3-dibromo-2-amino-naphthalene. Consden and Kenyon (J. C. S., 1935, 1596) had found it possible to remove the bromine atom attached to C_1 by means of tin and hydrochloric acid to give 2: 3-amino-bromo-naphthalene, i. e. the bromine atom attached to C_1 was more labile than that attached to C_3. This fact may be explained by the presence of a double bond between C_1 and C_2 and a single bond between C_2 and C_3.

Attempts to oxidise the amino group to the nitro graup, following the work of Meisenheimer (Ber., 1919, 52, 1172) using potassium persulphate and sulphuric acid as oxidising agent, or the work of Dino, Bigiavi and Corrado Albanese (Zentralblatt, 1935, 1348) (who obtained nitrobenzene from acetanilide by means of perhydrol) gave no satisfactory results, and it became necessary to resort to a method of diazotisation. A. Hantzsch and J. W. Blagden (Ber., 1900, 33, 2554) described an experiment whereby they obtained from β-naphthalene diazonium sulphate and potassium nitrite solution, in the presence of cupro-cupri-sulphite ($CuSO_3, Cu_2SO_3, 2H_2O$), β-nitro-naphthalene. The mixture yielded the desired compound, though the yield was small.

The preparation of the bromonitrotetralins and hydrindenes, seemed on first sight quite straight forward, but the early stages in both series involved some tedious processes. The Friedel-Craft Reaction was found to be most easily and satisfactorily manipulated when less than 50 gms. of hydrocarbon was treated at one time; it was therefore necessary to repeat this stage many times to give an adequate supply of acetotetralin or acetohydrindene. Oxime formation took place readily but the transformation from oxime to acetamino compound proved a temporary obstacle, to be overcome finally by using benzene sulphonyl chloride as Beckmann Reagent. The heat produced in the transformation prohibited work on a large scale; when 10 gm. portions were used it was found difficult to control the temperature adequately. Therefore 5 gm. portions were treated throughout. The efficiency of the transformation seemed to vary to some extent but an average yield would be approximately 55%.

Borsche and Bodenstein (Ber., 1926, <u>59</u>, 1909) claimed to obtain 6-bromo-5-acetamino-hydrindene and 4-nitro-5-acetamino-hydrindene by bromination and nitration respectively of 5-acetamino-hydrindene. From the amines of those we hoped to obtain 6-bromo-5-nitro hydrindene which would have reactive bromine and 5-bromo-4-nitro-hydrindene which would have inactive bromine.





Having obtained the products of the two processes, we measured the activity of the bromine in each and found it to be the same. This seemed suspicious and since the samples had melting points within two degrees of each other it was decided to find the melting point of a mixed sample. The result of this investigation proved conclusively that the products from the two preparations were identical. It seemed most likely that they were the 5:6-compound and reference to the work of Sidgwick and Springal (loc. cit.) proved this. Investigation then showed that doubt had already been cast on Borsche's results by Lindemann and Bruhin (Ber., 1927, <u>60</u>, 439).

Apparently it is difficult to attach a substituent to C_4 in a hydrindene molecule already substituted at C_5. Therefore, by analogy with the naphthalene series it was decided to experiment with the strongly ortho directing p. toluenesulphon-amido-group in pyridene solution. 6-bromo-5-amino-hydrindene was converted to 6-bromo-5-p-toluenesulphon-amino-hydrindene and brominated in pyridene solution. By this means a dibromo-p-toluenesulphonaminohydrindene was obtained, and by hydrolysis a dibromoaminohydrindene.

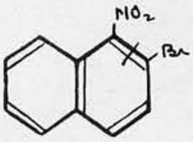
Again by analogy with the naphthalene series, it was thought that it might be possible to remove the bromine attached to C_6 and to $-C-NH_2$ through a double bond by means of tin and hydrochloric acid. Actually a monobromo-amine was obtained which was shown by the method of mixed melting points to be different from 6-bromo-5-amino-hydrindene and was presumed to be 4-bromo-5-amino-hydrindene. The amino group was replaced by a nitro giving an oil. The amount obtained was so small that it was impossible to effect further purification of the product than that afforded by steam distillation and extraction of the distillate with ether. It was decided to perform a reactivity measurement on this crude product, for which analysis figures showed the halogen content to be rather high and the nitrogen to be correspondingly low for a compound of composition $C_9H_8NO_2Br$. The result - 8% of halogen apparently removed in 22 hours - was sufficiently low when compared with 70% removed from pure 5:6-compound to justify an assumption that halogen attached to C_4 was really inactive.

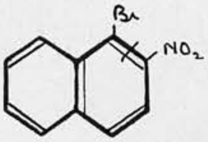
After nitration of acetamino-tetralin, difficulty was experienced in separating the isomers when Schroeter's method was followed exactly. 6-acetamino-7-nitro-tetralin was easily obtained pure but the 6-acetamino-5-nitro-compound had to be extracted from a tarry residue. In a second experiment the tar was removed by washing with cold alcohol before any separation was attempted, and two clean products were obtained although the 5-nitro-6-acetamino-tetralin was in small yield.

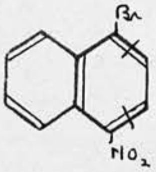
Theoretical.

The detection of double bonds by this principle of activation was previously used by Mills and Smith in the isoquinoline series (J.C.S., 1922, 121, 2724).

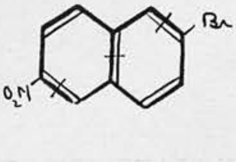
In all compounds in the naphthalene series, in which, on the Erlenmeyer formula, bromine was linked to nitro through a double bond or conjugated system of double bonds the bromine was reactive towards piperidine.





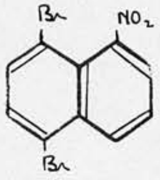


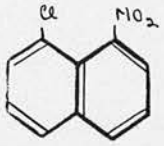
In 2-bromo-6-nitro-naphthalene the bromine and nitro groups were linked by a conjugated system of three double bonds but the bromine was non-reactive.

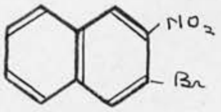


This conjugated system involved the double bond common to the two rings. The properties of the double bond common to the two rings can scarcely be normal and therefore it was not unexpected that this bond should be incapable of transmitting the activating effect.

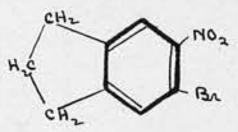
Particularly interesting and important was the non-reactivity of the bromine in certain ortho and peri positions; this also was predicted from Fuson's theory.

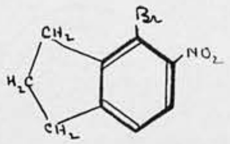






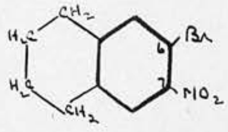
This non-reactivity seemed to indicate that the activation really was due to the presence of a double bond or conjugated system of double bonds in a fixed position and not to the mere proximity of the groups. Further, substituents in the peri positions are normally very reactive, yet in the bromo-nitro-series the bromine atom was not activated by the nitro-group.

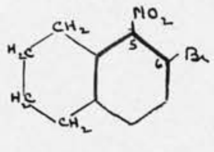




Of the two bromo-nitro-hydrindenes investigated, the 5:6-compound, in which on former evidence the nitro and bromine groups were linked by a double bond, had a very reactive bromine atom - 70% of bromine being removed in ½ hr. The 4:5-bromo-nitro-compound was obtained in too small quantity as an oil to permit of adequate purification but a measurement on the crude product gave 8% as the amount of bromine removed in 22 hours. An analysis of this crude material showed the halogen content to be higher than that of the pure substance and it is possible that the above 8% was entirely attribututable to impurity.

In any case the difference in activity of the bromine atom in the two compounds is sufficient to justify the assumption that the double bond is the controlling factor in activation.

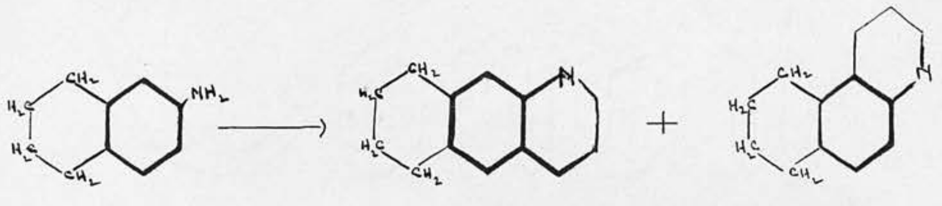




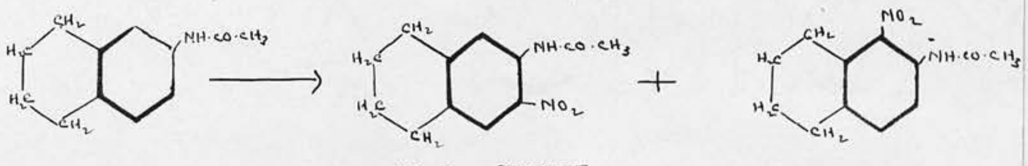
Examination of the tetralin compounds brought to light a strange anomaly. The 6-bromo-7-nitro-compound had reactive bromine (but not nearly so reactive as in the hydrindene or naphthalene series) whereas the 5-bromo-6-nitro-compound had completely inactive bromine. This fact cast some doubt upon the structure and composition of the compound but analysis showed it to contain both a nitro group and a bromine atom, and from the method of synthesis it must have been the 5-bromo-6-nitro compound.

In the naphthalene series, activity measurements, based on Fuson's theory of activation of one group by another linked to it through a double bond or conjugated system of double bonds, indicated the same arrangement of bonds in the nucleus of bromo-nitronaphthalenes as Fieser had supported for the nucleus of hydroxynaphthalenes by investigation of the coupling reaction between naphthols and diazonium salts. The same parallelism exists between the arrangement of bonds in bromonitrohydrindenes, methyl hydroxyhydrindenes, and 5:6- dibromo-hydrindene examined by Sidgwick and Springal, but in the tetralin series Fieser's and Sidgwick's work indicated oscillation of the bond arrangement in methyl hydroxy-tetralins and 5:6-dibromotetralin while activity measurements indicated a fixed arrangement in bromonitrotetralins.

It is interesting to note the following reactions of 6-aminotetralin and 6-acetaminotetralin.

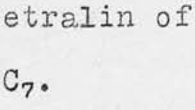


MAIN PRODUCT

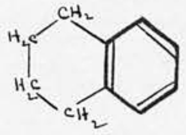


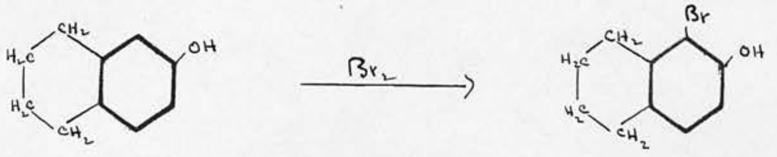
MAIN PRODUCT

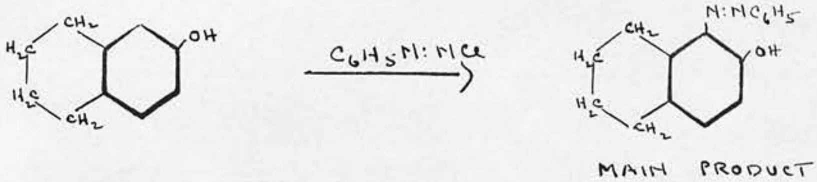
These reactions probably indicate a preponderance in ordinary 6-aminotetralin of the form having a double bond between C_6 and C_7.



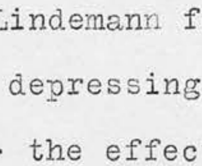
On the other hand in the case of 6-hydroxytetralin there would appear to be an excess of the form having a double bond between C_5 and C_6.







Lindemann (Ann., 1928, 462, 24) showed that certain chloronitrobenzenes can be deactivated by introduction of a methyl group or of an amino group and in the latter case reactivated by subsequent acetylation. This showed that different substituents have a different effect on the activity of halogen in nitrochlorobenzene.



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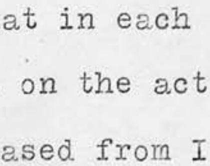
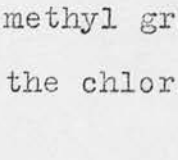


II



III

Lindemann found that in each case the methyl group had a depressing effect on the activity of the chlorine atom - the effect increased from I - III.

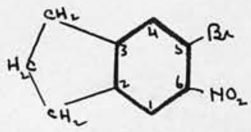
It appears from observations in the tetralin, hydrindene and naphthalene series that the arrangement of bonds in a substituted benzene ring attached to another hydrocarbon ring (which may be regarded as a side chain) depends upon two factors:-

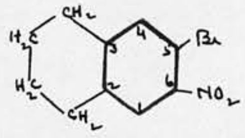
(1) The nature of the side chain.

(2) The nature of the substituents or perhaps the polarity of the substituents.

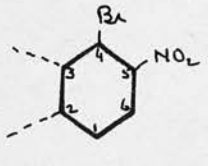
The first of these conditions was demonstrated stereochemically by Mills and Nixon (J.C.S., 1930, 2510).

Bromonitrohydrindenes and bromonitrotetralins can be regarded as ortho bromonitrobenzenes with further substituents on C_2 and C_3.





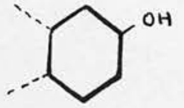
The trimethylene and tetramethylene side chains both permit activity in 5:6-bromo-nitrobenzenes but not in 4:5- nor 5:4-bromo-nitrobenzenes. Naphthalene too is a 2:3-substituted benzene molecule where the side chain is a butadiene chain; this unsaturated chain permits activity of 4:5- and 5:4-bromonitrobenzenes but not of 5:6-bromonitrobenzenes.



If activity of the bromine is to be attributed to the presence of a double bond between the carbon atoms to which the nitro and bromine groups are attached in the benzene ring then trimethylene and tetramethylene chains have the effect of fixing the arrangement of double and single bonds in one way and the butadiene chain in another way.

This is as would be expected from the chemically similar nature of trimethylene and tetramethylene chains.

By starting from the reactive bromonitrobenzene a satisfactory theory of the effect of hydrocarbon side chains on the arrangement of bonds can be worked out but an attempt to apply the same theory to 5-hydroxybenzene to be further substituted at C_2 and C_3 is not quite so simple.

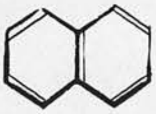


In this case tetramethylene has an effect intermediate between that of trimethylene and butadiene, similarly for 5-aminobenzene.

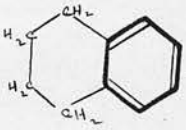
What is the effect of trimethylene, tetramethylene and butadiene substituents on a simple benzene ring ? For the case of butadiene we have the Raman Spectra observations of Kohlrausch (Ber., 1935, <u>68</u>, 893) that the molecule of naphthalene must be symmetrical suggesting the same arrangement of bonds in the hydrocarbon as exists in the bromonitronaphthalenes.

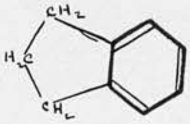
The combined effect which the tetramethylene ring and the substituents on the benzene ring will have on the arrangement of double and single bonds in the benzene ring of a particular compound varies as the substituents are changed. In bromonitro compounds this combined effect is similar to that of the trimethylene chain; in hydroxy compounds it is similar to that of the butadiene chain; and in the methyl hydroxy compounds it is intermediate between these two effects.

In so far as Fuson's theory of activation is applicable to the determination of the positions occupied by double bonds in an aromatic molecule, throughout the series of halogenonitronaphthalenes examined the arrangement of bonds is:-



In bromonitrotetralins and hydrindenes the arrangements are:-



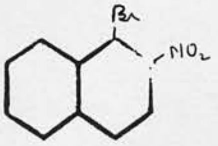


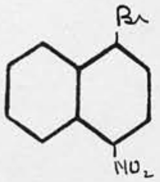
Investigations in the hydrindene and tetralin series have forced the conclusion that the arrangement of double and single bonds in the benzene nucleus of an aromatic molecule depends largely on the nature of any substituents and side chains attached to the ring. Therefore, from the experiments on bromonitronaphthalenes no definite conclusions can be drawn concerning the arrangement of bonds in an unsubstituted naphthalene molecule, nor in a molecule having different substituents.

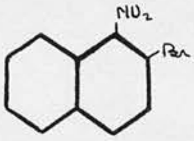
SUMMARY.

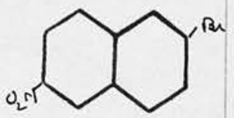
The following compounds were prepared for the purpose of measuring the reactivity of the halogen atom in each.

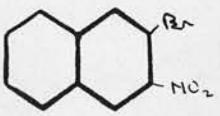
Naphthalene Series.

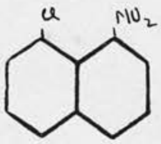


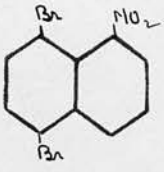




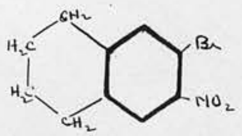


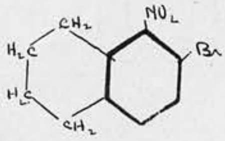




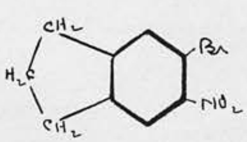


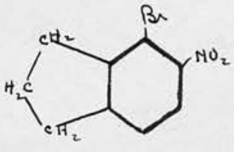
Tetralin Series.



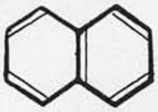


Hydrindene Series.

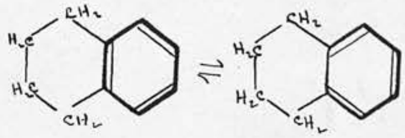




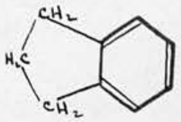
The reactivity of the halogen towards piperidine was determined volumetrically. Regarded for the most part qualitatively the results were as predicted from Fuson's theory of activation by unsaturated groups and from the formulae for naphthalene and hydrindene but not that for tetralin predicted by previous workers.



NAPHTHALENE



TETRALIN



HYDRINDENE

From evidence obtained here and from the work of previous authors it was concluded that the nature of the substituents on an aromatic ring had a powerful influence on the arrangement of bonds in the ring and therefore although our results with regard to the naphthalene series were in agreement with the Erlenmeyer formula for naphthalene we do not consider ourselves justified in claiming this work to be evidence in favour of the Erlenmeyer formula for an unsubstituted naphthalene molecule.

In conclusion the author wishes to acknowledge the guidance and encouragement given by Dr. Neil Campbell throughout this research, a grant from the Moray Fund and the award of a Research Scholarship by the Carnegie Trust.

ADDENDUM.

It should be pointed out that the references to the phenomenon of resonance given on pages 4 and 6 do not represent the most recent conceptions. In the older theory a fluctuation between the various structural forms was postulated. This has now been discarded and the theory accepted is expressed by Sidgwick (Sidgwick's Organic Chemistry of Nitrogen. Revised by Taylor and Baker p. xv) "If a molecule can have two or more different structures in the ordinary organic sense of the term, then under certain conditions its actual state is neither one nor the other, but something intermediate between the two, which partakes to some extent of the properties of both but cannot be expressed in the usual structural symbols."

It was however felt that the time was not ripe to attempt an interpretation of our results in the light of the resonance theory.