SOME DERIVATIVES OF

9-AZABENZANTHRONE

by

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Doctor of Philosophy

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C O N T E N T S

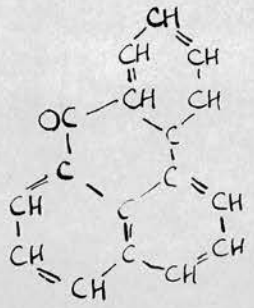
INDEX OF PREPARATIONS

INTRODUCTION

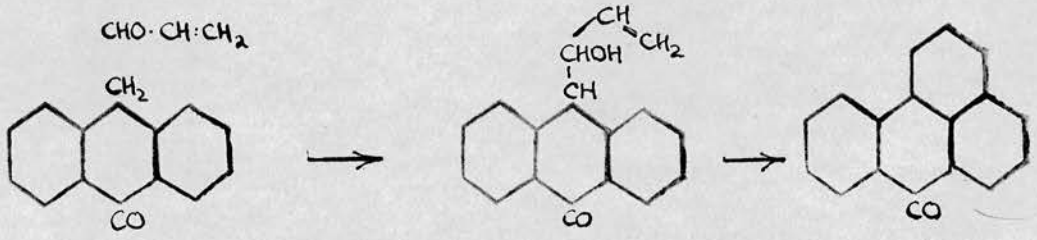
The bewildering array of organic aromatic compounds falls naturally into numerous classes, each class being characterised by the presence in the molecule of a certain basic ring structure. The simplest class is that wherein the benzene ring constitutes the base. All the derivatives of naphthalene may be said to form the second group. And so every ring structure gives rise to its own division of organic aromatic nomenclature.

The compounds of the more complex ring structures have not been so fully investigated as those with simpler basic systems and consequently provide a fruitful field for further research.

Among the more complex ring structures the benzanthrone system was first discovered by Bally in 1905 in the course of his investigations of the Skraup reaction on anthraquinone (Ber. 1905, 38, 194). He treated anthraquinone with glycerol and concentrated sulphuric acid in the presence of a reducing agent and obtained what has since been proved to be benzanthrone:-



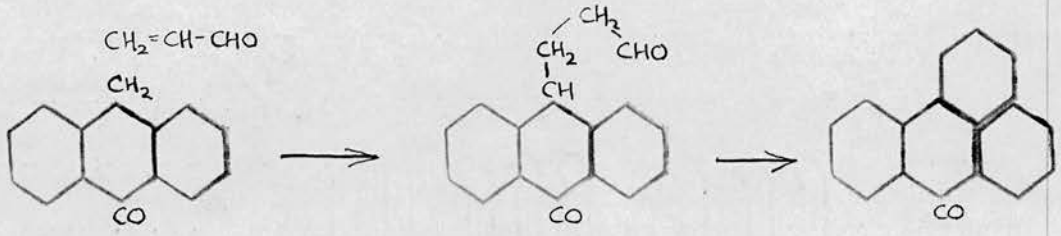
Benzanthrone proved to be the parent substance of a large class of compounds and one of great value technically for the production of dyestuffs. Since the original discovery this method of synthesis has been slightly modified, the anthraquinone being reduced to anthrone by means of copper powder and sulphuric acid before the addition of the glycerol. The mechanism of the reaction has given rise to considerable discussion. Bally and Scholl (Ber. 1911, 44, 1656) postulate that some of the anthraquinone is reduced to anthrone which combines with acrolein, from the glycerol and concentrated sulphuric acid, to form an aldol:-



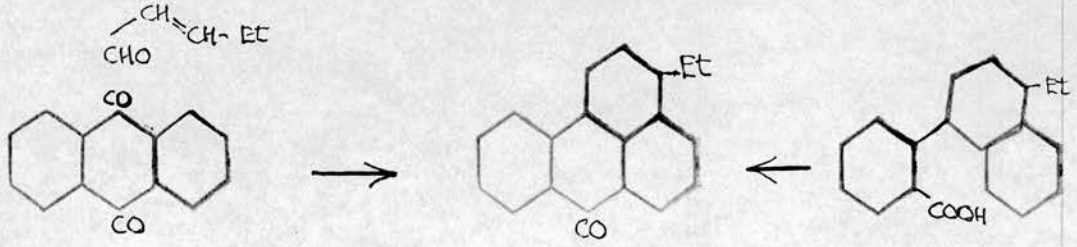
The aldol then undergoes loss of water to form benzanthrone, the liberated hydrogen reducing more anthraquinone.

Meerwein has proposed an alternative mechanism to avoid this unusual cyclisation (J. prakt. Chem. 1918, (2) 97, 284).

Since it is known that anthrone adds to unsaturated substances such as benzal-malonic ester, the anthraquinone nucleus becoming attached to the carbon of the double bond further removed from the ester group, Meerwein suggests that the first stage of benzanthrone formation is of this type, followed by ring closure of the aldehyde group:-

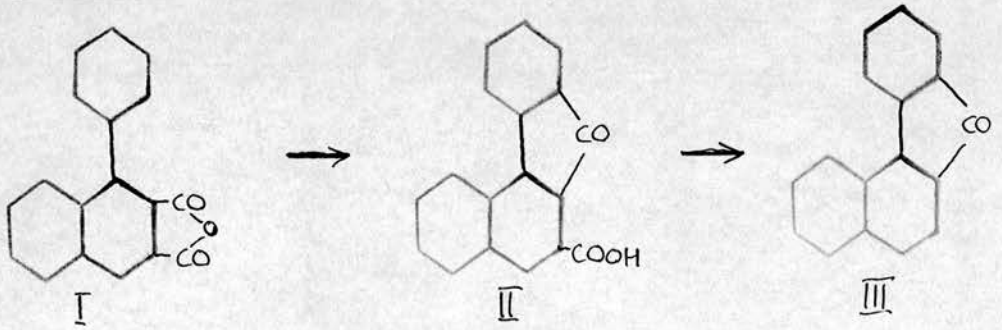


Positive evidence in favour of the mechanism advanced by Bally and Scholl has recently been forthcoming in the work of Baddar and Warren (J.C.S. 1938, 401). These workers condensed a-ethylglycerol, which is converted into b-ethylacraldehyde by concentrated sulphuric acid, with anthranol under the conditions of Bally's reaction and obtained 3-ethylbenzanthrone, the constitution of which was verified by ring closure of o-4'-ethyl-1'-naphthylbenzoic acid:-



A later synthesis of benzanthrone carried out by Scholl and Seer (Ann. 1912, 394, 111), involved "baking" α-benzoylnaphthalene with aluminium chloride, a process of aerial oxidation which also finds application in the synthesis of substituted benzanthrones.

Another synthesis of benzanthrone which leaves no doubt as to its constitution was that carried out by Schaarschmidt (Ber. 1918, 51, 1082). Allochryso-ketone-carboxylic acid (II) was prepared by the action of aluminium chloride in hot benzene on 1-phenyl-naphthalene-2:3-dicarboxylic anhydride (I). When II is slowly heated above its melting point it loses carbon dioxide to form benzofluorenone (III). Fusion with alkali converts this compound into o-1-naphthyl-benzoic acid (IV). The acid chloride of this compound is converted quantitatively into benzanthrone by solution in benzene and treatment with aluminium chloride.



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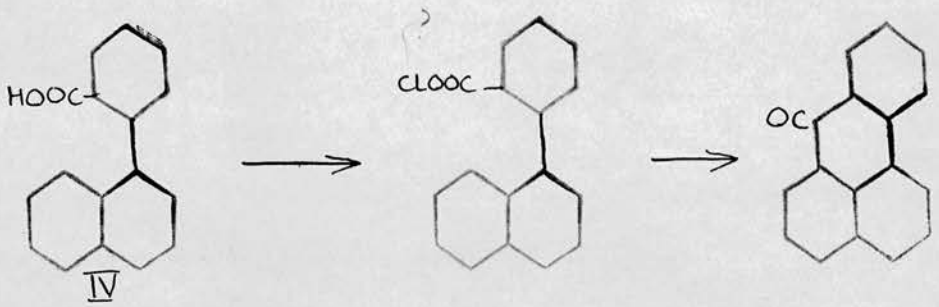
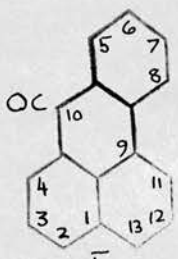


IV

Benzanthrone forms yellow needles of melting point 170 - 171°C., dissolving in concentrated sulphuric acid with deep red colour. On chlorination it yields a monochloro derivative m.p. 182°C. described as 3-chlorobenzanthrone and on further chlorination a mixture of isomeric dichloro derivatives (Cahn, Jones and Simonsen, J.C.S. 1933, 444). Bromo derivatives are also known, the 3-bromo being prepared by direct bromination of benzanthrone in acetic acid. Others have been prepared by coupling reactions (see page 14). Nitration of benzanthrone in nitrobenzene gives 3-nitrobenzanthrone while in acetic acid or sulphuric acid solution a mixture of mononitro derivatives is obtained. The hydroxy and methoxy derivatives have a special interest in connection with dyestuffs.

The systematic numbering of benzanthrone and its derivatives is somewhat confusing. The first systems in use took the anthracene nucleus as their basis and are given below (I) and (II), the latter still being employed in the Journal of the Chemical Society and American Chemical Society publications. The Inter-

national system of nomenclature (III) which is used almost exclusively in the present day technical literature and recommended by Heilbron in his Dictionary of Organic Compounds will be used throughout this thesis.



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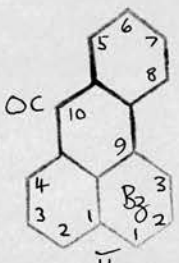
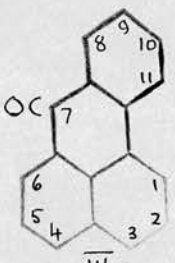
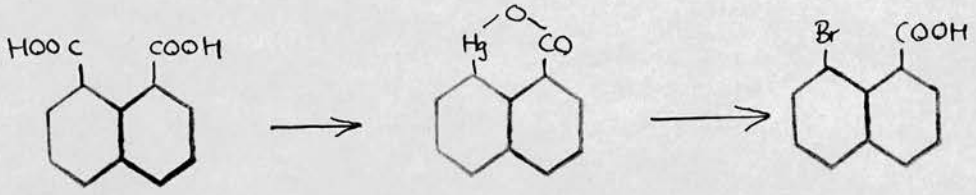


II



III

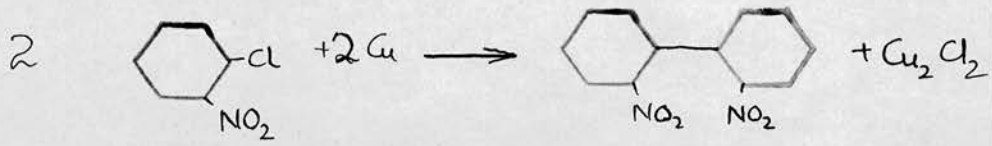
A modern method of wide applicability in the synthesis of benzanthrones uses as starting materials, certain peri-derivatives of naphthalene. During recent years the 8-halogeno-1-naphthoic acids have attracted considerable interest. Rule and co-workers (J.C.S. 1934, 170) employed the mercuration method of Whitmore and co-workers (J.A.C.S. 1929, 51, 1831, 3363) and have found it an eminently satisfactory source of these acids. Naphthalic acid or the anhydride can be mercurated by use of mercuric acetate to give anhydro-8-hydroxymercuri-1-naphthoic acid. This compound on treatment with bromine or chlorine yields the 8-halogeno acid.



The importance of these acids in benzanthrone syntheses rests in their ability to take part in the Ullmann reaction. This reaction, discovered by Ullmann in 1900 (Ber. 1901, 34, 2174; Ann. 1904, 332, 38), consists of treating halogenated aromatic compounds with finely divided copper (copper bronze) at high temperatures. The halogen is eliminated as cuprous halide and a dinuclear product is obtained. Ullmann's investigations showed that the reaction proceeded smoothly with almost all iodo compounds. For example on heating iodobenzene with copper at 230°C. in a sealed tube, diphenyl is formed:

In the case of the corresponding bromo and chloro compounds, however, the halogen was found to be unreactive unless an increased lability was conferred upon it by the presence of other substituents in certain positions. Thus o-nitrochlorobenzene readily under-

goes the reaction to give 2:2'-dinitrodiphenyl.

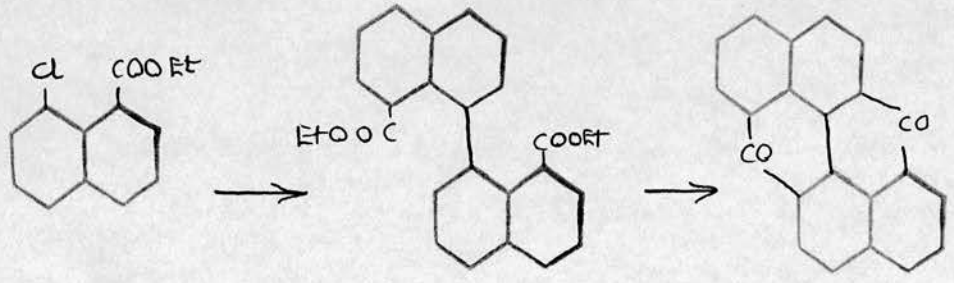


In striking contrast the m- and p- nitrochlorobenzenes are quite unreactive.

A carboxyl group in the ortho position has apparently an activating effect on the halogen similar to that of the nitro group.

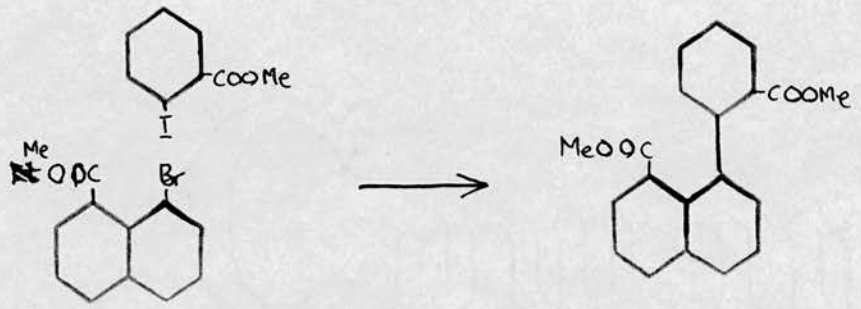
An important extension of the Ullmann reaction lies in the utilisation of mixtures of halogeno compounds to give unsymmetrical products.

Kalb in his synthesis of the dyestuff anthanthrone (Ber. 1914, 47, 1724) was the first to employ the 8-halogeno-1-naphthoic acids, in the form of their esters, in the Ullmann reaction. The ethyl ester of 8-chloro-1-naphthoic acid was treated with copper powder at 290°C. and the diethyl-1:1'-dinaphthyl-8:8'-dicarboxylate formed in small yield was converted quantitatively to anthanthrone by the action of concentrated sulphuric acid.

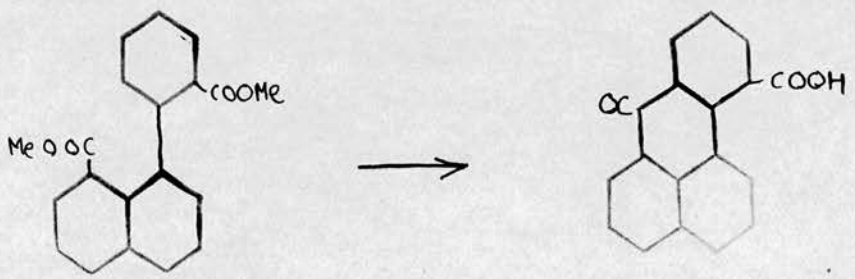


Rule and Barnett (J.C.S. 1932, 2728) in an inves-

tigation of the reactivity of the bromine atom in 8-bromo-1-naphthoic acid concluded that the halogens in methyl-8-bromo-1-naphthoate and methyl-o-iodobenzoate were comparable in reactivity with one another. Barnett (Thesis, Edinburgh 1932) on subjecting these two compounds to the Ullmann reaction at 190 - 200°C. was successful in obtaining a 40% yield of methyl-8-(o-carbomethoxyphenyl)-1-naphthoate:



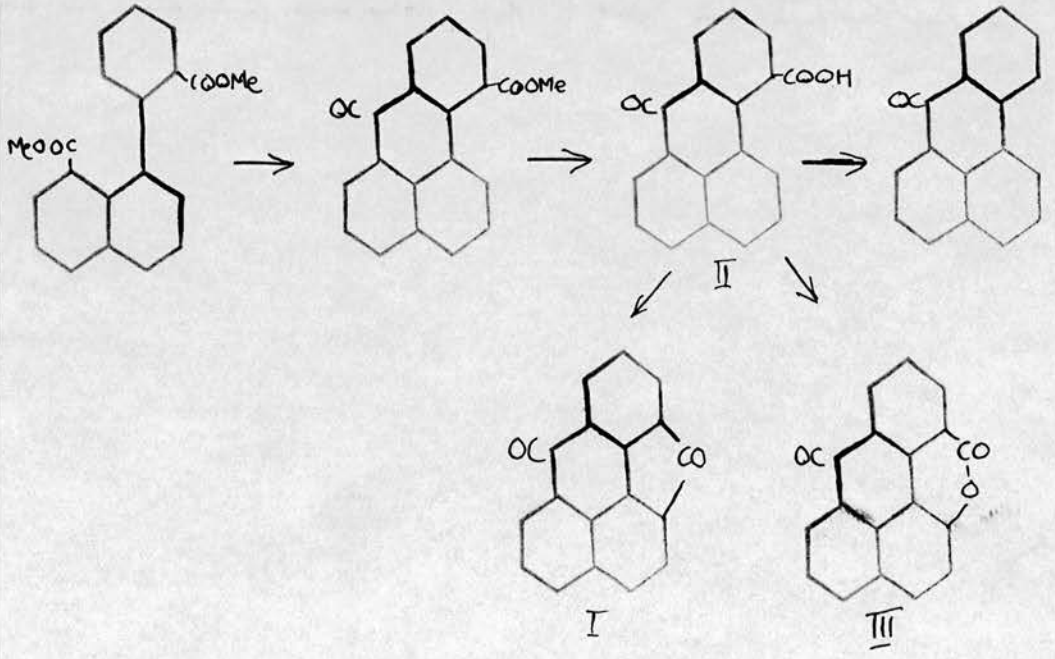
Rule and Pursell (J.C.S. 1935, 571) showed that the phenyl-naphthyl-dicarboxylate obtained by Barnett was, on treatment with concentrated sulphuric acid, converted quantitatively into 11-carboxy-benzanthrone:



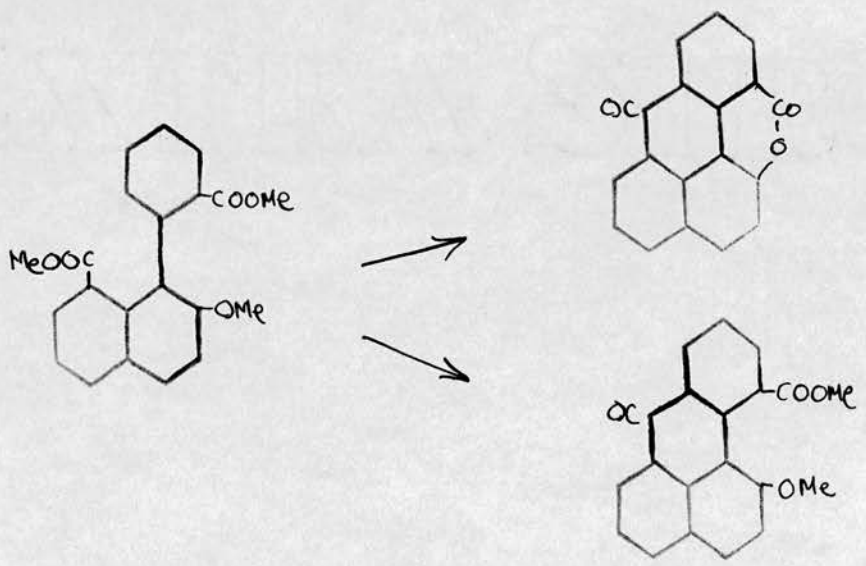
Barnett's preparation has since been examined more thoroughly and by employing a lower temperature in the Ullmann reaction and using excess of the iodobenzoate,

the yield of unsymmetrical product has been considerably increased (F. R. Smith, Thesis, Edinburgh 1935).

Rule and Bigelow (J.C.S. 1935, 573) in an attempt to prepare 1:11-ketobenzanthrone (I) by a further cyclisation of 11-carboxy-benzanthrone (II), showed that on more vigorous treatment of the acid with concentrated sulphuric acid a partial decarboxylation to benzanthrone resulted. This was also accompanied by some oxidation, indicated by the smell of sulphur dioxide, while the yield of the expected ketobenzanthrone was very small. The oxidation product obtained in this reaction was provisionally formulated as the lactone of 1-hydroxy-11-carboxy-benzanthrone. On treatment of the phenyl-naphthyl-dicarboxylate with sulphuric acid at 50°C. an intermediate product - 11-carbomethoxy-benzanthrone - was isolated.



The structure of the oxidation product (III) was later confirmed by J. L. Grieve (Thesis, Edinburgh 1936) who performed the Ullmann reaction at 175°C. with methyl 7-methoxy-8-bromo-1-naphthoate and methyl o-iodobenzoate and obtained a 46% yield of methyl 7-methoxy-8-(o-carbomethoxyphenyl)-1-naphthoate which with concentrated sulphuric acid at 100°C. gave the lactone of 1-hydroxy-11-carboxy-benzanthrone. This compound was identical with the product obtained by the sulphuric acid oxidation of 11-carboxy-benzanthrone. Grieve also prepared 1-methoxy-11-carbomethoxy-benzanthrone by cyclisation of methyl 7-methoxy-8-(o-carbomethoxyphenyl)-1-naphthoate with glacial acetic acid and sulphuric acid at 80°C.:

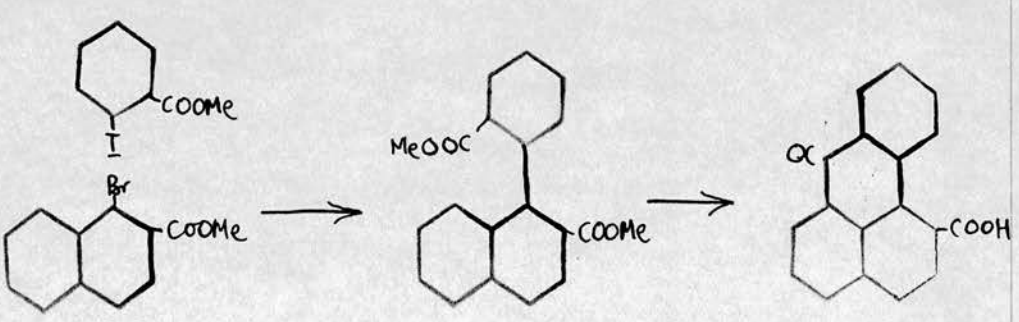


Although the yield of 1:11-keto-benzanthrone obtained by the action of concentrated sulphuric acid on 11-carboxy-benzanthrone was poor, the compound was

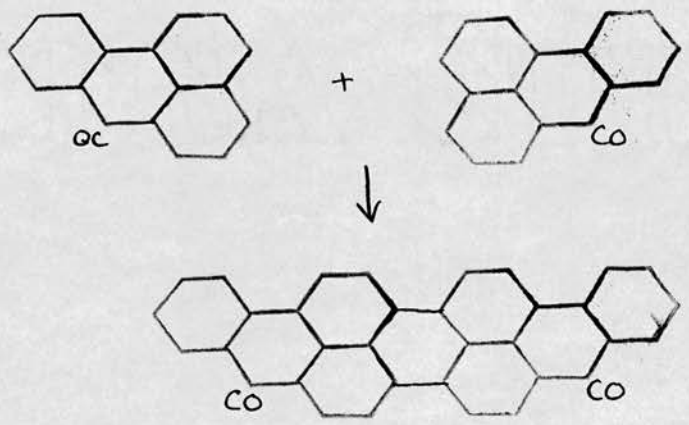
found to be readily prepared by the action of phosphorus pentoxide on a solution of 11-carboxy-benzanthrone in molten phthalic anhydride at 200°C.

1:11-Keto-benzanthrone when heated under reflux with dilute caustic soda, is slowly hydrolysed to give, presumably, a mixture of 1-carboxy-benzanthrone and 11-carboxy-benzanthrone (Rule and Sigelow, J.C.S. 1935, 574). After repeatedly unsuccessful attempts to separate these acids, J. S. Flanders (Thesis, Edinburgh 1938) has obtained a 15% yield of pure ethyl benzanthrone-11-carboxylate from the reaction by partial separation of the mixed ethyl esters by chromatographic adsorption on aluminium oxide from benzene solution.

1-Carboxy-benzanthrone, however, has been synthesised by J. L. Grieve (loc. cit.) by coupling methyl 1-bromo-2-naphthoate with methyl o-iodobenzoate at 175 - 180°C., and cyclising the product with concentrated sulphuric acid. The yield was 3% whereas 90% of the diphenic ester was isolated from the reaction mixture.



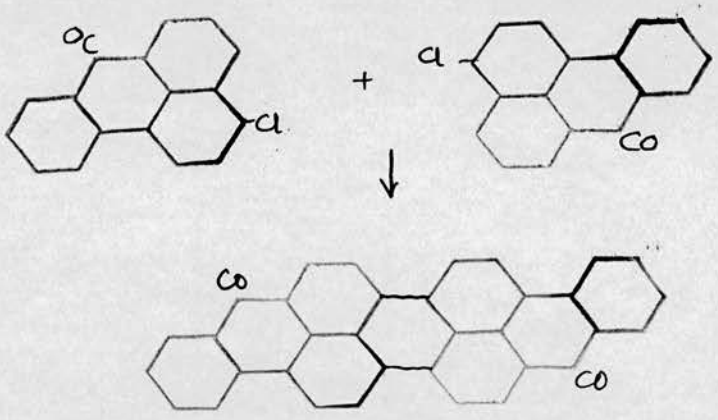
The great technical value of benzanthrone and its derivatives lies in their ability to undergo alkaline fusion to yield dibenzanthrones which are of great value as vat dyes. The parent benzanthrones are not highly coloured and doubt has been cast upon their capacity for vat dye formation. Bally, however, fused benzanthrone with caustic alkali at 230 - 240°C. and obtained a dark blue vat dye (Ber. 1905, 38, 195; G.P. 185221) which Scholl and Seer (Ann. 1912, 394, 126) showed to have the structure indicated below, the union of the two benzanthrone molecules occurring at the positions 3 and 4.



This product, known at first commercially as Violanthrone, now appears on the market as Indanthrene Dark Blue B.O., Caledon Dark Blue B., etc. From a red violet hydrosulphite bath it dyes cotton in very fast dark blue shades.

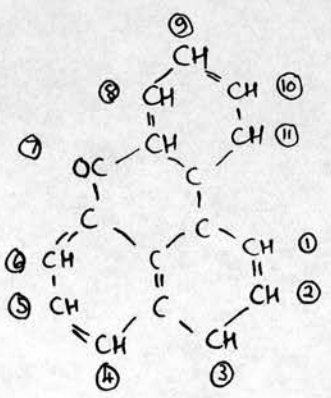
The symmetrical isomeride, iso-dibenzanthrone, is

the parent compound of a second class of dyes. It is also known as Isoviolanthrone and was prepared originally by the action of alcoholic potassium hydroxide on 3-chlorobenzanthrone.



The action of alcoholic potassium hydroxide on the 3:3'-dibenzanthronyl sulphides and selenides is also productive of isoviolanthrone and forms a more recent method of preparation (G.P. 443262; B.P. 367462).

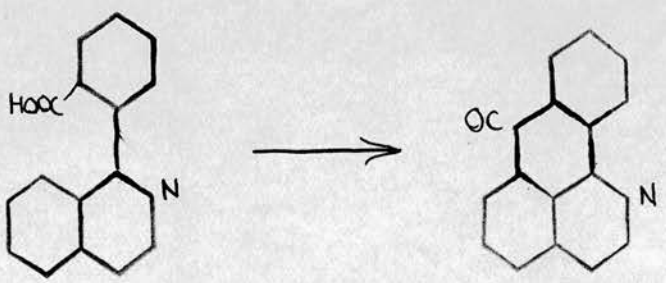
This value of benzanthrones as dyestuffs has stimulated a vast amount of industrial research and among derivatives investigated in the hope of procuring further dyestuffs or intermediates are the azabenzanthrones, in the molecules of which a nitrogen atom is substituted for one of the :CH. groups of the nucleus:



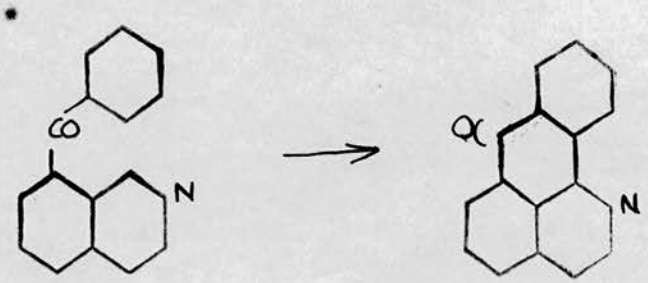
From the formula it can be seen that ten different azabenzanthrones are theoretically possible, namely those with a nitrogen atom in positions 1, 2, 3, 4, 5, 6, 8, 9, 10 and 11. Of these either the parent or derivatives are known of six with certainty, viz. 1-, 2-, 3-, 8-, 9- or 10- and 11- azabenzanthrone. Derivatives of others may be known but a certain amount of confusion has arisen in the literature regarding the nomenclature despite the three systems quoted on pages 10 and 11.

All the azabenzanthrone literature is patent literature as the research has all been carried out industrially and indeed the present thesis appears to be the first to deal academically with a member of the group.

Reverting to cases where there is no confusion, 1-azabenzanthrone has been prepared by heating b-phenyl-ethyl-phthalimide to 160°C. for 8 hours with a mixture of sodium chloride and anhydrous aluminium chloride, giving 1-phenyl-isoquinoline-2'-carboxylic acid, m.p. 235 - 237°C. Heating this to 100°C. with fuming sulphuric acid yields 1-azabenzanthrone, (G.P. 614196; Chemical Abstracts (hereafter C.A.) 1935, 29, 5859).



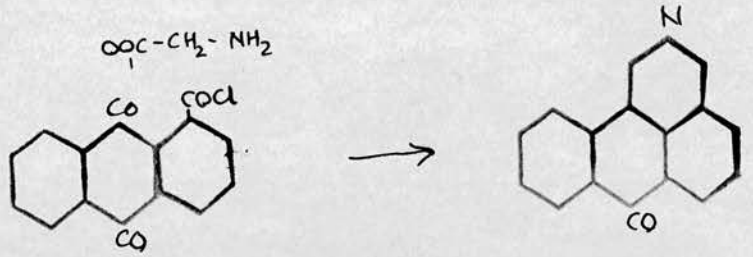
It may also be prepared by heating 4-benzoyl-isoquinoline with aluminium chloride (B.P. 450244; C.A. 1936, 30, 8638).



It is also described in F.P. 781562; C.A. 1935, 29, 6249.

Numerous derivatives are known; among them are 6-chloro-1-azabenzanthrone, m.p. 168 - 170°C., prepared from 1-phenyl-7-chloroisoquinoline-2'-carboxylic acid (F.P. 781562; C.A. 1935, 29, 6249: U.S.P. 2086704; C.A. 1937, 31, 6478); 9-chloro-1-azabenzanthrone made from b-phenyl-ethyl-4-chlorophthalimide (loc. cit.); and a methyl-1-azabenzanthrone, m.p. 208 - 209°C. (F.P. 780041; C.A. 1935, 29, 5859). A 1:3-diaza-benzanthrone is also described in the same patent. It melts at 180°C. Condensation products of 1-azabenzanthrone, its homologues and derivatives, are described in B.P. 421264; C.A. 1935, 29, 3531.

2-Azabenzanthrone and its derivatives may be prepared from anthraquinone-1-carboxylic acid halides by condensing with amino-acetic esters, treating with alcohol, saponifying and splitting out carbon dioxide.

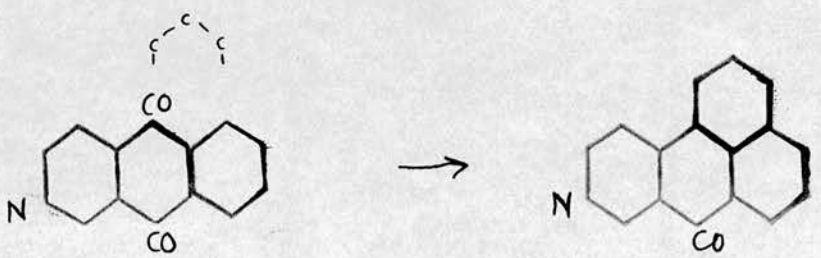


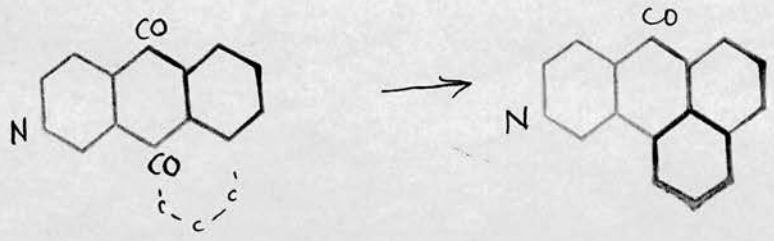
The parent compound is described in B.P. 450244; C.A. 1936, 30, 3638, and in G.P. 621455; C.A. 1936, 30, 1069, wherein also is described the 3-hydroxy-2-azabenzanthrone of melting point 334°C.

3-Azabenzanthrones are described in F.P. 780041; C.A. 1935, 29, 5859. Among the compounds mentioned are 8-amino-4:9-dimethyl-3-azabenzanthrone, 1-dibenzyl-3-azabenzanthrone, p-chloro-benzal-3-azabenzanthrone, a methyl-3-azabenzanthrone and an ethyl-3-azabenzanthrone.

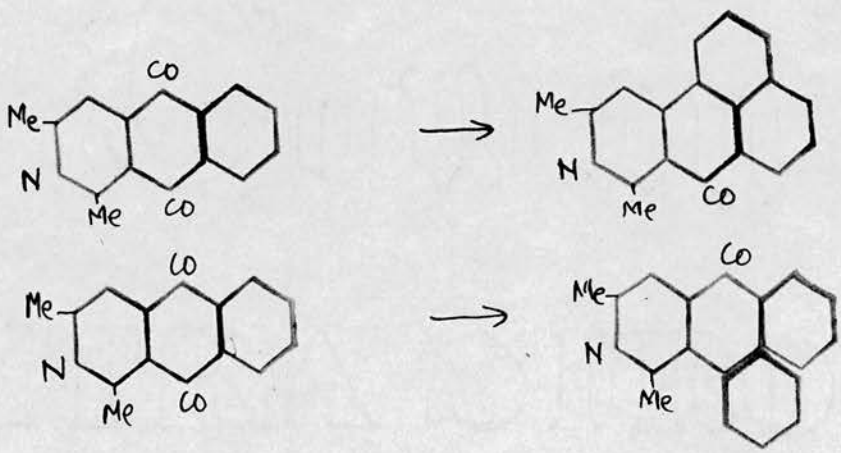
The preparation of 8-azabenzanthrone and its derivatives is described in F.P. 753828; C.A. 1934, 28, 1060, and condensation products of it, its homologues and derivatives in B.P. 421264; C.A. 1935, 29, 3531.

A very useful method of preparation is the Skraup reaction on b-azanthraquinones:





This reaction can give either 9-azabenzanthrone or 10-azabenzanthrone and probably gives a mixture of both, (G.P. 634968; C.A. 1937, 31, 417) but there is no certainty on this point. Treatment of 1:3-dimethyl-2-azabenzanthrone is described and the product will be either 8:10-dimethyl-9-azabenzanthrone - the goal of this part of the work - or 9:11-dimethyl-10-azabenzanthrone, but no distinction is mentioned.



Similarly are described the production of 11-methyl-9-phenyl-10-azabenzanthrone or 8-methyl-10-phenyl-9-azabenzanthrone; 9:11-dimethyl-4-benzyl-10-azabenzanthrone

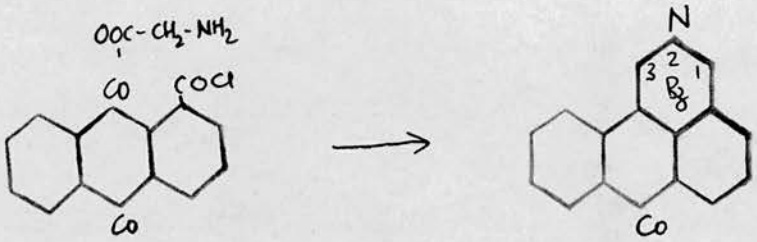
or 8:10-dimethyl-5-benzyl-9-azabenzanthrone and a bromo derivative of the 8:10-dimethyl-9-azabenzanthrone or of the 9:11-dimethyl-10-azabenzanthrone.

The preparation of 9- and 10- azabenzanthrones may also be described in B.P. 450244; C.A. 1936, 30, 8638, (see pages 22 and 23). Also in this group are, presumably, the b-azabenzanthrones of F.P. 802157; C.A. 1937, 31, 1429, wherein apparently no attempt is made to distinguish the two possible isomers.

Numerous derivatives of 11-azabenzanthrones are known, prepared from pyridinonaphthalenes by the Skraup reaction (F.P. 753828; C.A. 1934, 28, 1060). Among derivatives mentioned are 3-bromo-11-azabenzanthrone, m.p. 214 - 215°C.; 3:9-dibromo-11-azabenzanthrone, m.p. over 300°C.; 2-nitro-11-azabenzanthrone (U.S.P. 2013659; C.A. 1935, 29, 6905); 1-hydroxy-11-azabenzanthrone and its methyl ether, an amino-11-azabenzanthrone, a sulpho-11-azabenzanthrone and a cyano-11-azabenzanthrone, (G.P. 622464; C.A. 1936, 30, 1584); and 3-a-anthraquinonyl-11-azabenzanthrone (F.P. 753828; C.A. 1934, 28, 1060). Condensation products of the parent, its homologues and derivatives are described in B.P. 421264; C.A. 1935, 29, 3531.

The confusion in the literature mentioned on page 20 may be illustrated by reference to the British Patent 450244 (C.A. 1936, 30, 8638) wherein it is stated that Bz-2-azabenzanthrones may be obtained by condensing anthraquinone-1-carboxylic acid chloride

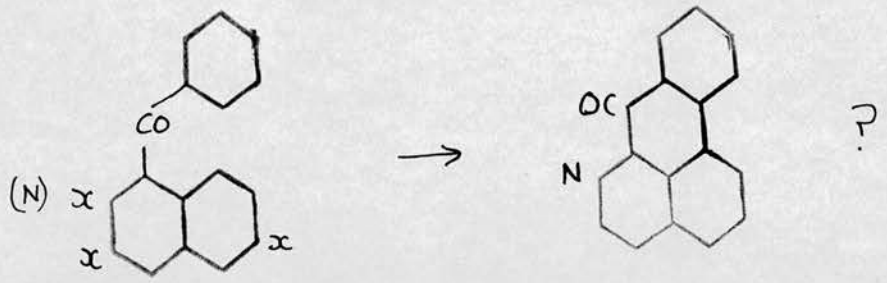
with amino-acetic esters, etc.



This accords with the first scheme of numbering on page 11 , giving 2-azabenzanthrones on the International system. The patent then states that Bz-3-azabenzanthrones are prepared by treating 4-benzoyl-isoquinolines having a reactive 5 position with a condensing agent of the aluminium chloride type. This must be formulated:

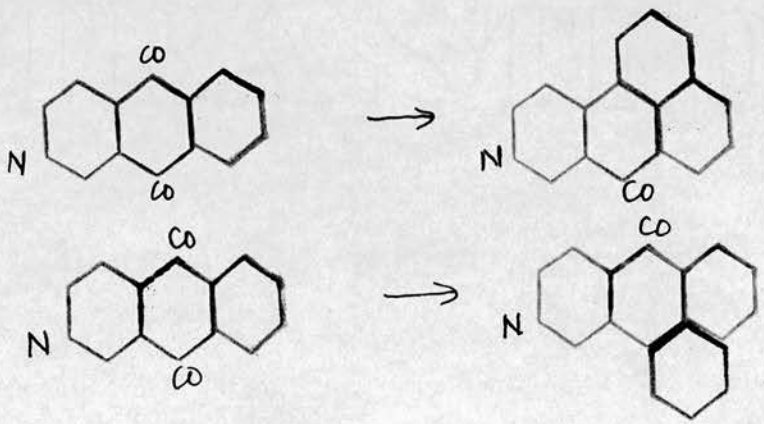
giving 1-azabenzanthrones on the International notation.

This is comprehensible but the next statement is that Bz-4-azabenzanthrones are similarly derived from 1-benzoyl-isoquinolines having a reactive 8 position. On no known system of numbering is there a Bz-4-position. The reaction itself must be formulated:



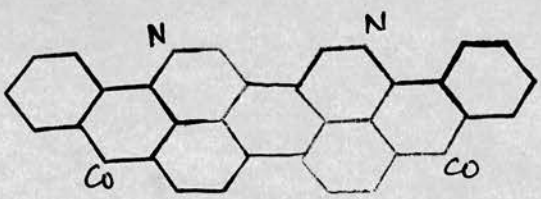
and the nitrogen atoms must be in one of the positions X. It is conceivable that Bz-4- is a misprint for 4- but the matter could not be verified by a reference to the Chemisches Zentralblatt for the patent was not abstracted in that Journal. Assuming 4- for Bz-4- gives the nitrogen atom in position 2 in the isoquinoline and 6 in the product on the International system and hence 6-azabenzanthrones may be known.

The next statement in the patent is that Bz-6- and Bz-7- azabenzanthrones are obtained from b-azanthraquinones or their reduction products by treatment with glycerol and concentrated sulphuric acid. Assuming the same misprint we have



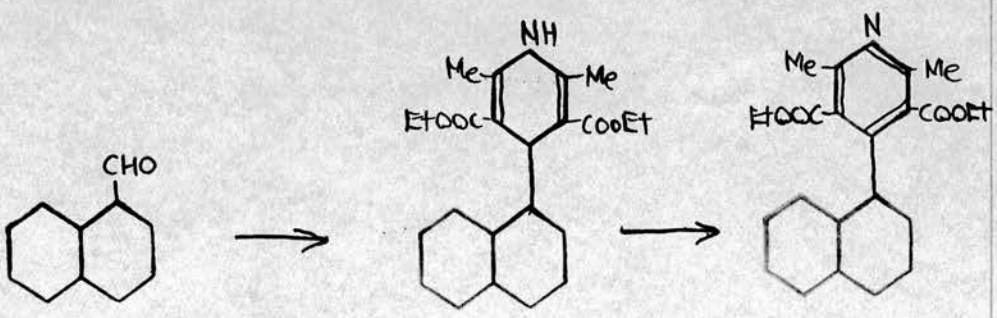
a series of reactions already known (pages 22 and 23).

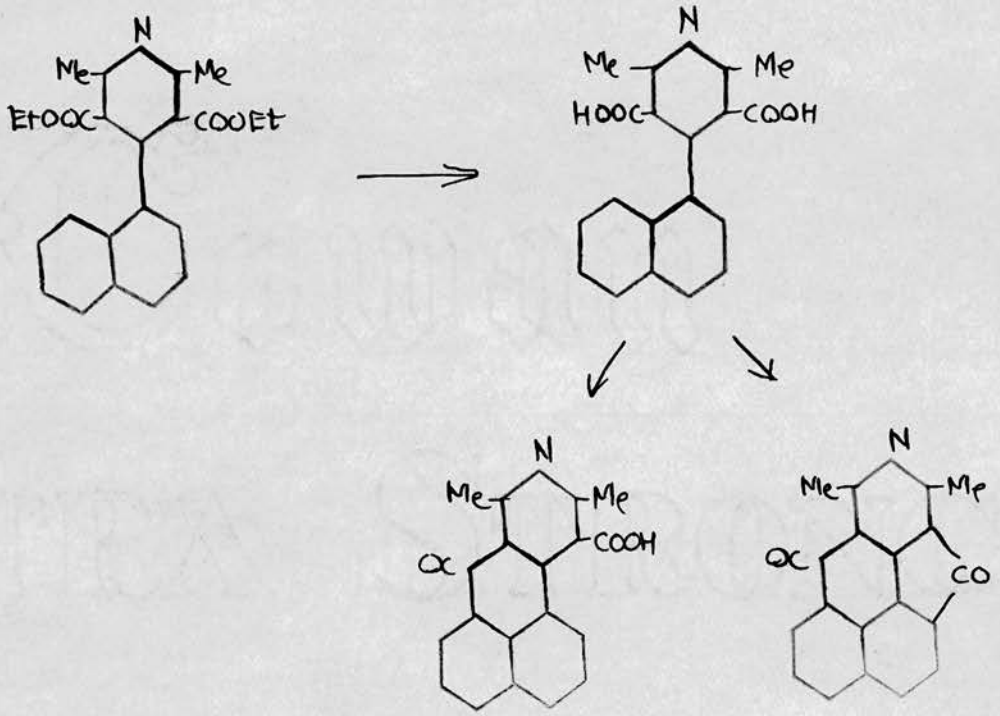
It is very significant that throughout the whole of this mass of patent literature there is no mention whatever of diazadibenzanthrones. Analogous with dibenzanthrones such compounds would have the formula, to take the case of 1:1'-diazadibenzanthrone



This indicates that azabenzanthrones do not generally undergo fusion with alkali to diazadibenzanthrones to give dyes as this surely would have been the most important property to patent.

In view of the uncertainty as to whether derivatives of 9-azabenzanthrone are known in the free state the present work is an attempt to prepare derivatives of 9-azabenzanthrone by an entirely new method of approach, viz. a Hantzsch synthesis on α-naphthaldehyde, oxidation of the resulting ester, complete hydrolysis to the dicarboxylic acid and cyclisation to derivatives of 9-azabenzanthrone:




N
Me
Me
EtOOC
COOEt
N
Me
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HOOC
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N
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Me
COOH
O
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O
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SUMMARY OF EXPERIMENTAL WORK

AND DISCUSSION OF RESULTS

The scheme proposed for the synthesis of the azabenzanthrone derivatives dealt with in this thesis is a new method of approach to the azabenzanthrone molecule, but it is a synthesis that can be applied only to derivatives of 9-azabenzanthrone.

The process uses as starting material α-naphthaldehyde, on which is performed the specialised synthesis associated with the name of Hantzsch. It was anticipated at the outset of the work that the preparation of sufficient quantities of the starting material might present considerable difficulty and this was borne out in the first attempts to prepare the aldehyde.

The older methods of preparation either involve just as inaccessible starting material or the process is extremely tedious and for these reasons recourse was had to the idea of reducing α-naphthoyl chloride with hydrogen in the presence of a palladium catalyst. α-Naphthoic acid was treated with thionyl chloride on

the water bath under reflux for ninety minutes and the excess thionyl chloride was removed from the brown liquid by vacuum distillation. The remaining liquid was distilled in an all glass apparatus. The a-naphthoyl chloride obtained was yellow in colour and distilled at 293°C.

The palladium catalyst was prepared by adding 20 grams of freshly prepared barium sulphate to 450 mils. of hot water, then 1.7 grams of palladium chloride in 50 mils. of water and also 1 gram of 40% formalin solution. This mixture was made slightly alkaline with sodium hydroxide and heated to boiling for a time. When the supernatant liquid was clear and colourless the grey material was filtered off and washed with hot water until it was neutral to litmus. The catalyst was dried in vacuo over potassium hydroxide.

The reduction of the a-naphthoyl chloride was then attempted. 22 grams of this acid chloride were dissolved in 60 grams of xylene and the mixture placed in a round bottomed flask with a ground-in condenser. Four grams of catalyst were added and dry hydrogen was passed down a narrow tube inside the condenser into the solution. When all the air had been displaced the flask was heated cautiously with a bunsen flame and the solution boiled for eight hours, carefully dried

hydrogen being passed in continuously all the time. On cooling, the contents of the flask crystallised and the crystals melted at 150°C. and proved to be a-naphthoic acid. In spite of precautions taken, it appears, therefore, that moisture had gained access to the reactants.

An alternative method of aldehyde preparation under examination was that discovered by Stephen, (J.C.S. 1925, 1874) which consists in reducing the corresponding nitrile through the imino chloride to the aldehyde with anhydrous stannous chloride in dry ether saturated with hydrogen chloride. The method has proved of value in the preparation of b-naphthaldehyde and althoughtStephen declares that the yield is very poor in the case of a-naphthonitrile, the preparation was attempted. Anhydrous stannous chloride was prepared by cautiously adding 35 grams of acetic anhydride (2 mols.) to 35 grams of $SnCl_2.2H_2O$ (1 mol.). The mixture was filtered and the solid washed with dry ether.

The finely powdered stannous chloride was suspended in dry ether and saturated with hydrogen chloride until two layers formed. The two layers later appeared to vanish and a homogeneous suspension remained. The a-naphthonitrile, 15 grams, was added

with shaking and a yellow-green solution formed. The reaction was continued when a white powder appeared. The mixture was placed on a shaking machine and after shaking overnight yellow crystals were deposited. These were filtered off, washed with dry ether and hydrolysed by being boiled with water for thirty minutes. The solution was then steam distilled but only water came over. a-Naphthaldehyde is volatile in steam.

Attention by this time had been directed to a recent and more promising method of preparing a-naphthaldehyde and Stephen's method was not pursued further. The method of Hinkel, Ayling and Benyon, (J.C.S. 1936, 340) was not at first tried because of the necessity of using anhydrous hydrogen cyanide. As other methods, however, proved unsatisfactory, this one was attempted.

The method consists in treating the corresponding hydrocarbon with the double compound of aluminium chloride and hydrogen cyanide in the presence of hydrogen chloride for a specific time at a specific temperature, hydrolysing the product and steam distilling. The process is applicable only to aromatic hydrocarbons.

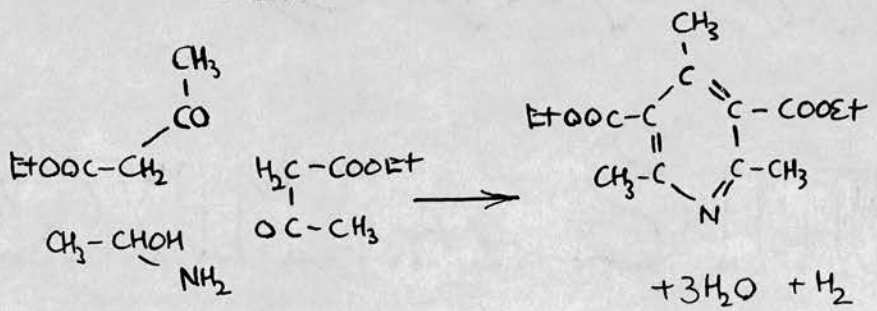
Anhydrous hydrogen cyanide is not readily available commercially and it was prepared by the method described

in Organic Syntheses, volume 7, page 50. This involved simultaneously dropping solutions of 500 grams of concentrated sulphuric acid in 500 grams of water and of 406 grams of sodium cyanide in a litre of water into a large flask. The hydrogen cyanide liberated was dried in a calcium chloride tube and condensed by being passed through a coil immersed in ice water. The product, generally 210 grams, or 84% theoretical, was slightly yellow in colour but was quite satisfactory for use without further purification.

Powdered aluminium chloride was suspended in chlorobenzene, the medium in which the reaction was conducted, and hydrogen cyanide dropped in. Stirring was employed throughout the reaction. Naphthalene was added and hydrogen chloride passed in. The reaction was conducted for 5 hours at 70°C., when the reactants were poured on to a mixture of ice and concentrated hydrochloric acid. After boiling the product was submitted to steam distillation and the aldehydic distillate extracted with ether and shaken with saturated sodium bisulphite solution. The aldehyde-bisulphite compound was separated and decomposed with dilute sulphuric acid and the free aldehyde isolated by steam distillation, extraction with ether and distillation. α-Naphthaldehyde was obtained as a yellow liquid boiling

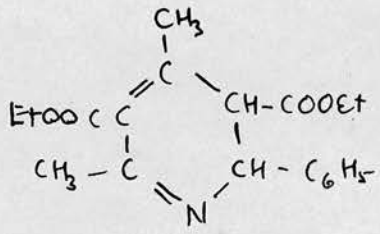
at 290°C. The yields obtained in later experiments were 35%. This figure was considered quite satisfactory and the reaction was deemed to be a very useful means of preparing a-naphthaldehyde which had hitherto been regarded as rather inaccessible.

The aldehyde was a yellow liquid with a characteristic smell. It appeared to keep quite well. The next stage of the series of reactions was the performance of a Hantzsch synthesis on the aldehyde. This reaction was first described by Hantzsch (Ann. Chem. Pharm. 215, 1; 215, 75) when he warmed aldehyde ammonia with ethyl acetoacetate and obtained what, after further oxidation, proved to be a dicarbethoxy-collidine. Hantzsch postulated the mechanism of the reaction to be (Ber. 1884, 17, 1512):

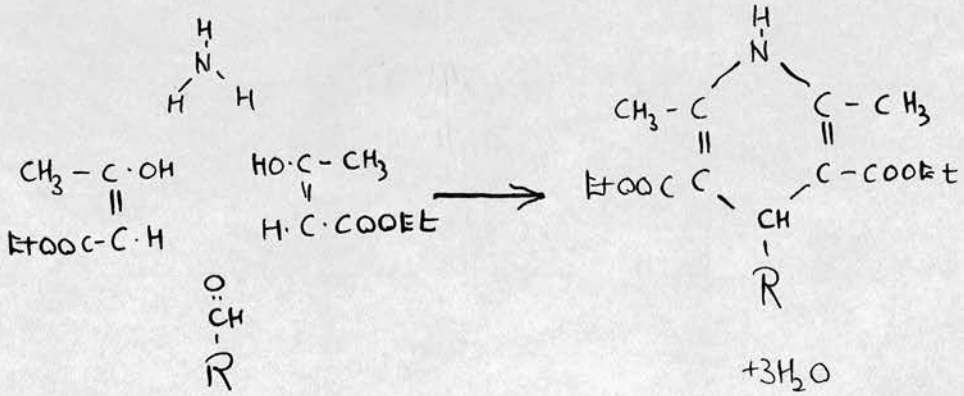


The reaction was extended to benzaldehyde by Schiff and Puliti (Ber. 1883, 16, 1607) who showed that an analogous phenyl dihydrolutidine dicarboxylic ethyl

ester was obtained and for which they proposed the constitution



The exact orientation of the substituents in the pyridine ring proved a fruitful field for investigation about that period and it was eventually shown by Hantzsch in a series of papers (Ber. 1884, 17, 1437; Ber. 1885, 18, 1744; Ber. 1885, 18, 2579) that the group of atoms attached to the aldehyde group taking part in the reaction was in the para position to the nitrogen of the pyridine ring. The mechanism of the reaction can best, therefore, be interpreted as



The mode of carrying out the reaction appeared to be perfectly simple, these earlier workers having merely warmed the mixture of reactants when the product separated out. The reaction was carried out in ethyl alcohol solution.

Accordingly 15 grams of a-naphthaldehyde and 25 grams of freshly distilled ethyl acetoacetate were mixed in a flask and 40 mls. of a saturated solution of ammonia in ethyl alcohol added down the condenser. The reactants were heated on the water bath for thirty minutes but on cooling no crystals separated out. The mixture was then refluxed for two hours and allowed to stand. After standing for several days, violent shaking led to the deposition of yellow crystals which soon filled the whole solution. Having stood overnight these yellow needles were filtered off, washed with ethyl alcohol and recrystallised from ethyl alcohol when the melting point was 200 - 202°C. Benzene proved to be a better agent and after a further two recrystallisations the melting point remained unchanged at 201.5°C. The yield was 30% of the theoretical.

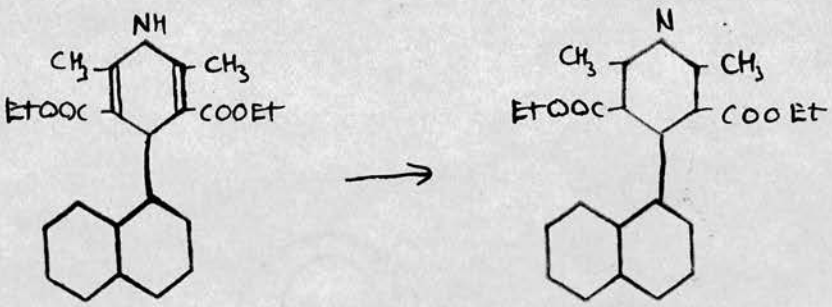
A modification was introduced later by which ammonia gas was passed continuously into the reaction mixture by means of a long tube passing down the condenser. This procedure raised the yield to 62% of the

theoretical.

The product consisted of fine white crystals which did not dissolve in alkali; they were also insoluble in acids which is somewhat unexpected in a pyridine derivative. The analysis figures, however, corresponded almost exactly to those expected for the anticipated 4-a-naphthyl-3:5-dicarbethoxy-2:6-dimethyl-1:5-dihydropyridine. To confirm this point the preparation of Schiff and Puliti was repeated and the phenyl dihydrolutidine dicarboxylic ethyl ester was found also to be insoluble in dilute acids. This indicates that the observed behaviour towards aqueous acids is probably general for complex esters of this type.

The next stage in the process was accomplished in the original Hantzsch synthesis and in later adaptations of it by oxidising the ester obtained, by nitrous fumes and in this case it was found that nitrous fumes oxidised the dihydro compound to the normal pyridine derivative quite satisfactorily. The white crystals of the ester were mixed with an equal weight of ethyl alcohol and nitrous fumes passed in over two and a half hours, the all glass reaction vessel being cooled in running water. The crystals of the ester slowly dissolved leaving a reddish solution. The alcohol was

distilled off on the steam bath and the acid residue neutralised with sodium carbonate. The excess carbonate was removed by filtration and the filtrate extracted with ether. When the red ethereal extract was warmed to remove the ether a red oil was left. The yield was 91% of the theoretical.



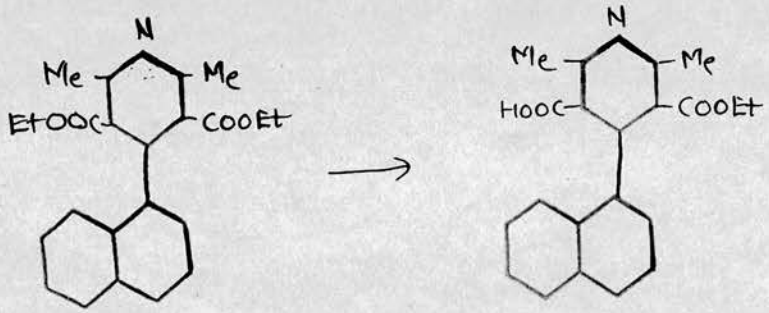
It was found that this oil could very well be used in the crude state for the next stage of the synthesis and this was the practice generally employed. On one occasion however, the treatment with nitrous fumes was continued for twelve hours, and when the product was treated with ether a pink solid was thrown down. This was filtered off and when the ether was removed from the ethereal extract the usual red oil was obtained. The pink solid was first of all supposed to be a nitro-derivative of the oxidised ester. It was recrystallised twice from ethyl alcohol when the melting point remained unchanged at 99.5 - 100°C. On analysis, how-

ever, the figures did not agree with those required by a nitro-derivative but coincided almost exactly with those calculated for the nitrate of the oxidised ester. If this was the case confirmation would be simple because treatment with dilute ammonia solution should leave the free oxidised ester, viz. 4-α-naphthyl-3:5-dicarbethoxy-2:6-dimethyl-pyridine. The presumed nitrate was treated with hot dilute ammonia when the solid melted to a discrete pink oil. A portion of the solution gave a positive brown ring test for a nitrate, confirming the constitution as the nitrate. When the oil was cooled it solidified and was then washed with water and dried. The solid was recrystallised from ethyl alcohol until the melting point remained unaltered at 59 - 60°C. On analysis the figures found coincided with the values calculated for the free ester.

As mentioned above, the usual practice in carrying out this series of reactions was not to obtain the oxidised ester in the pure state but to hydrolyse the crude oil resulting from two and a half hours' treatment with nitrous fumes.

Hydrolysis proved difficult to effect. In the first instance the oil was boiled for four hours with a slight excess of alcoholic potassium hydroxide. On pouring the reaction mixture into water and acidifying

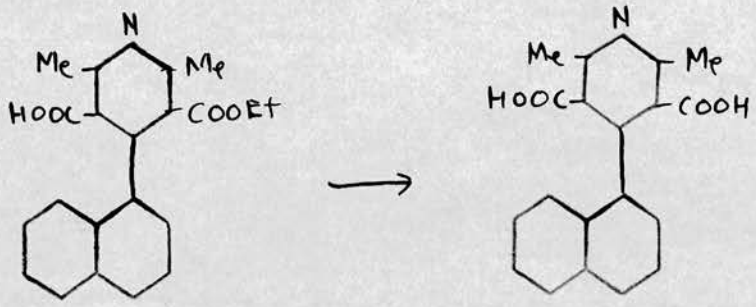
with sulphuric acid, a cream coloured solid was thrown out, which was found on analysis to be the half-hydrolysed ester, 4-a-naphthyl-3-carboxy-5-carbethoxy-2:6-dimethyl-pyridine.



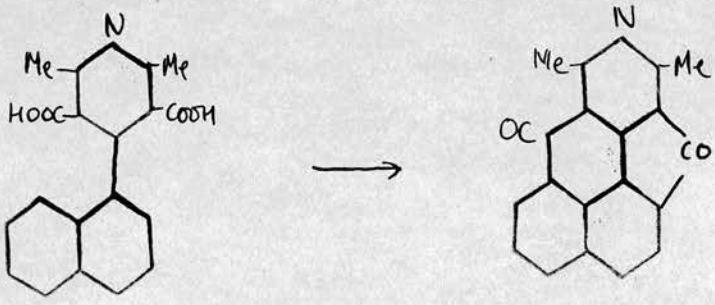
In order to bring about complete hydrolysis it was necessary to employ a considerable excess of alkali and to heat under reflux for 100 hours. Hydrolysis was also effected by use of a mixture of glacial acetic acid, concentrated sulphuric acid and water in the ratio 4:2:1. The respective yields from these two methods were 98% and 68% theory. Both products could be recrystallised from ethyl alcohol and melted with vigorous gassing about 329°C. The individual figures varied a few degrees on either side of this temperature with each treatment but as the figures represent decomposition temperatures the small observed differences are of little significance and are probably due to variations in the rate of heating. A mixture of the two products also

gassed at 329°C.

Although ethyl alcohol appeared the best solvent for recrystallisation the process was so uneconomical that the material was generally used in the crude state. One portion, however, was recrystallised three times and analysed satisfactorily.



The next stage in the series of reactions was the cyclisation of 4-a-naphthyl-3:5-dicarboxy-2:6-dimethyl-pyridine. Treatment with phosphorus pentachloride followed by aluminium chloride was found to effect complete ring closure giving 1:11-keto-8:10-dimethyl-9-azabenzanthrone.

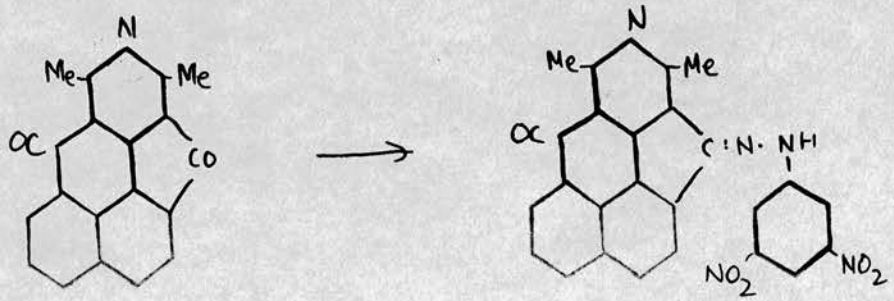


The process was carried out by treating 4-a-naphthyl-3:5-dicarboxy-2:6-dimethyl-pyridine with dry phosphorus pentachloride in dry benzene until no more hydrogen chloride was evolved. The benzene and phosphorus oxychloride formed were removed in vacuo and aluminium chloride, freshly powdered, and carbon tetrachloride were added and the mixture refluxed for six hours. On cooling and pouring on to ice a dark solid was obtained. This was digested with ammonia for thirty minutes to dissolve alkali soluble impurities, whereupon the solid material was filtered off, washed and dried. The digestion was repeated after which the solid consisted of a dark coloured powder with a tinge of green. The yield was 20% and the material did not melt below 360°C. but melted and burned on a platinum foil. It was quite insoluble in ammonia but sparingly soluble in dilute hydrochloric acid. It was slightly soluble in ethyl alcohol and more so in normal propyl alcohol. It was recrystallised from propyl alcohol, six litres being required for one gram, from which it separated as an orange powder and was further purified by being recrystallised from hydrochloric acid. On analysis the figures were found to agree closely with those for the hydrochloride of the ketoazabenzanthrone.

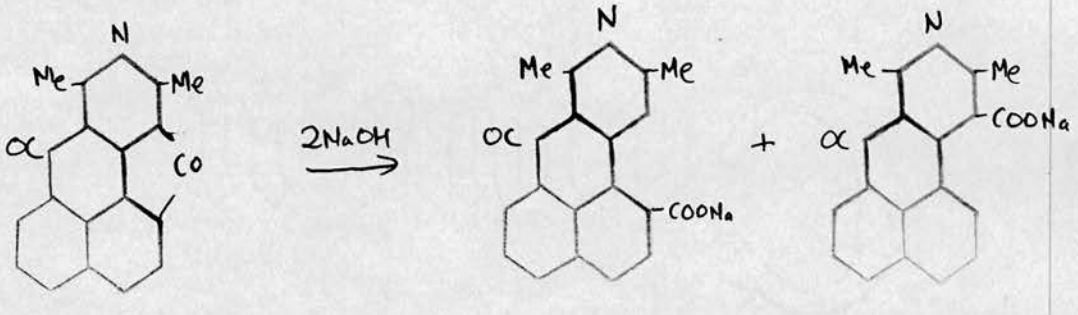
To prepare the pure free 1:11-keto-8:10-dimethyl-9-azabenzanthrone the hydrochloride was digested with

dilute ammonia and filtered and the process repeated until the filtrate contained no chloride ion. The compound was similar in appearance to the hydrochloride. It did not melt below 360°C. but melted and burned on a platinum foil. It analysed satisfactorily.

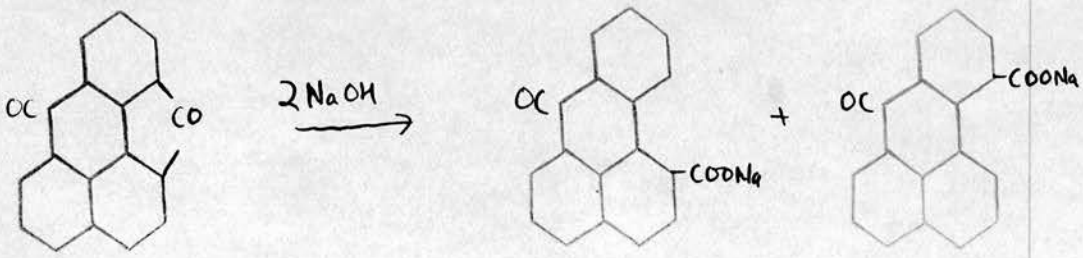
The formation of ketoazabenzanthrone was confirmed by its conversion into the dinitrophenyl hydrazone. The usual procedure was carried out and fine clusters of orange crystals were obtained. These were recrystallised from ethyl alcohol with some difficulty and orange crystals obtained which did not melt below 360°C. The nitrogen percentage was 15.8. The calculated percentage was 15.1; that for the reagent 28.3 and that for the starting material 4.9. There is thus no doubt that the dinitrophenyl hydrazone of 1:11-keto-8:10-dimethyl-9-azabenzanthrone had been prepared, confirming the constitution of the cyclised product.



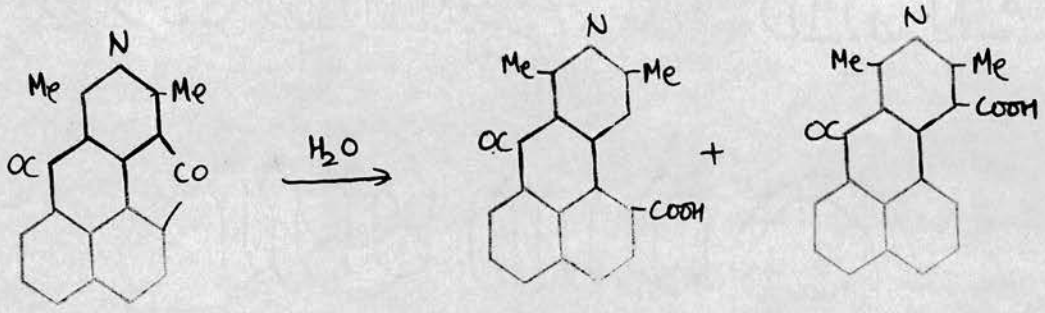
Two hydrolysis experiments were carried out on the ketoazabenzanthrone. In the first it was found that the compound was hydrolysed to, presumably, a mixture of 1-carboxy-8:10-dimethyl-9-azabenzanthrone and 11-carboxy-8:10-dimethyl-9-azabenzanthrone, to an extent of about 25% on being boiled with dilute sodium hydroxide for six hours.



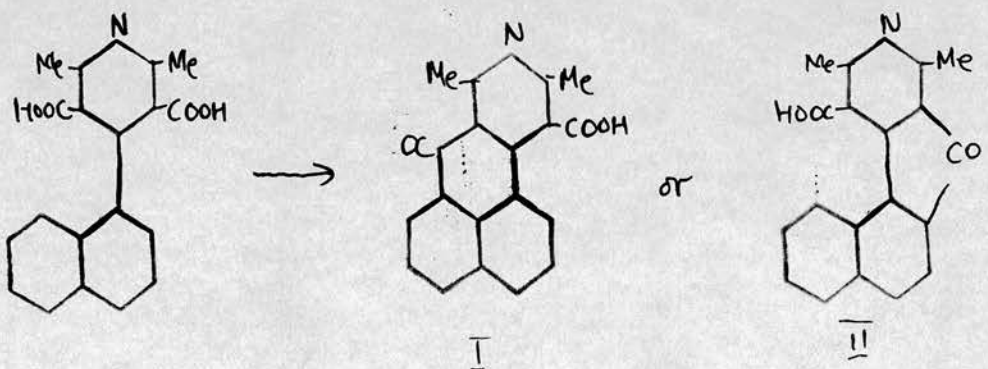
This behaviour is comparable with that of the corresponding nitrogen-free compound, 1:11-ketobenzanthrone, which on prolonged heating with aqueous alkali suffers rupture at the ketonic link to give presumably, a mixture of 1-carboxybenzanthrone and 11-carboxybenzanthrone (J.C.S. 1935, 573; J.S.Flanders, Thesis, Edinburgh 1938; J.C.S. 1938, 1834).



In the second experiment the hydrolytic agent was distilled water and after boiling for 100 hours the extent of the hydrolysis was about 5%. This is in striking contrast to the behaviour of 1:11-ketobenzanthrone which is completely unaffected by water, and is indeed a very unusual reaction.



Partial cyclisation of 4-α-naphthyl-3:5-dicarboxy-2:6-dimethyl-pyridine involving only one carboxylic group should give either 11-carboxy-8:10-dimethyl-9-azabenzanthrone (I) or a fluorenone derivative (II):



I II

Identification of such a ring-closed product should be a simple matter for the fluorenone derivative should react as a ketone and form a dinitrophenyl hydrazone whereas the azabenzanthrone derivative ought not to function as a ketone, none of the benzanthrones behaving in this manner.

Several reagents were employed in attempts to effect this cyclisation. On account of its value in the case of benzanthrones concentrated sulphuric acid was the first reagent to be employed. Several treatments for differing times and at different temperatures gave negative results, no product being thrown out when the solution in concentrated sulphuric acid was poured into water. It is very probable that sulphonation occurred in the unsubstituted ring of the naphthalene nucleus giving a product soluble in water. Treatment with 70% sulphuric acid also proved fruitless for probably the same reason.

Experiments with phthalic anhydride and a drop of concentrated sulphuric acid gave negative results and use was then made of chlorosulphonic acid, which has occasionally been employed in the study of benzanthrone derivatives to effect cyclisation.

This agent proved successful giving an orange product. After a variety of experiments the most

satisfactory treatment was found to be as follows: the dicarboxylic acid was treated with 10 to 20 times its weight of chlorosulphonic acid for three hours at room temperature and the rich ruby red solution poured into water drop by drop with vigorous mechanical stirring in a closed vessel. Chlorosulphonic acid reacts violently with water and loss from spurting will ensue if these precautions are not observed. After separation, the orange product was dissolved in dilute ammonia and reprecipitated with hydrochloric acid in an attempt to purify it and also to form the hydrochloride as presumably, all these derivatives will form salts as in the case of the ketoazabenzanthrone. The material did not yield a dinitrophenyl hydrazone and thus is not a fluorenone derivative but may be presumed to be the desired carboxyazabenzanthrone derivative.

Organic solvents were found to be useless for purifying the compound as hydrochloric acid was the only liquid in which it dissolved appreciably on heating and from which it separated out on cooling. A chlorine analysis showed the preparation to be a mixture of the hydrochloride and the free acid. Recrystallisation from concentrated hydrochloric acid failed to raise the percentage of chlorine and it was thus concluded that the hydrochloride was not being formed quantitatively.

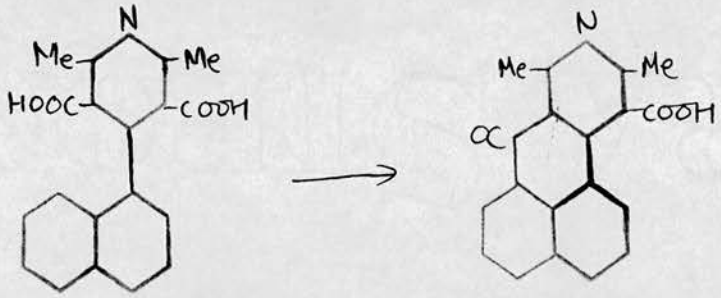
It was then thought that the hydrochloride might be more soluble in water than the free acid and that, consequently, boiling out with water might leave a residue of free acid. The mixture was therefore boiled out repeatedly with water until the compound had dissolved entirely. On every occasion ionic chlorine was found to be present in the aqueous extract. This method of separation thus also failed.

A third idea was to dissolve the compound in ammonia and reprecipitate with acetic acid in the hope that the acetate salt would not be stable in presence of excess water. When this procedure was adopted, however, acidification with dilute acetic acid failed to cause any precipitation and the compound remained in solution. A possible explanation of this might be that the carboxyazabenzanthrone was a stronger acid than acetic acid.

The fourth attempt to separate the hydrochloride from the free acid was no more successful. This involved solution of the mixture in dilute ammonia and then boiling vigorously in the hope of driving off ammonia and leaving a neutral solution from which the free acid would deposit. No solid was deposited on prolonged boiling of such an alkaline solution.

No other method of separating this mixture pres-

ented itself; it was therefore concluded that if this mixture could be made to yield a pure derivative it could be reasonably maintained that the material actually was a mixture of 11-carboxy-8:10-dimethyl-9-azabenzanthrone and its hydrochloride.



The derivative it was proposed to make was the corresponding dimethyl-azabenzanthrone and accordingly attempts were made to decarboxylate the 11-carboxylic acid mixture. The first method to be tried was treatment with copper bronze in boiling quinoline and the product of this reaction was found to be so insoluble in organic solvents that it could not be usefully purified. An alkaline fusion on the black impure product developed no characteristic colour and the recovered material did not act as a vat dye.

A second method of decarboxylation, however, proved more successful. This consisted in subliming the crude acid in a high vacuum at 360°C. in a Pyrex

apparatus. A 10% yield of an orange sublimate was obtained which was quite insoluble in alkali and which dissolved readily in ethyl alcohol. Inferior results were obtained when copper bronze was mixed with the material to be sublimed. The yield of sublimate was constant whether the vacuum was 0.01 mm. or 10 mm. The product did not give a characteristic colour on fusion with alkali and it did not act as a vat dye. The solubility in ethyl alcohol and xylene was in striking contrast to the general insolubility observed with the other derivatives so far examined. It was, indeed, so pronounced that the solvent had to be taken down almost to dryness before the material would crystallise out.

The mode of formation and the insolubility in alkali suggest very strongly that the product is 8:10-dimethyl-9-azabenzanthrone and this was confirmed on analysis.

It must be admitted, however, that the material melted over a range, between 110 and 120°C. On the other hand the German Patent (page 22) quotes no melting point for the product of the Skraup reaction on 1:3-dimethyl-2-azanthraquinone, whereas it does quote a melting point of 196 - 198°C. for the product of the Skraup reaction on 1-methyl-3-phenyl-2-azanthraquinone, and this derivative might be expected to have a higher melting point than the former.

Two attempts were made to oxidise the mixture of 11-carboxy-3:10-dimethyl-9-azabenzanthrone and its sulphate. In the first the material was dissolved in concentrated sulphuric acid and reprecipitated by addition of water. The suspension was boiled and treated with chromic acid, whereupon the reactants were refluxed for twelve hours. The colour of the solid changed from red brown to vivid orange yellow. On filtration about half the weight of the starting material of this bright product was obtained and this proved to be the unchanged 11-carboxylic acid, this time free from any chloride, chromate or sulphate. Why such treatment should effect separation is very difficult to see but the tests for these ions were emphatically negative.

The remainder of the material, whether oxidised or not, remained in the mother liquors of chromic and sulphuric acids and no attempt was made to isolate any product.

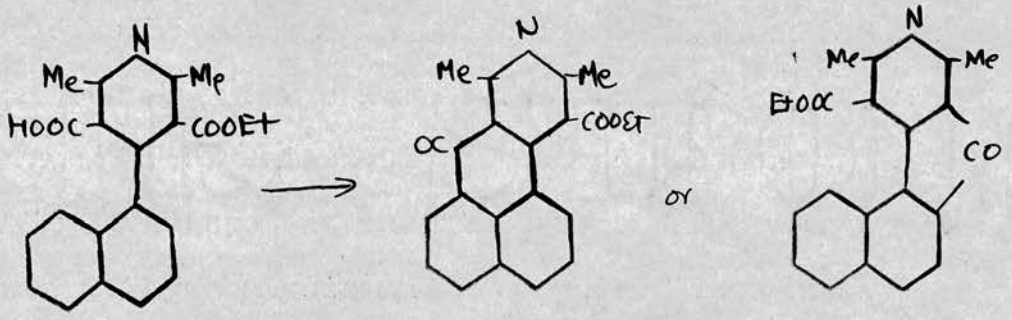
In the second oxidation the material was refluxed for 24 hours with alkaline potassium permanganate. The reactants were filtered and the filtrate taken down to dryness after acidification with dilute

hydrochloric acid. The mixture of brown material and sodium chloride was extracted with pyridine, a preliminary experiment under the same conditions having shown that sodium chloride did not dissolve in pyridine. The pyridine was removed in vacuo and a dark brown material was left which possessed slight fluidity. Thus if a portion was removed, in a short while the surface had again become intact. The product was unaffected by heat up to 360°C. and did not sublime after treatment for four hours. With zinc dust and sodium hydroxide the colour of the solution was that brown colour obtained by dissolving the material in sodium hydroxide. The material cannot thus be an azanthraquinone derivative. It was very soluble in water to give an acid solution and dissolved in concentrated sulphuric acid to give a brown solution with a darker brown fluorescence in daylight and a milky light blue fluorescence in ultraviolet light. Apart from its acid nature no positive evidence regarding the actual structure of the product was obtained.

A sodium hydroxide fusion was performed on the 11-carboxylic acid hydrochloride mixture and on the 1:11-keto-8:10-dimethyl-9-azabenzanthrone and in neither case was a distinctive colour developed nor did

the melts act as vat dyes.

Attempts were made to cyclise 4-α-naphthyl-3-carboxy-5-carbethoxy-2:6-dimethyl-pyridine in the hope of preparing 11-carbethoxy-8:10-dimethyl-9-azabenzanthrone. The product would be either this desired derivative or the fluorenone compound, distinction being established as in the case of the partially cyclised 4-α-naphthyl-3:5-dicarboxy-2:6-dimethyl-pyridine.



Several reagents were employed with disappointing results in every case. Treatment with phosphorus pentoxide in boiling toluene gave no alkali insoluble material nor did various treatments with concentrated sulphuric acid. Treatment with chlorosulphonic acid yielded a minute amount of orange solid too small to be worked up.

Accordingly the acid chloride was formed by treatment with thionyl chloride and aluminium chloride was

added to effect cyclisation. Alkali soluble material was removed by treatment with dilute ammonia and a very intractable dark brown powder was obtained in 20% yield melting above 370°C. No means could be found of effecting purification. The preparation was repeated with use of phosphorus pentachloride in place of the thionyl chloride and an 85% yield of impure black product obtained. This, too, defied all attempts at purification.

The impure material was brominated in the hope that the bromo compound might more readily undergo alkaline fusion. The derivative appeared to form readily but the product could not be purified nor did it undergo alkaline fusion to yield a vat dye.

As a group the derivatives of 9-azabenzanthrone examined in this work are characterised by a pronounced difficulty in handling and purification. It must be remembered that most of the compounds dealt with were amino acids in virtue of the carboxylic groups and the tertiary amino nitrogen of the pyridine ring, they contain and their working involved the usual difficulties associated with such compounds. Perhaps the most striking example of this was the difficulty of separating 11-carboxy-8:10-dimethyl-9-azabenzanthrone from its hydrochloride.

Other factors tending to make the work no less difficult were the lack of solubility in usual organic solvents and the fact that most of the azabenzanthrone derivatives melted above 360°C. These two properties proved of particular prominence in endeavours to purify the compounds. This difficulty can be most readily exemplified by the necessity of using six litres of normal propyl alcohol to recrystallise one gram of 1:11-keto-8:10-dimethyl-9-azabenzanthrone. The only derivative to show appreciable solubility was the 8:10-dimethyl-9-azabenzanthrone which could be recrystallised with comparative ease from ethyl alcohol. This property is in accordance with the information contained in German Patent No. 634968, (C.A. 1937, 31, 417), a copy of which was kindly provided by Imperial Chemical Industries, Ltd. This patent states that b-azabenzanthrones (page 24) can be purified in the usual way by crystallisation, and in particular specifies ethyl alcohol as a solvent for the azabenzanthrone prepared by the performance of a Skraup reaction on 1:3-dimethyl-2-azanthraquinone, the product of which may possibly be 8:10-dimethyl-9-azabenzanthrone (page 23).

The derivatives of 9-azabenzanthrone examined give characteristic colours with concentrated sulphuric acid with fluorescence. The 11-carboxy-8:10-dimethyl-9-aza-

benzanthrone gives a bright orange brown colour with green fluorescence in daylight and strong yellow fluorescence in ultraviolet light; the 1:11-keto-8:10-dimethyl-9-azabenzanthrone gives a red brown colour with concentrated sulphuric acid with no appreciable fluorescence in daylight but brown fluorescence with a tinge of green in ultraviolet light; the 8:10-dimethyl-9-azabenzanthrone gives a pure red colour with strong green fluorescence in daylight and very strong milky blue fluorescence in ultraviolet light.

It appears a general conclusion that derivatives of 9-azabenzanthrone do not undergo alkaline fusion to form diazadibenzanthrones, none of the compounds examined so doing. This is in accordance with the properties generally associated with the azabenzanthrones as a group, no diazadibenzanthrones being reported in the literature. The products of the attempted alkaline fusions did not act as vat dyes and it seems justifiable to conclude that derivatives of 9-azabenzanthrone are, in themselves, of no value as dyestuffs.

EXPERIMENTAL SECTION

The experimental work carried out is described in the following pages. Yields are quoted as percentages of the theoretical amount obtainable and all melting points are corrected, the thermometers employed having been calibrated against standard short stem thermometers. Melting points were determined in an electrically heated coil apparatus with which temperatures of 370°C. could conveniently be obtained. When only very small quantities of material were available the melting point determinations were performed on a special micro melting point apparatus consisting of an electrically heated plate mounted on the stage of a low power microscope.

All new compounds obtained in the pure state have been analysed by micro methods by Mr W. Brown of the Department of Medical Chemistry of the University of Edinburgh.

Preparation of Hydrogen Cyanide

(Organic Syntheses, volume 7, page 50)

Anhydrous hydrogen cyanide was prepared by simultaneously dropping fairly slowly a solution of 450 grams of sodium cyanide in a litre of water and a litre of a 1:1 solution of concentrated sulphuric acid and water into a large flask, care being taken to maintain an excess of the acid in the flask. When all the solutions had been added to the flask the contents were boiled to drive over the remaining gas. The gas evolved was led through calcium chloride drying tubes and through a coil of lead tubing cooled in ice, and the liquid hydrogen cyanide was collected in a special bottle. It was a clear liquid tinged slightly yellow. About 210 grams were obtained in each experiment being 84% of the theoretical yield. The liquid was used without further purification.

Preparation of α-Naphthaldehyde

(Hinkel, Ayling and Benyon, J.C.S. 1936, 340)

Aluminium chloride	340 grams
Hydrogen cyanide	120 mils.
Chlorobenzene	500 mils
Naphthalene	126 grams

The aluminium chloride was powdered in a mortar and introduced into a two litre Pyrex flask with three necks and the chlorobenzene immediately added. The centre neck of the flask carried a stirrer, one side neck a water condenser with a calcium chloride tube and the other a dropping funnel of 130 mils. capacity. The flask was placed in ice water and the hydrogen cyanide gradually added from the dropping funnel, the contents of the flask being stirred. The addition of the hydrogen cyanide should take about thirty minutes. The ice water was then removed and the flask allowed to stand for fifteen minutes at room temperature to complete the formation of the white addition compound $AlCl_3.2HCN$. The naphthalene was added and the funnel replaced by a wide tube for the introduction to the flask of a stream of hydrogen chloride which was generated by the action of concentrated sulphuric acid on ammonium chloride voltoids and dried by being passed through concentrated sulphuric acid.

A slow stream of hydrogen chloride was passed in for fifteen minutes at room temperature and then the flask was surrounded with a water bath and heated to $70^{\circ}C.$ for five hours, stirring and the stream of hydrogen chloride being continued throughout. The time and the temperature must be rigorously adhered to. The contents of the flask, a black viscous liquid, were then poured

on to a mixture of concentrated hydrochloric acid and ice, an operation best performed out of doors owing to the copious evolution of hydrogen chloride. The mixture was then steam distilled until no more yellow liquid - a-naphthaldehyde - passed over, an operation requiring about thirty hours.

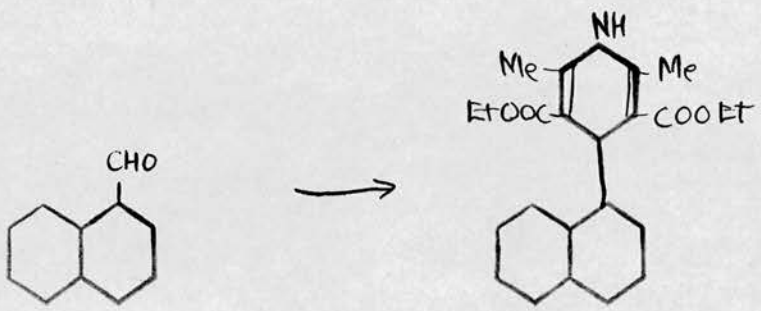
The distillate which consisted of water, chlorobenzene and a-naphthaldehyde, was extracted with ether and the ethereal extract shaken for eight hours with a saturated aqueous solution of sodium bisulphite. This was prepared by passing sulphur dioxide into a solution of sodium carbonate until it went apple green, about twelve hours being necessary. The white naphthaldehyde-bisulphite compound was filtered off and placed in a five litre bolt head flask. Dilute sulphuric acid was added and the contents of the flask steam distilled until no more a-naphthaldehyde passed over (eight hours). The distillate was extracted with ether, the ether evaporated off and the a-naphthaldehyde redistilled.

Yield 55 grams, i.e. 35% theoretical.

Boiling point 287 - 290°C.; quoted 291 - 292°C.

The filtrate from the bisulphite compound filtration was distilled and the chlorobenzene recovered and used again. It is purely a solvent.

Preparation of 4-a-Naphthyl-3:5-dicarbethoxy-2:6-dimethyl-1:4-dihydropyridine.



a-Naphthaldehyde	55 grams
Ethyl acetoacetate	92 grams
Saturated alcoholic ammonia	150 mils.

The above three reactants were mixed in a 500 mil. bolt head flask and boiled on the water bath under a reflux condenser for six hours. During this time ammonia gas was passed into the reaction mixture through a tube passing down the condenser. The gas was generated by boiling concentrated ammonia in a 2 litre flask, another 2 litre flask being fitted as a trap and the gas finally dried by means of a soda lime tower. At the end of the reaction the red solution was poured into a beaker and on cooling yellow crystals were deposited. These were filtered off, washed with ethyl alcohol and dried.

Yield 84 grams, i.e. 62% theoretical.

The ester was recrystallised twice from benzene when fine, almost white, crystals were obtained.

Melting point 201 - 202°C.

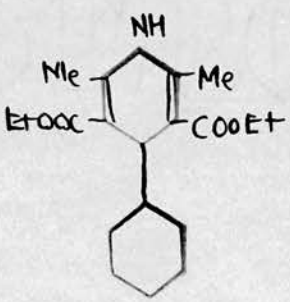
Analysis:

calculated for $C_{23}H_{25}O_4N$ - C - 72.8%; H - 6.6%; N - 3.7%,

found C - 72.8%; H - 6.8%; N - 3.7%.

The compound was insoluble in alkali and in dilute acids. It instantly decolourised bromine in carbon tetrachloride solution and so is unsaturated.

Preparation of 4-Phenyl-3:5-dicarbethoxy-2:6-dimethyl-1:4-dihydropyridine.



The product of the Hantzsch synthesis on α-naphthaldehyde, 4-α-naphthyl-3:5-dicarbethoxy-2:6-dimethyl-1:4-dihydropyridine, was found to be insoluble in dilute acids. This is contrary to the expected behaviour of a pyridine derivative. The corresponding

phenyl compound was first prepared by Schiff and Puloti in 1883 (Ber. 1883, 16, 1607) and this preparation was repeated in order to examine its behaviour to acids.

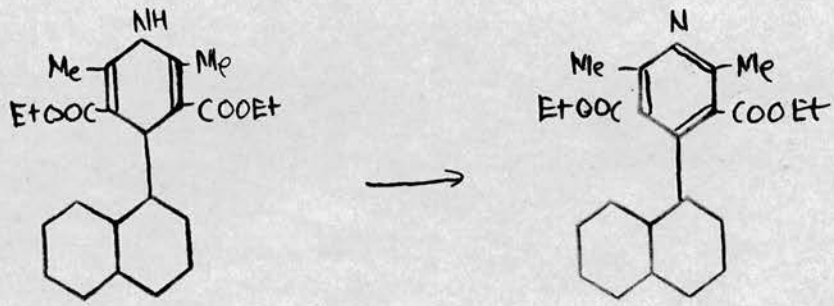
Benzaldehyde	10 grams
Ethyl acetoacetate	25 grams
Saturated alcoholic ammonia	40 mils.

The liquids were mixed and a white precipitate appeared immediately. The mass was warmed to 30°C. solution being then complete. Most of the alcohol was evaporated off and on standing overnight well-formed yellow crystals developed. These were filtered off, washed and recrystallised from ethyl alcohol.

Yield 9 grams, i.e. 30% theoretical.
M.p. 155 - 157°C.; quoted 155 - 157°C.

The compound, which was white in the pure state, was insoluble in hydrochloric acid, dilute or concentrated, and in dilute sulphuric, showing this somewhat abnormal property to be a general one of the series.

Preparation of Crude 4-a-Naphthyl-3:5-dicarbethoxy-2:6-dimethyl-pyridine.

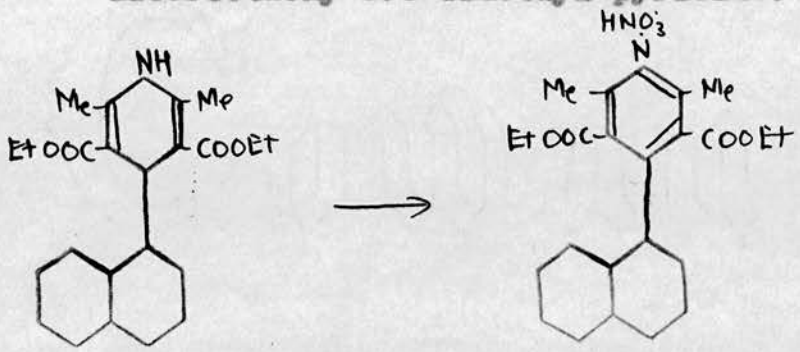


100 grams of the ester prepared by the Hantzsch synthesis on a-naphthaldehyde were mixed with an equal amount of ethyl alcohol in a 500 mil. bolt head flask. Nitrous fumes, generated by the action of concentrated nitric acid on lumps of arsenious oxide in a litre bolt head flask connected by glass tubing to a small gas bottle as a trap, were passed into the mixture in a fairly vigorous stream over two and a half hours, the reaction vessel being cooled in running water. At the end of the time almost all the ester had gone into solution leaving an orange liquid. The small residue was filtered off and the alcohol removed from the filtrate on the steam bath. Powdered sodium carbonate was added to neutralise the acid present and when the effervescence had ceased the excess was filtered off. The filtrate was extracted with ether and the extract on removal of the ether by warming, left a red oil. This last operation was conducted in a litre Jena flask in which vessel the next operation was to be carried

out.

Yield 91 grams, i.e. 91% theoretical.

Preparation of the Nitrate of 4-α-Naphthyl-3:5-dicarbethoxy-2:6-dimethyl-pyridine.



In a repeat experiment 10 grams of the dihydro-pyridine derivative were oxidised by the action of the nitrous fumes over the longer period of twelve hours. After removal of the alcohol and neutralisation of the acid by sodium carbonate, ether was added to extract the red oil. At this stage a pink solid was thrown down. The ether extract was filtered and the ether evaporated leaving the usual product of the shorter reaction as the red oil.

Yield of oil 6 grams.

The pink solid was washed with ether and dried on

on a porous plate.

Yield 4 grams.

M.p. 96 - 99°C.

The pink solid was recrystallised twice from ethyl alcohol when the melting point rose to 99 - 100°C. and 99.5 - 100.5°C.

Analysis:

calculated for

$C_{23}H_{23}O_4N.HNO_3$ - C - 62.7%; H - 5.5%; N - 6.4%,

found - C - 62.5%; H - 6.2%; N - 6.3%.

Preparation of Pure 4-a-Naphthyl-3:5-dicarbethoxy-2:6-dimethyl-pyridine.

4.00 grams of the pure pink crystals of the nitrate, prepared above, were treated with 25 mils. of dilute ammonia solution and warmed to the boiling point. The solid melted to a paler pink oil which remained discrete. A portion of the solution gave a positive brown ring test for a nitrate confirming the supposition that the pink crystals were those of the nitrate

of 4-a-naphthyl-3:5-dicarbethoxy-2:6-dimethyl-pyridine. After standing for an hour the solution was filtered and the solidified ester well washed with water and dried on a porous plate.

Yield 3.42 grams; calculated for loss of

HNO_3 - 3.43 grams.

M.p. 60 - 65°C.

The material was recrystallised from ethyl alcohol in the hot solution of which it was very soluble. Large flaky crystals, tinged pink, separated out in the refrigerator and these were filtered off, washed and dried in the air.

M.p. 58 - 59°C.

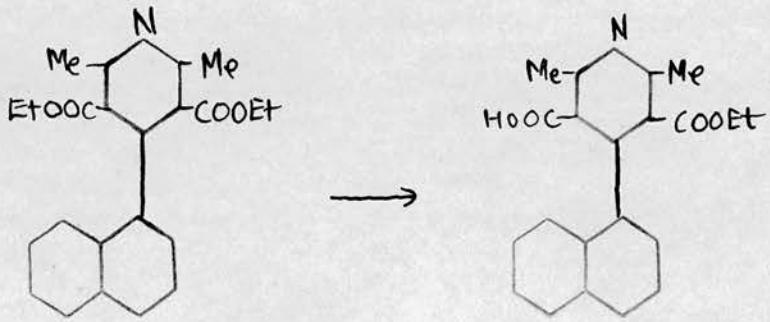
Recrystallisation was again effected leaving colourless crystals, melting at 59 - 60°C. This figure was unchanged after another recrystallisation.

Analysis:

calculated for $C_{23}H_{23}O_4N$ - C - 73.2%; H - 6.1%; N - 3.7%,

found C - 73.4%; H - 6.4%; N - 4.0%.

Preparation of 4-a-Naphthyl-3-carboxy-5-carbethoxy-2:6-dimethyl-pyridine.



Crude 4-a-naphthyl-3:5-dicarbethoxy-2:6-dimethyl-pyridine	26 grams
Potassium hydroxide (slight excess)	8 grams
Ethyl alcohol	250 mils.

The potassium hydroxide was dissolved in the alcohol by gentle warming and the solution poured on to the red oil contained in a litre Jena flask. The mixture was refluxed on the water bath for four hours and poured in to a solution of 10 mils. concentrated sulphuric acid in a litre of water. A cream coloured solid was thrown out which was filtered off, washed with water and dried.

Yield 23 grams, i.e. 100% theoretical.
M.p. 231 - 232°C. with gassing.

The material was recrystallised three times from

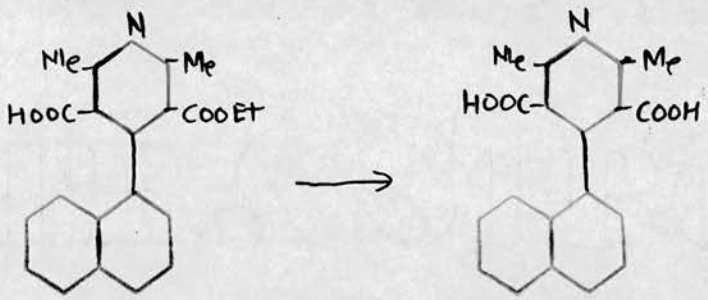
ethyl alcohol; the melting point from the last two operations remained unchanged at 238°C. with gassing.

Analysis:

calculated for $C_{21}H_{19}O_4N$ - C - 72.2%; H - 5.4%; N - 4.0%,

found C - 71.4%; H - 5.5%; N - 4.1%.

Preparation of 4-a-Naphthyl-3:5-dicarboxy-2:6-dimethyl-pyridine.



4-a-Naphthyl-3-carboxy-5-carbethoxy-2:6-dimethyl-pyridine	1.62 grams
Potassium hydroxide (fourfold excess)	1.00 grams
Ethyl alcohol	10.00 mils.

The potassium hydroxide was dissolved in the alcohol by slight warming and the solution poured on to the solid in a 50 mil. Jena flask and the mixture refluxed on the water bath for 100 hours. The solution was then poured into 100 mils. of water acidified with 12

mils. of dilute sulphuric acid when a light buff powder was thrown down. This was filtered off, washed and dried.

Yield 1.45 grams, i.e. 98% theoretical.
M.p. 334°C. with gassing.

On successive recrystallisations from ethyl alcohol the melting point varied

1. 329°C. with gassing.
2. 336°C. with gassing.
3. 324.5 - 325°C. with gassing.

As gassing indicates a decomposition point and not a true melting point, these fluctuations are without significance and probably arise from differences in the rate of heating. The material was insoluble in cold water and in cold hydrochloric acid; it was soluble in hot water, hot hydrochloric acid and cold sodium hydroxide.

The hydrolysis of the diethyl ester was also carried out in an acid medium.

4-a-Naphthyl-3-carboxy-5-carbethoxy-2:6-dimethyl-pyridine	2.00 grams
Glacial acetic acid	28 mils.
Concentrated sulphuric acid	14 mils.
Water	7 mils.

The above mixture of acids and water is known to be an efficient hydrolysing agent. The reactants were carefully mixed and refluxed on the water bath for 100 hours. The dark liquid product was poured into 300 mils. of water when a greyish solid was thrown down. This was filtered off, washed with water and dried.

Yield 1.25 grams, i.e. 68% theoretical.

M.p. 330°C. with gassing.

The material was successively recrystallised from ethyl alcohol when the melting points were

1. 328 - 328.5°C. with gassing.
2. 331 - 332°C. with gassing.
3. 330.5 - 331°C. with gassing.

A mixed melting point of the once recrystallised product, m.p. 328 - 328.5°C. and the once recrystallised product of the previous preparation, m.p. 329°C. melted sharply with gassing at 329°C. As these are decomposition points, however, not very much importance can be attached to these observations.

The more efficient alkaline hydrolysis was then repeated on the large scale.

Crude 4-α-Naphthyl-3:5-dicarbethoxy-2:6-dimethyl-pyridine	91 grams
Potassium hydroxide (fourfold excess)	105 grams
Ethyl alcohol	450 mils.

The potassium hydroxide was dissolved in the ethyl alcohol by warming and poured on to the red oil contained in a litre Jena flask. The mixture was refluxed on the water bath for 100 hours and then poured into 35 mils. concentrated sulphuric acid in 2500 mils. water. From the red solution a buff coloured solid was thrown down, which was filtered off, washed with water and dried in the steam oven.

Yield 65 grams, i.e. 85% theoretical.

M.p. 328°C. with gassing.

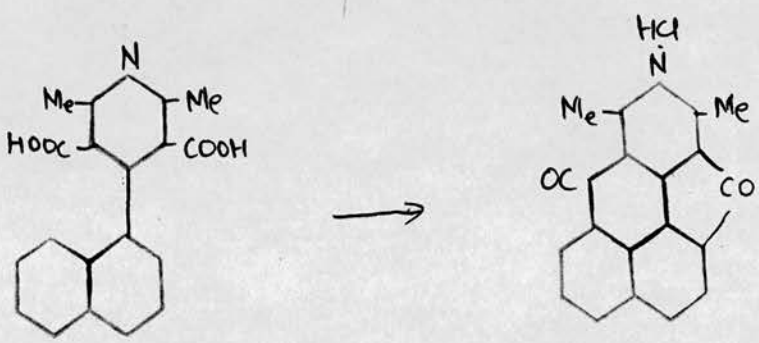
Of solvents for recrystallisation ethyl alcohol appeared to be the best but the process was so uneconomical that the material was used unchanged. A portion, however, was recrystallised three times for analysis.

Analysis:

calculated for $C_{19}H_{15}O_4N$ - C - 71.0%; H - 4.8%; N - 4.4%,

found C - 70.8%; H - 4.8%; N - 4.4%.

Preparation of 1:11-Keto-8:10-dimethyl-9-azabenzanthrone hydrochloride.



10 grams of 4-a-naphthyl-3:5-dicarboxy-2:6-dimethylpyridine were refluxed on an oil bath at 80 - 100°C. for two hours with 8 grams of dry phosphorus pentachloride and 150 mils. of AnalaR benzene. The condenser was fitted with a calcium chloride tube and copious evolution of hydrogen chloride was observed. The benzene and phosphorus oxychloride formed were removed in vacuo at 50°C. 10 mils. of benzene were added and also removed in vacuo. 30 grams of freshly powdered aluminium chloride were added and 150 mils. of sulphur-free carbon tetrachloride and the reactants refluxed at 100°C. for six hours. Evolution of hydrogen chloride was observed during the first two hours. The dark solution was cooled and poured on to 100 grams of ice. The dark solid was removed from the flask with a spatula and added to the ice. The mixture was filtered washed with water and dried on a porous plate.

Yield 10 grams, possibly containing alumina.

The material was digested for thirty minutes with dilute ammonia to remove alkali soluble impurities. Filtration of the product was slow due to the slimy nature of the solid. Washing was effected with a little water and the solid was dried on a porous plate over a bunsen flame.

Yield 2.60 grams.

The digestion with ammonia was repeated and the material washed until the wash liquid was colourless. The solid was then dried on a porous plate and consisted of a dark coloured powder with a tinge of green.

Yield 1.71 grams, i.e. 20% theoretical.

The material shrinks at 280°C. but does not melt below 360°C. It melts and burns on a platinum foil leaving no residue. It is quite insoluble in dilute ammonia, both hot and cold; it is soluble in dilute hydrochloric acid and insoluble in hot water. It is slightly soluble in ethyl alcohol to give a greenish solution, and more so in normal propyl alcohol to give a solution with a deeper green tint.

The ketoazabenzanthrone was therefore recrystallised from propyl alcohol from which it separated as an orange powder. To form the hydrochloride it was dissolved in boiling dilute hydrochloric acid and

allowed to crystallise out, when it was filtered off, washed with dilute hydrochloric acid, then water, and dried over calcium chloride in an unevacuated desiccator.

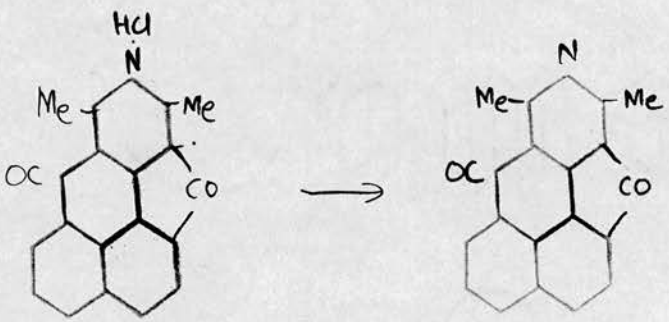
Analysis:

calculated for

$C_{19}H_{11}O_2N.HCl$ C - 71.0%; H - 3.7%; N - 4.4%,

found C - 70.9%; H - 4.0%; N - 4.5%.

Preparation of 1:11-Keto-8:10-dimethyl-9-azabenzanthrone.



About 0.5 grams of the hydrochloride of the keto-azabenzanthrone were digested with cold dilute ammonia for fifteen minutes and the solution filtered. The filtrate was quite colourless and the solid, which retained the same appearance throughout, was washed very thoroughly with water. A portion was boiled with

dilute nitric acid, cooled, filtered and silver nitrate added to the filtrate. A distinct opalescence developed showing ionic chlorine still to be present. The process was repeated and the compound dried in a clean desiccator. Ionic chlorine was now found to be absent from the orange powder. The compound was unchanged up to 370°C. but burned on a foil leaving no residue.

Analysis:

calculated for $C_{19}H_{11}O_2N$ - C - 80.0%; H - 3.9%; N - 4.9%,

found C - 80.1%; H - 4.4%; N - 5.0%.

Preparation of the Dinitrophenyl Hydrazone of 1:11-Keto-8:10-dimethyl-9-azabenzanthrone.

15 mils. of the dinitrophenyl hydrazine reagent, 5% in alcohol, were mixed with 15 mils. of ethyl alcohol and the solution boiled. A small quantity, about 0.1 grams, of 1:11-keto-8:10-dimethyl-9-azabenzanthrone was added and the solution boiled for about thirty seconds. The solution was then filtered and the filtrate treated with a few drops of concentrated hydrochloric acid and allowed to cool. Fine clusters of orange needles were deposited in reasonable amount.

These were filtered off, washed with ethyl alcohol and dried in the air. The hydrazone was boiled with 500 mils. ethyl alcohol for six hours and filtered and the residue boiled with another 500 mils. and filtered. The two filtrates were combined and on cooling deposited fine orange crystals which were separated by decantation and slow evaporation of the last traces of ethyl alcohol. The compound did not melt below 370°C.

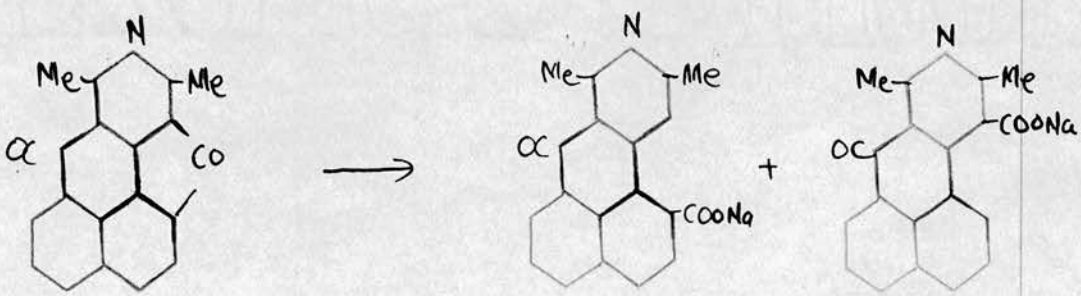
Analysis:

calculated for $C_{25}H_{15}O_8N_5$ - N - 15.1%

found N - 15.8%.

Nitrogen percentage for dinitrophenyl hydrazine reagent is 28.3%; nitrogen percentage for ketoazabenzanthrone is 4.9%.

Hydrolysis of 1:11-Keto-8:10-dimethyl-9-azabenzanthrone with sodium hydroxide.



0.300 grams of chloride-free 1:11-keto-8:10-

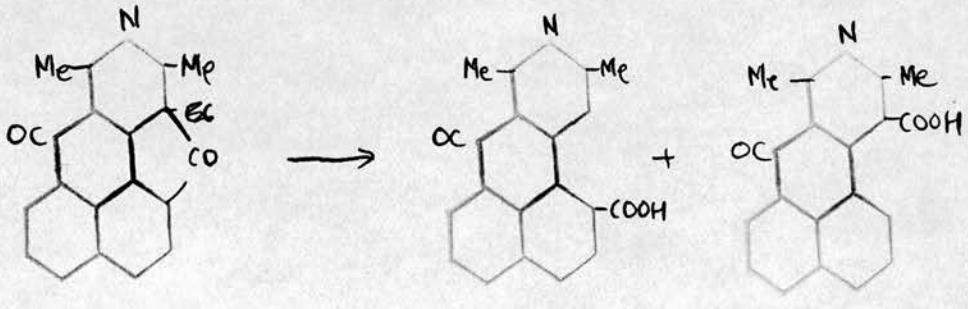
dimethyl-9-azabenzanthrone were refluxed with 20 mils. dilute sodium hydroxide solution for six hours and the rich brown solution that developed was filtered. The residue was washed and dried.

Yield 0.217 grams.

The filtrate was acidified with dilute hydrochloric acid and gave an orange-brown flocculent precipitate. This is in all probability a mixture of 1-carboxy-8:10-dimethyl-9-azabenzanthrone and 11-carboxy-8:10-dimethyl-9-azabenzanthrone.

The keto compound, therefore, is hydrolysed to an extent of about 25% on being boiled six hours with sodium hydroxide.

Hydrolysis of 1:11-Keto-8:10-dimethyl-9-azabenzanthrone with distilled water.



0.436 grams of the ketoazabenzanthrone were boiled with 500 mils. of distilled water for 100 hours and the faintly yellow solution filtered through a weighed sintered glass funnel, giving, when dry, 0.413 grams of ketoazabenzanthrone unattacked.

The filtrate was evaporated to dryness on the steam bath and a few mils. of dilute ammonia added, when the solid all dissolved. The ammonia was then evaporated to dryness.

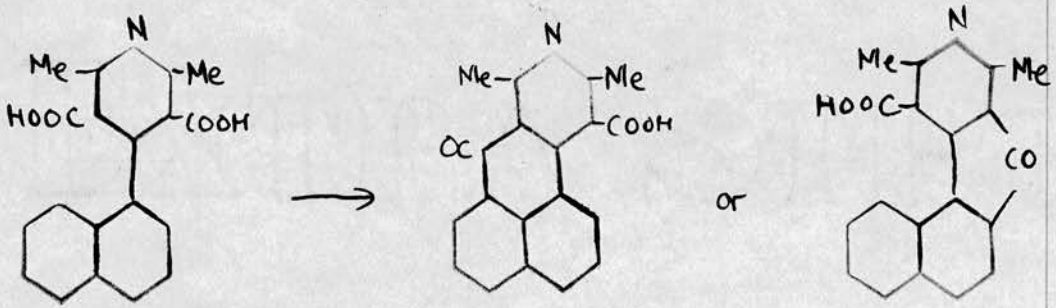
Yield of residue 0.025 grams.

The weight of ketoazabenzanthrone dissolved was 0.023 grams, or calculated as the ammonium salt of the 1- or 11- carboxy acid, 0.025 grams.

It thus appears that 1:11-keto-8:10-dimethyl-9-aza-benzanthrone is very slightly hydrolysed to the acids when subject to prolonged boiling with distilled water.

Attempts to Cyclise 4-a-Naphthyl-3:5-dicarboxy-2:6-dimethyl-pyridine Involving one Carboxylic Group.

If only one of the carboxylic groups reacts, ring closure of 4-a-naphthyl-3:5-dicarboxy-2:6-dimethyl-pyridine should yield either 11-carboxy-8:10-dimethyl-9-azabenzanthrone or a fluorenone derivative according to which group cyclises:



Identification of such a ring closed product should be easy for the fluorenone derivative should react as a ketone and give a dinitrophenyl-hydrazone whereas the azabenzanthrone derivative ought not to function as a ketone, none of the benzanthrone series so doing except those with additional ketone groups.

Several reagents were employed in attempts to cyclise partially 4-a-naphthyl-3:5-dicarboxy-2:6-dimethyl-pyridine.

On account of its value in the analogous case with benzanthrones, concentrated sulphuric acid was the first reagent to be employed.

(a) 0.2 grams of the dicarboxylic acid were treated with 2 mils. of concentrated sulphuric acid for 30 minutes at 50°C. The liquid turned red-brown and was poured into 50 mils. of water. The solution became yellow but no solid was thrown out.

(b) 0.1 grams were treated with 3 mils. of concentrated sulphuric acid for one hour at room temperature. The solution developed a golden colour with green fluorescence. It was poured into 50 mils. of water. No solid separated out.

One experiment was conducted with 70% sulphuric acid. 0.1 grams of the dicarboxylic acid were treated with 2 mils. of 70% sulphuric acid for 30 minutes at 100°C. This temperature was employed because the risk of sulphonation was less with the weaker acid. Some of the solid remained undissolved and was removed mechanically. The solution was greenish yellow and was poured into 50 mils. of water. No solid separated.

Experiments were conducted with phthalic anhydride

which has proved valuable in the case of benzanthrones. 1 gram of the dicarboxy acid was mixed with 3 grams of phthalic anhydride and one drop of concentrated sulphuric acid and the reactants boiled for 15 minutes, after which they were poured into water. Nothing appeared to dissolve in the water. The water was boiled and solid sodium carbonate added until the solution was alkaline. It was faintly lemon in colour. The black insoluble residue was filtered off - the carboxy-azabenzanthrone should be soluble in sodium carbonate - and the filtrate acidified with dilute hydrochloric acid. No solid separated.

In a second experiment 0.5 grams of the dicarboxy-acid were mixed with 1.5 grams of phthalic anhydride and two drops of concentrated sulphuric acid and heated to 150°C. for one hour on an oil bath. The mixture was stirred at intervals and at the end water was poured into the tube and all the solid dislodged. The mixture was boiled a few minutes to effect solution and then made alkaline with sodium carbonate. Filtration removed the insoluble material from the solution which had a green tint. Acidification with dilute hydrochloric acid produced some effervescence but no solid. The solid removed in the filtration was whitish in appearance and gassed at 128 - 130°C. Hence it was concluded to be phthalic anhydride.

Chlorosulphonic acid has been used occasionally in benzanthrone chemistry to effect ring closure and in view of the lack of success of the above experiments it was employed here.

(a) 1 gram of the dicarboxylic acid was treated with 5 mils. of chlorosulphonic acid for 5 minutes in the cold and the rich ruby red solution cautiously poured into water. The immediate product was in the form of clean yellow flakes which, on filtration, lost their clean appearance and after washing and drying were dark orange.

Yield 0.25 grams.

M.p. above 370°C.

Theoretical yields are not quoted in these preliminary experiments as the products were afterwards shown to be acid salts.

The product was soluble in sodium hydroxide.

(b) 0.1 grams of the dicarboxylic acid were treated with 3 mils. of chlorosulphonic acid for 30 minutes at 50°C. and the ruby red solution carefully poured into water, 100 mils. The solution turned a rich golden yellow and some yellow crystals separated out. On filtration and drying there was only enough material for a melting point determination, which was above 370°C.

(c) 0.1 grams were treated with 3 mils. of chlorosulphonic acid for one hour at 100°C. and the red solution poured into 100 mils. of water. A rich yellow solution developed and on standing overnight yellow crystals separated out. These were filtered off, washed and dried.

Yield 0.02 grams.
M.p. above 370°C.

The product was soluble in sodium hydroxide.

(d) 0.1 grams of the dicarboxylic acid were treated with 3 mils. of chlorosulphonic acid for one hour at room temperature and the red solution carefully poured into 100 mils. of water. Orange crystals appeared which were filtered off, washed with water and dried on a porous plate.

Yield 0.04 grams.
M.p. above 370°C.

The crystals were instantly soluble in sodium hydroxide solution and so still are acid. With concentrated sulphuric acid they give a rich orange colour with a greenish-yellow fluorescence - a characteristic of benzanthrones.

(e) 6 grams of the acid were treated with 10 mils.

chlorosulphonic acid for one hour at room temperature and treated as before.

Yield 1.7 grams.

M.p. above 370°C.

The product was soluble in alkali.

(f) 4 grams of the acid were treated with 20 mils. chlorosulphonic acid for three hours at room temperature and the rich red solution poured into a litre of water with mechanical stirring. A yellow precipitate which later turned orange was thrown down. This was filtered off, washed and dried.

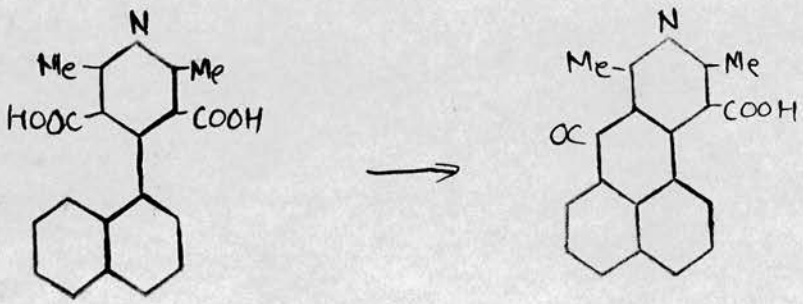
Yield 1.4 grams.

M.p. above 370°C.

The product was instantly soluble in alkali and did not yield a dinitrophenyl hydrazine derivative when subjected to the usual treatment. This shows the product is probably the azabenzanthrone derivative and certainly not the fluorenone derivative.

A review of the conditions employed and the results obtained shows three hours at room temperature to be the most satisfactory and these conditions were used in the larger scale operations described below.

Preparation of 11-Carboxy-8:10-dimethyl-9-azabenzanthrone.



10 grams of 4-a-naphthyl-3:5-dicarboxy-2:6-dimethylpyridine were treated with 100 grams of chlorosulphonic acid for three hours at room temperature. The rich red solution was then poured into a tap funnel fitted into the cork of a conical flask containing a litre of water and provided with mechanical stirring. Chlorosulphonic acid reacts very vigorously with water and considerable loss from spurting ensues if the above procedure is not carried out. Copious white fumes were evolved and a yellow solid precipitated in the water. After standing overnight the precipitate was filtered off, washed with water and dried on a porous plate. It was an orange powder.

Yield 4.81 grams.

M.p. over 370°C.

As the parent compound is a base by virtue of the nitrogen atom it was suspected that the product would be a salt, probably the sulphate. Accordingly the orange powder was dissolved in dilute ammonia in which it was instantly soluble to give a golden brown solution and reprecipitated by addition of dilute hydrochloric acid with stirring. After standing for some time the orange solid was filtered off, washed with water, and dried on a porous plate.

Yield 3.32 grams, i.e. 35% theoretical for the hydrochloride.

M.p. above 370°C.

Some of the material was recrystallised twice from concentrated hydrochloric acid in an attempt to convert it quantitatively into the hydrochloride. The fine orange-yellow powder was analysed for chlorine.

Analysis:

Calculated for $C_{19}H_{13}O_3N.HCl$ Cl - 10.4%,

found Cl - 3.4%.

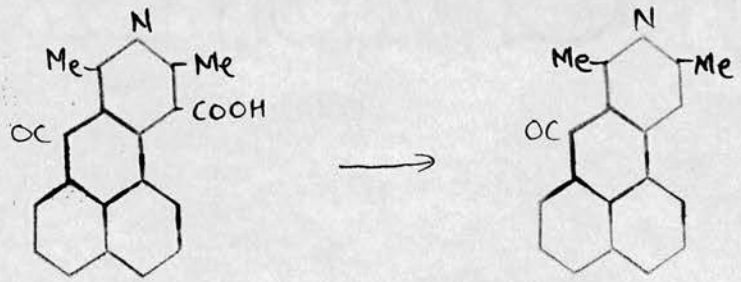
This shows that the material is apparently a mixture of the free acid and the hydrochloride.

When the matter of the separation of these compounds is considered it will be seen that no ready method presents itself. The chlorine can only be

separated by solution in alkali and the material can be recovered only by precipitation with an acid, again giving a salt.

It was decided, therefore, that if treatment of this mixture could be made to yield a pure product it would be legitimate to conclude that the 11-carboxy-acid had actually been prepared but could not be readily separated from the hydrochloride. Accordingly attempts were made to decarboxylate the mixture.

Attempted Preparation of 8:10-Dimethyl-9-azaben-zanthrone.



The commonest method of decarboxylation, treatment with copper bronze in boiling quinoline solution, was the first to be attempted.

0.5 grams of the 11-carboxylic acid mixture were boiled with 10 mils. of redistilled quinoline in a Pyrex test tube and 0.3 grams of copper bronze added in small quantities. A frothing occurred at each addition but this may have been merely increased boiling round the copper particles. The solution was boiled for two minutes and then filtered hot to remove the copper.

The quinoline solution was poured into 100 mils. of dilute hydrochloric acid and allowed to stand. A layer of flocculent green precipitate separated at the foot but filtration through a sintered glass funnel merely left a black coat that could not be removed.

The experiment was repeated with a different technique in the working up of the products.

0.5 grams of the carboxylic acid were boiled with 10 mils. of quinoline and the solution allowed to go off the boil when the copper bronze (0.3 grams) was added in small quantities. Frothing occurred as before and more copper was added until no frothing occurred on its addition. The solution was thereupon filtered to remove the copper bronze and steam distilled for four hours to remove the quinoline. A brown solution with a black scaly solid was left. The solid was removed by filtration, washed and dried.

Yield 0.5 grams.

The material was found to be soluble in dilute ammonia and consequently was extracted with 10 mils. and the solution filtered leaving a black scaly solid.

Yield 0.07 grams.

M.p. above 370°C.

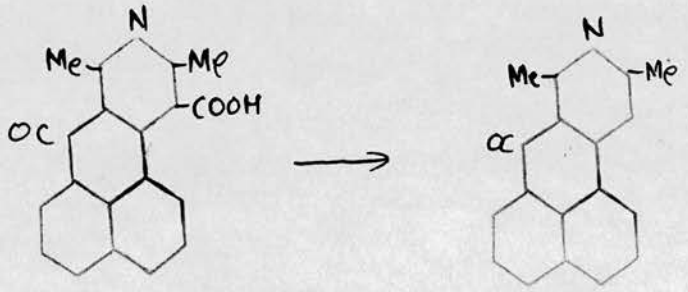
The material burned on a foil leaving no residue, did not contain halogen but was almost insoluble in alcohol, in striking contrast to the product of the sublimation, page . It proved to be almost insoluble in the usual organic solvents and could not be usefully purified.

An alkaline fusion was performed up to 320°C. but no characteristic colour developed and the melt did not act as a vat dye.

With concentrated sulphuric acid the material gave a brown solution with a strong green fluorescence.

In view of the successful sublimation method of decarboxylation, this method was not tried further.

Preparation of 8:10-Dimethyl-9-azabenzanthrone.



The goal of the research was attained by subliming the 11-carboxy-8:10-dimethyl-9-azabenzanthrone and its hydrochloride mixture in a high vacuum. The apparatus consisted of a Pyrex test tube, 8" by 1" on to which a short side tube was blown. The condenser consisted of a length of $\frac{8}{9}$" Pyrex tubing pointed at its lower end, the condensing surface. A rubber stopper was placed round this tube at such a height that the tip of the condenser was $\frac{1}{4}$" from the foot of the Pyrex test tube. The condenser tube carried a rubber stopper at its open end with two holes through which was passed a long and a short length of 3/16" glass tubing. Water was led down the long length which reached to the foot of the condenser and the short length was connected to a sink. The pump was a motor one giving a vacuum, generally between 0.03 and 0.05 mm. mercury.

0.20 grams of the 11-carboxylic acid mixture were placed at the foot of the Pyrex test tube and the condenser assembly placed in position. The tube was connected to the pump through a gauge and evacuated. When a high vacuum had been obtained the tube was heated on a metal bath up to 360°C. An orange yellow sublimate condensed and the reaction appeared to have terminated after about five hours. On removing the condenser 0.021 grams of sublimate were obtained, much carbonisation having occurred.

The process was repeated until sufficient material was obtained. Experiments in which an equal weight of copper bronze was mixed with the material were not so successful, the weight of sublimate being 0.003 grams. The sublimate was quite insoluble in dilute ammonia. It could be recrystallised from ethyl alcohol, in the hot solution of which it was vastly more soluble than any of the other azabenzanthrone derivatives examined. Fine orange crystals were obtained which dissolved in concentrated sulphuric acid to give an orange red solution with strong green fluorescence in daylight and very strong milky blue fluorescence in ultra violet light.

The mode of formation and the fact of its insolubility in alkali suggest very strongly that the product is 8:10-dimethyl-9-azabenzanthrone.

Analysis: calculated for $C_{18}H_{13}ON$ N - 5.4%,

found N - 5.3%.

On the other hand it must be pointed out that the material melted over a range of temperature, 110 - 120°C. This striking change in melting point from those hitherto observed is not without support from other quarters. The German Patent (page 22) quotes no melting point for the azabenzanthrone obtained by the performance of the Skraup reaction on 1:3-dimethyl-2-azanthraquinone, the product of which may be identical with the material now under examination, whereas the patent does quote 196 - 198°C. for the melting point of the azabenzanthrone obtained by the Skraup reaction on 1-methyl-3-phenyl-2-azanthraquinone. It is a generally recognised property that a phenyl group on introduction into a molecule tends to raise the melting point more than the introduction of a methyl group. It may thus be inferred that the product described in the patent would have a melting point lower than 196°C. and it would be interesting to know why no melting point was quoted.

It may also be mentioned in passing that no melting point is quoted in the patent for the products of the Skraup reaction on 2-azanthraquinone and a bromo-1:3-dimethyl-2-azanthraquinone.

Oxidation of 11-Carboxy-8:10-dimethyl-9-aza-benzanthrone with Chromic Acid.

Two grams of the mixture of the 11-carboxylic acid and its sulphate were dissolved in 20 mils. of concentrated sulphuric acid and reprecipitated by addition of 160 mils. of water. The fine suspension was boiled and eight grams of chromic acid were added in portions. The solution was refluxed for twelve hours when the solid changed in colour from a red brown to a vivid orange yellow. The solid was filtered off, washed with water and dried.

Yield 0.90 grams,

M.p. above 360°C.

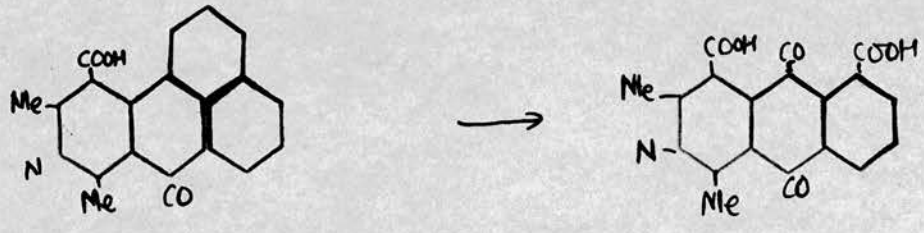
The material was completely soluble in a moderate amount of water and in aqueous alkali. When a given weight was dissolved in standard alkali and the excess alkali determined the values obtained agreed closely with those calculated for a monobasic acid of molecular weight in the region of the starting material.

The material was sparingly soluble in ethyl and normal propyl alcohols and soluble in concentrated sulphuric acid to give an orange solution with a yellow

fluorescence with a tinge of green in ultraviolet light. The compound contained nitrogen and did not give a dinitrophenyl hydrazone, nor did it give a characteristic colour on being heated with zinc dust and sodium hydroxide.

In all these properties it resembles closely the starting material and it can thus be concluded that the 11-carboxylic acid was unaffected by the oxidation, the rest of the material remaining in the sulphuric acid-chromic acid mother liquors, for separating it from which no ready means presented itself.

It had been thought that if oxidation occurred the course of the reaction might be as follows



giving 4:5-dicarboxy-1:3-dimethyl-2-azanthraquinone, (cf. oxidation of 11-carboxybenzanthrone; J.L.Grieve, Thesis, Edinburgh 1937).

Anthraquinones however, give derivatives with dinitrophenyl hydrazine although not true hydrazones,

do not fluoresce in ultraviolet light in concentrated sulphuric acid solution and do give characteristic colours with zinc dust and sodium hydroxide.

Oxidation of 11-Carboxy-8:10-dimethyl-9-aza-benzanthrone with alkaline Potassium Permanganate.

Two grams of the 11-carboxylic acid and sulphate mixture were mixed with two grams of sodium hydroxide and four grams of potassium permanganate and dissolved in 300 mils. of water. The solution was refluxed for 24 hours. The product was filtered free of the manganese dioxide and the filtrate acidified with dilute hydrochloric acid. No precipitate formed. The solution was evaporated almost to dryness when the residue consisted of a brown jelly-like material. This was filtered and washed with small quantities of water in which the brown colour was carried down into the filtrate. The residue was a white solid which gave an instant white precipitate with silver nitrate when dissolved in water and seemed thus to be pure sodium chloride.

The filtrate was evaporated completely to dryness, and extracted with pyridine, a preliminary experiment having shown that under similar conditions sodium chloride was not soluble in pyridine. On removing the pyridine in a vacuum desiccator a dark brown material was left which possessed slight fluidity. Thus if a portion was removed the surface in a short while again became intact.

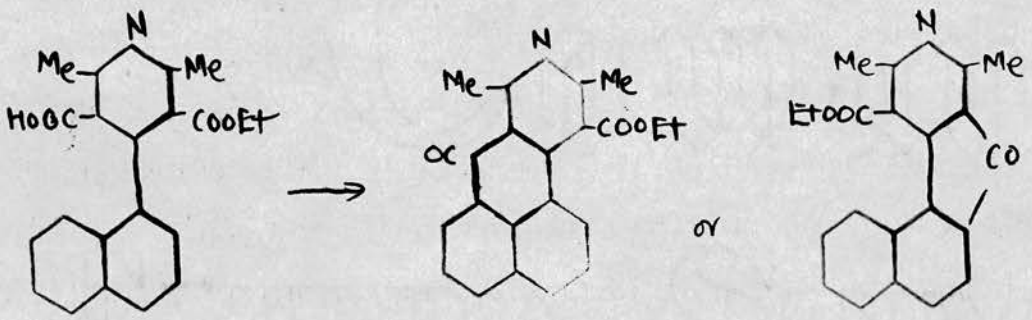
The material was unaffected by heat up to 360°C. and did not sublime after treatment for four hours. With zinc dust and sodium hydroxide the colour of the solution was the brown colour obtained by dissolving the material in sodium hydroxide.

The material was very soluble in water to give an acid solution. It dissolved in concentrated sulphuric acid to give a brown solution with a darker brown fluorescence in daylight and a milky light blue fluorescence in ultraviolet light. An elements test showed nitrogen to be present but the material could not befreed from the smell of pyridine even after several days' evacuation.

The product is obviously not an azanthrequinone derivative and apart from its acid nature no positive evidence regarding the actual structure was obtained.

Attempts to Cyclise 4-a-Naphthyl-3-carboxy-5-carbethoxy-2:6-dimethyl-pyridine.

Ring closure of 4-a-naphthyl-3-carboxy-5-carbethoxy-2:6-dimethyl-pyridine should give either 11-carbethoxy-8:10-dimethyl-9-azabenzanthrone or a fluorenone derivative and discrimination should be easy depending upon whether or not the product yields a dinitrophenyl hydrazone.



A variety of agents was employed with disappointing negative results in every case.

0.68 grams of the acid ester were boiled with toluene, phosphorus pentoxide added and the whole refluxed on an oil bath for one hour. The solid residue in the flask was red-brown in colour. Extraction with aqueous sodium hydroxide dissolved

everything to give a yellow solution. As the desired product should be insoluble in alkali it had obviously not been formed.

2.5 grams of the acid ester were treated with 20 mils. of chlorosulphonic acid for 3 hours at room temperature and the red solution carefully poured into a litre of water. A small amount of a yellow solid, turning orange, was thrown out and was allowed to stand in the refrigerator for a week. After filtration the solid was so small in amount that it could not be removed from the filter paper.

Four experiments were conducted with concentrated sulphuric acid. 0.1 grams of the acid ester were treated with 3 mils. of concentrated sulphuric acid for 5 minutes at 50 - 70°C. and cooled. The solution changed from lemon yellow to brown yellow. Concentrated ammonia was added until the solution was alkaline and the resulting solution was quite clear. The desired product should be insoluble in alkali and so had not been formed. Similar treatments for 15, 30 and 60 minutes also gave no precipitates.

The three reagents hitherto employed yielded nothing so the method used to prepare the ketoaza-benzanthrone - formation of the acid chloride and treatment with aluminium chloride - was tried.

1 grams of the acid ester was refluxed for two

hours with 5 mils. of thionyl chloride, care being taken to exclude water. Hydrogen chloride was evolved at the beginning of the reaction. Excess thionyl chloride was removed at the pump and 3 grams of powdered aluminium chloride and 10 mils. of carbon tetrachloride added and the whole refluxed for six hours. The reactants were then poured on to 50 grams of crushed ice and allowed to stand. On filtration a dark coloured product separated. This solid was partially soluble in ammonia and so still contained unchanged material. It was therefore treated with 20 mils. of dilute ammonia, warmed to boiling point and allowed to stand for 15 minutes. It was then filtered off, well washed with water and dried on a porous plate, giving a dark brown powder.

Yield 0.19 grams, i.e. 20% theoretical.
M.p. above 370°C.

The material was completely insoluble in boiling dilute ammonia and in boiling water. It was slightly soluble in boiling dilute hydrochloric acid to give a faintly green solution. It proved to be so insoluble in organic solvents that no purification could be effected by their use.

1 gram of the acid ester was treated with 1 gram of phosphorus pentachloride and 20 mils. of AnalaR benzene and refluxed on an oil bath at 80 - 100°C. for two hours. For the first portion of the period considerable evolution of hydrogen chloride was observed at the calcium chloride tube at the top of the condenser. The reaction was effected in a 250 mil. wide neck conical flask for ease of removal of the final product. The benzene and phosphorus oxychloride were removed at the pump between 50 and 100°C. Another 10 mils. of benzene were added and removed. 3 grams of freshly powdered aluminium chloride and 25 mils. of carbon tetrachloride were then added and the whole refluxed for six hours at 80 - 90°C. Evolution of hydrogen chloride persisted for about three hours. The contents of the flask were then poured on to 50 grams of crushed ice and the solid scraped out with a spatula. After filtration the solid was dried on a porous plate.

Yield 2.10 grams, probably still moist.

This material was boiled for 5 minutes with dilute hydrochloric acid to remove aluminium compounds and filtered. The rich orange filtrate, on neutralisation with sodium hydroxide, gave a white flocculent precipitate presumably aluminium oxide. The solid residue was

treated with dilute ammonia for 15 minutes, warmed to the boiling point and filtered, leaving a uniform brown powder after thorough washing and drying.

Yield 0.81 grams, i.e. 86% theoretical.

M.p. above 370°C.

The material was insoluble in dilute ammonia, dilute and concentrated hydrochloric acid, water and benzene. It was very slightly soluble in propyl alcohol to give a faintly green solution. Very slight solubility in glacial acetic acid, chlorobenzene and n-amyl alcohol was noted, none of these being of the slightest use for purification. The compound appeared to dissolve in boiling nitrobenzene but did not separate out on cooling. In pyridine complete solution occurred but the solid could be recovered only by adding alcohol, and even then the process was very uneconomical. After one treatment 0.33 grams were obtained, melting above 370°C. and apparently no purer than the starting material. Another treatment did not alter the appearance at all. The compound was very dark brown and obviously seriously impure. With concentrated sulphuric acid the material gave a very dark brown solution.

An attempt was made to form the dinitrophenyl hydrazine derivative and proved negative showing the

compound to be probably of azabenzanthrone type and certainly not of fluorenone type.

Bromination of the presumed 11-Carbethoxy-8:10-dimethyl-9-azabenzanthrone.

0.30 grams of the material obtained in the previous preparation were dissolved in concentrated sulphuric acid, giving a very intense brown solution, and precipitated by addition of water. A 25% excess of bromine, 2 mils. of 0.5N bromine water, was added and the reactants were heated very gently so as not to drive off the bromine. After 15 minutes the colour of the bromine had disappeared and the solution was filtered, washed with water and dried.

Yield 0.23 grams.

M.p. above 370°C.

On being boiled with dilute nitric acid the material gave a strongly positive test for ionic halogen. Accordingly it was digested twice with dilute ammonia, filtered off, well washed with water and dried in the steam oven.

Yield 0.19 grams, i.e. 51% theoretical.

The material then gave a negative test for ionic halogen but a positive elements test for halogen, the silver halide being tinged yellow. It thus appears that the bromination had been successful. The material was completely insoluble in alcohol, chlorobenzene, glacial acetic acid and other usual organic solvents. It was soluble in pyridine, but less so than its precursor, to give a brown solution. Purification was attempted by adding hot ethyl alcohol to the hot pyridine solution until the first trace of precipitation appeared, when the solution was placed in a refrigerator. Overnight a very small amount of solid separated, which it was impossible to work up. The pyridine was taken down to dryness and the dark impure bromo-compound recovered.

It melted above 370°C., did not melt on a platinum foil but sublimed away leaving no residue.

The material was fused with sodium hydroxide up to 230°C. The melt remained the same dirty brown colour showing no change and the recovered product did not act as a vat dye.

As purification proved impossible the matter was not investigated further.

S U M M A R Y

A Hantzsch synthesis has been performed on α-naphthaldehyde, the resulting ester oxidised by nitrous fumes and the oxidised product completely hydrolysed by a fourfold excess of alcoholic potassium hydroxide to give 4-α-naphthyl-3:5-dicarboxy-2:6-dimethyl-pyridine.

This compound has been cyclised by use of phosphorus pentachloride and aluminium chloride to yield 1:11-keto-8:10-dimethyl-9-azabenzanthrone hydrochloride. Treatment with ammonia gave the free ketoazabenzanthrone and the compound formed a dinitrophenyl hydrazone. The ketoazabenzanthrone could be hydrolysed by prolonged treatment with dilute alkali and also water.

Treatment of 4-α-naphthyl-3:5-dicarboxy-2:6-dimethyl-pyridine with chlorosulphonic acid yielded a mixture of 11-carboxy-8:10-dimethyl-9-azabenzanthrone and its sulphate from which the free acid could not be obtained. Decarboxylation by sublimation, however, gave 8:10-dimethyl-9-azabenzanthrone.

The compound 4-α-naphthyl-3-carboxy-5-carbethoxy-2:6-dimethyl-pyridine was also prepared and attempts to ring close this yielded products that could not be usefully purified.

None of the azabenzanthrones examined yielded diazadibenzanthrones on alkaline fusion or acted as vat dyes.

In conclusion an acknowledgement here can but very inadequately express the author's appreciation of his indebtedness to Dr H. Gordon Rule for his guidance and interest throughout the course of this work.