Factors Governing the Reactivity of the Unsymmetrical Benzils.

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Factors Governing the Reactivity of the Unsymmetrical Benzils.

I. Introduction.

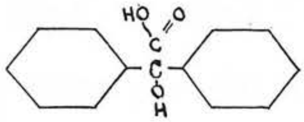
The original discovery that led to the remarkable series of compounds including the benzoins, the benzils and their derivatives, was made in one of the classic researches in the history of Chemistry.

In the year 1832, Liebig and Wöhler published the results of their famous work on the benzoyl derivatives in a paper entitled," On the Radical of Benzoic Acid". (Ann., 1832,3,266) In this paper was recorded the preparation of benzoin by the action of caustic potash on benzaldehyde. It was later shown by Zinin (Ann., 1870,155,92), that in reality this reaction was due to the presence of prussic acid in the benzaldehyde, which had been obtained from natural sources (viz. oil of bitter almonds). He was able to effect the condensation by the action of caustic potash on the crude benzaldehyde, or by treating pure benzaldehyde in aqueous alcoholic solution with potassium cyanide.

This unusual reaction between the carbonyl groups of two molecules of benzaldehyde to form a ketonic secondary alcohol has been found to apply to a large number of substituted benzaldehydes.

It was found that the benzoin was readily oxidised, for example, by the action of boiling nitric acid, to form a compound which was at first called benzoyl, but which is now known to be a dimeric form of this radical, viz. dibenzoyl or benzil.

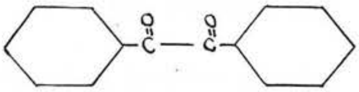
Mention must be made here of another reaction which was discovered in the same period of Organic Chemistry. Laurent,(Ann.,1836,17,91), found that the action of alcoholic potassium hydroxide on benzil produced a purple coloration which disappeared on boiling and he showed the presence in the solution of a new acid now known to be benzilic acid.



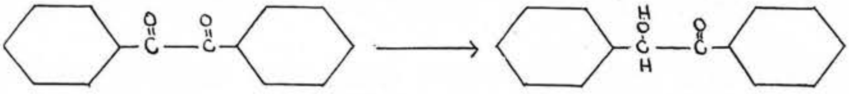
Laurent observed that this compound had a colour reaction with conc. sulphuric acid - a bright red colour was produced - and this property is still used as the most characteristic test for benzilic acid, and may even be used as a colorimetric method for its determination, (Lachmann J.A.C.S.,1922,44,336)

Enough has been said here to show how far the present research is related to the very foundations of Organic Chemistry, and it is now necessary to give a short account of the scope and purpose of the present work, before writing a detailed account of the past researches leading up to it and the various theoretical matters involved.

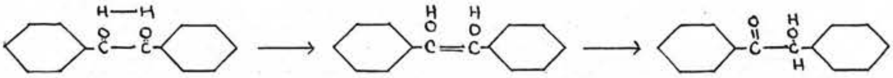
The compound benzil has been shown to have the well-defined structure



and it has many of the characteristic reactions of an aromatic ketone, including the formation of oximes, hydrazones, etc. By careful reduction it may be converted into benzoin, which is a ketonic alcohol.

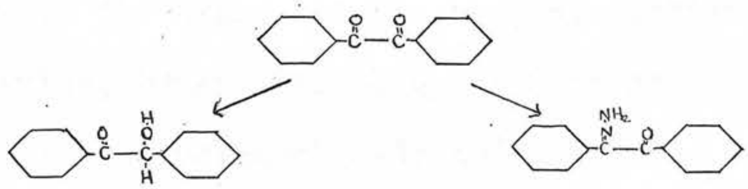


This last reaction must, however, be accepted with some reserve as there is some possibility that the benzoin may be formed in the enolic form, and that hence it is not a normal ketonic reduction.

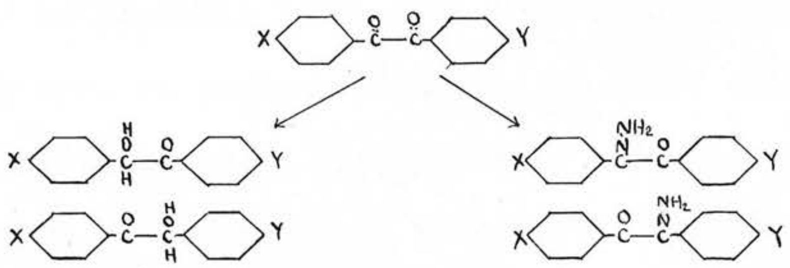


Benzil also undergoes several reactions which are not so obviously ketonic in nature, though they involve the carbonyl groups. Of these, the best example is the benzilic acid change which was discovered, as stated above, by Laurent.

Now, any reaction that involves but one of the ketonic groups of benzil, has, of necessity, only one product, for the ketonic groups are identically situated with respect to the rest of the molecule. For example, in the reaction with hydrazine to form the monohydrazone, or the reduction to benzoin, the product is the same whichever group is attacked.



When a substituent is introduced into one of the benzene rings, a different state of affairs is at once evident, for now each reaction has two possible products, as illustrated below in the case of the two specific reactions mentioned.



The first reference to this fact which had any general experimental basis, was the statement by Buck and Ide, (J.A.C.S., 1932, 54, 4359), that in the catalytic reduction of such unsymmetrical benzils, by the action of one mol. of hydrogen in the presence of platinum black, only one benzoin was produced from each benzil, in every case so far examined.

This statement has, however, not been further examined, and the object of the present research is to see how far it applies to ketonic reactions in general in connection with the mixed benzils.

To this end it was proposed to prepare a number of mixed benzils in fairly large quantity, and to act on them with the usual ketonic reagents including hydroxylamine, hydrazine, phenyl hydrazine, dinitrophenylhydrazine, semicarbazide and aniline. It was intended in each case to find out whether or not only one of the ketonic groups reacted, and in the first case to determine the structure of the resulting compound. It was thought that such reactions might possibly follow some sort of general law, and that it might be feasible to connect this theoretically with the benzoin condensation, the benzilic acid reaction and other reactions of the typically aromatic carbonyl groups such as are found in substituted benzaldehydes.

During the course of the research it was decided to measure the absorption spectra of the benzils used. This decision was made in view of the stress that has been laid by modern spectroscopists on the relation between the reactivity of a group and its absorption spectrum.

It is a curious fact that the two fundamental reactions on which this thesis is based were discovered in the dawn of Organic Chemistry and are not yet thoroughly understood in spite of a great deal of experiment and much speculation on the subject. These reactions are intimately connected with the most modern work on the theory of organic reactions and are fully discussed later, in this connection.

The Benzoin Condensation.

The condensation of two molecules of benzaldehyde under the influence of potassium cyanide, to form benzoin, was discovered , as stated above, by Liebig and Wohler in the year 1832. It was later shown by Zinin that the reaction could be brought about by such other cyanides as gave the cyanide ion in solution.

Though the benzoin condensation was discovered thus early in the history of organic chemistry, it was not until 1880 that the first unsymmetrical benzoin was prepared. In that year Fischer obtained a mixed benzoin, but though he realised that two isomers were possible, he did not pursue the matter further. (Ber.,1880,13,1104)

During these 48 years, research in this field had been devoted to the preparation of new benzoins, and to the determination of the conditions of the reaction, and especially the exact function of the catalyst. The most important fact ascertained during this period was the influence of polar substituents on the reaction. It was shown by Ekecrantz and Ahlquist (C.1908-1) that the reaction would not occur with aldehydes containing strongly electropositive groups such as $-NO_2$ and $-OH$ or even negative groups such as $-NH_2$

The work in the field of the mixed benzoins was carried on by Staudinger (Ber., 1913,43,3537), Horbye(Dissertation Dresden 1917), Brass (Ber.,1931,64,503) and more recently by Buck and Ide (J.A.C.S., 52 to date) and by Tiffeneau and Levy (Bull., 1930,49,725).

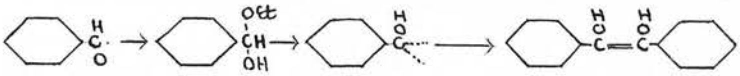
Give actual references.

Staudinger gave a striking illustration of the influence of polar groups which had been suggested by Ekecrantz. He found that dimethylaminobenzaldehyde, which will not condense with itself, readily reacts with benzaldehyde to give 80 pc yield of a mixed benzoin.

Staudinger suggested that the peculiar behaviour of this aldehyde was due to the fact that it existed in only one of two possible forms, both of which were necessary for a benzoin condensation to take place.

These forms he associated with a reactive carbonyl and an activated hydrogen respectively, and on the basis of the reactivity of dimethylaminobenzaldehyde with diphenyl ketene and also its rate of auto-oxidation, he assigned to it the form with reactive carbonyl. It has now been shown that the benzoin formed has the structure which invalidates this reasoning. (J.A.C.S. 1930,52,5197)

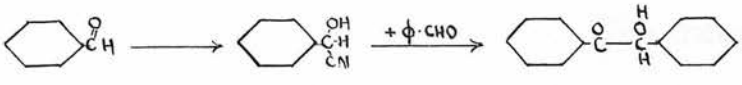
In the year 1896 Nef advanced a novel theory (Ann., 1897, 298, 313) which, in spite of several attractive points, has been shown by later work to be quite untenable.



The chief objections against this theory are as follows :-

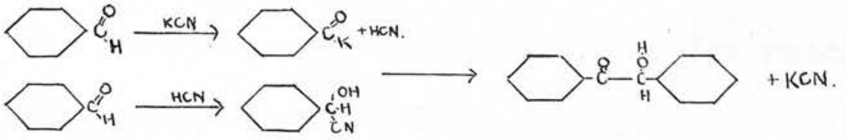
Firstly, the isolation of mandelonitrile as an intermediate product shows that the fundamental idea behind Nef's theory is incorrect. Secondly, the theory cannot explain the formation of mixed and optically active benzoins, and finally it has been shown that the reaction proceeds equally well in petrol ether solution where the first stage of the reaction shown above is impossible.

The most important work in this field was done by Lapworth (J.C.S., 1903, 83, 955) who suggested the following scheme for the reaction.

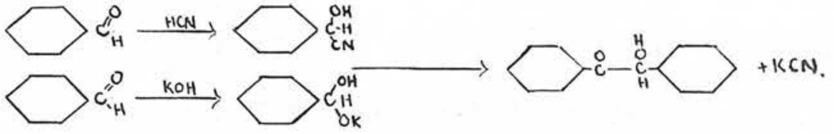


This mechanism explains all the phenomena associated with the simple benzoin condensation and has been successfully applied to the symmetrical substituted benzoins, by Hodgson (J.C.S., 1930, 14). It is probable that the theory also applies to the mixed benzoin condensation if appropriate modifications be made.

A very similar theory was put forward by Chalanay and Knoevenagel (Ber., 1892,25,293) and quantitative work by Bredig and Stern (Z.Ph.Ch.,1905,50,513) has shown that either of these mechanisms is possible.



Lachmann (J.A.C.S., 1925,46,722) suggested that the theory of Lapworth might be modified and corrected by the introduction of a further addition compound of benzaldehyde - viz. Ø.CHO,H_2O or Ø.CHO,KOH. This mechanism which claims to explain also the Cannizzaro reaction of benzaldehyde, has been disproved by the discovery that the condensation will occur readily in the entire absence of ionising solvents. (see later)



The experimental evidence for the various theories may be summarised as follows:-

The reaction between two molecules of benzaldehyde to form benzoin occurs by the influence of cyanides of the alkali metals or the alkaline earths, and no other catalyst for the reaction has been found. No benzoin is formed in the absence of cyanides and none has been detected in the heating of benzaldehyde within wide limits.

The condensation will proceed in the presence of alkali, though it is accompanied in this case by the Cannizzaro reaction, while it is completely inhibited by the action of acids, even acetic acid.

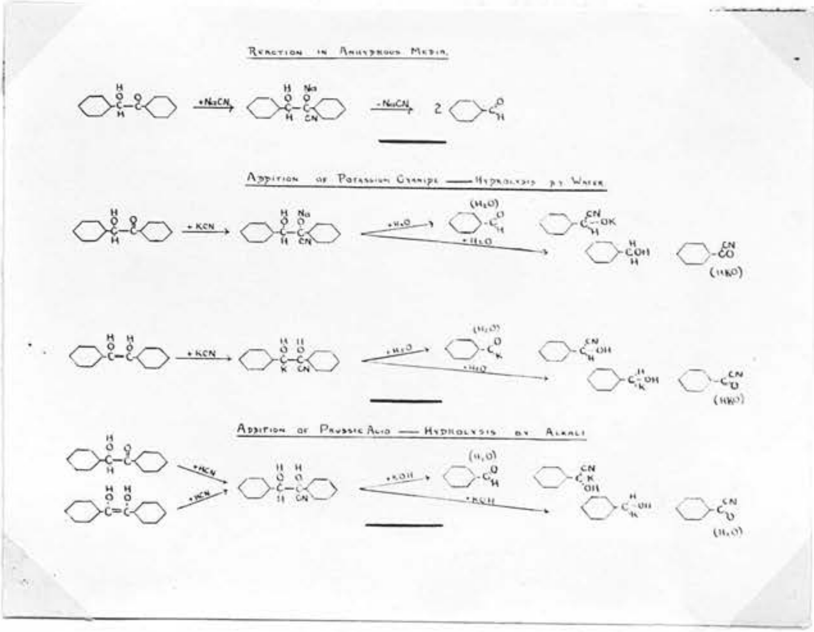
The most favourable condition for the reaction is in boiling aqueous-alcoholic solution, but it will also proceed in dry petrol ether or pyridine. In these solvents, allowing for the comparative insolubility of the cyanide used, the reaction is more rapid than in aqueous-alcoholic solution.

The dynamics of the reaction which were studied by Bredig and Stern show that the reaction contains a measurable stage corresponding to a reversible reaction of the second order. It is proportional to the concentration of cyanide within wide limits and increases with the proportion of water in the solvent. The reversibility of the reaction was definitely proved by Buck and Ide who prepared benzanisoin from benzoin and anisaldehyde in the presence of potassium cyanide.

It was shown by Lachmann (loc.cit.) that on drastic treatment of benzoin - for example by dry heating with solid potassium cyanide - the products are varied and include benzaldehyde and reduction products of benzoin, as well as a series of products which appear to be formed by splitting of the benzoin about the central bond. The last mentioned products are also found, though only in traces, in the benzoin condensation itself, especially if it be heated for a time much longer than that necessary to complete the reaction. The reduction products of benzoin are accounted for by the fact that benzoin decomposed by heat evolves hydrogen, which is obtained in the free state only in presence of metallic palladium (J.A.C.S., 45,1592 and46,712)

The crucial evidence, on which the theory of Lapworth rests consists of the slow condensation of mandelonitrile and benzaldehyde in presence of tripropylamine in dry pyridine solution. This reaction was applied by Horbye to the mixed benzoins. He condensed the calcium salt of anisaldehyde with benzaldehyde. Unfortunately, his experimental conditions are not known but it seems likely that in this case the reaction might proceed at a rate comparable with that of the benzoin condensation.

A final piece of evidence which appears to support this modified form of Lapworth's mechanism, while at the same time inconsistent with the original equation given by him, was published by Morton and Stevens (J.A.C.S.1928,52,2031). These workers showed conclusively that the condensation could proceed in solution in anhydrous petrol ether, and actually


REACTION IN ANHYDROUS MEDIA.
+NaCN
-NaCN
ADDITION OF POTASSIUM CYANIDE — HYDROLYSIS BY WATER
+KCN
+H₂O
ADDITION OF PRUSSIC ACID — HYDROLYSIS BY ALKALI
+HCN
+KOH

isolated an addition compound of benzoin and sodium cyanide, which probably corresponds to the benzoin cyanhydrin of Lapworth's theory.

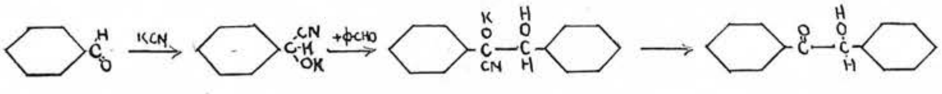
The reverse action does not appear to have been studied theoretically, and it is important to notice that of the six possible cases only three yield benzaldehyde as a product, while the other three give products similar to those isolated by Lachmann from benzoin by dry heating with potassium cyanide.

There is no case exactly corresponding to the equations of Lapworth and Lachmann, but the slightly modified formulation of Horbye, which fits in with the work of Morton and Stevens, finds an exact parallel.

So far no explanation has been given for the results of the mixed benzoin condensation by the authors responsible for them. In the first place it must be mentioned that in no case does the mixed condensation give as good results as the condensation of benzaldehyde. The products are generally obtained as oils and the yields are smaller and the mixed benzoin is not in general the sole product of the reaction. It appears however that in all cases, whatever the nature of the substituent present, the carbinol group in the resulting benzoin is adjacent to the unsubstituted benzene ring, or that containing a chlorine atom in the p- position, where such is present.

The mixed benzoin condensation is dealt with later, and the present knowledge of the reaction in general may be summed up as follows:-

The first step in the benzoin condensation is the addition of potassium cyanide or prussic acid to a benzaldehyde molecule to form a mandelonitrile or its salt. It appears that under different conditions either or both of these possibilities may occur. The mandelonitrile and a molecule of benzaldehyde then condense by some unknown mechanism to form benzoin cyanhydrin, and finally this decomposes to give benzoin and the regenerated cyanide.



Of these stages, all must be reversible under the conditions of the reaction, and the first and the last stages are very rapid.

The Benzilic Acid Transformation.

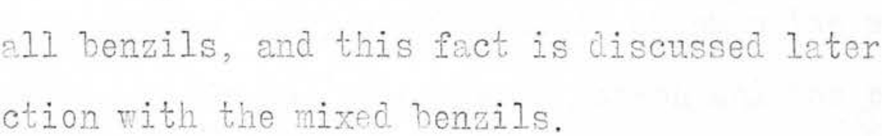
It was discovered by Laurent (Ann., 1836,17,91) that the action of alcoholic potash on benzil produced a purple colour, and he showed that an acidic compound was present in the solution. This compound is now called benzilic acid and the reaction may be represented as follows.

This acid was isolated several years later by Liebermann and Homeyer (Ber., 1879,12,1972) who regarded the colour as characteristic of benzil. It was later shown by Bamberger that the colour was developed with other diketones and he suggested that the colour was characteristic, not of benzil alone, but of diketones in general. Later still, Bamberger and Scholl proved that, though the reaction was given by a mixture of benzil and benzoin, a very pure sample of benzil did not react with alcoholic potash in the cold. (Ber., 1899, 32, 1809)

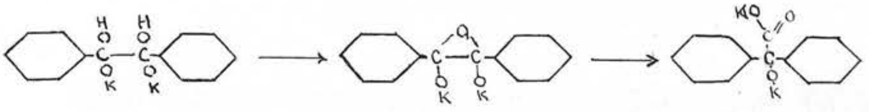
The colour reaction was also studied by Hantzsch and Glover (Ber 1907,40,1519) who showed that the colour produced from benzil on heating with alkali differed from that given by a mixture of benzil and benzoin in the cold, which disappeared on shaking in the air. These workers also distinguished between the coloured product given by the action of benzil and potassium ethoxide in dry ether and that produced in benzil by metallic potassium, which is now known to be caused by the formation of benzil dipotassium.

The production of benzilic acid does not occur with all benzils, and this fact is discussed later in connection with the mixed benzils.

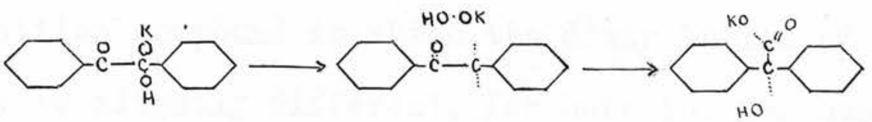
The mechanism of the benzilic acid reaction was first discussed by Nef (Ann., 1897, 298, 372) He assumes the addition to the benzil of one molecule of water and splitting of the intermediate compound so formed into benzophenone and dihydroxymethylene. This last compound isomerises to formic acid and adds on to benzophenone.



Tiffeneau (Rec.Gen.Sci., 1907, 18, 584), by analogy with the pinacol change, assumes that the reaction involves the addition to the benzil of two molecules of potassium hydroxide followed by the elimination of a molecule of water, the formation of a C.C.O ring and isomerisation to benzilic acid. This has been severely criticised by Lachmann on the grounds that it has no experimental basis, that benzilic acid does not form a disodium salt, and lastly that ring formation is improbable under the conditions of the reaction. In addition this theory leaves the mechanism of the reaction no clearer than before.



Schroeter (Ber., 1909, 42, 2336) assumes the addition to the benzil of one molecule of potash and the elimination of HO.OK. This residue isomerises and HO.OK adds on again.



The most important objection to this theory is that diphenyl ketene is unstable and under these conditions it would give diphenylacetic acid. It must also be noted that the second stage of the reaction involves the formation at the same time of a powerful oxidising agent and a highly unsaturated compound. Lachmann (J.A.C.S., 1922, 44 330) has also objected that the third stage involves an increase in the free energy of the system and hence a violation of the laws of thermodynamics.

The application of thermodynamical principles to the benzilic acid change has been treated by Michael (J.A.C.S., 1920, 42, 1787) in a paper on the application of thermodynamics to the mechanism of organic reactions.

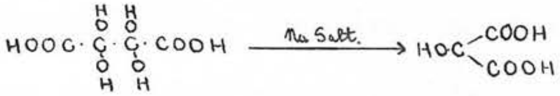
It may be pointed out that this treatment is too speculative to be seriously considered, as there is no way of proving the various points raised and the theory neither makes any definite advance nor clears up any existing mechanism.

The theory assumes that the C-C bond in benzil has been weakened by the influence of the phenyl groups, and hence the molecule readily ruptures at this point, e.g. by the action of alcoholic hydrogen cyanide at room temperature. In the presence of potash, benzil forms an addition compound in which the distribution of binding energy is slightly different, for here the C-Ø bond is weak and the C-C bond is stronger and so there exists a tendency to the transformation. This takes place by the action of alcoholic potash in accordance with theory but the application of the method to the splitting of benzil by the action of alcoholic potassium cyanide is by no means clear.

A very comprehensive study of the benzilic acid change has been made by Lachmann by analogy with several reactions of a similar nature. His papers include a considerable amount of experimental work in which the benzilic acid change and similar reactions both of benzoin and benzil have been studied.

The starting point of the research is the dis-

discovery that the dihydroxy tartaric acids undergo a similar reaction to the benzilic acid change.



$$HOOC\cdot\overset{\overset{H}{O}}{\underset{\underset{H}{O}}{C}}\cdot\overset{\overset{H}{O}}{\underset{\underset{H}{O}}{C}}\cdot COOH \xrightarrow{\text{Na Salt.}} HOC\begin{matrix}\diagup COOH\\ \diagdown COOH\end{matrix}$$

The sodium salt of hydroxytartaric acid decomposes even at room temperature, and more quickly on heating, to form tartronic acid, and it seems possible that the transformation in the case of benzil is due to the formation of a similar hydroxy-compound.

In this connection an observation by Klinger (Ber 1886,<u>19</u>,1868) assumes considerable importance. This worker found that on long standing in moist ether, benzil gave at least traces of benzilic acid. It should be noted that even traces of benzilic acid may be estimated by means of the red colour which is produced by the action of conc. sulphuric acid.

The experimental evidence cited by Lachmann may be summarised as follows:-

The benzilic acid change proper occurs in traces by the prolonged action of water, or ether containing a little water. The acid is most readily prepared by the action of aqueous or aqueous-alcoholic potash, and the reaction is very rapid on heating. It has been shown that the increased rate of reaction due to the potash compared with that of water, is less than the increase in the concentration of the hydroxyl ion. It has been suggested that, as the heat change in the reaction is small, therefore the reaction is probably reversible, but as no evidence of the production of benzil from benzilic acid has been recorded, this point can not be settled.

In the purest benzilic acid formed by the action of potash, there is always present a trace of benzoic acid. The explanation of this has been found in the study of another reaction which appears to be related to the benzilic acid change. This reaction involves the splitting of benzil by the action of sodium ethoxide intobenzaldehyde and ethyl benzoate.

The corresponding compound -benzoin- is affected by these reagents in a different manner. Potash in the presence of air and aqueous alcohol causes splitting about the central bond to form benzyl alcohol and benzoic acid (at temperatures over 100° and with alkali over 7N).

Benzil has been shown to have addition compounds of potash and sodium methoxide and ethoxide (Ber., 1923, 56,253 and Lachmann-loc.cit.) and it is probable that benzoin has similar derivatives, though these have not been isolated in a state of purity. The potash compound of benzil readily decomposes to form benzilic acid;

the methoxide and ethoxide are split up by alcohol into benzaldehyde and the corresponding benzoic ester, and by water to the benzil. If water be present in the alcohol, benzilic acid is formed, and in any case a trace of this compound appears.

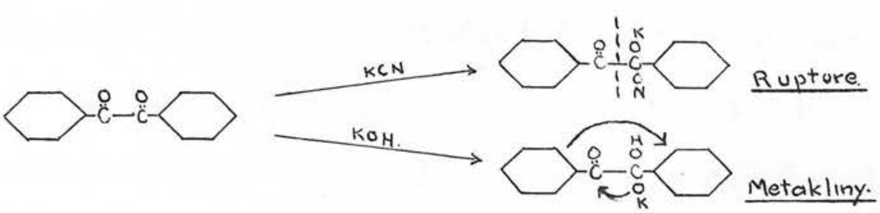
In many of these reactions a compound, ethyl dibenzyl, appears to be formed, and it is thought to be a benzilic acid derivative, though its structure has never been determined.

Benzil is decomposed by aqueous or alcoholic potassium cyanide to benzaldehyde and benzoic acid or its ester. In the action of benzil and anhydrous prussic acid, the dicyanhydrin is formed, and this compound has a tendency to rupture in a manner analogous to the reactions described above.

Benzoin is stable to the action of cyanides, though it is split up by the action of alcoholic prussic acid, apparently via benzoyl cyanide, in the usual manner.

With acids benzoin gives the compound corresponding to benzilic acid, viz. diphenyl acetic acid, though the yield is small owing to side reactions, and to the action of the reagent on the acid formed.

Lachmann's theory of the reaction may be summed up as follows. The first step of the reaction is the addition of one molecule of potash to the benzil to give a compound analogous to dihydroxytartaric acid



Now under different conditions this compound can undergo two alternative reactions, splitting or metakliny (i.e. the transformation). In the case of the addition compound with sodium ethoxide, as stated above, splitting of the molecule occurs in the absence of water, and otherwise benzilic acid is formed. In this addition compound wandering of the OEt or the ONa group cannot occur, since in these cases the product would include ethylbenzilic acid or the ethyl ester of benzilic acid, which is not the case. The action of water probably first involves the decomposition of the ethoxide compound and the formation of a hydrate or a potash addition compound. In either of these compounds, which are also formed by the action of water and of aqueous potash on benzil, benzilic acid may be formed by the wandering of a group, in one case a hydroxyl and in the other an ONa group.

It has been suggested that the splitting of benzil by the action of alcoholic potassium cyanide is due to the momentary formation of the mono-cyanhydrin.

In the foregoing part of the introduction are discussed two reactions of organic carbonyl compounds which have been extensively studied from many angles, and in all cases experiment shows that none of the theories advanced explains all the facts or completely depicts the reaction.

This fact applies to organic reactions in general, and has not escaped the notice of the more far-sighted chemists, especially within recent years. The considered opinions of several noted chemists may be quoted to illustrate this point. Schönbein for example (J.Pr.Ch.,1868,105,228) states it in the following words :- (cf. Ann., 298,215)

" I have repeatedly expressed the opinion that very many, if not all, chemical reactions, and especially those in which oxygen is involved, do not proceed directly ,but rather by a series of intermediate reactions. The final formation of a synthetic product is, so to speak, but the closing scene of a chemical drama of several acts. That one has not as yet observed these intermediate processes is due chiefly to the fact that they usually occur so rapidly that they cannot be followed by ordinary chemical means."

Similar opinions are expressed by Goldschmidt (Stereochemie) in connection with the Walden inversion

" Numerous attempts have been made to give a theoretical explanation of the Walden inversion. All these however give only a mechanical picture, and in no case do they enable us to predict the occurrence or absence of the phenomena."

Rice (Am.Ch.Monograph) in his consideration of the same reaction says,

" From this review we must regretfully conclude that chemical methods alone in spite of the enormous amount of work done, do not appear to be sufficient to explain and predict the many vagaries that occur when studying the Walden inversion"

The same applies, as has been stated above, to the majority of organic reactions, and indeed as shown by the authors quoted, the time is ripe for the organic chemist to radically alter his point of view. It seems almost as if the limits of purely organic methods had been reached, and the next steps must lie with the physical chemist. At present, the chemical methods of investigation show us the starting materials of a reaction, and the end-products, and in some cases the presence of intermediates can be shown. In other words, the reaction has been resolved into two simpler ones, and there the matter rests for the meantime. The causes of such reactions cannot be probed except by methods involving the molecule as a whole and as an individual, and treating of its internal relations - for example the various spectrometric methods which have been developed within recent years.

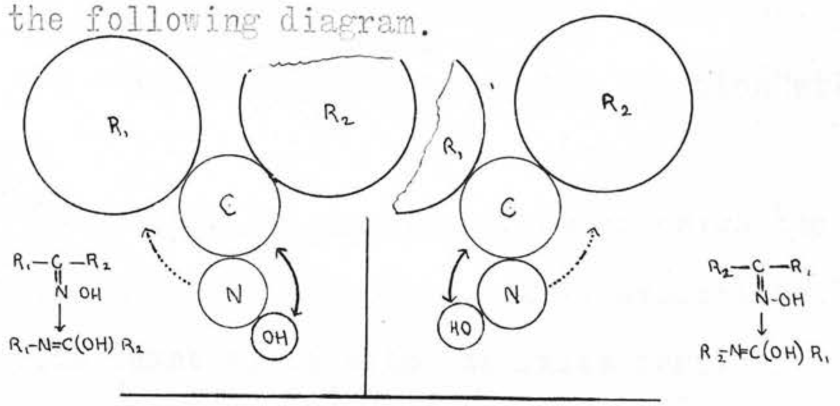
In the two cases considered above, for example it must be emphasised that the starting materials and the products are 'per se' perfectly stable substances. Now, by the addition to the starting materials of a more or less specific reagent, a reaction occurs between them and the product is extremely unstable. A second reaction is put in train and so on the system goes till a stage is reached, at which the product is stable under the conditions of the experiment, and the reaction is'complete' In all cases, the facts are perfectly clear, but the motive power of the various reactions is completely unknown.

It is this drawback which has led to the introduction of such aids to the imagination as partial valencies, which in the long run amount merely to a vague statement of the underlying truth; yet it is evident that ordinary ideas of valency are not competent to explain the motive power of organic reactions.

In his presidential address to the B.A. in 1932 Mills threw out a suggestion, which though merely conjectural, and without any experimental basis, has considerable bearing on the reactions discussed above and points out in a decided manner the entire inadequacy of present day chemical equations.

His suggestion refers especially to the Beckmann Transformation and may be expressed qualitatively by the following diagram.

a.

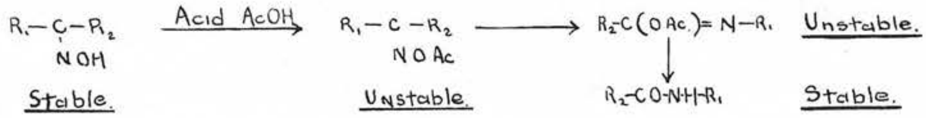


All previous theories of the Beckmann transformation fail when confronted by the fact that the reaction results in the interchange of positions between two groups in the trans- position with respect to one another. This has been found to occur in all cases of the Beckmann reaction of the first type in which it was possible to put the matter to the proof. Now, on Mills' theory, all difficulty vanishes if the simple and reasonable assumption be made that the driving force of the reaction is the stability of the C-O bond as compared with that of the C-N or the N-O bond present in the oxime.

As it stands, the theory will not apply to ordinary conditions, for an oxime is normally stable and the transformation is brought about by the application of strongly acidic reagents such as benzene sulphonyl chloride and phosphorus pentachloride or, as was shown by Kuhara, of acetylating agents in the presence of hydrochloric acid. This modification does not alter the validity of the idea, but merely defines the conditions under which the reaction will take place.

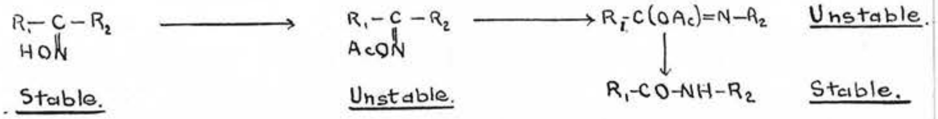
Thus, from the conditions under which the reaction is known to take place, it is evident that the reaction takes place with the oxime derivatives of the ester type, and the true distribution of forces may be represented by diagrams b. and c. .

b.



$$\underset{\text{Stable.}}{\underset{NOH}{R_1-C-R_2}} \xrightarrow{\text{Acid AcOH}} \underset{\text{Unstable.}}{\underset{NOAc}{R_1-C-R_2}} \longrightarrow R_2-C(OAc.)=N-R_1 \ \text{Unstable.} \downarrow R_2-CO-NH-R_1 \ \text{Stable.}$$

c.



$$\underset{\text{Stable.}}{\underset{HON}{R_1-C-R_2}} \longrightarrow \underset{\text{Unstable.}}{\underset{AcON}{R_1-C-R_2}} \longrightarrow R_1-C(OAc)=N-R_2 \ \text{Unstable.} \downarrow R_1-CO-NH-R_2 \ \text{Stable.}$$

It is evident from consideration of the benzoin condensation, benzilic acid change, and indeed of organic reactions in general, that the first step in a reaction can often be shown to be definitely the addition of the reagent to the starting compound. In the benzil series this has been shown to be the case in the benzilic acid change as well as in the splitting of benzil by sodium ethoxide and by potassium cyanide, and it seems possible that the true reactivity of a carbonyl must be measured by the tendency for the addition of the reagent. The subsequent course of the reaction depends entirely on the properties of the addition compound so formed. For example in the benzilic acid reaction, the addition compound of potash and benzil undergoes metakliny, while the similar compounds of sodium ethylate and potassium cyanide split about the central bond. In the case of the benzoin condensation it has been stated that the properties of the substituted benzoin cyanhydrins are one factor determining whether a benzoin condensation shall occur.

Unfortunately, there is at present no method of determining this additive power, and the reactivity must be judged by the final products of the reaction.

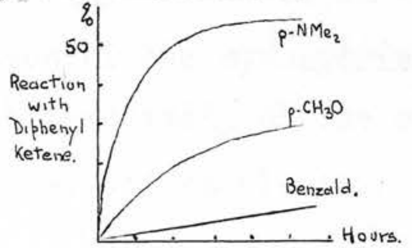
In the field of the mixed benzils, effectively there has been no work done on the ketonic derivatives.

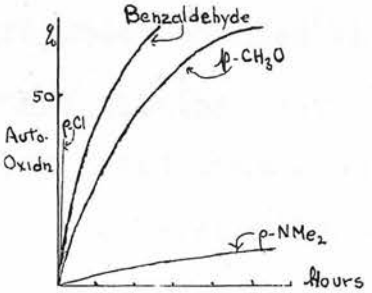
and the same applies to the substituted symmetrical benzils. Evidently, then, any attempt to predict the properties of a mixed benzil must be based on a knowledge of the reactivity of the carbonyl groups in much simpler compounds.

The fallacy of predicting the effect on the reactivity of a carbonyl group, of a substituent in an adjacent benzene ring is at once evident on considering the available data for aromatic carbonyl groups. It is at once seen from a search in the literature that the reactivity of such a group is a comparatively unexplored field, and even in the results already recorded, there are discrepancies and anomalies.

In the aliphatic series considerable work has been done with valuable results, and in the year 1906 Stewart (J.C.S., 1906, <u>87</u>, 185 and 1907, <u>89</u>, 489) studied the reactivity of the carbonyl group in this series towards sodium bisulphite, and later studied the subject spectroscopically. He showed definitely that the reactivity of the carbonyl was largely governed by the nature of the surrounding radicals. In this connection it may be mentioned that the introduction of an aromatic radical into the molecule effects a considerable decrease in the reactivity of the characteristic group.

In such investigations, the most direct method is the measurement of the rates of reaction with the standard carbonyl reagents such as hydroxylamine, hydrazine and sodium bisulphite and also with other less known reagents. In the year 1913 Staudinger (Ber. 1913, 46, 3537) studied in this manner the rates of auto-oxidation of some benzaldehydes and also their rate of reaction with diphenyl ketene and obtained curves of the type illustrated.





The results were applied, wrongly as it now appears, to the mechanism of the formation of the mixed benzoins.

Several years later, Hibbert (J.C.S. 1912, 101, 3421) measured the amount of hydrogen liberated in a Grignard reaction in which the ketone was competing with β-naphthol for a Grignard reagent. In this way a quantitative measure of the influence of phenyl radicals in a ketone was obtained. Later still, the same author describes a measure of the reactivity of ketones by the lowering of the cathode potential of an electrolytic cell by the presence of the ketone. (J.A.C.S., 46, 983)

Quite recently Weissberger (Ber., 1932, 65, 1816) has correlated the speed of auto-oxidation of the α-ketols with the dissociation of the corresponding acids, and also with the Cannizzaro reaction (J.C.S., 1934,535)

Other quantitative measurements, in the aliphatic series include Echner (Ann., 1898 ,302,335) on the heat of formation of Schiff's bases and Petrenko-Kritschenko (J.Pr.Ch., 1900 ,61,431 , 1900 ,62,315 , Ber., 1901 ,34,1699,1702 Ann., 341,150) on the formation of the oximes phenylhydrazones and bisulphite compounds.

Lapworth (J.C.S., 1928,2544) studied the dissociation of the cyanhydrins and obtained several values for the reactivity of the substituted benzaldehydes , and Hinkel and Madel (J.C.S., 1939,75)recently measured the reactivity of similar aldehydes in the Hantzsch pyridine synthesis.

Now, in order to form any general conclusion about the reactivity of carbonyl groups, even those of the substituted benzaldehydes alone, a large amount of data is required. As yet however, this is not available and the data are only comprehensive enough to show that the alternating polarity theory of organic reactions is wholly inadequate to explain the results of these reactions. This conclusion was arrived at by Lapworth (loc.cit.) and also by Flürscheim in his study of the ionisation of the substituted benzoic acids.

The recent work on the mixed benzoins, which was undertaken partly to throw some light on the reactivity of the substituted aldehydes, appears at the moment to confuse the issue still further. In this case also there does not seem to be a sufficient amount of information available, and the authors have drawn no general conclusions. It has, however, been definitely shown that in the condensation of benzaldehyde and a substituted benzaldehyde, the structure of the resulting benzoin is always the same irrespective of the nature of the substituent in the benzene ring. In the case of such mono-substituted benzoins, the carbinol group is always remote from the unsubstituted ring.

This fact is quite unforseen on any of the current theories of the benzoin condensation, and is not accounted for by the alternating polarity theory developed by Ingold, Lapworth and others.

Evidently then, since such matters as this, which have been fully investigated, have led to no definite regularities in the reactivity of the carbonyl group, it is impossible to predict, a priori, the properties of a ketonic group under a series of slightly different circumstances such as are to found in the case of the mixed benzils. In this series, the properties of the carbonyl are governed by the presence of another ketonic group in the α-position as well as that of the two phenyl radicals. For example, it has been shown that under normal circumstances benzil will react as a monoketone. It is readily possible to prepare the mono-substituted derivatives of benzil, and the di-substituted derivatives are, in general, only formed under more strenuous conditions. Another illustration of this property appears in the work of Auwers and Siegfeld on benzil-monoxime, when it was found that under certain circumstances the second carbonyl group would not react with the usual reagents, and in some cases the oximino group was even replaced by such carbonyl reagents while the other ketonic group remained untouched. Under these circumstances it is evidently impossible to give any theoretical treatment until at least a few cases have been examined experimentally.

In the year 1932, an important paper was published by Mme. Ramart-Lucas (Bull.Soc.Chim., 1932,51,512) on the relation between the structure of organic molecules and their absorption spectra.

This paper first of all discusses in a general way, the fact that a group of atoms contained in an organic molecule exhibits the properties, not of the group itself, but rather of the group as modified by the presence of the adjacent radicals. This is well illustrated by the fact that in a homologous series of compounds, the first member, in which the alkyl group present may be regarded as hydrogen, is invariably exceptional in its chemical properties. Another example of this influence is that hexamethylacetone is so much altered by the replacement of six hydrogen atoms by methyl groups that the compound no longer reacts with semicarbazide and other ketonic reagents.

While it is possible in the case of simple molecules to predict the properties of a radical from its environment, in the more complex cases it becomes difficult to do so. Hence, the study of any property related to the chemical reactivity is important, and in this instance the special importance of the quantitative measurement of absorption spectra lies in the fact that they are directly related to the energy changes within the molecule, and are very sensitive to the mutual influence between two groups. According to the method of investigation due to Ramart-Lucas the saturated hydrocarbons do not absorb ultraviolet light between 2000Å and the visible, and a group which, when attached to a hydrocarbon residue, gives a definite and characteristic absorption is called a chromophore. This corresponds to the characteristic chemical groups such as C=O, CO-OH, CN etc and the exact colour (absorption spectrum) of the resulting compound depends on the influence of the other part of the molecule. In the case of a molecule containing a single chromophore, Ramart-Lucas has found that the hydrocarbon radical, excepting the first member of a homologous series, has little effect on the absorption spectrum.

The work has been extended by her to the study of compounds containing two chromophores. It has been found that the two chromophores may influence each other to such an extent that the fundamental properties as shown by the spectra differ totally from those associated with the two chromophores separately. In a more extended study it was shown that this was only the case when the two chromophores were directly united, and as they were separated by carbon atoms, the spectra became more like that of the individual chromophores, till when more than two carbon atoms intervened, the spectra corresponded to simple combinations of the bands due to the two chromophores themselves. It has been shown that the speed of hydrolysis of aliphatic amides obeys similar rules, as well as the speed of esterification of acids. The general conclusions may be summed up as follows:-

> In the case of any chromophore, for all compounds having the same absorption, the reactivity of the group is the same.
>
> At the same time, two chromophores connected by a chain of less than two carbon atoms will show a spectrum more or less modified, and if they are directly united the bands will be wholly different.

The application of this to the mixed benzils is dealt with in the discussion, but it is evident that as they are diketones, they will show a modified ketone band - a diketone band - . For diketones of the same reactivity, the band should have the same position and intensity, according to the conclusions of Ramart-Lucas quoted above.

Summary of Introduction.

The source of the present work has been shown to originate with Liebig and Wohler, and the object and scope of the work has been stated.

The benzoin condensation has been discussed because of its intimate connection with the reactivity of the carbonyl group, and since the relations existing in a molecule of similar structure seem likely to have some bearing on the reactivity of benzil. It was seen that the experimental evidence leads only to the conclusion that the reaction is due to the additive capacity of the aldehydes concerned, and various possible additions are discussed.

The benzilic acid change has been discussed, and it has been shown that this reaction is due to the addition of one molecule of potash to the benzil and that hence it may be possible to use it to measure the reactivity of the carbonyl groups of a mixed benzil.

The mechanism of organic reactions in general is reviewed and the unsatisfactory state of ideas on the subject commented upon.

It has been shown that no generalisations can be based on previous work on the reactivity of aromatic carbonyl groups.

The relation of structure of organic molecules to their absorption spectra is discussed and applied to the mixed benzils.

Note:-

In the experimental part of this thesis all preparations have been worked out, and fully described in the case of simple benzil. For the other benzils described, conditions were similar, and in such cases only such modifications of the standard methods as were found necessary or desirable are described. In all preparations described, the method given is the best and most convenient in the simple benzil series.

Factors Governing the Reactivity of the Unsymmetrical Benzils.

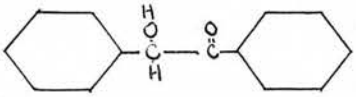
II. Experimental.

Standard Experiments with Simple Benzil.

Benzaldehyde.

The benzaldehyde used in all the benzoin condensations was prepared by distilling the commercial product over a range of one degree, through a long air-condenser. This was found sufficient to remove impurities of which benzoic acid was the chief, and the process was repeated immediately before use.

Benzoin.



Methods for the preparation of benzoin are found frequently in the literature, and those used in this work are given in Organic Syntheses and in Vanino's Präparative Chemie (Organic Part). The latter method was more convenient in the case of smaller quantities and the product was slightly purer. The yield, however was decidedly less.

a) In a three-litre flask fitted with a water reflux condenser, were placed 625 ccs R.S. alcohol, 500 ccs water, 500 ccs benzaldehyde and 50 gms potassium cyanide and the whole was boiled for half an hour. At the end of twenty minutes crystals usually began to appear and an evolution of heat took place so rapidly that the solution boiled almost explosively, while at the same time the whole became solid. Yield 90 pc m.p. 132°

b) A weight of 20 gms of potassium cyanide was dissolved in 400 ccs water contained in a two-litre flask, 200 ccs benzaldehyde in 500 ccs alcohol were added, and the mixture was boiled for half an hour. On cooling, the benzoin separated, and was purified as described below. Yield 80-90 pc m.p. 137-8°

The product from both methods was slightly yellow or brownish in colour, and as this was not quite removed by recrystallisation from alcohol it was found preferable to give a preliminary recrystallisation from glacial acetic acid. The product was then pure white and had a sharp m.p., but a further recrystallisation from alcohol was found advisable to remove traces of acetic acid. It was noted that the product of the method of Vanino had a m.p. 4-5° higher than that usually recorded in the literature and higher than that of the benzoin prepared by the other method (Heilbron in his recently published dictionary of organic compounds records a m.p. of 137°). No explanation for this was found, though the benzoin was recrystallised several times from alcohol and acetic acid. The difference in m.p. was found even when acetic acid was not used in the purification.

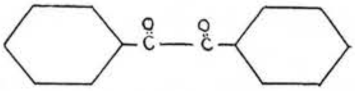
It was found that in the case of the mixed benzoins, as mentioned by Buck and Ide and by Kinney,(p 42 c) a more complicated method of conducting the condensation was not necessary, and the technique described above was used throughout, though in the purification of the mixed benzoins it was often necessary to remove any excess of aldehydes, usually by steam-distillation, before crystallisation would take place.

Cannizzaro Reaction.

A permanent emulsion was made by shaking together 5 gms benzaldehyde and a solution of 4·5 gms potassium hydroxide in 3 ccs water. The reaction was allowed to proceed in the cold overnight, and the product was treated with 25 ccs water and extracted twice with ether. The ether extract contained the benzyl alcohol formed, and the acid was isolated by acidifying the aqueous layer.

The ether soluble portion was tested with dinitrophenyl hydrazine for the presence of unchanged aldehyde and the benzyl alcohol was characterised by means of the phenyl isocyanate m.p.76°.

Benzil.
a) Org. Syn., 6,46
b) Berichte., 1913,46,3537
c) J.A.C.S., 1929,51,1592



It was found that the simplest method of preparing benzil from benzoin, namely the oxidation by conc. nitric acid, gave excellent results, but as it is not applicable to all the mixed benzoins (as was discovered by Kinney, loc.cit., in the case of p-methoxybenzoin), other methods were tried.

The most convenient method, and that which was generally adopted, was found to be oxidation by a concentrated Fehling's solution. This was described by Staudinger, and was later found satisfactory by Buck and Ide. Though the yields were not so good as in the other methods the product was comparatively pure. The method used by Kinney, which involves the use of copper sulphate in aqueous solution in the presence of pyridine, was found to be troublesome on the small scale.

a) In a three litre flask were placed 410 gms benzoin and one litre of concentrated nitric acid. The mixture was then heated on the water-bath for one hour with occasional shaking till no more brown fumes were evolved, and then poured into four or five litres of cold water Yield 90-5 pc m.p.96-7°

b) A hot concentrated solution of the benzoin in alcohol was treated with small quantities of Fehling's solution, till the liquid remained blue on further heating. The mixture was then heated for quarter of an hour, and, after cooling, the benzil, along with the precipitated cuprous oxide, was filtered off and extracted with alcohol. Yield 80 pc m.p.95°

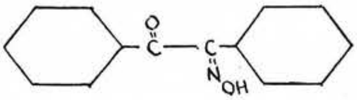
c) In a twelve litre flask, fitted with a mercury sealed stirrer, a reflux condenser, and an air inlet tube were placed 4000 ccs pyridine and 1400 ccs water along with 4100 gms copper sulphate crystals. The flask was then heated till all was dissolved and 1696 gms benzoin were added with stirring which was then continued for two hours. After cooling, the copper sulphate solution was decanted off, and the benzil washed with hot water and then heated with three to four litres of ten per cent hydrochloric acid to remove pyridine. Yield 86 pc m.p.94-5°

In all cases, in the preparation of ordinary benzil, the product was pure after recrystallisation once or twice from alcohol or carbon tetrachloride. The latter solvent was especially useful in the case of an oxidation by a copper solution.

Benzil-α-monoxime. J.C.S., 1930,2305.

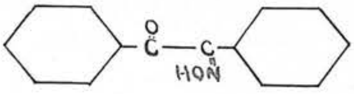
A method for the preparation of this oxime has been worked out, using hydroxylamine hydrochloride in alkaline solution at ice temperature, and its latest form is due to Taylor (loc.cit.). The procedure is simple,a good yield is obtained, and the product is readily purified.

A suspension of ten gms benzil, in a finely divided state, in enough alcohol to form a thin paste was mechanically stirred and one mol. of hydroxylamine hydrochloride in the minimum of water was added. The whole was cooled to -5° and was vigorously stirred by means of a water-turbine, while three mols. (30 ccs) of 20 pc caustic soda solution were dropped in. After one and a half hours stirring at this temperature the mixture was diluted to 400 ccs, filtered and neutralised with the minimum of glacial acetic acid. The precipitated oxime was filtered off and recrystallised from 60 pc alcohol and then from benzene till pure.



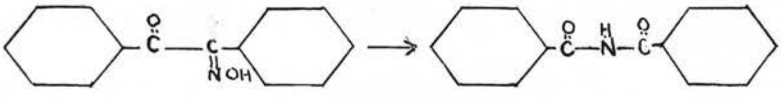
The oxime crystallises from benzene and from alcohol in thin lustrous plates. Yield 95 pc m.p.140°
Under these conditions the oxime is almost completely free from benzilic acid, and from the β-oxime.

Benzil-β-monoxime. J.C.S., 1930, 2305

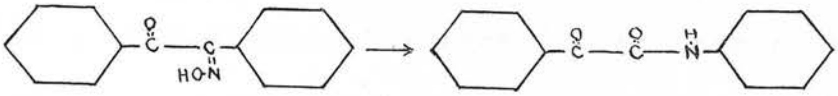


This oxime is the stable form, and may be obtained from the α-form in a variety of ways. It was prepared by heating the pure α-oxime with one tenth of its weight of animal charcoal in the minimum of benzene for ten minutes, or by heating with alcohol in a sealed tube to a temperature of 100° for eight hours. This oxime crystallises from benzene or alcohol in long shining needles or prisms, and it may readily be distinguished from the α-form, or from a mixture, by the use of the microscope. Yield theoretical. m.p. 113°

Beckmann Transformation. Ann., 274, 1 (1893)



The oxime was dissolved in absolute ether and an equal weight of phosphorus pentachloride added. The reaction was allowed to proceed for quarter of an hour, the ether solution decanted from the excess reagent and shaken with a saturated sodium carbonate solution. On evaporation of the ether an oil was obtained which was shown by Beckmann to contain benzoyl chloride and benzonitrile which could be decomposed to ammonia and benzoic acid.



On similar treatment of the β-oxime with phosphorus pentachloride, great heat was developed and the reaction mixture had to be cooled in running water. on shaking with sodium carbonate solution (and not until then) a strong odour of phenyl isocyanide was observed, and by the procedure outlined above an oil was isolated which had a smell of phenyl isocyanide and benzoyl chloride. This oil on standing deposited crystals of aniline hydrochloride m.p.198° and then yellow crystals which were not further investigated (probably benzoyl formanilide as described by Beckmann).

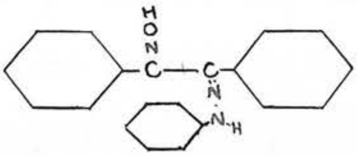
The equations represent the course of the reaction as shown by Meisenheimer.

For the sake of completeness the work of Forster and of Auwers and Siegfeld on the benzil oximes was confirmed.

<u>Phenylhydrazine and Oximes.</u> Ber., 1893, 26, 788

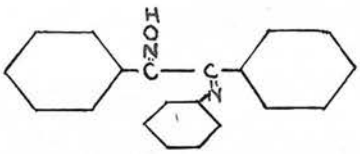
One mol. of the α-or β-oxime was heated to a temperature of 30-40°for a period of three hours with one mol. of freshly distilled phenylhydrazine

(b.p. 132-3° at 18 mms) dissolved in 10 ccs alcohol and acidified with 1 cc of glacial acetic acid. In the case of the α-oxime the phenyl hydrazone of benzil oxime was formed and crystallised out during the reaction. This did not occur with the β-oxime which reacted only under more vigorous conditions to give the dihydrazone of benzil.



Aniline and Oximes. Ber., 1893, 26, 788

Similar experiments were made using aniline instead of phenylhydrazine, and heating under reflux on the water-bath for twelve hours in each case. It was found that both oximes gave the same product, namely an oximanil, though the α-form reacted more readily.

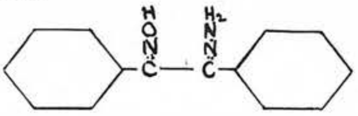


It was not found possible to prepare either of these compounds by the action of hydroxylamine on the monoanil or mono-phenylhydrazone of benzil.

Hydrazine and Oximes. J.C.S., 1913, 2236

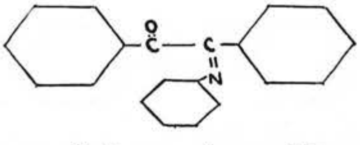
A mixture of one mol. (.·5 gm) of the oxime with alcohol(20 ccs) and one mol. of hydrazine hydrate (50 pc aqueous solution) was refluxed over a small flame for four hours. At the end of the time a little water was added and the solution was allowed to crystallise.

In the case of the α-oxime it was found that the oximino group had apparently been replaced, and the product was found to be benzil-monohydrazone, while with the β-oxime a good yield of benzil hydrazoxime was obtained.



Benzil-anil.

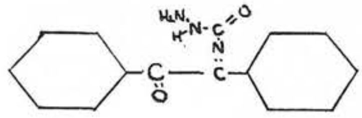
J.Pr.Ch., 89,40,(1909)



A mixture of 1 gm benzil and 1 gm aniline was heated with ·01 gm iodine to a temperature of 130° for ten minutes, the mixture was diluted with alcohol and allowed to crystallise. Yield 90 pc m.p.100°

Alternatively a mixture of equivalent weights of benzil and aniline were boiled with ten times their weight of nitrobenzene till no more water was expelled. The nitrobenzene was steamdistilled off and the residue recrystallised from alcohol. Yield 90 pc m.p.100°

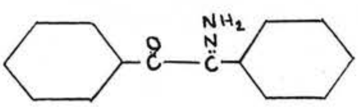
<u>Benzil-semicarbazone</u>. Ann., 1905 ,<u>339</u>, 250



a) Benzil (2 gms) and potassium acetate (1 gm) were dissolved in alcohol and treated with semicarbazide hydrochloride (1 gm) in the minimum of water. The solution was cleared by the addition of alcohol or water as necessary and allowed to stand for one day.

b) The benzil was dissolved in a little methyl alcohol and the potassium acetate and semicarbazide hydrochloride in the minimum of water. The two cold solutions were mixed and alcohol or water added to clear the turbid solution so produced. Yield 2 gms m.p. 175°

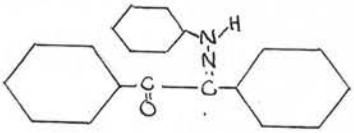
<u>Benzil-hydrazone</u>. J.Pr., 1891,<u>44</u>,176



A solution of 20 gms benzil in the minimum of boiling alcohol was made and treated with 6 gms. hydrazine hydrate (12 ccs 50 pc aqueous solution) The mixture was boiled for one minute and on cooling the hydrazone crystallised out and was recrystallised from alcohol. Yield theoretical m.p. 151°

In the case of the mixed benzils a longer heating was usually necessary and the time was adjusted for each experiment by trial.

Benzil-phenylhydrazone.



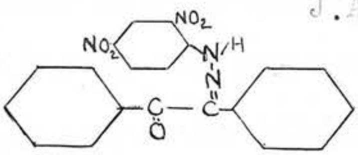
a) One gram of benzil in a finely divided state was treated with a solution of one gram of phenylhydrazine, an equal volume of 50 pc acetic acid and six volumes of water. Yield 80 pc. m.p. 129°.

b) In this modified procedure, the benzil was dissolved in a little hot alcohol and the phenyl hydrazine in a similar volume of water with one drop of acetic acid per cc. The two solutions were mixed and boiled till a red precipitate appeared on cooling.

Yield 80 pc. m.p. 129°.

Benzil-dinitrophenylhydrazone.

Analyst, 1926, 51, 77
J.A.C.S. 1930, 52, 2955



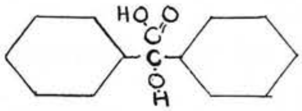
The stock reagent for the preparation of this derivative was a suspension of 1 gm of 2,4-dinitrophenylhydrazine in 200 ccs alcohol. Five ccs of this reagent were boiled and about 0.1 gm of the ketone was added and the mixture boiled till all was dissolved. Two drops of conc. hydrochloric acid were then added and the solution boiled for one minute. In the case of benzil dinitrophenylhydrazones a precipitate

appeared on cooling and adding a little water.
Benzil dinitrophenylhydrazone m.p.185°.

In cases where a larger quantity of this derivative was required the method of Brady was used J.C.S.<u>1930</u>,756. In this modification of the procedure 1 gm. of the solid dinitrophenylhydrazine was dissolved in 2 ccs conc. sulphuric acid, and an alcoholic solution of the ketone was added. The derivative was precipitated immediately without heating.

Benzilic Acid.

Organic Syntheses.

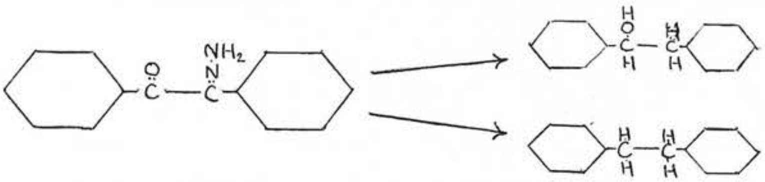


The benzilic acid transformation was brought about by the reaction of 350 gms benzil with an equal weight of potassium hydroxide dissolved in 1400 ccs 50 pc alcohol. A deep bluish-black solution was produced and the mixture was boiled under reflux for about 15 minutes. It was then poured into a large basin and allowed to crystallise overnight. The potassium salt of benzilic acid which crystallised was filtered off and washed with a little alcohol. The salt was then dissolved in 3-4 litres of water and hydrochloric acid slowly added. The benzilic acid was filtered off, well washed with water, dried, and recrystallised from benzene.

Yield 75-80 pc. m.p.150°.

EX BIBL. UNIV. E

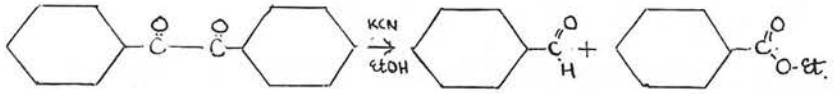
Reduction of Benzil-hydrazone.



A five gram portion of benzil hydrazone was heated in a sealed tube to a temperature of 180° for eighteen hours with a solution of one mol. of sodium in 50 ccs alcohol. On cooling the tube was opened. Ammonia was copiously evolved and the contents of the tube were poured into 250 ccs water. The product was an oil which could not be crystallised. No desoxybenzoin was isolated, and as it was found in the literature that this compound can be reduced by sodium ethoxide it was thought that the mixture might contain unchanged hydrazone along with the reduction products of desoxybenzoin. The experiment was therefore repeated with three mols. of sodium. The product was an oil which was dissolved in alcohol and allowed to crystallise out. The crystals, which had a m.p. of 125° were probably dibenzyl (yield 60 pc), and on evaporation of the mother-liquor a quantity of crystals was obtained. These had a m.p. of 75° and consisted of benzyl phenyl carbinol (yield 30 pc).

Action of Potassium Cyanide on Benzil.

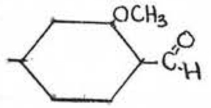
Lachmann J.A.C.S., v.45 (1923)



A solution of 2 gms benzil in 20 ccs absolute alcohol was shaken with 1 gm potassium cyanide for fifteen minutes in a test-tube filled with nitrogen. At the end of this time the solution was diluted with ether and treated with a saturated solution of sodium bisulphite. The benzaldehyde bisulphite compound was filtered off and the ethereal solution extracted with sodium carbonate solution to remove any benzoic acid due to oxidation of the benzaldehyde in the air. On acidification of this extract it was found that no acid was present. The bisulphite compound was decomposed by dilute sulphuric acid and the benzaldehyde extracted with ether. The ether was then evaporated and the aldehyde characterised as the dinitrophenylhydrazone. The ethereal solution was now evaporated and heated under reflux to decompose any mandelonitrile present. It was found that no prussic acid was evolved (tested by a drop of ferrous sulphate on a glass rod, held in the vapour for a minute and then acidified.-absence of prussian blue shows that no hydrogen cyanide is present). The residual ester was hydrolysed by cold alcoholic potash, poured into water and the free acid precipitated by dilute sulphuric acid.

o-Methoxybenzaldehyde.

Ber., 1905,38,1676



Commercial salicylaldehyde was methylated as follows. A mixture of 24 gms salicylaldehyde and 50 gms dimethyl-sulphate was added to a boiling solution of 20 gms caustic soda in 200 ccs water, at such a rate that the solution continued to boil. On cooling, the mixture was extracted with ether and the extract was washed with alkali, then with water, dried and distilled. Yield 85 pc. b.p.124-7°at 16 mms.

o-Methoxy-benzoin.
o-Methoxy-benzil.

Bull., 1930,49,743

According to Tiffeneau and Levy,(loc.cit.) this benzoin has been prepared by the benzoin condensation in the form of an oil which was purified by formation of the semicarbazone. Actually it was found that the product of the condensation was already dark in colour and after steam-distilling, a reddish black oil was obtained. From this oil it was not found possible to obtain other than a meagre yield of the semicarbazone, and in consequence it was thought advisable to convert the whole directly into the benzil. Both the nitric acid and the Fehling's solution methods of oxidation (see page 42) gave a similar product, namely a dark-coloured sticky oil. Attempted purification of this oil resulted in grave wastage and it was ultimately decided to distil the remaining oil. It was found possible by careful heating and using an Anschutz flask to obtain about one-third of this product in the form of a pale yellow oil which soon solidified and was recrystallised from alcohol. Yield about 10 pc m.p.85°.

Contains
75·1 p.c. C & 5·0 pc H.
Required for $C_{15}H_{12}O_5$
7·50 & 5·0.

o-Methoxybenzil-α-oxime.

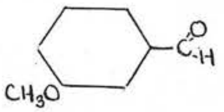
A quantity of the benzil (2 gms) was finely divided and suspended in 10 ccs of alcohol. To this suspension was added one mol. of hydroxylamine hydrochloride in a little water and the whole was cooled to -5° with vigorous mechanical stirring, and finally 3 mols. of 8 pc caustic soda were dropped in slowly. The oxime was isolated exactly as described in the case of simple benzil-oxime. Yield 1·9 gms. m.p.130°.

o-Methoxybenzil-β-oxime.

This was prepared by heating 1·5 gms of the α-oxime in alcohol to a temperature of 100° in a stoppered bottle for four hours. The alcohol solution was then poured into water, extracted with ether, dried and the ether evaporated. The oxime formed an oil which solidified slowly in the icebox Yield 1·3gms. m.p. 150-2°. Contains 9·2 pc Nitrogen ($C_{15}H_{13}O_2N$ = 103)

From a Beckmann Transformation of this oxime the only product isolated was o-anisic acid m.p. 98-100°

m-Methoxybenzaldehyde. Ber., 1882, 15, 2048
ibid 1900, 33, 1826

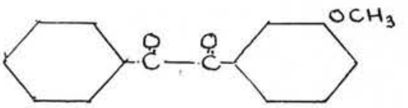


a) m-Hydroxybenzaldehyde was supplied by the B.D.H. in the form of a buff-coloured amorphous powder A methyl alcoholic solution of this aldehyde (137 gms) 56 gms potash and 136 gms methyl iodide were heated to a temperature of 100° in a stoppered bottle for a period of several hours. After cooling, the bottle was opened and the contents diluted with water and steam-distilled.

b) An alternative method demanded the use of dimethyl sulphate. A solution of 250 gms m-hydroxybenzaldehyde in 750 ccs methyl alcohol was treated with 85 gms caustic soda in the minimum of water and the solution was boiled. Dimethyl-sulphate was then added; the first 290 gms were added at such a rate that the solution continued to boil, and finally 200 gms were added in one lot along with enough 50 pc caustic soda to keep the solution alkaline. The methyl alcohol was then evaporated off and the mixture was steam-distilled In this method the yield was somewhat smaller but though the manipulation is less simple there is no risk of total loss of the product as there is in the first method Yield 60-70 pc. b.p. 129-30°at 60 mms.

m-Methoxybenzoin
m-Methoxybenzil

Bull., 1930, 49, 729



The course of the benzoin condensation was exactly as described by Tiffeneau and Levy, but the benzoin was converted directly to the benzil.

The benzil has not previously been described and was prepared by oxidation of the oily product of the benzoin condensation by means of Fehling's solution. The yield was good and the benzil was readily purified. It forms stubby yellow needles from alcohol, and shows the tendency to the formation of large crystals which is also characteristic of the o- and p-isomers.

Contains 74·8 pc C &
5·2 pc H
Required for $C_{15}H_{12}O_5$
75·0 & 5·0.

Yield 60 pc. m.p. 70·5°.

m-Methoxybenzil-α-oxime.

By the action of hydroxylamine hydrochloride and caustic soda on the benzil in the usual manner, a red oil was obtained which showed no signs of crystallising even on three weeks standing in the ice-box.

m-Methoxybenzil-dioxime.

It was found that the benzil would also react readily under the same conditions with two mols. of hydroxylamine to form the dioxime. This oxime recrystallised from benzene was pure white and had a sharp m.p.

Yield theoretical. m.p. 200°.

Nitrogen content 10·6 pc (Required for $C_{15}H_{14}O_3N_2$ 10·4)

m-Methoxybenzil-β-oxime.

By heating the red oily α-oxime with alcohol in a sealed tube, diluting with water and extracting with ether a yellowish brown oil was obtained. This crystallised slowly in the icebox. m.p. 124°.

Beckmann Transformation.

The Beckmann transformation of the β-oxime yielded no identifiable products.

m-Methoxybenzil-hydrazone. m.p. 113-5°

This hydrazone crystallised from the reaction mixture in the usual manner and was recryst. from alcohol.

Contains 11.1% N
$C_{15}H_{14}O_2N_2$ = 11.0%

m-Methoxybenzil-phenylhydrazone

The phenylhydrazone was only obtained as an oil.

m-Methoxybenzil-dinitrophenylhydrazone.

This derivative was prepared in the usual manner and was found to have a m.p. of 149-53°. Contains 13.3% N: Required for $C_{21}H_{16}O_6N_4$ = 13.4%

m-Methoxybenzil-semicarbazone.

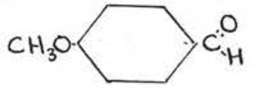
After one week at room temperature this derivative was obtained in the usual manner. m.p. 155-7°.

Contains 14.1% N
$C_{16}H_{15}O_3N_2$ = 14.2%

Benzilic Acid Reaction.

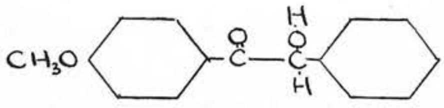
An attempt was made to prepare the benzilic acid from m-methoxybenzil, by the method described on page 51 using in this case 2 gms of the benzil, but the product was an oil which could not be crystallised.

p-Methoxybenzaldehyde.



Anisaldehyde was obtained from the B.D.H. and was vacuum-distilled and kept in sealed bottles till required for use. b.p. 251° at 760 mms.

p-Methoxybenzoin. Bull., 1930,49,729



This benzoin was prepared by the method of Tiffeneau and Levy (loc.cit.) and was obtained from the condensation as an oil which solidified in the ice-box. Yield 80-90 pc.

It has been noted by Kinney (J.A.C.S., 1929, 51,1592) that the benzoin so obtained is not pure, and it was found that when it was recrystallised from alcohol till pure the yield was but 40 pc or thereby.

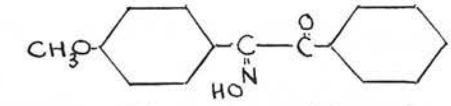
m.p. 105-6°.

p-Methoxybenzil.

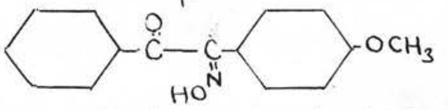
According to the method of Staudinger (see simple benzoin) the benzoin was dissolved in boiling alcohol, treated with a slight excess of Fehling's solution, and heated on the water-bath for half an hour. An equal volume of water was added and the solution extracted with small quantities of ether till the extract was no longer coloured. Yield 85 pc. m.p.62°.

p-Methoxybenzil-α- and β- monoximes.

α.



β



When an attempt was made to oximate this benzil in a manner exactly analogous to that used for simple benzil, an oil was obtained in a yield of about 80 pc. On standing in the ice-box this oil deposited about half its weight of crystals of m.p. 110-20° After washing with alcohol and recrystallising from the same solvent, these had a m.p. of 110°. The alcohol mother-liquors were then added to the residual oil and the mixture was heated in a sealed tube with a further qua ntity of alcohol in order to convert the oxime or oximes present into the stable β-form. The product was poured into water, the oxime extracted with ether, the ether evaporated and the oily residue allowed to crystallise in the ice-box. The oxime so produced was recrystallised from alcohol and had a m.p. of 170-1°. Animal charcoal was also used to effect the transformation from the α- to the β- form, but this method was found less convenient than that described above. It was also noted that an alcoholic solution of the α-oxime containing some calcium chloride became converted to the β- form on standing several days at room temperature, but this phenomenon was not further investigated.

From the solution of the β-oxime there was left finally about 5 pc of an oil which could not be induced to crystallise by any means whatever. This oil may contain, besides impurity, and decomposition products, other oximes of the benzil. Evidence for this was obtained from a microscopic examination of the oil from which all the β-oxime had not been removed. This showed the presence of a small quantity of a plate-shaped crystal differing optically from that of the α- and β-oximes. It was thought that this might be due to the presence of some of the isomeric oxime, but it was not found possible to isolate from the oil anything but the β- and α- forms described above.

Yield of α-oxime 40 pc. Yield of β-oxime 45-50 pc.

Beckmann Transformation of the β-oxime.

The product of the Beckmann transformation of this oxime was a yellow compound melting at 97° ; on hydrolysis it split up and crystals of p-anisidine were isolated m.p. 57°. The identity of this substance was established by a mixed m.p. with an authentic sample of the amine supplied by B.D.H. Contains 5.5 pc N ($C_{15}H_{13}O_3N$)

Actually, the structure of this oxime has been proved by Meisenheimer (Ann., 1925, 444, 94) and this Beckmann transformation was only studied as there is no previous record of it.

Action of Phenylhydrazine on the Oximes of p-Methoxybenzil

The procedure of Auwers and Siegfeld, quoted in the section regarding simple benzil, was applied to the oximes of p-methoxybenzil with the following results.

In the case of the α-oxime the phenyl hydrazone of the oxime began to crystallise out during the course of the reaction. It crystallised from alcohol in long silky needles and was found to contain 12·5 pc of nitrogen (required for $C_{21}H_{19}O_2N_3$ 12·8 pc) m.p. 195-6°. yield ·5 gm.

In the case of the β-oxime though the solution darkened in colour, the only product was the unchanged oxime even after several days standing at the temperature given by Auwers. These results are in accordance with the results for simple benzil.

Action of Aniline on the oximes of p-Methoxybenzil.

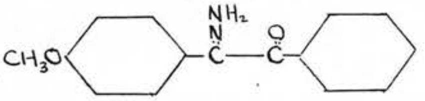
It was found that the oximes did not react with aniline and were recovered unchanged. This is contrary to the results of Auwers and Siegfeld who prepared the oximanil from both oximes by this method.

Action of Hydrazine on the oximes of p-Methoxybenzil.

In the case of both oximes the product of the action of hydrazine hydrate according to the method of Forster (cf. simple benzil oximes) was the same namely the hydrazone of p-methoxybenzil m.p. 105-6°.

and containing 10·7 pc of nitrogen (required for $C_{15}H_{14}O_2N_2$ = 11·0 pc). This hydrazone is not the same as that produced by the action of hydrazine on the benzil. Apparently the hydrazido group has replaced the oximino group of the original oxime, and hence it may be inferred that there is a structural difference in the compounds resulting from the action on the benzil of hydroxylamine and hydrazine respectively.

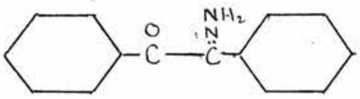
This illustrates the peculiar value of the oximes where questions of molecular structure are involved, for their structure is readily determined by means of the Beckmann transformation. In this case the hydrazone of m.p. 105-6° is probably



p-Methoxybenzil-anil.

This preparation was attempted by both the methods described for benzil-anil, but in both cases the product was an oil which could not be crystallised

p-Methoxybenzil-hydrazone.



This compound was readily prepared by the action of hydrazine hydrate on the benzil. It was found to crystallise from alcohol in tangled rosettes of long hair-like needles which melted at 164°. Yield theoretical. The compound was found to contain 10·9 pc of nitrogen (required for $C_{15}H_{14}O_2N_2$ = 11·0 pc).

As this compound is not identical with the hydrazone described above it must have the alternative structure.

p-Methoxybenzil-semicarbazone.

It was not found possible to prepare this compound in spite of several attempts under different conditions, and in all cases the benzil was recovered unchanged.

p-Methoxybenzil-phenylhydrazone..

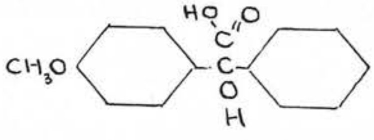
The phenylhydrazone was readily prepared by the method described as b., in the case of benzil-phenylhydrazone. It was pure after one recrystallisation from alcohol. It formed clumps of flat orange prisms m.p. 180-1° and contained the calculated amount of nitrogen, viz. 8·5 pc .

p-Methoxybenzil-dinitrophenylhydrazone.

This derivative had a m.p. of 187-90° when recrystallised from acetic acid. Contains 13·4 pc N ($C_{21}H_{16}N_4O_6$= 13·2)

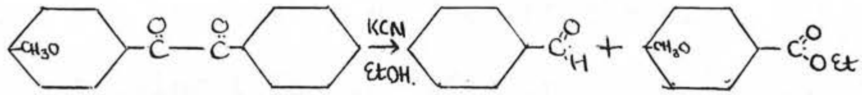
p-Methoxybenzilic Acid.

The benzilic acid prepared from this benzil was found to have a sharp m.p. in the crude state, and when recrystallised from benzene the m.p. remained at 148-9°. As the yield is theoretical the benzilic acid must have the structure shown. Contains 69.8% C 5.4% H (Correct value)



Potassium Cyanide Splitting.

The reaction of this benzil with potassium cyanide was carried out exactly as described in the case of benzil. It was found that the aldehyde dinitrophenylhydrazone was identical with that derived from benzaldehyde (The m.p. of an authentic sample was not depressed on addition of this compound) m.p.235-6.° On hydrolysis, the ethyl ester was found to be that of anisic acid. The acid had a m.p. of 184°, and a mixed m.p. with pure anisic acid showed no depression.



Nitrobenz-aldehydes.

All the mono-nitrobenzaldehydes were obtained from the B.D.H. and m-nitrobenzaldehyde was also prepared by nitration of benzaldehyde. (Vanino)

A mixture of two litres of concentrated sulphuric acid and 170 ccs fuming nitric acid was cooled to 0° and well stirred while 500 ccs benzaldehyde were dropped in at such a rate that the temperature did not rise. When all the benzaldehyde had been added, the mixture was heated to 60° and poured on to ice. The product was recrystallised from a mixture of alcohol and ether. Yield 500 gms. m.p.59-61°.

Benzoin Condensation.

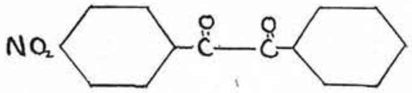
In no case was it found that the nitrobenzaldehyde would undergo the benzoin condensation either with itself or with benzaldehyde; the product of the reaction was invariably a black sticky oil. After steam-distilling this yielded a tarry semisolid mass which could not be crystallised and which did not yield a benzil on oxidation with conc. nitric acid or Fehling's solution. This black product smelt strongly of benzaldehyde and much of this reactant was recovered in the steam-distillation. No simple benzoin was isolated.

Cannizzaro Reaction.

It was found that by the action of a conc.

solution of potash on the o- and m- aldehydes a most vigorous reaction took place, and the product appeared to consist solely of the corresponding acid, while in the case of the p-nitrobenzaldehyde a condensation product involving the nitro- group was obtained. (It appears from Beilstein that with a less concentrated alkali solution these undergo a normal Cannizzaro reaction)

p-Nitrobenzil. J.C.S., 1928, 1080.



An attempt was made to prepare p-nitrobenzil by the method described by Chattaway and Coulson (loc. cit.), by the nitration of benzoin in the presence of acetic anhydride, and it was found necessary to modify the procedure considerably.

Even on mixing conc. sulphuric acid with acetic anhydride, heating took place accompanied by considerable charring and it was found that the solution of benzoin in this mixture was already quite dark-coloured and sticky. When the nitration was completed the product was a dark sticky oil which hardly even merited the name semi-solid. When this oil was converted into the benzil it was found that the m.p. was considerably

Not if kept cold.

lower than that quoted by the previous workers and only after a number of recrystallisations was it raised to its maximum of 140°. Acetone and alcohol were used for this purpose, but it was found that amyl alcohol and ethyl acetate were also good solvents. The modified procedure for the preparation of this benzil is described below in two stages namely the preparation of p-nitrobenzoin acetyl derivative and its oxidation to the p-nitrobenzil.

Acetyl p-Nitrobenzoin.

A mixture of 200 gms benzoin and 1000 ccs of acetic anhydride (b.p. 138-40°) was vigorously stirred and 200 ccs conc. sulphuric acid were dropped in while the flask was cooled in ice. After this operation, the whole was cooled to -5° and 110 gms potassium nitrate were added in small portions. The amber-coloured reaction mixture was allowed to stand for two days at room temperature while white crystals separated. These were filtered off and washed with acetic anhydride and then with ether. The residual solution was then poured on to ice and the oily product removed and drained. It was later found that this oily product on treatment with ether yielded further crystals identical with those described above, and that also the oily product obtained by the method of Chattaway and Coulson deposited the same compound on similar treatment. Yield 60 pc. m.p. 127-8°.

This product has been identified as the acetyl derivative of p-nitrobenzoin described by Francis (J.C.S., Year ? 111,344) and its identity was proved by a mixed m.p. with a sample prepared by his method. The compound prepared as described above was found to be pure after two recrystallisations from alcohol or acetone. It is only moderately soluble in both these solvents even on boiling, and it crystallises in thin shining plates or short flat needles.

After the isolation of the acetyl derivative from the nitration there remained about 30-40 pc of dark-coloured oil, from which there was isolated by shaking with sodium carbonate solution and long standing in the cold, a yellowish solid of m.p. 118° which was not further investigated.

Structure of p-Nitro-acetyl benzoin.

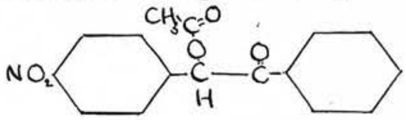
It was found that the acetyl compound of m.p. 127-8° was oxidised by boiling with conc. nitric acid to form the nitrobenzil, in a relatively pure state. m.p. 140°.

The acetyl compound could not be benzoylated in pyridine solution, nor could it be acetylated either by the method described in Organic Syntheses for acetylbenzoin, or by the action of acetyl chloride and pyridine.

The oxime of this compound was readily prepared by the action of hydroxylamine hydrochloride on the acetyl derivative in solution in about thirty times its weight of pyridine. Yield theoretical m.p. 159-61°, contained 8·7 pc nitrogen (required for $C_{16}H_{14}O_5N_2$ 8·9 pc).

Two grams of the compound were boiled for eight hours with 10 ccs 20 pc methyl alcoholic potash and the alkaline solution was extracted with ether. On evaporation of the ethereal solution about one gram of p-nitrobenzaldehyde was obtained m.p. 105-6°, mixed m.p. with pure aldehyde 104-5°. The aldehyde oxidised in air to the corresponding benzoic acid m.p. 232-5° (compared with B.D.H . product m.p. 234-5°). From the alkaline solution, by acidification with sulphuric acid, was obtained a little p-nitrobenzoic acid, along with an infusible product, probably a condensation product involving the nitro-group.

This evidence tends to confirm the structure established for the compound by Francis in which the substituted benzene ring is adjacent to the acetylated carbinol:



Attempts to hydrolyse the acetyl compound of nitrobenzoin have been recorded by Francis, but these led to the formation of the benzil, and of furane derivatives. Hence it was thought advisable to make no systematic attempt to prepare the benzoin in this way, but it may be said that hydrolysis by conc. sulphuric acid leads to very extensive charring and that 50 pc acid leads to the formation of an infusible product which was not further investigated. Boiling the acetyl compound with a mixture of conc. hydrochloric acid and methyl alcohol in an attempt to prepare the benzoin gave an intensely yellow solid of m.p. 185° This compound is again mentioned under the oximation of the p-nitrobenzil.

It was not found possible to isolate from a nitration by the method described above, any of the isomeric benzoins or their acetyl derivatives, and it was found that a mixture of nitric acid and acetic anhydride, cooled in ice, failed to nitrate the benzoin, while at room temperature the reaction became violent and was accompanied by almost complete charring.

p-Nitrobenzil.

When this compound was prepared exactly as described by Chattaway and Coulson it had a m.p. many degrees lower than that quoted by these workers, and only after a number of recrystallisations was it raised to its maximum of 140°. On the other hand, when the acetyl-nitrobenzoin was isolated as described above, the crude benzil had a m.p. as high as 140° and it was readily purified. Yield 80 pc m.p. 142°.

This benzil has been prepared by a number of workers other than those quoted above, but only in poor yields and mixed with the o-isomer. The methods described here proved to be superior both to the method of Francis for the preparation of the acetyl nitrobenzoin, and to that described by Chattaway for the p-nitrobenzil.

Oximation of p-Nitrobenzil.

Oximation by the method of Taylor as described for simple benzil-oximes gave in this case an infusible acidic product which did not melt even on strong heating on a nickel spatula and slowly burned away leaving no residue. It could not be sublimed even in vacuo. In several attempts, a white platy product was obtained by extraction with benzene. This product which was in exceedingly small yield had a m.p of 145-6° and was not identified.

A similar oximation using sodium carbonate in place of the hydroxide had no result and all the benzil was recovered unchanged.

By heating the benzil with one mol. of hydroxylamine hydrochloride and 3 mols. of sodium carbonate for ten hours, the benzil was recovered unchanged.

Similar experiments were carried out with potassium acetate, barium carbonate, borax, and potassium dihydrogen phosphate in order to find a medium which would be alkaline enough to cause the formation of the oxime and if possible to dissolve it as formed, and yet which would not be sufficiently alkaline to cause the benzilic acid change or the formation of condensation products of the benzil. In every case the experiment failed and the benzil was recovered.

In a similar experiment with baryta, an infusible product was formed as in the case where alkali was used.

When 4 mols. of dilute ammonia solution were added to a solution of the benzil in alcohol, with one mol. of hydroxylamine hydrochloride, an intensely yellow solid was formed. This compound was identical with that formed from p-nitrobenzoin acetyl compound by the action of methyl alcohol and hydrochloric acid

It was shown that the action of either conc. nitric acid or Fehling's solution did not oxidise it to the benzil, and that hence it could not be the p-nitrobenzoin.

When the benzil was heated in a sealed tube with hydroxylamine hydrochloride in alcohol, the product was a clear oil which could not be crystallised but which was completely soluble in sodium carbonate solution and was apparently reprecipitated by acetic acid. None of the benzil was recovered from the oil and it probably consisted wholly of the oximes of the nitrobenzil. When the oxime was heated with animal charcoal in alcohol or benzene no crystalline compound was obtained

In view of this experiment, the benzil was héated in alcoholic suspension with one equivalent of hydroxylamine hydrochloride on the water-bath for half an hour. At the end of this time, the benzil was completely dissolved and the solution was a palé yellow in colour. A sample of the mixture dissolved completely when poured into dilute caustic soda solution showing that the reaction was complete and that no more benzil was present. The whole was then poured into water and extracted with ether. On evaporation of the ether, an almost theoretical yield of the oxime was obtained in the form of a clear, almost colourless, oil which would not crystallise even on cooling to -15° for some time and scratching with a glass rod, or standing in the ice-box for several weeks. The oxime could not be obtained in the crystalline state from solution in alcohol or benzene, and it was therefore heated in alcoholic solution with animal charcoal in order to ensure that all the oxime should be converted to the β-configuration (as described in the case of simple benzil). Attempts to crystallise the oil from a wide variety of solvents were then made without success.

A Beckmann transformation of this oil as described in the case of benzil-oxime gave a bright yellow solid of m.p. 127-8° which was recrystallised from alcohol. It was shown by means of a mixed m.p. that this compound was not p-nitraniline, and similarly that it could not be p-nitrobenzonitrile or benzoyl-p-nitraniline or p-nitrobenzoyl-aniline. 15·6 pc Nitrogen.

Attempts were made to hydrolyse this product. The action of hydrochloric acid produced a similar compound of m.p. 150° and hydrolysis by caustic soda gave only a small quantity of black tar. It was found that on dissolving the original yellow solid in conc.

sulphuric acid and pouring into water, a white compound with an unsharp m.p. was formed (recrystallised twice from alcohol) and when pure it melted at 175-6°. On gentle warming with alkali, the compound dissolved, but none of the original substance could be recovered by extraction with ether. This shows that the compound of m.p. 176° was probably not a sulphate of the yellow substance m.p. 127-8°.

An attempt was made, without success, to prepare an oxime-semicarbazone of the benzil by the action of semicarbazide on the oily oximation product. The reaction was allowed to proceed in the usual manner for several weeks at room temperature, and finally a little water was added, but no crystalline product was obtained.

It was found that by the action of excess hydroxylamine hydrochloride on p-nitrobenzil, a small quantity of the dioxime was formed, and crystallised out from the oily product.

p-Nitrobenzil-hydrazone

This derivative was prepared in the usual manner, and was a slightly yellow solid of m.p. 120-2° It contained 15·9 pc of nitrogen (required for $C_{14}H_{11}O_3N_3$ = 15·7 pc). An attempt was made to reduce this hydrazone by the action of sodium ethoxide as described for benzil hydrazone, in the hope of isolating products which would enable the structure of the hydrazone to be determined. The reaction mixture became dark, and on pouring into water, a reddish oil was obtained from which no identifiable products could be isolated. In this case owing to the presence of the easily reduced nitrogroup, the reaction is probably much more complex than in the reduction of simple benzilhydrazone.

p-Nitrobenzil-phenylhydrazones.

The action of phenylhydrazine on p-nitrobenzil yields a mixture of two phenyl hydrazones m.p. 174° and 200° respectively, the latter being present in greater amount, as described by Chattaway and Coulson (loc.cit.). It was found that both these phenyl-hydrazones were recovered unchanged after three hours boiling with alcohol and hydroxylamine hydrochloride. As in the case of the hydrazone, it was not found possible to assign a structure to this derivative.

p-Nitrobenzil-dinitrophenylhydrazone.

This compound as prepared by the usual method had an unsharp m.p., and after recrystallisation from acetic acid it was found to melt at 180-5°. Contained 16.6% N
Required 16.1%

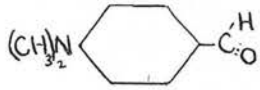
It was not found possible to prepare the semicarbazone or the anil of this benzil, possibly owing to the extreme insolubility of the benzil in cold alcohol.

p-Nitrobenzilic acid.

An attempt was made to prepare the benzilic acid corresponding to this benzil by the standard method described on p51 . The product was an infusible solid which burned when strongly heated and left no residue. It was insoluble in acid, but dissolved in alkali and liberated carbon dioxide from sodium carbonate solution, showing that it contained a free acidic group. The molecular weight was estimated by solution in standard alkali and back-titration with standard acid. . The end-point was quite sharp using phenol phthalein as indicator, and the compound was reprecipitated , apparently unchanged, by the addition of excess acid. The molecular weight , assuming that only one acidic group is present per molecule, was 140-6 and analysis by the micro-Dumas method showed a nitrogen content of 5·6 and 6·0 pc .

An attempt was made to prepare the methyl ester of this acid, but owing to the extreme insolubility of the starting material in the methyl alcoholic sulphuric acid used, the yield was very small. The m.p. of the ester so obtained was 110°.

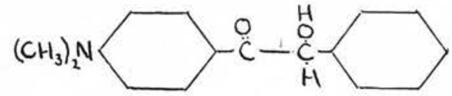
p-Dimethylaminobenzaldehyde.



This aldehyde was obtained from the B.D.H. in the form of the Analar or A.R. chemical which was sufficiently pure for the preparation of the benzoin, though the quality of the aldehyde appeared to vary with different samples.

p-Dimethylaminobenzoin.

Ber.,1913,46,3537



The method of Staudinger for the preparation of this benzoin by the condensation of the dimethylaminobenzaldehyde with simple benzaldehyde was found to be satisfactory. The benzoin crystallised from the mother-liquor and was readily purified by recrystallisation from alcohol. Yield 75-85 pc . m.p. 165°.

p-Dimethylaminobenzil.

It was found that this benzil was readily prepared from the benzoin by the action of Fehling's solution . The crude benzil had a good m.p. and it was readily purified to give a good yield of the pure compound. Yield 80 pc. m.p. 114°.

p-Dimethylaminobenzil-α-oxime.

It was found that when this preparation was carried out in the usual way only half of the benzil reacted, even if the reaction was allowed to occur at room temperature for ten hours. This, along with the fact that the m.p. was remarkably high and that the oxime was only moderately soluble in alcohol and insoluble in benzene led to the suspicion that the benzil had been converted into the dioxime. Yield 40 pc. m.p. 208°.

It was found that the oxime contained 15·1 pc nitrogen (calculated for the dioxime 14·9 pc). This shows conclusively that the compound is the dioxime.

No different methods were used to prepare the monoxime, as the results of this experiment are quite definite and show that under the standard conditions p-dimethylaminobenzil gives a good yield of the dioxime along with unchanged benzil.

The configuration of the oxime described above was not determined.

p-Dimethylaminobenzil-phenylhydrazone.

Under the conditions laid down for simple benzil a good yield of this derivative was readily obtained and it was pure after one recrystallisation from benzene in which it is rather soluble. Yield 80 pc m.p. 157-8°. Contained 12·0 pc nitrogen (required for $C_{22}H_{21}ON_3$=12·3 pc).

p-Dimethylaminobenzil-dinitrophenylhydrazone.

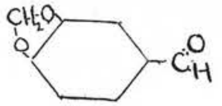
This derivative was prepared by the method given for benzil, and it was found to have a deep reddish black colour m.p. 235-40°. Contains 15.6% N $C_{22}H_{19}O_5N_5$ = 16.2.

It was found that the other ketonic derivatives of this benzil were not readily prepared under the standard conditions and the benzilic acid change did not take place to an appreciable extent after heating the benzil with alcoholic potash for an hour.

Action of Alcoholic Potassium Cyanide.

The only product of splitting the benzil by potassium cyanide in absolute alcohol, which was identified was benzaldehyde (characterised by means of the dinitrophenylhydrazone. m.p. 235°).

Piperonal.

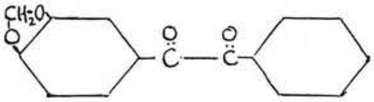


This aldehyde; obtained from the B.D.H., was a massy white solid with a remarkably pleasant odour m.p. 37°.

Piperobenzoin.

This benzoin was prepared as described by Buck and Ide and by Tiffeneau and Levy (loc.cit.). It was found that the benzoin obtained had a m.p. of 110° and there was no sign of any other isomer.

Piperobenzil.



The benzil was prepared from the benzoin described above, by the Fehling's solution method.

Yield 65-70 pc. m.p. 117°.

Piperobenzil-oximes.

It was found that as in the case of p-methoxybenzil, oximation gave an oil which was crystallised by standing in the ice-box to give an oxime of m.p. 110-111°. (containing 5·2 pc nitrogen - required for $C_{15}H_{11}O_4N$ = 5·1 pc).

When the residues of this crystallisation were heated in alcohol with animal charcoal to form the β-oxime,(as for simple benziloxime), the oily product crystallised readily and had a m.p. of 152-3°. It contained 5·2 pc nitrogen. The total yield of oxime was about 80-90 pc showing that in this benzil only one ketonic group is subject to attack by hydroxylamine.

Beckmann Transformation of the β-Oxime.

The Beckmann transformation of this oxime gave a deep yellow micro-crystalline solid of m.p.134-5which did not yield any identifiable products on hydrolysis. It was found that this compound gave a characteristic jade green with conc. sulphuric acid, but no recognisable hydrolysis products were obtained on diluting with water.

Piperobenzil-hydrazone.

There is no abnormality about this reaction, but the m.p. of the product was only sharp after three recrystallisations from alcohol m.p. 117-4 Yield 90 pc.

10.7% Nitrogen
$C_{15}H_{12}O_3N_2$ = 10.5%.

No identifiable products were obtained on the reduction of this hydrazone by sodium ethoxide.

Piperobenzil-phenylhydrazone.

This derivative was prepared by the method -b- on page 50 and was obtained in the form of a reddish oil which deposited about 5 pc of crystals m.p. 115-7°. These contained 9·9 pc nitrogen (calculated for $C_{21}H_{16}O_3N$= 10.4 pc). The residual oil did not solidify.

Piperobenzil-dinitrophenylhydrazone.

This derivative has a characteristic bright red colour similar to that of the corresponding aldehyde. m.p 181-2° . Contains 13pc N. $C_{21}H_{14}O_7N_4$=12.9pc.

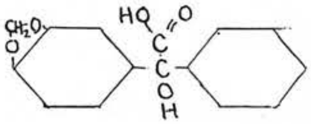
Piperobenzil-semicarbazone.

It was found that the semicarbazone was readily prepared by method b., after one week standing in the cold. m.p.106-7° 13.7pc N $C_{16}H_{13}O_4N_3$=14.0pc.

Action of Potassium Cyanide.

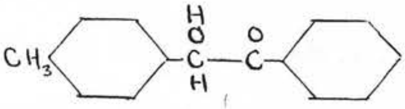
The products of the potassium cyanide splitting of this benzil were benzaldehyde (characterised by the dinitrophenylhydrazone,) and piperonylic acid m.p.284°

Piperobenzilic acid.



The benzilic acid was readily prepared from piperobenzil in the usual manner. m.p. 133-4° Contains 66·1pc C and 4·6pc H $C_{15}H_{12}O_5$= 66·1 and 4·4.

p-Methylbenzoin. Ber., 1916, 49, 1382

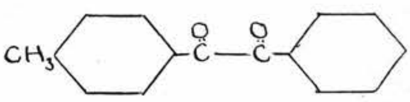


This benzoin was prepared by means of a simple Grignard reaction.

A solution of benzaldehyde cyanhydrin prepared by shaking 10·6 gms benzaldehyde in 50 ccs ether with 13 gms potassium cyanide and 22 gms ammonium chloride in water, was dried with calcium chloride and added to a Grignard solution prepared from 58 gms p-bromotoluene, 8 gms magnesium and 160 ccs absolute ether. During the most vigorous reaction, the flask was cooled in ice, and thereafter it was heated on the water-bath for fifteen minutes and the contents poured on to ice acidified with hydrochloric acid. The benzoin separated from the water-layer in the course of several hours. Yield 20 pc m.p 108-9°.

The yield is calculated in terms of the bromotoluene, and it must be noted that three mols. of this reactant are required for the formation of one mol. of benzoin.

p-Methylbenzil.



The Fehling's solution method of oxidation of the benzoin was found to give incomplete conversion and it was decided to try the action of nitric acid, though it was feared that this might lead to oxidation of the methyl group. The product melted unsharply and by recrystallisation from petrol ether (b.p. 40-60°) it was found possible to isolate about 30 pc of this material with a sharp m.p. of 97-8°. At the end of this long and tedious fractional crystallisation it was found that the compound contained nitrogen (3·7pc) corresponding to a little more than half a nitro-group per molecule of benzil. (Required for a mono-nitro compound 6.9 pc). In view of this failure to isolate the required benzil the matter was not further investigated.

Additional Experimental Results.

Attempts were made to prepare mixed benzoins by the condensation of benzaldehyde with each of the following aldehydes:- o-,m-,andp- hydroxy- and nitrobenzaldehydes. The only recognisable product was in the case of m-hydroxybenzaldehyde, where all the benzaldehyde was recovered as simple benzoin m.p.130°

In connection with the benzilic acid change the following colours were observed in the reaction of the benzil with aqueous-alcoholic potash.

p-Methoxybenzil.	Reddish-purple
p-Dimethylaminobenzil.	Dirty brown.
p-Nitrobenzil.	Insoluble - no colour
Piperobenzil.	Evanescent purple
m-Methoxybenzil.	Transient purple
Simple Benzil.	Violet colour.

In all cases the colour disappeared slowly, but was not affected by shaking in the air.

On treating a mixture of each benzil and the corresponding benzoin with aqueous-alcoholic potash, in all cases a purple colour was developed (excepting the case of p-dimethylaminobenzil where there was no colour). This colour disappeared instantly on shaking

As stated above, the action of alcoholic potassium cyanide on each benzil was investigated. This is described in the case of each benzil, and the results are brought together here for purposes of comparison.

	Products Isolated.
p-Methoxybenzil.	Benzaldehyde and Anisic acid
p-Dimethylaminobenzil.	Benzaldehyde formed.
Piperobenzil.	Benzaldehyde and piperonylic acid.
Simple benzil.	Benzaldehyde and benzoic acid.

Dinitrophenylhydrazones.

All the aldehydes and ketones used were characterised by means of the dinitrophenylhydrazone.

Substituent	Benzaldehyde	Mixed Benzoin	Mixed Benzil
o-Methoxy			
m-Methoxy			143°
p-Methoxy	252°	236-8°	187-90°
o-Nitro	249°		
m-Nitro	286°		
p-Nitro	above 300°d.		180-5°
o-Hydroxy			
m-Hydroxy			
p-Hydroxy	260°d.		
p-$N(CH_3)_2$	243°d.	210°	235-40°
Pipero	269°d.	243-4°	187-8°
p-Methyl	237°	233°	

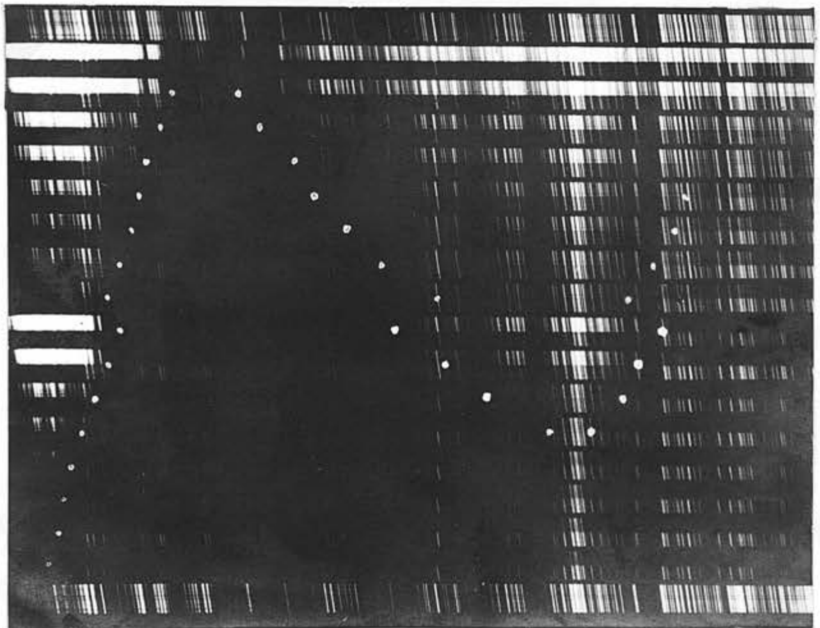
Absorption Spectra.

The absorption spectra of the benzils described above were measured by means of a Bellingham and Stanley medium quartz spectrograph using the rotating sector method.

This method is in common use with spectroscopists and is described in modern text-books. The principle on which it is based is that two spectrum photographs of an iron arc are recorded, by a special apparatus, side by side on a photographic plate. One spectrum is due to the light after passing through the solution to be measured, and the other after passing through the pure solvent. The iron spark spectrum contains a great many lines, and it is possible to plot a dispersion curve for the spectrograph used so that the wavelength of any line may be determined from its distance from any one of the most prominent lines. The light passing through the solvent is cut down by a rotating shutter which has a variable opening graduated in terms of the logarithm of the absorption. Now, if the spectrum of the solvent and the solution have been given the same exposure to the same amount of light, the two spectra will have lines of the same intensity only at such wavelengths as the absorption is zero. In addition, where the exposures (governed by the rotating shutter) are different, the absorption at lines of equal intensity is proportional to the ratio of the two exposures (registered on the adjustable shutter).

A determination by this method involves the taking of a series of pairs of photographs in which the ratio of the two exposures is varied regularly, and in some cases it is necessary to take further plates using different thicknesses of solution and different concentrations in order to plot the whole spectrum within the range of the instrument.

A print taken from a specimen plate is annexed here and it is seen how the lines of equal intensity appear in the two photographs of each pair. The wavelength of each such point is determined from the dispersion curve referred to above, and the values obtained plotted against the corresponding values of the absorption obtained from the reading of the graduated shutter.



No.	Shutter	Tube.	log kc	log c	log k
1	1·5	1 cm.	·185	5·699	4·486
2	1·2		·088		4·389
3	·95		1·987		4·288
4	·75		1·884		4·185
5	·60		1·787		4·088
6	·48		1·690		3·991
7	·38		1·586		3·890
8	·30		1·489		3·787
9	1·5	4 cms.	1·586	5·699	3·887
10	1·2		1·489		3·790
11	·95		1·388		3·689
12	·75		1·285		3·586
13	·60		1·188		3·488
14	·48		1·091		3·392
15	·38		2·990		3·291
16	·30		3·188		3·188

The values of log k derived as above must be plotted against the corresponding wavelengths for each benzil. Actually the lines having this absorption were not identified, but their distance from the line at 500A, which is prominent in the iron spark spectrum was measured, and the wavelength obtained from a dispersion curve.

log k	Benzil	p-CH_3O	m-CH_3O	o-CH_3O	p-NO_2	Pipero	NMe_2	Pipero	
4 486									
4 389 4 288							349 372		
4 288				265 255			378		
4 185	249 266			269	269		382		
4 088	244 2735	296		272	255 2825		386	308	
3 991	2785	284 303	315	2775	284	325 316	3915		
3 890	283	307		287	293	2825 310 328	3975	280	
3 787	287	3135	3185	293	296	290 3085 339	401	342 301 286	
3 887 3 790	283 286	3185 322	280	2925	3025 308			344 346	
3 689	2915	328	286 3015 343	2985	313	299 342	408	3475	
3 586 3 488 3 392 3 291 3 188	294 297 299 300 3045	332 3355	346 347 3485	3055 322	3165 323	345 350 3575 362	416 424 432 435	348 3515 358	N.B. See also p. 133

The constant k, which measures the absorption of a compound in solution is obtained from Beer's law:

$\log\frac{I}{I_0} =$ kcd (where c is concentration
d is thickness)

The following dinitrophenylhydrazones have not previously been recorded, and their composition was checked by the micro-Dumas method of nitrogen estimation.

*p-Methoxybenzaldehyde	Found 13·3pc	Calc. 13·4 pc
o-Nitrobenzaldehyde	21·6	21·2
m-Nitrobenzaldehyde	21·1	21·2
p-Hydroxybenzaldehyde	18·2	18·5
p-Methylbenzaldehyde	18·6	18·7
p-Methoxybenzoin	13·6	13·3
Dimethylaminobenzoin	16·2	16·5
Piperobenzoin	12·8	12·9
p-Methylbenzoin	11·3	11·7
m-Methoxybenzil	13·3	13·4
p-Methoxybenzil	13·3	13·4
p-Nitrobenzil	16·6	16·1
Dimethylaminobenzil	16·2	16·2
Piperobenzil	12·9	13·0

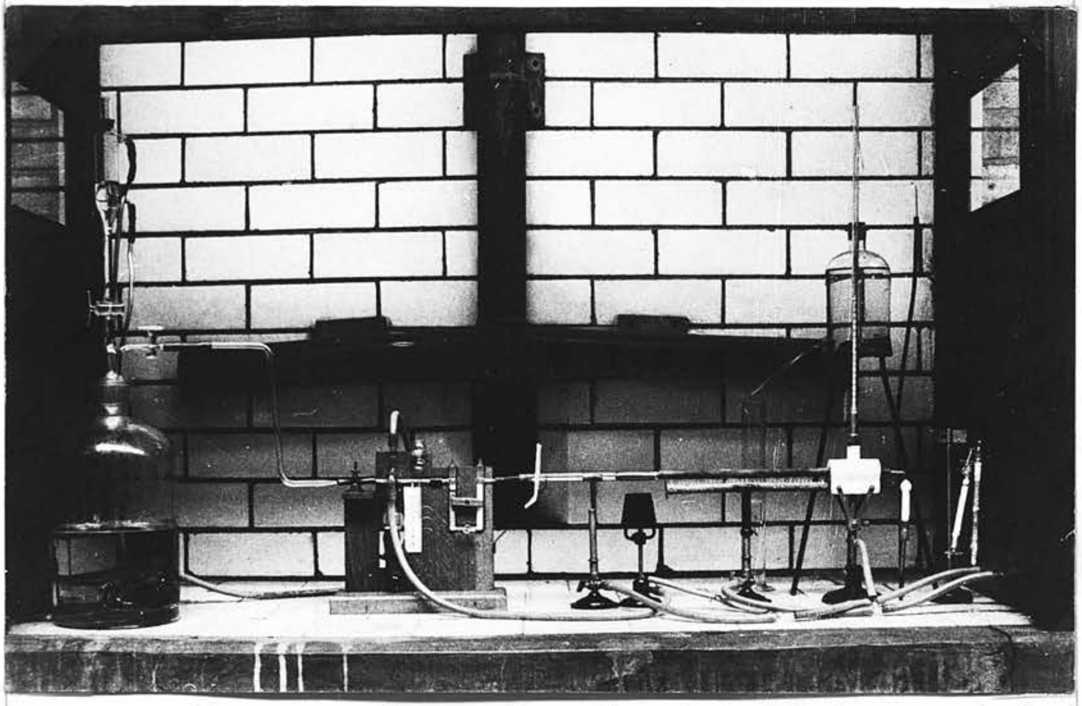
*prepared by Brady

Methods of Analysis.

In the course of this investigation it was found necessary to perform a large number of analyses, and a short account of the methods employed is given here.

Semi-Micro Carbon and Hydrogen.

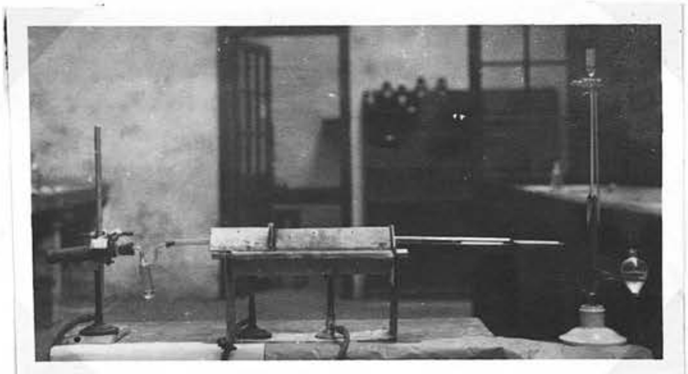
The method used in the course of this work for the determination of carbon and hydrogen, requires from 20-30 milligrammes of compound for a determination, and with these quantities the results are in general correct to within ± 0·2 pc for carbon and hydrogen.



The apparatus, shown in photograph, consists of a gasholder from which oxygen is supplied, under a constant head of water, via a combined precision tap gas regulator manometer and purification tubes, to the combustion tube. The latter is filled with a mixture of equal parts of lead chromate and copper oxide wire and at the end remote from the oxygen supply, a plug of platinised asbestos packed so that the oxygen would flow at a rate of about 4 ccs per minute when under a total pressure of 80 mms water. The whole of this part of the tube is heated to dull redness. The filling is completed by a layer of lead peroxide on asbestos with a short packing of silver wool on either side. This section of the tube is heated to 170° in a special oven. The end of the combustion tube is attached to the absorption tubes by means of a capillary tube which is formed at the end. The absorption tubes which are straight with a normal filling are finally connected through a calcium chloride tube to a Mariotte's bottle which serves both to measure the volume of oxygen used, and to regulate the pressure within the latter part of the apparatus. The procedure is carefully standardised and need not be described here except to say that the compound in a small boat, is volatilised by means of the burner G which is regulated, by the pressure within the apparatus a cting on the apparatus C, so that the combustion automatically proceeds regularly and smoothly.

Determination of Nitrogen.

For the determination of nitrogen two methods were used. These were the method of ter Meulen as described by Thorpe and Whiteley in their book of organic analysis, and a form of semi-micro Dumas estimation. The latter method was found to be the most speedy and satisfactory, and in the present work at least it was found that the apparatus required was very simple.



Carbon dioxide was generated by heating A.R. sodium bicarbonate in a hard-glass test-tube protected by wire gauze and asbestos. This gas was not purified in any way, but was passed through a small washbottle to collect water evolved in the reaction. The carbon dioxide was passed over the boat containing the substance covered by ignited copper oxide, over a column of fine copper oxide (any other filling was found superflous), and finally into a nitrometer (1·5 ccs capacity) The tube and filling were well roasted in an atmosphere of dry carbon dioxide-free air, and then in an atmosphere of carbon dioxide till no more air was evolved from the filling. The boat was then inserted as quickly as possible and carbon dioxide passed through the tube while the copper oxide filling was heated strongly. When it was found that all the gases evolved from the end of the tube could be absorbed in the potash solution which filled the nitrometer (i.e. the tube was free from nitrogen) the boat was gently heated. Under these conditions the combustion was usually over in about five minutes and the carbon dioxide was passed for a further ten minutes till all the nitrogen was carried over . Otherwise the proceeding was exactly as in the ordinary Dumas method of nitrogen determination.

Factors Governing the Reactivity of the Unsymmetrical Benzils.

III. Discussion.

The choice of the mixed benzils for this work is important for several reasons. Firstly, the benzils are typically aromatic ketones, and study of them should show quite clearly the reactivity of the carbonyl in the aromatic series. The benzils are readily available by way of the benzoins, and it should be quite possible to show the influence of the substituents on the carbonyl. An important factor influencing the choice of such a series of compounds is that the Beckmann products of an aromatic ketone appear, from the literature, to be much more easily identified than the corresponding compounds in the aliphatic series, and hence the structures of the oximes are more readily available. In addition to these factors, it must be remembered that whereas several mixed benzils have been prepared, the only other work on them is that of Buck and Ide and of Jenkins who have reduced several of them. In consequence, this thesis may be regarded in the light of exploration of a new field.

The reactivity of a carbonyl group may be measured in two ways, chemically and by physical means, and both methods were adopted in the course of this research. In the case of the estimation of reactivity by means of chemical reagents, the ultimate aim is, of course, to measure the reaction quantitatively, and this is impossible till the general trend of the reaction is understood. It would be ridiculous for example (to quote from the present work) to determine accurately the rate of formation of p-dimethylaminobenzil monoxime when, as has been shown above, the dioxime is formed immediately, even under very mild conditions of oximation.

The aim of this thesis is to investigate qualitatively the action of various chemical reagents on several mixed benzils with a view to forming some conclusions as to the relative reactivity of the two carbonyl groups compared with those of simple benzil.

Though it was not intended to make the investigation quantitative in nature, it was thought advisable to make the experiments with the various benzils comparable by performing them under the same conditions irrespective of questions of yield etc. These conditions are described in the experimental section of this thesis, and are those found most convenient in the case of simple benzil.

As it has been stated that the reactivity of a carbonyl group can be correlated with the position and intensity of the absorption band associated with this group in the spectrum of the compound examined, the absorption spectra of the benzils described above were determined by means of the rotating sector method and the results are discussed in the light of previous work in the field.

At the outset it has been stated that the object of this research is to study the effect of various factors on the reactivity of the two ketonic groups in various mixed benzils. In the course of an examination of the previous work on a series of related reactions, it has been shown that even the most satisfactory of theories is far from representing the whole truth of the matter in any of the examples studied, and that'a priori', no prediction can be made as to how the diketones will react. This is owing chiefly to our lack of precise and comprehensive data about the reactivity of the carbonyl group even in simpler compounds and under less complex circumstances.

The most important deduction from previous work is that the reactivity of a carbonyl depends on its environment. This influence may be resolved into two factors which depend on internal and outside circumstances respectively. Now, in a mixed benzil, the internal factors are evidently the presence in the molecule of the two benzene rings, and of the second carbonyl, while the external influence is due to the different reagents employed, as well as the effect of solvent on the various reactions.

The effect on a carbonyl group of an adjacent benzene ring can best be studied in the case of the substituted benzaldehydes, but, as stated above, this comparison is not possible in practice owing to the lack of data about the reactivity of these particular compounds.

The influence of two adjacent carbonyls on one another is seen in simple benzil which has been shown to react in certain circumstances as a monoketone. This factor is not readily measured, except possibly by the comparison of the reactivity of the substituted benzils with that of the corresponding benzophenones and of the desoxybenzoins, and here too there is an almost complete lack of data. It has been found that in the case of benzophenones, so little is known that in some cases, the oximes have not yet been prepared. Similar remarks apply also to the substituted (symmetrical) benzils.

The discussion falls naturally into several divisions. The first deals with the preparation of the starting materials - the mixed benzils. Any previous work on these compounds has only been done casually in the course of other investigations, and a considerable amount of work was necessary in preparing the benzils used in the research.

The best way to approach the mixed benzils appeared to be the formation of the mixed benzoins by means of the benzoin condensation and oxidation of the products by one method or other to the benzils. Now, for the sake of simplicity it is advisable, and for a start quite imperative, that the benzils used should contain but one substituent in the benzene rings. Obviously the introduction of a second substituent leads to unmanageable complications.

At first sight, the experimental work in this section appeared relatively simple, yet from the start considerable difficulty was encountered. The number of mixed benzoins which contain but one substituent and are readily available in good yield,is strictly limited, and indeed the difficulty in the preparation of these compounds is commented upon by Buck and Ide in several places in their series of papers.

Actually it was found that only three mixed benzoins could be prepared from readily available aldehydes in good yield and in a reasonably convenient manner. These are the p-methoxy, p-dimethylamino, and piperobenzoins. o-Methoxy and m-methoxybenzoins were also obtainable, less readily, in the form of oils which were oxidised directly to the benzils. One benzoin, the p-methyl compound was obtained by means of a simple Grignard reaction in fair yield, and the acetyl derivative of p-nitrobenzoin was obtained from benzoin by a special nitration method.

Repeated but unsuccessful attempts were made to prepare the new mixed benzoins from the condensation of benzaldehyde and the following substituted benzaldehydes - the three isomeric mononitrobenzaldehydes, the three hydroxybenzaldehydes and chlorobenzaldehyde.

With one exception, the benzoins actually prepared were oxidised to give the benzils in fair yield but in most cases it was found necessary to sacrifice a considerable portion of the yield in order to obtain a really pure compound. In the case of p-methylbenzoin it was found that Fehling's solution did not give complete oxidation and when nitric acid was used, some nitration appeared to take place, and the product was an inseparable mixture of isomers containing nitrogen corresponding to about half a nitro group per molecule of the benzil.

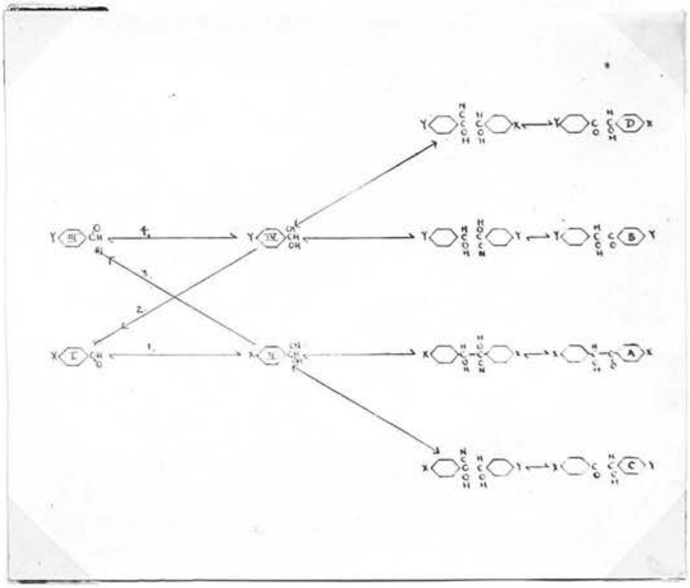
It is evident that the work of this thesis is not directly connected with the mixed benzoins as no new mixed benzoins have been prepared and only a few negative results recorded. At the same time, it emphasises in a manner hardly possible to the original workers in this field that the benzoin condensation is by no means so simple as might be expected. There seems no doubt that the mixed benzoins produced by the condensation are not in general quite pure, (they are generally obtained in the form of oils and gums which crystallise only very slowly) and the other products of the reaction have yet to be identified. No general conclusion has yet been drawn from their work by the original researchers in this field, and as stated before the relation of the benzoin condensation to the reactivity of the aldehydes concerned has still to be definitely worked out.

The theoretical interest of the condensation is due to the fact that the reaction is affected by the presence of substituents just as is the reactivity of the various benzaldehydes concerned. In fact from the theoretical consideration it appears that the condensation may be intimately related to the reactivity of the carbonyl group in these compounds and possibly in the mixed benzils also. It has been stated that one object of the preparation of a number of mixed benzoins by Buck and Ide was to enable worth while deductions to be made as to the reactivity of the aldehydes concerned. From this point of view it is important to notice that some mixed benzoins are formed only in very poor yields and in an impure state. In the case of p-methoxybenzoin for example, if the product is purified, the yield is only about 40 pc, which is poor compared with the simple benzoin condensation where yields of 90 pc are common.

Until the mechanism of the simple benzoin condensation is properly understood it is difficult to deal with the mixed benzoins in a satisfactory manner. The most promising basis on which this may be done is a consideration of the fact that the reaction includes as a first stage the formation of mandelonitrile, and apparently the last stage is the formation of an addition compound of benzoin and prussic acid, - in all probability benzoin cyanhydrin.

Now, obviously both these stages are subject to the influence of substituents in the benzene ring, and it must also be remembered that the various side reactions are involved.

It has been shown by Buck and Ide that the condensation is reversible, and, restricting the discussion to the main issue at stake, the reaction may be represented by an equilibrium scheme as follows:-



It may be remarked that this is only one of the possible mechanisms for the benzoin condensation. This matter is fully dealt with in the introduction, and the scheme given here may readily be adapted to an alternative formulation such as that of Horbye.

In a mixed benzoin condensation the composition of the product will depend firstly on the extent to which the mandelonitriles are formed in the first step of the reaction. If one of the aldehydes (say X.∅.CHO) forms no cyanhydrin, then reactions 2 and 1 will be suppressed, and only the benzoins D and B can be formed. By extending this form of discussion it may be seen that the product in a general case will be A +B +C +D and the relative proportions will depend on the capacity of the two aldehydes for addition of prussic acid. As the mechanism of the reaction is not completely understood it is impossible to say whether there is any reason why an aldehyde $X.\phi.CHO$ and a mandelonitrile $Y.\phi.CHOH.CN$ should or should not react to form the benzoin cyanhydrin but the reaction is evidently reversible, and the proportions of the two possible benzoin cyanhydrins will depend on individual circumstances. The last stage of the reaction - the decomposition of the cyanhydrin to the benzoin - will also affect the final proportions of the two benzoins formed.

It seems probable that there should be an intimate relation between the simple benzoin condensation and the mixed reaction, and it is evident from the diagram that in the ideal case one benzaldehyde forms a cyanhydrin and the other none, and the product may contain one simple and one mixed benzoin e.g. B and D - the formation of all others is impossible. Now, within this system there is still a network of reversible reactions and, obviously, the resulting mixture will depend on the tendency of the two benzoin cyanhydrins to split up into the benzoins and hydrocyanic acid, as well as the tendency of the two aldehydes to unite with the one possible cyanhydrin, and the simple and mixed benzoins are, in this sense complementary.

In the case where neither aldehyde forms a cyanhydrin no reaction is possible, and if both form this derivative the whole equilibrium system comes into play.

For a start, it may be taken simply that all benzaldehydes containing strongly polar groups give no simple benzoin condensation. Such are p-dimethylamino-benzaldehyde as well as nitro and hydroxy benzaldehydes, and in consideration of this matter it is unfortunate that in the most interesting cases the substituents have a strong tendency to enter into side reactions which obscure the main issue, chiefly by the formation of oils and tars. Furthermore, there is a variety of side reactions which have been dealt with by Lachmann; these have only been fully investigated in the case of simple benzaldehyde and benzoin, and apparently not at all in the case of substituted benzaldehydes. This explains to some extent the formation of oils and tars in benzoin formation, especially considering the extraordinary reactivity of the aromatic aldehydes.

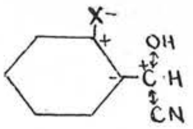
At the same time, such side issues seem hardly adequate to explain the fact that in some mixed benzoins the yields are as small as 10-30 pc . This is probably primarily due to shift of the equilibria of the reactions towards the benzaldehydes as shown in the scheme above, but for a complete proof of this complete equilibrium data and reaction velocities for all the reactions involved are necessary.

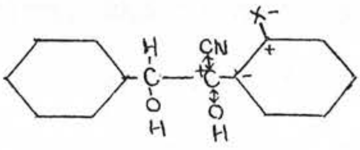
Evidently then, the composition of the product from a benzoin condensation in homogeneous solution will depend primarily on the equilibrium constants and reaction velocities of the various reactions involved, and until these physical data are available for a large number of benzaldehydes the matter cannot be profitably considered at any greater length. The nature of the final product isolated from a benzoin condensation will however depend on another factor about which very little is known · namely the solubility of the various possible products in the reaction mixture. Thus , in the case of a system where one possible benzoin is much more insoluble than the others, on cooling, the benzoin will crystallise out, and if the reactions involved are very rapid, the whole scheme will be upset and a preponderant amount of that benzoin will be formed. The least soluble of the possibilities will not, of course, be formed unless the corresponding cyanhydrin is stable, and indeed the question of solubility is entirely a secondary one dependant on the equilibrium scheme given above.

A third factor influencing the product was discovered by Buck and Ide who found that in certain cases addition compounds of two benzoins could be formed, with, of course, corresponding complication of the equilibria.

Consideration of the reaction diagram given above suggests a possible explanation of the anomalous effect of substituents on the condensation. In the case of a reaction where both aldehydes form cyanhydrins, as shown above, the resulting mixture, in solution, will contain the benzoins A + B + C + D in equilibrium with the corresponding other compounds as illustrated. Now, in practice, the benzoin isolated from such a mixture is always found to have the carbinol group adjacent to the unsubstituted phenyl, and apart from the solubility factor which cannot lead to any such regularities, the explanation must be sought in the effect of substituents on the benzaldehyde and benzoin cyanhydrins respectively.

These two effects are shown in the diagram below. It will be noted that the influence of the substituents is represented by a system of + and - signs, which does not accord with the latest ideas of Ingold and other theorists in this field. This has been done for the sake of simplicity, as the theories of today are too complex to be applied properly here. Such simplification is justified by the example of Aarhenius, who, it is said, never made an exact measurement lest it should obscure the general law by its very exactitude.





While it is extremely difficult to predict with certainty the stability of a compound from a consideration of its structural formula alone, yet it is evident that the conditions in the molecule of benzaldehyde and benzoin cyanhydrins must be very similar. Thus, if the influence of an electronegative substituent is to increase the stability of the benzaldehyde cyanhydrin, then it must also stabilise that of the corresponding benzoin. Now, these two effects will immediately be followed by the promotion and inhibition respectively, of the benzoin condensation as will be seen from the diagram (p106). While this line of reasoning is too speculative to be carried further without the backing of collateral evidence, it at any rate shows that there is no reason why an electronegative and an electropositive group should necessarily have the effect of causing the formation of benzoins of opposite structure.

For the purposes of discussion, the results of the experimental part of this work are summarised in two tables. One table contains descriptions of all the ketonic derivatives prepared, while the other shows various other reactions of the benzils, along with several reactions of the corresponding benzaldehydes. which appear to be analogous to those of the benzils.

In addition, a section is annexed dealing with absorption spectra in general and especially those of aromatic carbonyl compounds including particularly the mixed benzils.

Benzil	Oxime	Hydrazone	Phenyl-hydr.	Semicarb.
p-Methoxy	Cryst. in icebox 110	One formed q.v. 164	Only one 180-1	No data
p-Nitro	Oil by sp. method	One compd. 120-2	? Two	No data
p-NMe_2	Dioxime at once	None	One only 157-8	No data
Pipero	Monoxime 148-52 (β)	m.p. unsharp 117-25	Oily 115-7	m.p. 106-7 mono-
o-Methoxy	Dioxime 150-2	No data	No data	No data
m-Methoxy	Dioxime 210	One compd. 113-5	Oil	149-53 mono-

Unless otherwise stated, the compound formed was the monosubstituted one. Dinitrophenylhydrazones were formed in each case except that of o-methoxybenzil but are tabulated separately. The monoxime was first formed in each case except p-dimethylaminobenzil, and in the o- and m- methoxybenzils these were not isolated.

Benzil	Benzilic Acid.	KCN Splitting	Simple Benzoin	Mixed Benzoin
p-Methoxy	Only one	Ø.CHO +	E.Formed	40 pc.
p-Nitro	Cond.Pr.	Cond.Pr.	None	None
p-NMe_2	None	None	None	86 pc
Pipero	Only one	Ø.CHO +	E.Formed	30 pc
o-Methoxy	No Data		Known	Oily
m-Methoxy	Oil	Ø.CHO +	Known	Oil

From these results it is at once evident that there is no simple relation between the results, and no obvious agreement with the absorption spectra of the benzils.

This may be due to the fact that confusion arises due to the various factors involved which have been mentioned above and which can be dealt with more fully at this stage. Thus, to compare the effects of the reagent employed, it is necessary to consider the action of various reagents on the benzil, and to show the influence of substituents on the reactivity one must compare the reactions of one reagent with all the benzils. To study the effect of a carbonyl on its neighbour, the properties of a benzil may be compared generally with those of the corresponding benzophenones or desoxybenzoins, or alternatively the properties of a series of benzils in respect of one reagent may be compared with a series of benzophenones under similar circumstances.

It is evident that the structures of the oximes give the key to those of the other ketonic derivatives for their structure is readily determined by means of the Beckmann Transformation. Once the structure of the oximes is found it is possible, by means of the methods of Auwers and Siegfeld and of Forster (which have been described in the case of benzil and p-methoxybenzil) to obtain the structures of the other carbonyl derivatives.

It soon became evident that this could not be done in the course of this research, for it was found that only a limited number of benzils gave monoximes readily in a state of purity, and furthermore, these oximes did not give the Beckmann reaction of the second type. Invariably, they gave yellow solids which could not be identified, but were probably of the type of benzoyl formanilide. In every case attempts to hydrolyse these products failed, except in the case of p-methoxybenziloxime whose structure was already known. This difficulty has been noted by Buck and Ide in treating of the corresponding products from the oximes of the mixed desoxybenzoins. As the synthesis of a compound like benzoyl formanilide is long and difficult it was not thought advisable to attempt it in the short time available.

As the only satisfactory methods for the determination of the structure of the ketonic derivatives depends entirely on the structure of the oximes, it was only possible to apply it in one place. (see p-methoxybenzil)

The only other method for the determination of these structures which showed any promise was the action of alkali and sodium ethoxide on the hydrazones and semicarbazones. This method was found to be of little service, since a trial experiment showed that it required modification to suit each derivative. In the case of benzil hydrazone sodium ethoxide not only expels the hydrazido residue, but also reduces the desoxybenzoin so formed to benzyl phenyl carbinol and dibenzyl. The first part of the reaction is a general one for all hydrazones, and desoxybenzoin has been reduced by this method by Wolf (Ann., 1912, 384) to yield the same products. It was not found possible to investigate the use of caustic alkali in a similar reaction with a view to the preparation of the desoxybenzoin .

It must therefore regretfully be concluded that until the monoximes of these benzils have been prepared and their structures determined, it will be difficult to determine the structure of the other ketonic derivatives.

It appears that in the reactions of the carbonyl group, the effect of the reagent employed is much more than was at first suspected. This is most strikingly evident in the case of p-methoxybenzil in which it has been shown that hydrazine and hydroxylamine and hydrazine attack different groups. With p-dimethylaminobenzil, hydroxylamine attacks both carbonyls while phenyl hydrazine only appears to attack one and neither caustic soda or hydrazine react at all. p-Nitrobenzil appears to give the two phenyl hydrazones, though it has yet to be proved that these are individuals and not dimeric forms. It has definitely been shown that only one hydrazone is formed in this case and it seems probable that the oxime which is an oil, contains two isomeric forms. Piperobenzil gives but one oxime, while the m.p. of the hydrazone originally formed is unsharp, suggesting that here too there is at least a trace of an isomeric form, and the phenyl hydrazone has not been obtained in the solid form probably owing to the same cause. In all cases, the dinitrophenylhydrazones are formed by the reaction of only one ketonic group of the parent benzil.

These resılts appear to suggest that under certain circumstances a compound may react as a diketone while by a change of reagent it may become a monoketone and the other carbonyl may be quite unreactive. This is evident in the case of simple benzil which usually reacts as a monoketone and in which the other carbonyl can be caused to react only under more strenuous conditions. In this connection it must be mentioned that in view of the fact that the diketone is formed so readily, the failure of p-dimethylaminobenzil to give the benzilic acid change may be due to the fact that potash adds on to both the ketonic groups (see later).

In nearly all cases the m-compound reacts differently from the o- amd p- compounds, and the importance of this is realised when it is stated that this is the only instance in the present research in which there is any resemblance to a correlation of the results with the alternating polarity type of theory.

It is interesting to note that p-nitrobenzil and p-dimethylaminobenzil, which contain the most strongly polar groups considered in the course of the present research, though of opposite polarity give the dioxime readily, In the first case however, the monoxime is probably formed first, as a mixtureof the two possible forms (α and α_1) while in the other case it is not formed at all even under very mild conditions of oximation.

The effect of substituents on the behaviour of different benzils to the same reagent shows similar anomalies. For example, as will be seen from the table, p-methoxybenzil and piperobenzil are similar in their behaviour to hydroxylamine in contrast to p-dimethylamino and m-methoxy benzils which readily form the dioxime. As a matter of fact m-methoxybenzil reacts first to form the monoxime, but the above classification is justified by the ease with which the dioxime is formed by the action of excess hydroxylamine. Owing to the occurrence of a side reaction the case of p-nitrobenzil is not quite comparable, but by the application of a slightly different method it was found possible to prepare a monoxime in the form of a gummy oil from which neither the benzil, nor the dioxime separated on seeding with these compounds. The dioxime was formed by the reaction with excess hydroxylamine as is the case with m-methoxybenzil.

This reaction shows no definite regularities and it should be noted that the benzils are associated in groups different from these shown by the examination of the spectra, except that in both cases p-dimethylaminobenzil is entirely different from all the others

The hydrazones show a similar type of anomaly and the benzils are associated with each other in still a third manner. Here benzil nitrobenzil and m-methoxybenzil are similar while piperobenzil and p-dimethylaminobenzil are different from these and from each other.

The case of the phenyl hydrazones is again different for here p-methoxybenzil and p-dimethylaminobenzil are similar while p-nitrobenzil and possibly also piperobenzil and m-methoxybenzil give two phenyl hydrazones.

As far as could be shown, the dinitrophenylhydrazones of the benzils were all of the same type.

Of the eight benzils studied, only benzil, piperobenzil and m-methoxybenzil gave any semicarbazone, - in each case only one was formed and it was the monosubstituted derivative.

These results are summarised in a table (p.120) which demonstrates the fact that the result of these reactions is largely governed by the reagent employed. Of all the reagents tabulated, only one gives similar results with each benzil and in all probability this reagent -dinitrophenylhydrazine - is the most suitable one for the estimation of the reactivity of a carbonyl group.

Compound	Oxime	Hydrazone	Ø-Hydrazone	Semicarb.
Di-substituted	NMe$_2$. (m-CH$_3$O.) (o-CH$_3$O.) (p-Nitro.)		NMe$_2$.	
One monosubstituted	Benzil p-CH$_3$O. Pipero.	Benzil p-CH$_3$O p-Nitro m-methoxy	p-CH$_3$O p-NMe$_2$	Pipero m-CH$_3$O Benzil
Two monosubstituted	(Nitro)	Pipero	(p-Nitro) (Pipero) (m-CH$_3$O)	
None		NMe$_2$		p-CH$_3$O p-NMe$_2$ p-Nitro o-CH$_3$O
No data		o-CH$_3$O	o-CH$_3$O	

From this table it is evident that the reactivity of the two carbonyl groups of benzil is affected by the presence of substituents in the benzene ring in such a manner that the substituted benzils react in most cases as monoketones. At the same time one very important fact emerges, namely that it is impossible to define the reactivity of a chemical radical or group by reference to the formation of non-formation of only one or two derivatives as was done by Mme. Ramart-Lucas in her discussion of the absorption spectra of organic compounds, and it is obvious that in consideration of such reactivity, not only the formation, but also the rate of formation must be considered. Indeed it is possible that if all the rates of reaction of benzils with the above reagents were known, a comparison of them would show some general rule for the reactivity of the carbonyl group. Obviously, this rule would not fit all the cases unless allowance were made for the individual peculiarities of the reactions concerned.

While the benzilic acid change can give no information about the relative reactivities of the two carbonyl groups in the molecule, since in all cases the two phenyl radicals are firmly attached to the same carbon atom, it still yields some interesting results

It is somewhat surprising to find that with p-dimethylaminobenzil no benzilic acid is formed in view of the fact that the dioxime is formed immediately as is the phenylhydrazone. This is however quite in accordance with the fact that no semicarbazone, hydrazone etc. are formed. The same applies to m-methoxybenzil and in the case of p-methoxybenzil and piperobenzil where there is but one monoxime, transformation takes place readily. It is possible to understand this if the addition compounds of benzil with hydrocyanic acid are considered. It was shown by Lachmann that benzil added two molecules of prussic acid to form the dicyanhydrin, which would not split up into benzaldehyde and ethyl benzoate in alcohol solution. Now, benzil is readily split up by the action of cyanides and Lachmann deduced that this was due to the momentary formation of the (unknown) monocyanhydrin. By analogy with this, it appears that the failure of p-dimethylaminobenzil to give the benzilic acid change may be due to the fact that this benzil adds on two molecules of potash to form a complex which cannot undergo metakliny. This explanation presupposes that the mechanism of the formation of an oxime and of the alkali addition compound is similar in nature, but if these are in fact dissimilar the problem is much simpler, for in this case the failure to react may be due to the fact that the benzil does not add on potash at all. In such a case, the metakliny of such compounds as readily form a monoxime is probably due to the addition of alkali to the carbonyl which remains unattacked by hydroxylamine.

The fact that p-methoxybenzil and piperobenzil form only one benzilic acid and that there is no trace of a mixture of the unsubstituted and disubstituted acids shows that the original assumption of the benzilic acid change taking place within a molecule, and not between two molecules, is justified.

It appears that some connection might be made between the reactions of benzaldehyde which were studied and which are probably related to the reactivity of the carbonyl groups in the aldehydes concerned. This was suggested by the fact that certain similarities of the benzoin condensation and of the Cannizzaro reaction led Lachmann to postulate a common mechanism for the two reactions. From the consideration of the table it appears that this might to a certain extent be justified, though from other evidence it appears that this author's mechanism cannot be sustained. Between the simple Cannizzaro reaction, and the simple and mixed benzoin condensations of any aldehyde there seems to exist the following relation. If both the simple benzoin condensation and the simple Cannizzaro reaction proceed readily, or not at all, then the aldehyde will condense readily with benzaldehyde to give one mixed benzoin.

This is evident in the case of p-dimethylamino benzaldehyde which has neither the Cannizzaro reaction nor benzoin condensation, yet gives a mixed benzoin with benzaldehyde. Piperonal furnishes us with the complementary example in which both simple reactions go readily as well as the mixed benzoin condensation. With o- and m- methoxybenzaldehyde where the Cannizzaro reaction proceeds readily, though the benzoin condensation is known, it gives very poor yields, and correspondingly the mixed benzoin reaction results in an oil which is obviously im

The case of p-nitrobenzoin is complicated by side reactions probably involving the nitro group, but it seems that the Cannizzaro reaction is possible, and here the mixed benzoin reaction is not known, though this may be due to such side reactions as mentioned above.

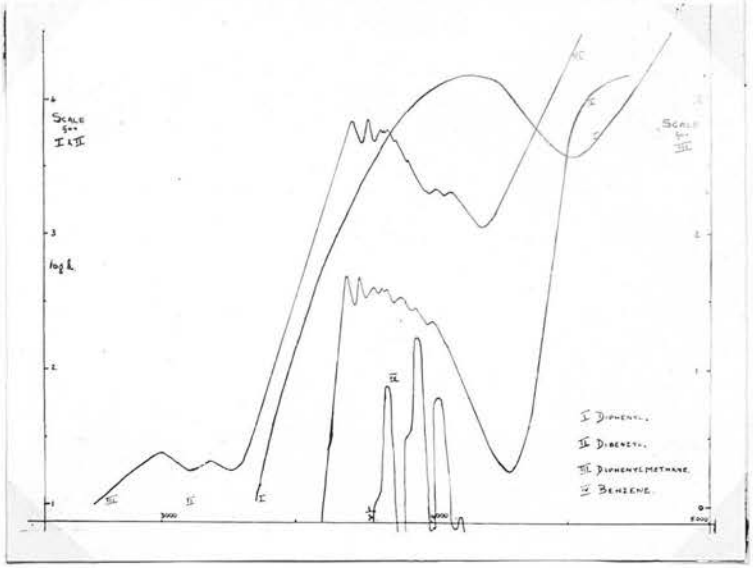
There is no obvious connection with the mixed Cannizzaro reaction, since in all cases the only product identified was ethyl benzoate, and in most cases the other aldehyde was recovered unchanged,

The splitting of benzil by the action of potassium cyanide, which has been related by Lachmann to the benzilic acid change was found to yield, in the case of every benzil examined, the same products, viz. benzaldehyde and the ester of the substituted acid. This appears to show that in these cases the same carbonyl is attacked by the reagent. Further, since the reaction is probably due to the addition of potassium cyanide to the carbonyl group this goes to show that in this reaction, in every case so far examined, the same carbonyl is active, namely that remote from the unsubstituted benzene ring.

Absorption Spectra and Structure.

It has been shown by Mme. Ramart-Lucas (loc. cit.) that several chemical groups, notably those which are associated with the chemical properties of a molecule have the property of imparting a definite absorption spectrum to an aliphatic hydrocarbon radical (the hydrocarbons have been shown to be quite transparent in the easily accessible regions of the ultra-violet). She has stated that though the position and strength of the bands due to such a combination of chromophore and hydrocarbon residue have a characteristic value for each chromophore, they may be slightly altered by the nature of neighbouring groups. This is true more especially of a system containing two adjacent chromophores, for it is found that if the two chromophores are directly united, the spectrum of the molecule is due to combination of the two and may bear no resemblance to the sum of the spectra due to the two groups separately. When carbon groups are introduced between the chromophores, the spectrum gradually reverts to normal, and when more than two carbon atoms are so introduced, the spectrum cannot be distinguished from that of a mixture of the two chromophores attached to different hydrocarbon radicals.

An illustration of this principle compiled from the literature is shown below.

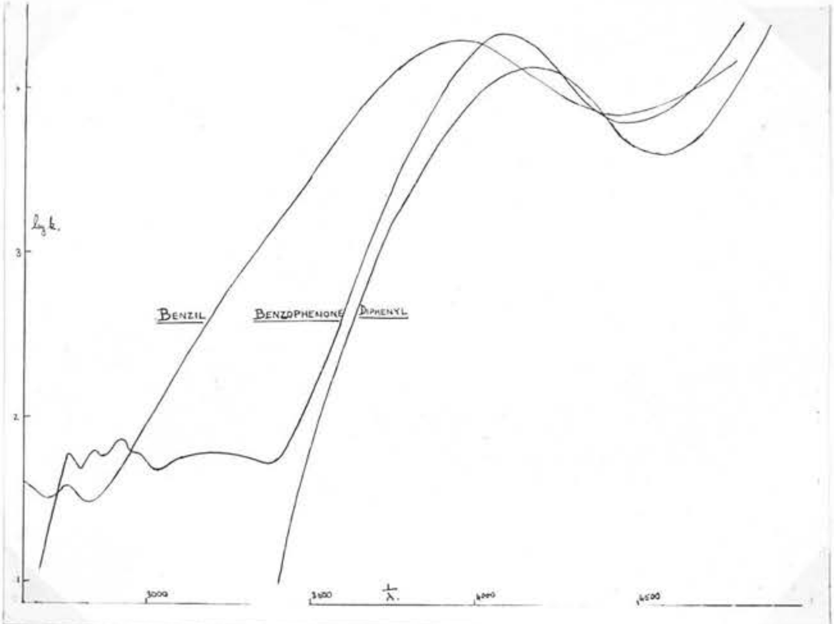


1.

N.B.
GRAPH III
IS ON A
DIFFERENT
SCALE.

The approach of the spectra to that of benzene with a maximum about 3900Å is so marked as to pass without comment. It has been shown by Mme. Ramart-Lucas that the band in dibenzyl between 3000 and 3500Å should not be present, but is due to a trace of stilbene, and it is quite possible that the same also applies to the spectrum of diphenylmethane.

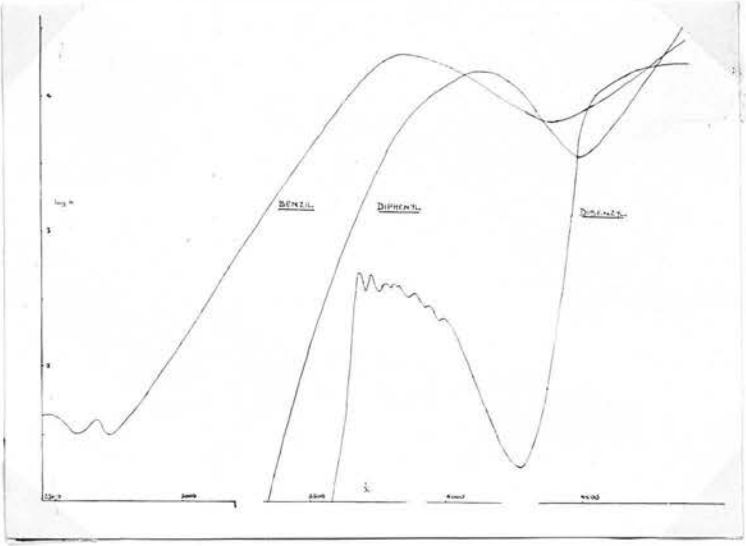
If it is desired to use the absorption spectra of benzils to assess the reactivity of the carbonyl group, it will first be necessary to show that one band in the spectrum may definitely be associated with that group. As the carbonyl band is always between the limits 3800 and 4500Å, in which region the spectra are readily measurable, the ultra-violet spectra of several related compounds are shown in figures 2 and 3 in an endeavour to show that the main band of benzil, which appears at about 4000 on the wave-number scale is substantially due to the ketonic group.



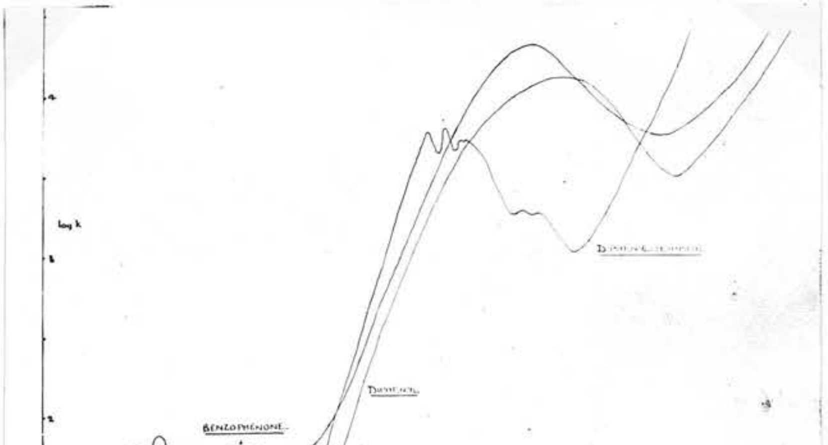
2.

Figure 2 shows in a most remarkable manner a totally unexpected feature. In it the spectra of benzil, benzophenone, and diphenyl are seen to be very similar, and in fact the position of the maximum of the main band is approximately the same. At first sight, this appears to indicate that the band is due chiefly to the association of two benzene rings, but on consideration of diagrams 3,4, and5 it is evident that the effect is much more complex.

In the first place it is important to notice that the phenyl groups in benzil are no longer directly joined, but are separated by two carbon atoms as in dibenzyl, and hence would be expected to give typical benzene bands such as are exhibited in the spectrum of dibenzyl (see fig 1.). Similarly, it appears that the spectrum of benzophenone is comparable, not with diphenyl, but with diphenylmethane. Figures 3, and 4 show these comparisons, and it is easily seen how far the spectra of the two ketones differ from those of the corresponding hydrocarbon nucleus.



3

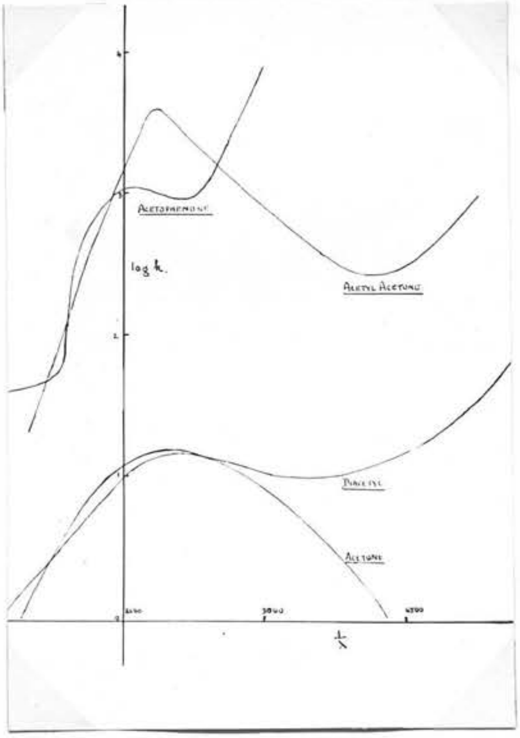


4

DEDUCT 1
FROM SCALE
FOR
DIPHENYLMETHANE

Benzophenone and benzil contain subsiduary bands at between 2500 and 3500Å, and the main band due to benzil is much wider than that of either diphenyl or of benzophenone. As the spectrum of benzil is due to five chromophores directly united in a chain it will not, according to Ramart-Lucas, show the spectrum characteristic of the sum of the ketonic and phenyl bands, but will be more or less distorted by the mutual influence of the chromophores. This effect is so complex that analysis of it is impossible at the present time. It has been shown above that the influence of the two phenyl groups is not predominant and it is therefore evident that the mutual effect of the phenyl and carbonyl, and the two carbonyl groups on each other is important. This is illustrated by diagrams 5 and 6

5.



6.

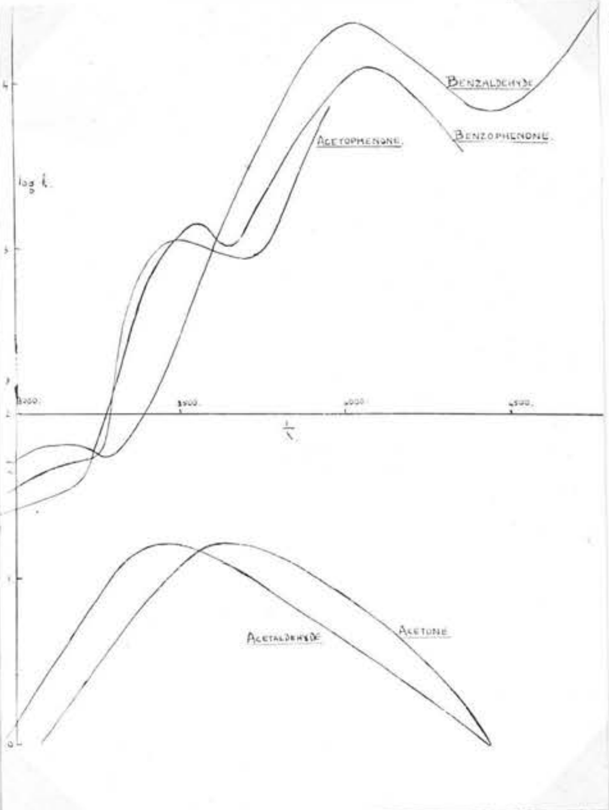


Figure 6 shows that the introduction of one benzene nucleus in place of methyl in acetone has an enormous effect on the spectrum and that the effect is not much different from that produced by the introduction of two phenyl groups to form benzophenone. Exactly the same effect is seen in the comparison of acetaldehyde and benzaldehyde. These two examples show that the mutual effect of the phenyl and carbonyl groups is comparable with that between two benzene rings.

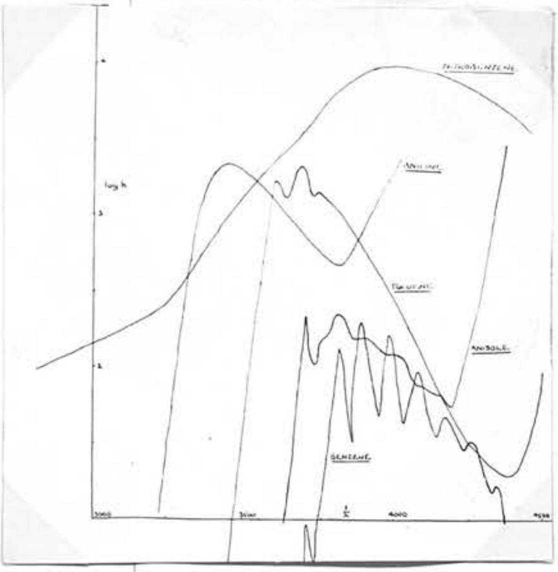
The other effect referred to in connection with the spectrum of benzil is the mutual effect of two carbonyl groups. This is seen in the comparison of acetone and diacetyl, and in the spectrum of benzil the only similar phenomenon is the broadening of the main band which is evident in comparison with benzophenone. In this connection it may be pointed out that the most valid comparison in this connection is really that of benzil and desoxybenzoin. It has been found however that the spectrum of desoxybenzoin determined several years ago is identical with that of benzophenone, within the experimental limits. (J.C.S., 1912, 1514)

It may be stated in summing up, that the spectrum of benzil is too complex to be handled theoretically or by analogy. It is evident however that, bearing in mind the principle, at least of the two main conclusions of Ramart-Lucas, a certain amount of information about the mutual influence of the various chromophores in this complex system may be obtained from the consideration of the spectra of related compounds.

Firstly, it is obvious that the presence of a phenyl group enormously increases the absorption of a carbonyl group and that this absorption is not much affected by the presence of a second benzene ring (cf. figure 5). Secondly, in benzil the mutual effect of the phenyl groups is not enough to account for nearly all the absorption (cf. figure 3). Again, the absorptions of benzaldehyde, acetophenone, and benzophenone (and desoxybenzoin) are not much different from each other and from that of benzil. In these cases the common factor is the presence of a phenyl and a carbinol adjacent to each other, and hence probably the spectrum of benzil is chiefly due to the association of these two radicals. The introduction of a second carbinol to form benzil is accompanied by considerable broadening of the main band, though there is but little change in the position of the maximum, and apart from this the influence of the two carbonyls on each other cannot be detected.

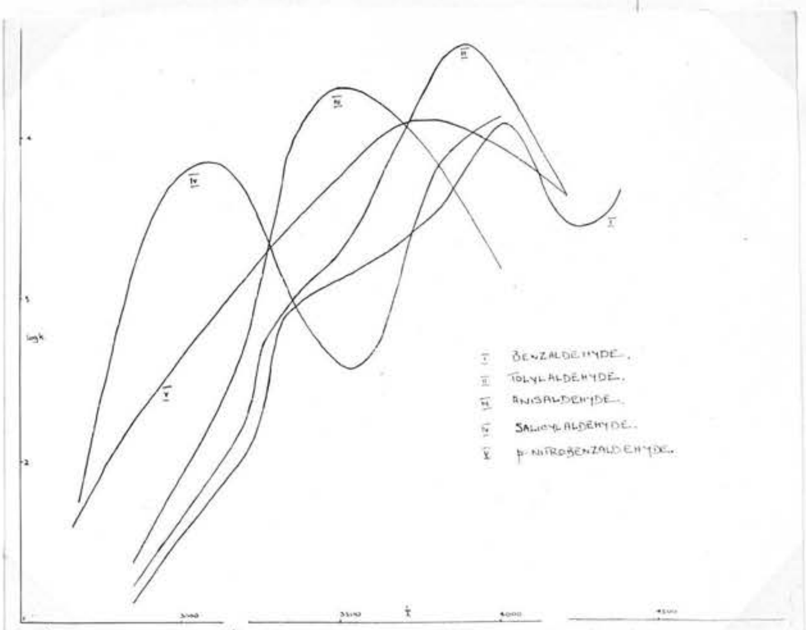
It seems therefore that though the spectrum of benzil is so complex it is possible to show that one of the chief factors in its genesis if not the predominant one is the mutual effect of the phenyl and carbonyl radicals, and it is this effect that is the most likely to be affected by variation of the reactivity of the carbonyl group due to the effect of substituents in the benzene ring.

The next two diagrams show the effect on the spectrum of benzene itself, and of benzaldehyde, of the introduction of substituents. There seems to be no simple correlation with the spectra of the mixed benzils.

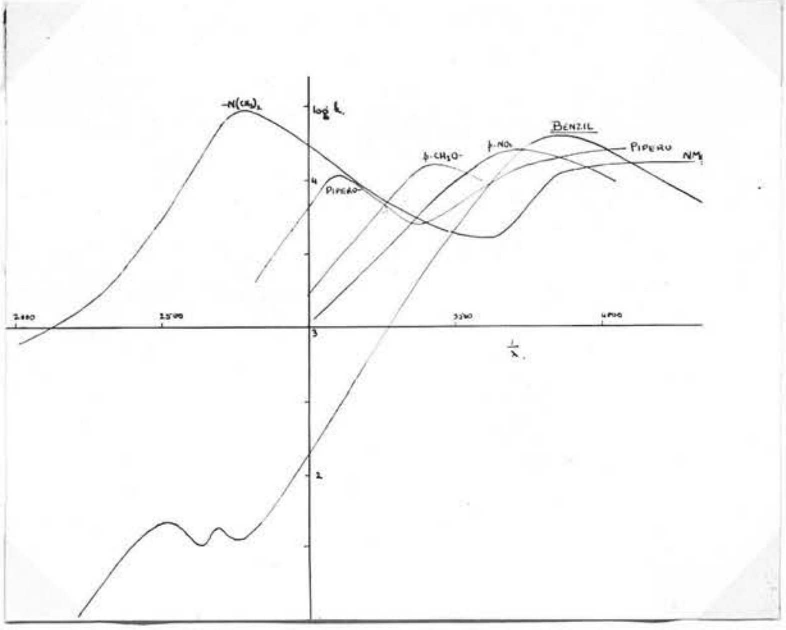


7.

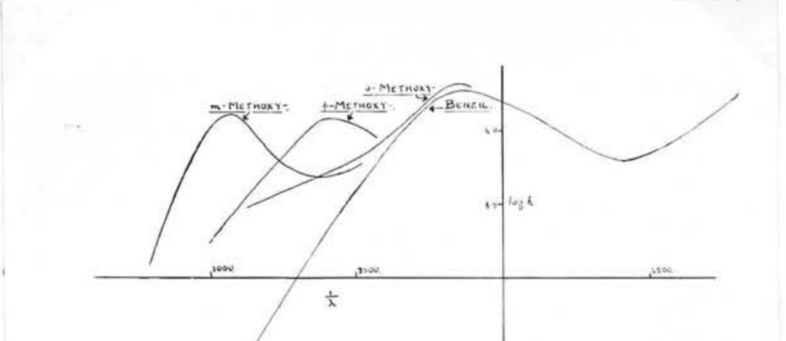
8.



It may be seen from the foregoing discussion that some considerable difficulty exists in interpreting exactly the absorption spectrum of benzil. In view of this fact it was not thought advisable to work out the subject fully, and the curves recorded for the various benzils in alcoholic solution are recorded below.



9.



10.

It should be emphasised that the purity of the benzils was not investigated thoroughly, and it is possible that their true spectra are considerably different from those recorded. The compounds used were however, the purest obtainable by ordinary methods, and as the the rigorous purification of these compounds would involve the synthesis of each benzil by at least two distinct methods and recrystallisation till a constant spectrum was obtained in each case, for a complete examination of these spectra a separate investigation would seem necessary. Incidentally it must again be emphasised that the importance of such a purification has only recently been realised and in consequence any or all of the spectra quoted here may be erroneous to a greater or less extent. A specific example of this fact may be seen in the case of dibenzyl which has always been represented as having two bands in its spectrum but was shown by Mme, Ramart-Lucas to have only one while the other was due to the presence of a trace of stilbene. It must always be remembered that the curves given above were quoted from International Critical Tables and are by a variety of different authors, presumably under different conditions and hence they are not strictly comparable.

In the above discussion, it will be noticed that no comparison is made of the reactivity of the benzils with that of the substituted benzophenones or desoxybenzoins or benzaldehydes. After an extensive investigation of the literature relating to these compounds it was felt that the matter could not be adequately dealt with here. It was found that though many derivatives of the substituted benzaldehydes had been made in the past, the conditions of the reactions were so divergent, and the data so scattered that the only possible method of comparison appeared to be a complete quantitative investigation of various reactions under identical conditions. The case of the benzophenones and desoxybenzoins was slightly different for here the data are simply non-existent, and in some instances even the oximes have not been prepared.

The data acquired in the course of this research are not yet sufficient to form a secure basis for any generalisation, yet in spite of many difficulties, it has been shown that the original statement of Buck and Ide that the two carbonyl groups of mixed benzils have widely differing reactivities, is amply justified. It has been shown that in the case of some reactions, (e.g. the reactions with potassium cyanide and with hydrogen) the same carbonyl is attacked in a series of different benzils containing one substituent. Further, it has been found that the effect of reagent employed is very important, for a benzil may react to one ketonic reagent as a diketone, while with another it will not react at all. (p.61) It has been demonstrated that the spectra of the benzils show a shift on the introduction of substituents, much greater than that produced in benzene, and also that the main band of benzil is probably associated with the combination of carbonyl and phenyl chromophores, and hence is probably associated with the reactivity of the benzils in question.

On the other hand, as has been pointed out, enough data have not been obtained to found any sweeping generalisation, and from a study of the results it is strikingly evident that the future comparison of such reactions of any carbonyl group can only be made by means of quantitative data such as reaction velocities. Again, before such work can be fully appreciated it is absolutely imperative that the simplest carbonyl compounds should be systematically examined. Though this has been done to some extent in the aliphatic series, where the very simplest carbonyl compounds are situated, the data for aromatic compounds is strictly limited. The inherent differences between the aliphatic and aromatic hydrocarbon nucleus render the former series of compounds useless for the purpose of a basis for investigations in the benzene carbonyl compounds.

In the circumstances it is not advisable to make any attempt to apply the current theories of organic reactions to the results, at least till some degree of generalisation is reached within the field itself. It has been proved, over and over again that an attempt to fit results into a preconceived theory is the surest way to unscientific reasoning, and this is especially true of work dealing, as does this thesis with the distribution of energy within the molecule. The problem is being attacked both from the side of the chemist and the physicist and as yet the connection between the two sets of results is not precise enough for practical application.

As Hückel points out in the closing paragraphs of his 'Theoretische Grundlage der Organische Chemie' it is a characteristic of chemical theory that as time goes on, the subject becomes more complex and less satisfactory. In the early days of a theory a simple postulate suffices to explain all the known phenomena associated with a reaction, but as investigation progresses, anomalies and discrepancies are found, which must be explained by modification of the theory, till finally a new theory must be evolved . Hückel points out how necessary it is to realise the limits of our knowledge in order to appreciate to the full the value of any new work, but on the other hand how essential it is not to stress these limits too much lest wholly destructive criticism should paralyse further progress into the fringes of the unknown.

Summary.

Several mixed benzils containing one substituent in the benzene ring have been prepared, and their reaction with various ketonic reagents considered. In addition the absorption spectra of these benzils have been recorded.

p-Nitro acetylbenzoin and p-nitrobenzil have been prepared by a greatly improved method.

Two methods for the determination of the structure of ketonic derivatives of benzils have been described, and the structure of p-methoxybenzil hydrazone determined.

The action of potash and of alcoholic potassium cyanide on the benzils has been described.

The mixed benzoin condensation has been discussed with the aid of a diagram and the importance of quantitative work in this connection is emphasised.

The reactivity of the mixed benzils was considered, and it was seen that though the effect of the reagent employed was very important, in many cases it was found that only one ketonic group reacted.

It was shown that the main band in the spectrum of benzil is probably intimately connected with the effect of substituents on the reactivity of the carbonyl. The spectra of the benzils were found to show considerable shifts due to the substituents.

The feasibility of chemical and of physical methods for the determination of the reactivity of a carbonyl group has been considered, and it has been shown that different methods give different values for the reactivity.

The lack of accurate quantitative data obtained under comparable conditions was felt in almost every phase of this work.

It was conclusively shown that the only reagent which gave parallel results for all the benzils, was dinitrophenylhydrazine, and that in consequence it is the most suitable reagent for the characterisation of carbonyl compounds.

In conclusion, the author wishes to express his cordial appreciation of the kindly and efficient supervision of Dr. Neil Campbell and Dr.H. G. Rule throughout the period of this research. Thanks are also due to the Department of Scientific and Industrial Research for a Maintenance Allowance during the years 1933-35.