

THE PREPARATION AND REACTIONS OF THE AMINO

METHYLENE DERIVATIVES OF DESOXYBENZOIN.

BY

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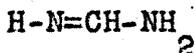
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The Nature and Reactions of Formamidines.

Formamidine is the ammonia analogue of formic acid.

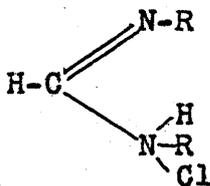
The simple formamidine



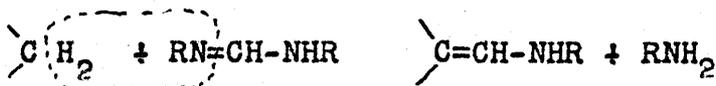
may be regarded as a sort of formic acid in which the aldo oxygen has been replaced by an imino group (as in the imino esters) while the hydroxyl radical is replaced by an amide group, (as in the acid amides). Hence it may be considered as imino formamide.

But the simple formamidine is not very stable and is exceedingly difficult to make.¹ Since the disubstituted aryl formamidines are quite stable and may be heated as high as 200° with little or no decomposition, they are universally used in reactions requiring a compound of this nature.

Like most compounds containing tri-valent nitrogen, the substituted formamidines are capable of forming ammonium compounds with strong acids, as

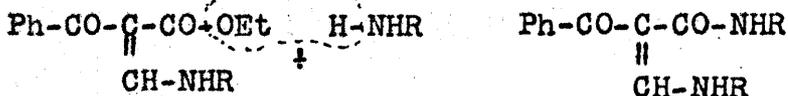


Similarly, it forms a double compound with picric acid. The most important reaction of the disubstituted formamidines, however is their ability to react with methylene hydrogen to produce amino methylene derivatives, as



1. Ber. 35, 2498; 31, 1770.

This "methylene" hydrogen, which is further alluded to under the discussion of benzylphenyl ketone, is characterized by its extreme activity. It is found in such compounds as acetoacetic ester, benzoylacetic ester, acetyl acetone, cyanacetic ester, thiazolones, isoxazolones, and pyrazolones.¹ In each case, these compounds, on being heated with formamidines, yield an amino methylene derivative, and a primary amine is split off. If the compound also contains a carbethoxy group, (as in benzoylacetic ester) a secondary reaction may set in, in which the amine, freed from the formamide, replaces the ethoxy group to produce a substituted amide, as



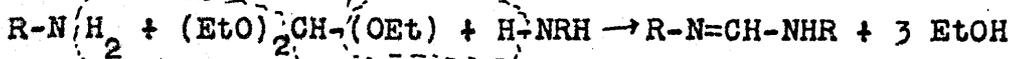
1. J.A.C.S. 31, 1148; 35, 959, 970; 38, 1510.

Ber., 35, 2497.

Preparation of Formamidines.

There are three general methods by which formamidines may be prepared. These are: (1) by heating the desired amine with ethyl orthoformate, (2) by the continued heating of an amine with formic acid, and (3) by treating a formamino derivative with the desired amine, in the presence of a condensing agent, such as phosphorus trichloride.

Of these methods, the first, when practicable, gives by far the best results. For example when di-p-tolyl formamidine is desired, it is only necessary to heat two mols of the purified amine with one mol of orthoformic ester, to about 140° for one hour. After cooling and allowing the formamidine to crystallize out, it is in such a pure state, that it is only necessary to filter and wash with a little gasoline. A yield of eighty percent is easily attainable. The reaction involved may be represented as follows:



The only difficulty with the method is that ethyl orthoformate is a very costly reagent; or if made, is rather difficult to prepare.

The second method is that of Weith.¹ Here two mols of the amine are heated with one mol of formic acid for about eight to ten hours. The reaction is:



The apparatus suggested consists of a reflux condenser fitted with a trap to catch the water given off during the course of the reaction. The compound thus obtained may be partially purified by repeated crystallizations from absolute alcohol, gasoline, or benzene. The former is much more efficacious.

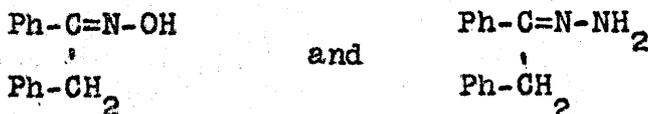
This method of making formamidines is not very satisfactory. In the first place, the amines, at their boiling points exercise a marked solvent action on stoppers, whether of cork or of rubber. This causes the solution of the formamidine to become deeply colored, and this color can be removed only with much difficulty. In the second place, it is difficult to effect a complete separation of the formamidine and unused amine (except with absolute alcohol). This is particularly true of the solid amines, as para toluidine. Vacuum distillation was tried as a means of obviating the difficulties of separation. Here further difficulties ensued, for at the boiling point of diphenyl formamidine, (205° at 14 mm.) considerable decomposition into phenyl isonitrile ensued. The yield of fairly pure product obtained by the Weith method ranged from 30-35% of the theoretical.

The third method of making formamidines is resorted to only when mixed formamidines are desired.¹

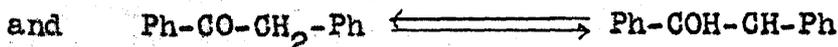
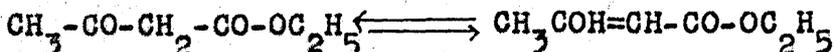
1. Wheeler and Johnson, (A.C.J. 20, 859)

Desoxybenzoin.

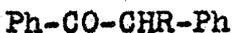
Because of its molecular structure, benzylphenyl ketone, or desoxybenzoin, exhibits (1) the properties of a ketone, (2) the properties of an alcohol, and (3) the properties due to its methylene hydrogen. As a ketone it forms an oxime and a hydrazone with hydroxylamine and hydrazine respectively:



Desoxybenzoin behaves as an alcohol by virtue of keto-enol tautomerism. Just as we have this tautomeric relationship in acetoacetic ester, so also do we find it in benzyl phenyl ketone:



The sodium salt of the enol form may readily be prepared by warming desoxybenzoin with sodium ethylate.¹ When the sodium salt is treated with alkyl halides, the alkyl derivative of desoxybenzoin is produced.

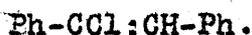


These are, like the parent substance, colorless crystalline bodies, possessing low melting points.

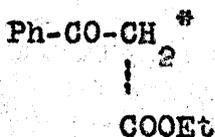
The keto-enol relationship is still further born out by the fact that when desoxybenzoin is treated

1. Meyer and Oelkers. (Ber., 21, 1295)

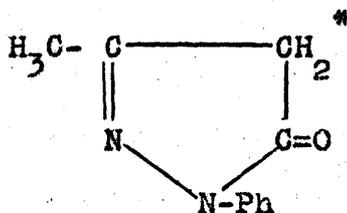
with phosphorus pentachloride, we have produced not a diphenyl dichlor ethane, but chlorostilbene.²



"Methylene" hydrogen refers to hydrogen on a carbon atom which may be replaced with comparatively great ease. It occurs in saturated, or partially saturated compounds, where a $-\text{CH}_2$ group is situated adjacent to a carbon atom loaded with "negative" elements, or groups; as for example

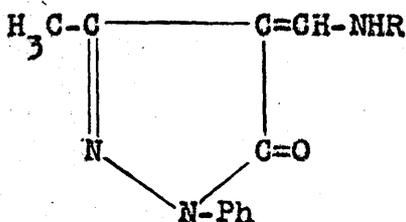


Benzoylactic ester.

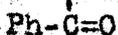


Phenylmethyl Pyrazolone.

This methylene hydrogen is quite "mobile", that is, it may be readily replaced by such compounds as aldehydes, ketones, and, as in the present work, by formamidines, giving such compounds as



Methylene hydrogen is possessed to a rather marked degree by desoxybenzoin. For example, it reacts with benzaldehyde to produce benzylidene desoxybenzoin:



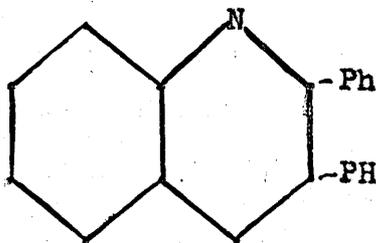
Benzylidene desoxybenzoin.

and when two mols of desoxybenzoin react with one of benzaldehyde, a substance known as benzamarone is produced:¹



This is of interest in that when treated with hydroxylamine hydrochloride, a derivative of pentaphenyl pyridine, is produced.

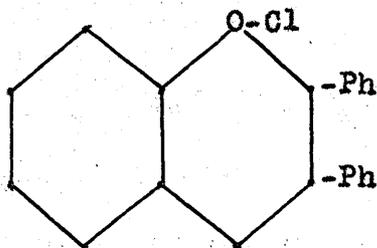
Before describing the experimental work, it might be well to mention some of the more important syntheses of various heterocyclic compounds from desoxybenzoin and its derivatives. M. Buddeberg prepared 2:3 diphenyl quinoline by first making orthonitrobenzyl desoxybenzoin (from o-nitrobenzyl chloride and sodio-desoxybenzoin) and then reducing this compound with iron and acetic acid.² The compound so formed, had the empirical formula $\text{C}_{21}\text{H}_{15}\text{N}$, corresponding to:



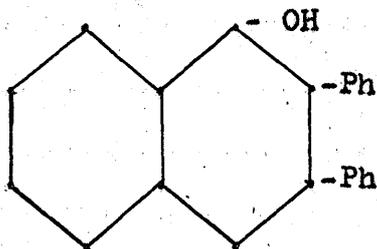
The compound is exceedingly stable, boiling at 420° , without decomposition.

1. Knoevengel (Ber., 26, 436-46)
2. Buddeberg (Ber., 23-2066)

Singh and Mazumdar¹ have prepared a variety of cyclic compounds from desoxybenzoin. Among these are 2:3 diphenyl benzopyronium chloride:



prepared by saturating a solution of desoxybenzoin and salicylaldehyde with dry HCl; and 4-hydroxy, 2:3 diphenyl quinoline:

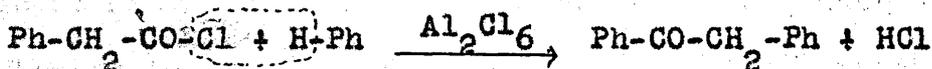


which was prepared by heating o-amino benzoic acid with desoxybenzoin.

1. Singh and Mazumdar (J.C.S. 115, 821)

The Preparation of Desoxybenzoin.

Desoxybenzoin has been prepared in a variety of ways. All of these, with the exception of the synthesis of Graebe and Bungener, involve a reduction of benzoin. Graebe and Bungener prepared the compound from phenylacetyl chloride and benzene;¹



This positively identified desoxybenzoin as benzyl-phenyl ketone.

Meyer and Oelkers² prepared desoxybenzoin by the following method: benzoin is added to 75% alcohol. Then a slight excess of granulated zinc is added to the solution and small quantities of a saturated solution of HCl in 80% alcohol are added from time to time. When reduction is complete, the desoxybenzoin is thrown from the solution with water, partially dried, and then subjected to a vacuum distillation. A yield of some sixty percent is claimed by the authors.

The simplest method for the preparation of desoxybenzoin is that of Juillard and Tissot³, which consists of dissolving the benzoin in five times its weight of glacial acetic acid, and adding an equal weight of zinc dust; then heating the whole for 20

1. Graebe and Bungener (Ber., 12, 1079)

2. Meyer and Oelkers (Ber. 21, 1295)

3. Chem. Centr., 11, 1891, 166.

to 24 hours. The mixture is then poured into cold water and allowed to stand for several hours, or at least until the yellow oil, which separates out, has become completely crystalline. By repeated crystallization from hot alcohol (6 to 10 crystallizations), the pure product is finally obtained.

The last named method is essentially the one used in this work for the preparation of desoxybenzoin. But, in order to avoid the tedium of repeated crystallizations, and to keep the yield as high as possible, the method was modified as follows: after pouring the reaction product into five to six times its volume of cold water, the crude desoxybenzoin was extracted with ether. The ethereal solution was dried with calcium chloride, the ether distilled off and the desoxybenzoin fractionated under diminished pressure. In the four preparations by this method, an average yield of about 60% was obtained, as compared with a yield of 37% when the compound was purified by repeated crystallizations. In an attempt to still further increase the yield, a quantity of benzoin was reduced, using a mechanical stirrer to insure proper contact of the acid solution with the zinc dust. No appreciable improvement of the yield was perceived. Desoxybenzoin boils at 185-90° under 15 mm. pressure. The compound so obtained is of a very light amber color, and melts sharply at 55°.

Experimental Work.I. THE PREPARATION OF AMINO-METHYLENE DERIVATIVES
OF DESOXYBENZOIN.A. ANILIDOMETHYLENE DESOXYBENZOIN.

Repeated preliminary attempts to condense diphenyl formamide with desoxybenzoin were unsuccessful. For example, ten grams of desoxybenzoin and ten grams of diphenyl formamide were heated on an oil bath at 125° for two hours. No product was obtained. The temperature was raised to 150° for two hours with the same negative result. Portions were heated at 175° , 200° and at 250° . No condensation product could be isolated from any of the material heated to these temperatures.

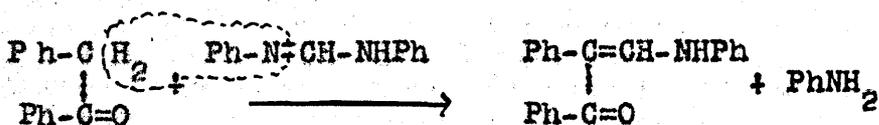
In the hope that by removing the aniline formed in the reaction that the condensation might be brought about, the following procedure was tried. Twenty-four grams of diphenyl formamide and twenty grams of desoxybenzoin were heated at 155° , in a distilling flask under reduced pressure for a period of two hours. An oil distilled over into the receiver. This proved to be aniline, for with acetic anhydride it gave acetanilide. The temperature of the oil bath was then raised to 190° for about fifteen minutes. The contents of the flask were then emptied into a beaker containing dilute HCl and warmed to destroy any formamide which might remain.

The oil which floated on top was then crystallized several times from alcohol until it gave a compound which melted sharply at 93.5° . The yield was about twelve grams of the purified product.

The following are the results of a Kjeldahl analysis for nitrogen:

	Sample I	Sample II.
Weight sample	0.4985 g.	0.5364 g.
Vol. acid used	10.4 cc.	11.0 cc.
1.00 cc. of acid = 0.00222 g. nitrogen.		
Percent nitrogen	4.63%	4.55%
Nitrogen (calculated) from formula $C_{21}H_{17}ON$ is 4.67%		

The anilidomethylene desoxybenzoin is a canary yellow crystalline substance. From the analysis, shown above, it is apparent that the reaction must progress as follows:



Subsequent attempts to produce anilido methylene desoxybenzoin were much less successful. The average yield was perhaps 15%. The problem of making the compound is largely one of temperature control. If it is heated much above 180° , decomposition occurs, with the production of a viscous brown oil, which it is impossible to crystallize. This decomposition also occurs if the mixture is heated for four or five hours,

even at 170° . In nearly all of the condensation products prepared, or attempted, the p-tolyl amino methylenedesoxybenzoin was used in preference to the anilido methylene derivative. The former is easier to prepare in a pure state, and the yield is better.

B. PARA TOLYL AMINOMETHYLENE DESOXYBENZOIN.

Fifteen grams of di-p-tolyl formamidine and thirteen grams of desoxybenzoin were heated in the manner described for the preparation of anilidomethylene desoxybenzoin. The product was crystallized from hot alcohol, from which it assumed the form of large, amber monoclinic crystals. These melted at 132° . On analysis by the Kjeldahl method, the following results were obtained.

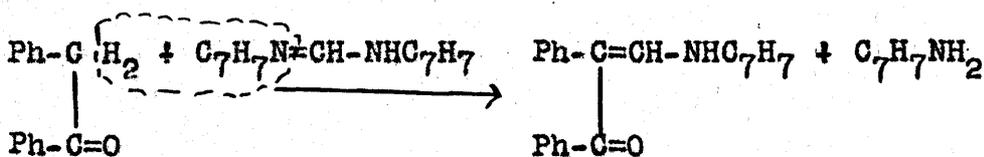
	Sample I	Sample II
Weight of sample	1.0232 g.	1.4412 g.
Vol. acid neutralized	20.8 cc.	28.8 cc.

One cc. of acid is equal to 0.00222 g. nitrogen.

Percent nitrogen	4.51%	4.43%
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The percentage of nitrogen, calculated from the formula, $C_{22}H_{19}ON$ is 4.47%.

The above figures, together with the fact that para toluidine was set free during the course of the reaction, indicates that condensation occurred as follows:



C. ATTEMPT TO PREPARE PARA ETHOXY-PHENYL AMINO-
METHYLENE DESOXYBENZOIN.

Twenty grams of di-para-ethoxyphenyl formamidine (prepared from p-phenetidine and ethyl orthoformate) and sixteen grams of desoxybenzoin were heated in vacuo at 165° for three hours. The mass was dissolved in hot alcohol, but no p-ethoxyphenyl aminomethylene desoxybenzoin crystallized out. The solvent was evaporated off, and benzene, then acetic acid was tried, but none of the above named compound was obtained.

D. PARA METHOXYPHENYL AMINOMETHYLENE DESOXYBENZOIN.

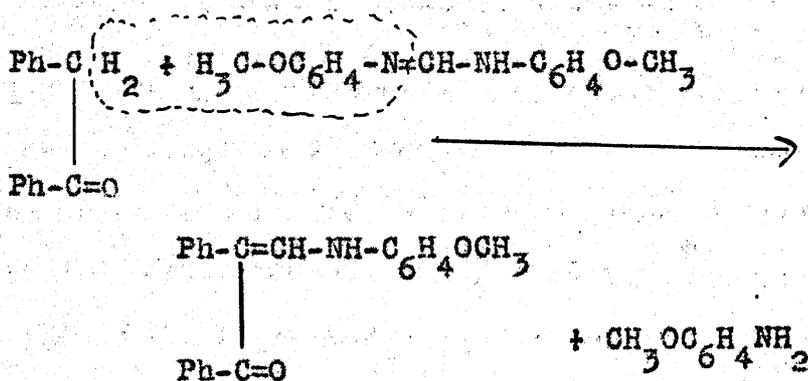
Twenty grams of di-p-methoxyphenyl formamidine (from p-anisidine and ethyl orthoformate) and 15 grams of desoxybenzoin were heated for three hours at 165°. After solution in hot alcohol, the compound finally crystallized out in amber cubes, which melted at 127°. The yield was very poor.

The following analytical data was obtained for the compound:

	<u>Sample I</u>
Weight of sample	0.5134 g.
Vol. acid neutralized	9.96 cc.
Percent nitrogen present	4.31%

The percent of nitrogen, as calculated from the formula $C_{22}H_{19}O_2N$ is 4.26%

The reaction may be formulated as follows:



E. ORTHO TOLYL AMINOMETHYLENE DESOXYBENZOIN.

Three separate attempts to prepare this compound from di-*o*-tolyl formamidine and desoxybenzoin. Each of these was absolutely unsuccessful.

F. Summary of Aminomethylene Derivatives.

It is of interest to note that all of the substituted formamidines do not react with desoxybenzoin with the same ease. The following table shows the yields in the preparation of aminomethylene derivatives:

Name	Attempts to prepare					Average.
	1st.	2nd.	3rd.	4th	5th.	
p-tolyl	22%	38%	26%	8%	14%	22%
phenyl	40%	12%	3%	8%	8%	14%
p-methoxyphenyl	3%					3%
p-ethoxyphenyl	0%					0%
<i>o</i> -tolyl	0%	0%	0%			0%

Perhaps the above may throw some light on the relative reactivity of the substituted formamidines.

II. Concerning the Reactions of the Amino-methylene Derivatives of Desoxybenzoin.

A. Reaction with Aqueous Acid.

That aminomethylene derivatives of desoxybenzoin are stable toward the action of acids is shown by the fact p-tolyl aminomethylene desoxybenzoin was not altered by boiling, in reflux, with 15% sulfuric acid for four hours.

B. Reaction with Aqueous Bases.

Five grams of p-tolyl aminomethylene desoxybenzoin was heated with 35 cc. of 20% NaOH for one hour. During the heating, a slight odor of isonitrile was apparent. Aside from this, no reaction took place, for a large portion of the compound was regained, unaltered.

C. Hydrolysis of p-tolyl aminomethylene desoxybenzoin.

Eight grams of the p-tolyl derivative were dissolved in 35 cc. of alcoholic potash, and refluxed for two hours. The yellow color of the compound disappeared during the process. Water was added in excess and the oil, which floated on top was extracted with ether. This ether was evaporated off, and the residue was treated with NaOH and benzoyl chloride. The compound thus prepared melted at 155°, and by mixed melting point with known substance was identified as identified as benz-p-toluide.

The basic mother liquor was then evaporated to about one-fourth its volume, made acid and allowed to

cool. A substance melting at 121° crystallized out. By mixed melting points, the compound was identified as benzoic acid.

The products of hydrolysis are, as might be expected, para toluidine, benzoic acid, and probably formic acid.

D. PARA ACETAMINOMETHYLENE DESOXYBENZON.

Ten grams of p-tolyl aminomethylene desoxybenzoin and thirty five grams of acetic anhydride were heated together for ten hours. During the heating, the color of the solution changed from deep yellow to a light amber. The reaction product was thrown into cold water and allowed to stand until the oil, which settled to the bottom had solidified. The mass was then crystallized from hot alcohol, from which the compound appeared in colorless cubes, m.p. 111° . Results obtained from a Kjeldahl analysis of the compound are as follows:

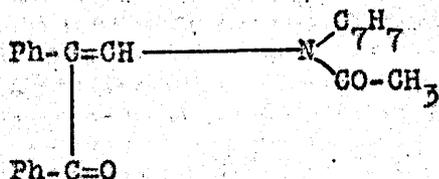
	<u>Sample I</u>	<u>Sample II</u>
Weight of sample	0.3167 g.	0.3997 g.
Acid used	5.3 cc.	6.77 cc.

1.00 cc. of acid = 0.00222 g. nitrogen.

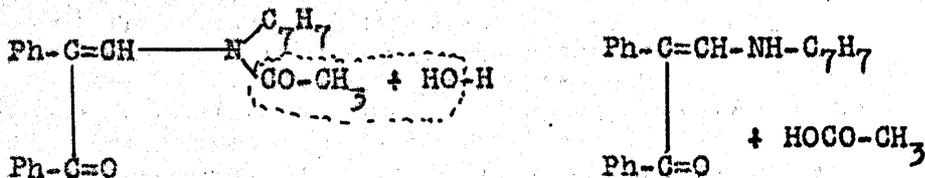
Percent nitrogen	3.71%	3.67%
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Percent nitrogen from formula $C_{24}H_{21}O_2N$ is 3.94%

These results tend to show that the compound is p-tolyl acetaminomethylene desoxybenzoin, which may be represented by the following formula:



The identity of the above compound was further demonstrated by boiling it with aqueous KOH. During the boiling, the color of the substance changed from colorless to yellow. The oil which floated on top of the alkali was removed and crystallized from alcohol. By its melting point, and mixed melting point, it was identified as p-tolyl aminomethylene desoxybenzoin.



E. THE ACTION OF BROMINE ON ANILIDOMETHYLENE DESOXYBENZOIN.

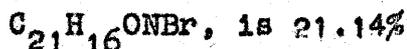
Five grams of pure anilidomethylene desoxybenzoin were dissolved in fifty cc. of chloroform. The solution was well cooled and two grams of bromine added. Hereupon, the mixture was placed in the dark and allowed to stand for two hours, when it was found that a crystalline yellow compound had separated out. This was filtered from the mother liquor and dried on a porous plate. The compound was found to melt at 144° , with decomposition. When a portion of the substance was thrown into water, it first turned liquid, then solid. On crystallizing the resulting compound from alcohol, in which it is sparingly soluble, it melted at 167° . It was assumed that the first compound was

was the hydrobromide of the free base (167°). The brominated base is of a light color, and separates from alcohol in fine, distinct crystals. The compound was analyzed for both bromine and nitrogen. The bromine was determined by the Garius method while the nitrogen was determined by the Kjeldahl.

Bromine.

	<u>Sample I</u>	<u>Sample II</u>
Weight of samples	0.2318 g.	0.2710 g.
Weight AgBr	0.1105	0.1388
Percent Bromine	20.28%	21.77

The percent bromine as calculated from the formula



Nitrogen.

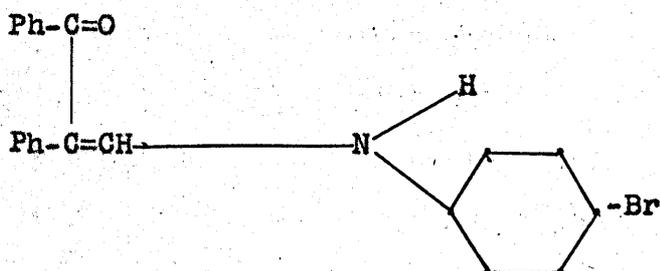
	<u>Sample I</u>	<u>Sample II.</u>
Weight of sample	0.3398 g.	.3724 g.
Vol. acid used	5.72 cc.	6.47 cc.
1.00 cc. of acid = 0.00222 g. nitrogen.		
Percent nitrogen	3.73%	3.86%

The percentage of nitrogen based on the formula,

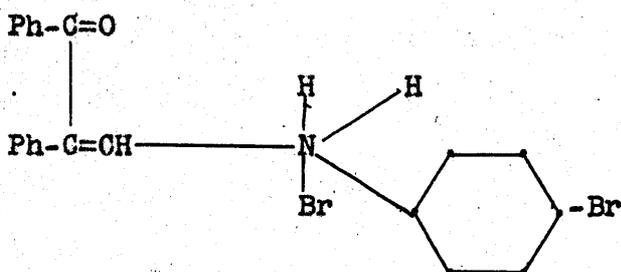


In order to more closely ascertain the position of the bromine atom within the molecule, two grams of the brominated compound (167°) were heated with 10 cc. of alcoholic potash. (see P. 16) The resulting product was then subjected to steam distillation, and

the oily distillate collected. On treatment with NaOH and benzoyl chloride, a compound was obtained, which by its melting point and mixed melting point with known pure substance, was identified as benz-p-brom aniline. We may therefore conclude that the bromine is present in the molecule as shown below.

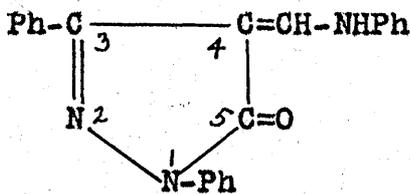
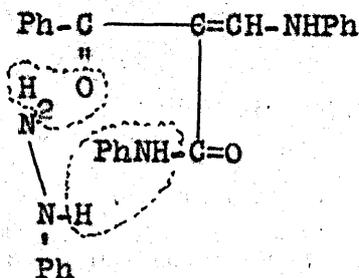


The hydrobromide of the brominated base may be represented as:

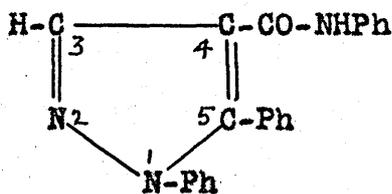
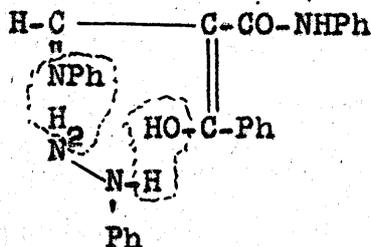


III. THE CONDENSATION PRODUCTS OF THE AMINO
METHYLENE DERIVATIVES OF DESOXYBENZOIN.

When, for example, the anilidomethylene derivative of benzoylacetanilide is treated with phenylhydrazine, a five membered heterocyclic ring is produced. Ruggenburg, who first investigated the reaction, interpreted it as occurring in the following manner:¹



Later work, by Dains and his co-workers², demonstrated that this assumption was erroneous, and that a pyrazole and not a pyrazolone derivative was formed. The reaction is, therefore:



As is shown in the above, the reaction assumes the formation of an -enol, which then reacts with the hydrazine to produce a pyrazole. The reaction is quite general for compounds in which the anilidomethylene group is in the beta position to the keto group.

1. Dissertation, Frieberg (1903)
2. J.A.C.S. 31, 1148; 40, 562

Since in the aminomethylene derivatives of desoxybenzoin, the aminomethylene group is in the beta position to the keto group, this reaction was tried.

A. Synthesis of 1:4:5:triphenyl Pyrazole.

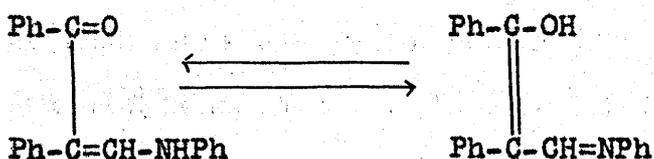
Seven grams of anilido methylene desoxybenzoin, and five grams of phenyl hydrazine were dissolved in thirty-five grams of alcohol and were heated on the water bath until the yellow color of anilido methylene desoxybenzoin had vanished. (about three hours). The reaction product was allowed to cool when a white crystalline substance separated out. These crystals were washed with cold alcohol and then re-crystallized from hot benzene. The compound thus obtained melted sharply at 212° , a temperature exactly coincident with that of the already known 1:4:5 triphenyl pyrazole.

On analysis, by the Dumas method, the following results were obtained:

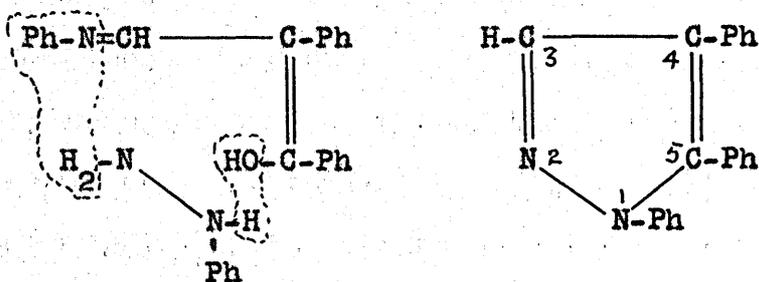
	<u>Sample I</u>
Weight of sample	0.2242 g.
Volume of nitrogen	19.7 cc.
Temperature	28° C.
Barometer	733 mm.
Percent nitrogen	9.41%

The percentage of nitrogen calculated from the formula $C_{21}H_{16}N_2$ is 9.46%

Subsequently this same reaction was carried out, using p-tolyl aminomethylene desoxybenzoin instead of anilidomethylene desoxybenzoin. The same compound, m.p. 212° , was obtained. Because of the fact that a pyrazole with phenyl groups at 4 and 5 is formed, it is necessary to assume that keto-enol tautomerism exists in the aminomethylene desoxybenzoin; thus:



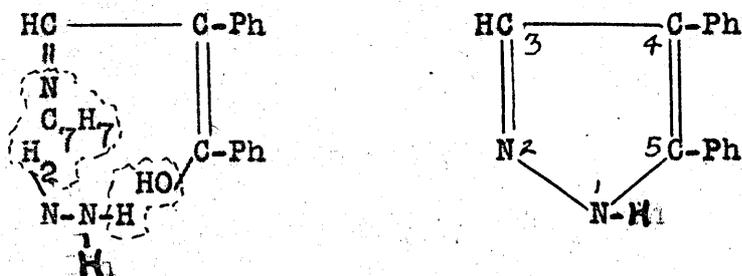
Assuming the formation of this enol, we may explain the reaction as follows:



B. The Synthesis of 4:5 diphenyl Pyrazole.

Ten grams of p-tolyl aminomethylene desoxybenzoin and five grams of finely powdered hydrazine sulfate were added to five grams of potassium carbonate in thirty-five cc. of alcohol. The whole was heated on a water bath, with reflux, for four hours. The compound was then poured into dilute acid and stirred vigorously for a few moments. It was then filtered and the precipitate crystallized from hot alcohol.

The compound thus obtained was in the form of colorless rhombs, m.p. 158° . The compound is exceedingly stable, for it distills at about 365° under normal pressure, with no decomposition. The acid filtrate, mentioned above was concentrated, made alkaline with NaOH, and treated with benzoyl chloride. The compound so prepared, after crystallization from alcohol, melted at 156° , and by its melting point when mixed with known pure substance was identified as benz-p-toluide. This shows conclusively that p-toluidine is split off in the reaction. We may therefore conclude that the reaction goes as indicated below:



Two attempts were made to analyze this compound by the Kjeldahl method, but, as is frequently the case with cyclic nitrogen compounds, low results were obtained. The Dumas method was therefore resorted to. The following analytical data was obtained:

	Sample I	Sample II
Weight of sample	.2243 g.	.1895 g.
Temperature	30°	25°
Barometer	26.5 cc.	21.85 cc.

Barometer	739 mm.	739 mm.
Percent nitrogen	12.61%	12.64%

Based on the formula $C_{15}H_{12}N_2$, the percent of nitrogen in the compound was calculated to be 12.72%, which coincides fairly well with the above.

C. The Synthesis of 4:5 Diphenyl Isoxazole.

As has previously been stated, anilidomethylene derivatives, in which the aminomethylene group is in the beta position to the keto group, behave as do ordinary beta diketones,¹ and possess the property of condensing with hydroxylamine to form compounds, cyclic in nature, called isoxazoles. Since p-tolyl amino methylene desoxybenzoin is such a compound, the reaction was carried out. The procedure used was that of Dains and Griffith.²

Ten grams of p-tolyl aminomethylene desoxybenzoin and five grams of hydroxylamine hydrochloride were refluxed for four hours with a mixture of twenty-five cc. of alcohol and ten cc. of pyridine (the latter to absorb the HCl from the hydroxylamine hydrochloride). The color of the solution, during the reaction changed from yellow to pale amber. After the refluxing was complete, the reaction mass was thrown into cold, dilute HCl and allowed to stand until the oil, which had settled out, had become crystalline. The product was then filtered, and the acid water was evaporated to one-fourth its volume, made basic with NaOH, and then treated with benzoyl chloride.

The product thus obtained was crystallized from hot alcohol, and by its melting point, and mixed melting point with pure known substance, was identified as benz-p-toluide. This shows conclusively that para toluidine is set free during the course of the reaction. The crystalline mass was then removed from the filter paper and crystallized from hot 80% alcohol. This was twice repeated until a perfectly colorless substance, m.p. 74-75°, was obtained.

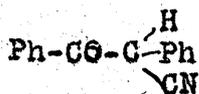
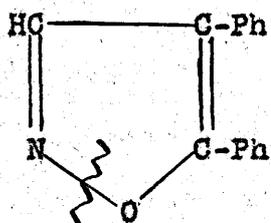
An analysis, (Kjeldahl) gave the following results:

	<u>Sample I</u>	<u>Sample II</u>
Weight of Sample	.4032 g.	.4485 g.
Acid used	11.71 cc.	12.1 cc.
1.00 cc. of acid = 0.00222 g. of nitrogen.		
Nitrogen present	6.44%	6.18%

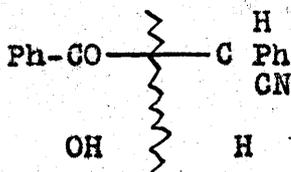
This coincides fairly well with the percent nitrogen calculated from the formula, $C_{15}H_{11}ON$, which is 6.34 percent.

In an attempt to demonstrate that the compound was an isoxazole, with phenyl groups at positions 4 and 5 hydrolysis was tried.

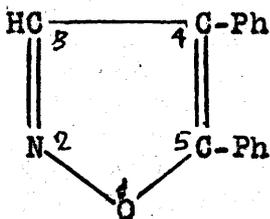
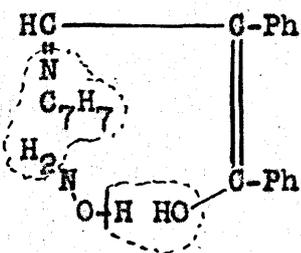
Two grams of the compound was boiled with 15% sodium hydroxide for several minutes. If the compound were 4:5 diphenyl isoxazole, the ring should be ruptured as follows:



The reaction evidently went further, for benzoic acid was produced, as well as an oily substance, possessing the odor of benzaldehyde. This, it was presumed, was benzyl cyanide, produced by the hydrolysis of the above compound.



Because of this, and the fact that para toluidine was split off during the course of the synthesis, it follows that the compound was 4:5 diphenyl isoxazole. The reaction for its formation being:



D. Attempts to Prepare Pyrimidines.

In the hope of preparing a pyrimidine derivative from p-tolyl aminemethylene desoxybenzoïn, this compound was heated at various temperatures, and under various conditions with (1) urea (2) benzamidine, (3) phenyl-thiocarbamide. All were unsuccessful.

In conclusion, the writer wished to express his thanks to Dr. F. B. Dains for his interest in directing this work, and for the many valuable suggestions received from him.