ON THE REACTIONS OF THE FORMAMIDINES:

THE SYNTHESIS OF CERTAIN
PYRAZOLE DERIVATIVES

by

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INTRODUCTORY
Primary aromatic amines react, as a rule, with ortho-formic ester to form substitution products of formamidine, \( \text{HC(OC}_2\text{H}_5)_3 + \text{RNH}_2 = 3\text{C}_2\text{H}_5\text{OH} + \text{RN:CH.NHR} \). This generalization may be put in the form of the equation following in which \( 'R' \) represents an aromatic radical:
\[
\text{HC(OC}_2\text{H}_5)_3 + \text{RNH}_2 = 3\text{C}_2\text{H}_5\text{OH} + \text{RN:CH.NHR}.
\]

Di-phenyl formamidine, the first representative product of this reaction, was prepared by Wichelhaus \( \text{(a)} \) by subjecting to heat a mixture of o-formic ester and aniline. In a similar manner a great number of substituted formamidines have been prepared since.

It has been shown that formamidines react with compounds containing methylene hydrogen with the formation of methylene compounds of the type, \( \text{R'CH:CH . NHR} \). This generalization may be stated as follows:
\[
\text{R'CH}_2 + \text{RN:CH.NHR} = \text{RNH}_2 + \text{R'CH:CH.NHR}.
\]

Should the methylene compound contain an ethoxy group a secondary reaction may occur, in which the above indicated products of reaction take part. Thus:
\[
\text{RNHCHCXCOOC}_2\text{H}_5 + \text{RNH}_2 = \text{RNHCHCXCONHR} + \text{C}_2\text{H}_5\text{OH}.
\]

Methylene derivatives of the type, \( \text{RCOR'CH:CH.NHR} \),
react with hydrazines with the formation of substitution products of pyrazole\(^6\), \(\text{HC} \longrightarrow \text{CH} \). The equation for this generalization follows:

\[
\begin{align*}
\text{RC} - \text{OH} + \text{HNH(R''')} & = \text{RNH}_2 + \\
\text{R'C} - \text{CH:NR} & = \text{H}_2\text{N} + \\
\text{H(N(R'''))}
\end{align*}
\]

As a concrete illustration of the above generalizations, the following reactions are given:

1. \(\text{HC(OC}_2\text{H}_5\text{)}_3 + 2\text{C}_6\text{H}_5\text{NH}_2 = \text{C}_6\text{H}_5\text{NH}_2 \cdot \text{CHNHC}_6\text{H}_5 + 3\text{C}_2\text{H}_5\text{OH}\),

2. \(\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_6\text{H}_5 + \text{C}_6\text{H}_5\text{NH}_2 = \text{CH}_3\text{CO(COOC}_2\text{H}_5\text{)} \cdot \text{CHNHC}_6\text{H}_5 + \text{C}_6\text{H}_5\text{NH}_2\),

3. \(\text{CH}_3\text{CO(COOC}_2\text{H}_5\text{)} \cdot \text{CHNHC}_6\text{H}_5 + \text{C}_6\text{H}_5\text{NH}_2 = \text{C}_6\text{H}_5\text{OH} + \text{CH}_3\text{CO(CONHC}_6\text{H}_5\text{)} \cdot \text{CHNHC}_6\text{H}_5\),

4. \(\text{CH}_3\text{COH:C(CONHC}_6\text{H}_5\text{)} \cdot \text{CH:NR} + \text{C}_6\text{H}_5\text{NHNNH}_2 = \text{RNH}_2 + \text{C}_6\text{H}_5\text{NH}_2 + \text{HC} \longrightarrow \text{C} \cdot \text{CONHC}_6\text{H}_5\)

\(^{-} \text{I-Phenyl,4-anilido,5-methyl pyrazole is the final product in this case.}\)

In conformity with the fourth generalization, phenylhydrazine reacts with certain amino-methylene derivatives of acetoacetic and benzoylacetic esters to form compounds of the type mentioned (pyrazole derivatives). Thus,

\(\text{CH}_3\text{COH:C(CONHR)} \cdot \text{CH:NR} + \text{C}_6\text{H}_5\text{NHNNH}_2 = \text{RNH}_2 + \text{H(C-CONHR)} \text{CH:NR} + \text{C}_6\text{H}_5\text{NHNNH}_2 = \text{RNH}_2 + \)
Illustrations of this type are the following \textit{pyrazoles} which have been prepared:-

(A) Pyrazoles from phenylhydrazine and aceto-acetic ester derivatives:

The phenyl-amide of 1-phenyl-5-methyl pyrazole-4-carboxylic acid,

\begin{align*}
&\text{HC} \quad \text{C-CONHC}_6\text{H}_5 \quad \text{N}\quad \text{C-CH}_3 \\
&\quad \text{N}<\text{C}_6\text{H}_5
\end{align*}

(a)

the p-tolylamide of 1-phenyl-5-methyl pyrazole-4-carboxylic acid,

\begin{align*}
&\text{HC} \quad \text{C-CONHC}_6\text{H}_4.\text{CH}_3(p), \quad \text{N}\quad \text{C-CH}_3 \\
&\quad \text{N}<\text{C}_6\text{H}_5
\end{align*}

(b)

the alpha-naphthalide of 1-phenyl-5-methyl pyrazole-4-carboxylic acid,

\begin{align*}
&\text{HC} \quad \text{CONHC}_6\text{H}_5.\text{H}_7(\alpha) \quad \text{N}\quad \text{C-CH}_3 \\
&\quad \text{N}<\text{C}_6\text{H}_5 \quad (\alpha)
\end{align*}

the beta-naphthalide of 1-phenyl-5-methyl pyrazole-4-carboxylic acid of structure similar to above, (\alpha)

the ethyl ester of 1-phenyl-5-methyl pyrazole-4-carboxylic acid,

\begin{align*}
&\text{HC} \quad \text{C-COOCH}_3 \quad \text{N}\quad \text{C-CH}_3 \\
&\quad \text{N}<\text{C}_6\text{H}_5
\end{align*}

(h)

the o-ethoxy anilide of 1-phenyl-3-methyl pyrazole-4-carboxylic acid,

\begin{align*}
&\text{HC} \quad \text{C-CONHC}_6\text{H}_4.\text{OC}_6\text{H}_5(o) \quad \text{N}\quad \text{C-CH}_3 \\
&\quad \text{N}<\text{C}_6\text{H}_5 \quad \text{(i)}
\end{align*}
(B) Pyrazoles from phenylhydrazine and benzoyl-acetic ester derivatives:

This condensation was investigated by Rüggebürg who concluded that phenylhydrazine reacted with anilidomethylene-benzoyl-acetanilide and with o-toluidomethylene-benzoyl-acet-o-toluidide to form aminomethylene derivatives of diphenyl pyrazolone.

Dains and Brown however showed that the compounds formed were pyrazole derivatives. They prepared the o-tolylamide of 5-diphenylpyrazole-4-carboxylic acid from phenylhydrazine and O-toluidomethylene-benzoyl-acet-o-toluidide and proved this to be identical with the product prepared by Rüggebürg.

The formula for this compound follows:

\[
\begin{align*}
\text{HC} & \quad \text{C-CONHC}_7\text{H}_7 \\
\text{N} & \quad \text{C-C}_6\text{H}_5 \\
\text{N} & \quad \text{C-C}_6\text{H}_5
\end{align*}
\]

The O-ethoxyanilide of 1,5-diphenyl-4-pyrazole-carboxylic acid, \(\text{HC} \quad \text{C-CONH}_2\text{C}_6\text{H}_4 \cdot \text{OC}_6\text{H}_5\) (o), has been made from phenylhydrazine and the O-ethoxy-anilide of O-ethoxyanilido-methylene-benzoyl acetic acid.
(C) Pyrazoles from hydrazine and aceto-acetic ester derivatives:

5-Methyl-pyrazole-4-carboxylic acid, \( \rightarrow (1) \)

![Chemical Structure](C)

by hydrolysis of the ethyl ester.

The anilide of 5-methyl-pyrazole-4-carboxylic acid,

![Chemical Structure](m)

The p-toluidide of 5-methyl-pyrazole-4-carboxylic acid,

![Chemical Structure](n)

The o-ethoxyanilide of 5-methyl-pyrazole-4-carboxylic acid,

![Chemical Structure](o)

The ethyl-ester of 5-methyl-pyrazole-4-carboxylic acid,

![Chemical Structure](l)
This completes the list of pyrazoles which have been made from hydrazines and methylene derivatives of the type, $\text{RCOR'C:CH.NHR}$. It will be observed that the list includes no derivatives made from hydrazine and methylene-benzoyl-acetic-ester compounds.

The work, the results of which are given in this paper, was undertaken with the view of investigating the action of hydrazine on benzoyl-acetic ester derivatives of the methylene type. A number of such derivatives were found to condense with hydrazine with the formation of pyrazole derivatives of the type, 

\[
\begin{align*}
\text{HN} & \text{N} \\
\text{H} & \text{H} \\
\end{align*}
\] 

\[
\text{RCOR} \quad \text{C-COR}
\]

on hydrolysis, 

\[
\begin{align*}
\text{N} & \text{N} \\
\text{H} & \text{H} \\
\end{align*}
\] 

\[
\begin{align*}
\text{E-CaH}_2
\end{align*}
\]

\[
\text{H-C-COCONH-CaH}_2 \quad \text{H-C-COCONH-CaH}_2
\]

The preparation of this acid completes the number of possible 5-phenyl-carboxyl pyrazoles. The two other possible 5-phenyl mono-carboxylic compounds have been prepared. The structural formulae for these follow:
In the course of the investigation referred to above, we were led to an examination of certain derivatives of the types which follow:

\[
\begin{align*}
\text{HCCOOR} & \quad \text{HCCOR} & \quad \text{HCCOR} \\
\text{H} & \quad \text{H} & \quad \text{H} \\
\text{N} & \quad \text{N} & \quad \text{N} \\
\text{C} & \quad \text{O} & \quad \text{O} \\
\text{NH} & \quad \text{NH} & \quad \text{NH} \\
\text{C} & \quad \text{C} & \quad \text{C} \\
\text{H} & \quad \text{H} & \quad \text{H} \\
\text{N} & \quad \text{N} & \quad \text{N} \\
\text{CsH} & \quad \text{CsH} & \quad \text{CsH} \\
\end{align*}
\]

The point in question was the effect of certain groups attached to \( \text{COR} \) and of certain atoms in the ring upon the hydroizability of the grouping, COR. The facts which led to this will be stated later in the course of this discussion.

Subordinate to the above work but necessary to its prosecution was the preparation of a number of formamidine derivatives and derivatives of benzoyl acetic ester. In connection with the work on these derivatives we had occasion to prepare a number of substances not directly connected with the investigation proper. Some of these required analysis and description. This work will be referred to in its proper place.

A more detailed reference to the experimental part of the work follows:
6-Phenyl-4-carbethoxy pyrazole may be prepared by condensing o-ethoxy-anilido-methylene-benzoyl acetic ester with hydrazine according the following reaction:

\[
\text{C}_6\text{H}_5\text{COOC}:\text{CHNMCH}_3\text{H}_4\text{OCCH}_5 + \text{H}_2\text{N.NH}_3 = \text{C}_6\text{H}_5\text{O.C}_6\text{H}_4\text{N.HN} + \]

\[
\begin{array}{c}
\text{H} \\
\text{N} \\
\text{C}\text{C}_6\text{H}_5 \\
\text{H}
\end{array}
\]

Melting point 84° to 85°.

This pyrazole is readily hydrolyzed to 5-phenyl-4-carboxyl pyrazole,

\[
\begin{array}{c}
\text{H} \\
\text{C} \quad \text{C}-\text{COOH} \\
\text{N} \\
\text{N} \\
\text{C}\text{C}_6\text{H}_5 \\
\text{H}
\end{array}
\]

, melting at 260°.

The acid at its melting point loses carbon-dioxide with the formation of 5-phenyl pyrazole,

\[
\begin{array}{c}
\text{H} \\
\text{C} \quad \text{C}\text{H} \\
\text{N} \\
\text{N} \\
\text{C}\text{C}_6\text{H}_5 \\
\text{H}
\end{array}
\]

, melting at 78°.

This product is described in the literature. (q)

The anilide of anilido-methylene-benzoyl-acetic acid and hydrazine react with the formation of 5-phenyl-4-carbanilido pyrazole,

\[
\begin{array}{c}
\text{H} \\
\text{C} \quad \text{C}-\text{CONHMCH}_3\text{H}_5 \\
\text{N} \\
\text{N} \\
\text{C}\text{C}_6\text{H}_5 \\
\text{H}
\end{array}
\]
melting at 184°.

This compound can be hydrolyzed, but with greater difficulty than the corresponding ester derivative, to the same 5-phenyl-4-carboxyl pyrazole,

\[
\begin{align*}
\text{H C} & \quad \text{C-COOH} \\
\text{N} & \quad \text{N} \\
\text{H} & \quad \text{C-C_6H_5}
\end{align*}
\]

, melting at 260°.

\[\text{p-Anisidomethylenebenzoylaceticp-anisidide}\]

and hydrazine condense with the formation of the p-

\[\text{Anisylamide}\]

of 5-phenyl-4-carboxylic acid,

\[
\begin{align*}
\text{H C} & \quad \text{O-CONHC_6H_4\cdot OCH_3\ (p)} \\
\text{N} & \quad \text{N} \\
\text{H} & \quad \text{C-C_6H_5}
\end{align*}
\]

, melting at 160° to 161°.

This pyrazole can be hydrolyzed fairly readily to 5-phenyl-4-carboxyl pyrazole,

\[
\begin{align*}
\text{H C} & \quad \text{C-COOH} \\
\text{N} & \quad \text{N} \\
\text{H} & \quad \text{C-C_6H_5}
\end{align*}
\]

, melting at 260°.

\[\text{o-Anisidomethylenebenzoylacetoanisidide}\]

and hydrazine react with the formation of o-anisylamide

of 5-phenyl-4-carboxyl pyrazole,

\[
\begin{align*}
\text{H C} & \quad \text{O-CONHC_6H_4\cdot OCH_3\ (o)} \\
\text{N} & \quad \text{N} \\
\text{H} & \quad \text{C-C_6H_5}
\end{align*}
\]

, melting at 138°.

Difficulty was experienced in hydrolyzing this derivative. By boiling with constant-boiling hyd-
robromic acid it gave 5-phenyl-4-carboxyl pyrazole,

\[
\begin{align*}
\text{H} & \quad \text{C} \quad \text{C-CONHCeHs} \\
\text{N} & \quad \text{N} \quad \text{C-CeHs} \\
\text{H} & \quad \text{H} \\
\end{align*}
\]

melting at 260°, as in the preceding instances.

The following characteristics were noted in connection with a study of these compounds:

The carboxyl pyrazole fails to form the anilide on heating with aniline, nor does it undergo benzoylation with benzoyl chloride. It will not add methyl iodide nor is it acted upon apparently by phosphorus pentachloride. It does appear to undergo nitration and forms well-defined salts with silver, copper and barium. It forms no salt with hydrochloric acid.

The ester pyrazole does not react with aniline, with hydrochloric acid, or with acetyl and benzoyl chlorides. It will not add methyl iodide. The anilido pyrazole crystallizes with a mole of alcohol. It will not form the hydrochloride.

The question of the hydrolyzability of the CONH group in the '4' position of the pyrazole ring arose as a result of a consideration of the following facts:

1. 5-Phenyl-4-carbanilido pyrazole can be hydrolyzed:

\[
\begin{align*}
\text{H} & \quad \text{C} \quad \text{C-CONHCeHs} \\
\text{N} & \quad \text{N} \quad \text{C-CeHs} \\
\text{H} & \quad \text{H} \\
\end{align*}
\]
The anilide of 1,5-diphenyl-4-carboxyl pyrazole,

\[
\text{H C} \quad \text{C-CONH}_{C_6H_5} \quad \text{H C} \quad \text{C-COOH}
\]


\[
\text{N} \quad \text{N} \quad \text{C-C}_6\text{H}_5
\]

was prepared by the
method of Rüggeberg from phenylhydrazine and anilidomethylenebenzoylacetanilide. Attempts to hydrolyze this derivative have given negative results. Some change in the mole apparently occurs but there is no evidence of the formation of aniline. A small quantity of material melting at a different temperature from that of the original compound.

The anilide of 5-phenyl-4-carboxyl isoxazole,

\[
\begin{array}{c}
\text{H} \\
\text{N} \\
\text{O} \\
\text{C-CaHs} \\
\text{C-CONHCaHs}
\end{array}
\]

was prepared by the method of Dains and Griffin from hydroxylamine and anilidomethylenebenzoylacetanilide. An attempt to hydrolyze this product with a mole of potassium hydroxide resulted in the formation of benzoylcyanoacetanilide, \( \text{CaHsCOCH(CN)CONHCaHs} \), melting at 208°. This was the result expected. An attempt to hydrolyze with a mixture of alcohol and concentrated hydrochloric acid gave anilinehydrochloride and a high proportion of the original compound. No other product was isolated, indicating decomposition of the acid probably.

With the view to forming 5-phenyl-4-carbethoxy isoxazole,

\[
\begin{array}{c}
\text{H} \\
\text{N} \\
\text{O} \\
\text{C-CaHs} \\
\text{C-COOCAHs}
\end{array}
\]
a mixture of hydroxylamine and o-ethoxyanilidomethylene benzoylacetic ester was heated in boiling water. An oil was recovered which is doubtless the compound sought but the quantity obtained was too small for identification. A more extensive investigation of ester derivatives of the above type has been impossible in that we have been unable to secure in quantity a methylene derivative of the type,

C₆H₅COC(COOC₆H₅):CHNR.

Anilidomethylenebenzoylacetanilide and semicarbazine react with the formation of a compound melting near 185°. The product has not been secured sufficiently pure for satisfactory analysis. The nitrogen content falls somewhat below that calculated for 1-carbamine-5-phenyl-4-carbanilido pyrazole,

\[
\begin{align*}
\text{H} & \quad \text{C} \quad \text{C-CONH}_2\text{C}_6\text{H}_5 \\
\text{N} & \quad \text{N} \quad \text{C-C}_6\text{H}_5 \\
\text{CONH}_2
\end{align*}
\]

Work on this compound is to be continued as well work on the above isoxazole derivative.

In addition to the above work the following may be mentioned:

It was found that di-o-ethoxy-diphenyl formamidine will react with benzoylacetic ester with the formation of o-ethoxyanilidomethylenebenzoylacetic ester
as follows:

$$(\text{C}_6\text{H}_5\text{O})\cdot \text{C}_{6}\text{H}_4\cdot \text{N} \cdot \text{CH} \cdot \text{NHC}_6\text{H}_4\cdot \text{OC}_{6}\text{H}_5 (\text{o}) + \text{C}_6\text{H}_5\text{COCH}_6\text{H}_4\text{COOC}_6\text{H}_5 =$$

$$\text{NH}_2\text{C}_{6}\text{H}_4\cdot \text{OC}_{6}\text{H}_5 (\text{o}) + \text{C}_6\text{H}_5\text{CO(COOC}_6\text{H}_5\text{):CHNH}_{6}\text{H}_4\cdot \text{OC}_{6}\text{H}_5$$

The compound melts at 108°.

It being desirable to secure, in quantity, a supply of a derivative of benzoylacetie ester of the type, $\text{C}_6\text{H}_4\text{CO(COOC}_6\text{H}_5\text{):CHNH}_{6}\text{H}_4\cdot \text{OC}_{6}\text{H}_5$, attempts were made to prepare such a derivative from benzoylacetic ester and diphenylformamidine. All attempts, however, gave as the product of condensation the anilide of anilido methylenebenzoylacetic acid.

Benzoylacetic ester and di-m-tolylformamidine react to form the m-tolylamide of m-toluidomethylene-benzoylacetic acid.

$$\text{C}_6\text{H}_5\text{CO}$$
$$\text{C:CHNH}_{6}\text{H}_4\cdot \text{CH}_3 (\text{m})$$
$$\text{CO}. \text{NH}_{6}\text{H}_4\cdot \text{CH}_3 (\text{m})$$
separating from alcohol as long slender needles melting at 134°.

O-Formic ester and acetphenylenediamine readily react with the formation of a product which separates from alcohol as crystals melting at 190°. The product is doubtless di-acet-diphenyldiaminiformamidine though analysis of the product has not as yet been attempted.

O-Formic ester and o-chloraniline easily react with the formation of di-o-chlor-diphenylformamidine,
\[
\text{H} \text{C}^=\text{N} \text{C}_6\text{H}_4-\text{Cl} (\text{o})
\]

\[
\text{NHC}_6\text{H}_4-\text{Cl} (\text{o}), \text{ which separates from}
\]
alcohol as pink flakes melting at 140°. It forms

a hydrochloride melting at 178°.

Benzylphenylhydrazine was prepared by the method
of Antrimick. It was found not to condense with

o-formic ester as do hydrazine and phenylhydrazine.

When p-form-toluide is treated with a mole of
bromine in acetic acid or chloroform solution,
the product formed is, m-dibrom-p-toluidine,
instead of o-brom-p-form toluide the product ex-
pected;

\[
\begin{array}{l}
\text{NMeCHO} \\
\text{CH}_2
\end{array}
+ \begin{array}{c}
\text{Br}_2 \text{in} \\
\text{HCl,} \text{ or CHCl}_3
\end{array}
\rightarrow
\begin{array}{l}
\text{NH}_{3} \\
\text{Br}
\end{array}
\begin{array}{l}
\text{Br} \\
\text{CH}_2
\end{array}
\]

From the chloroform solution the product separates
as a mixture of the hydrobromide and the free base.

By brominating in water solution, the o-brom-p-
form toluide is obtained in good yield. This com-

pound is easily reduced to the corresponding o-
brom-p-toluidine which forms a benzoyl derivative
melting at 147° to 148°, and a well defined hydro-
chloride.

\[
p-\text{Nitro-quinoline and the corresponding p-}
\]

amino-derivative were prepared by the methods of
The amine with o-formic ester gave a product melting at 185°. This product forms with hydrogen chloride a compound which decomposes at 230°. The nitrogen content fell a little short of that calculated for di-p-quinoliniformamidine.

\[
\begin{align*}
\text{HN} & \quad \text{HN} \\
\text{HC} & \quad \text{HC}
\end{align*}
\]

The product which is doubtless the formamidine reacts with acetoacetic ester to form a solid melting at 280°. This may be the methylene derivative but the yield was so small that identification was not attempted.
EXPERIMENTAL
PART I.

RING CLOSURE:

PYRAZOLE SYNTHESSES,

REACTIONS.
5-PHENYL-4 CARBA-NILIDO PYRAZOLE

Anilidomethylenebenzoylacetanilide, 7.0 grams,
Hydrazine Sulphate, 11.0 grams,
Sodium carbonate, an equivalent, anhydrous,
Alcohol, 75 cc.

To the alcohol-suspension of the anilidomethylene compound, the neutralized solution of the hydrazine sulphate was added. The mixture was heated at the boiling point for five hours. White crystals separated on slowly evaporating the alcohol. The residue was extracted with hot methyl alcohol. To the methyl alcohol solution ice was added whereupon the product separated in the form of white crystals melting at 182°. In the case of a second preparation, the methyl alcohol extract was first acidified with acetic acid
acid and then diluted with water.

Yield, 5.07 grams.
Percentage yield, 97.0
Melting point, 184°.

ANALYSIS COMBUSTION

Samples, 0.1798, 0.1868, 0.1816, 0.1904
Moist gas, 22.8, 24.1, 23.5, 25.0
Pressure, 737.5, 743.0, 740.5, 730.0
Temperature, 17.8°, 19.8°, 23.6°, 22.1°
Vapor pressure, 8.2, 9.3, 11.5, 10.6

Percent Na found, 14.39, 14.34, 14.63, 14.38
(calculated for \( \text{C}_{12}\text{H}_{10}\text{O}_{12}\text{Na} \cdot \text{CH}_2\text{O} \), 14.23)

Note: While determining the melting point of this product, it was noticed that a liquid was given off at about 120°. After drying at 120°, the product gave the following analysis:

ANALYSIS COMBUSTION

Samples, 0.2035, 0.2028
Moist Gas, 30.00, 30.00
Pressure, 735.5, 734.0
Temperature, 20.9°, 24.5°
Vapor tension, 18.5, \( (\text{H}_2\text{O}) \), 12.1 (40% KOH)

Percent Na found, 16.15, 16.08
(calculated for \( \text{C}_{12}\text{H}_{10}\text{O}_{12}\text{Na} \), 15.96)
The behavior of 5-phenyl-4-carbanilido-pyrazole on melting indicated methyl alcohol of crystallization and the analysis confirmed this conclusion. Some of the preparation freshly crystallized from ethyl alcohol and air-dried was subjected to analysis. It was found that the loss in weight on drying a sample at 120°, corresponded to a loss of one mole of ethyl alcohol. The data for the determination follow:

- Weight of sample, 1.1348 grams,
- Loss at 120°, 0.1662 grams,
- Percentage loss, 14.64
- Calculated for (C<sub>9</sub>H<sub>7</sub>ONa.C<sub>6</sub>H<sub>5</sub>0), 14.88
ATTEMPTED REACTIONS

(a)

ATTEMPT TO FORM THE HYDROCHLORIDE:

Dry hydrogen chloride was passed into a boiling benzene solution of 5-phenyl-4-carbanilidopyrazole until a precipitate ceased to form and the solution was saturated with the gas. A dense, white, gelatinous precipitate came down.

Melting point, 182°.
Melting point of the 5-phenyl-4-carbanilidopyrazole, 182° to 183°.
Melting point of a mixture, 175°.

Product is partially soluble in N/10 sodium hydroxide.

Air-dried sample taken for analysis, 0.1606 grams.
N/10 NaOH, 20.0 cc
N/10 HCl, 15.7 cc
Percent HCl, found, 9.7

calculated for (C₉H₇NO₃S⋅HCl) 12.50
Analysis of the sample oven-dried at 120°:

Sample, 0.1235 grams.
N/10 NaOH, 15.00 cc,
N/10 HCl, 15.00 cc.
Percent HCl, found, 0.00.

The above results suggest the possibility of the formation of an unstable hydrochloride.

(b)

HYDROLYSIS:

A half-gram of 5-phenyl-4-carbanilido-pyrazole was digested with boiling concentrated hydrochloric acid for three hours. A crystalline precipitate formed on diluting with water. Washed with water and dried these melted sharply at 260°.

The filtrate was evaporated to dryness. The residue gave a strong positive reaction for aniline with bleaching powder, indicating that hydrolysis had taken place. The product of hydrolysis, 5-phenyl-4-carboxyl pyrazole, was prepared in larger quantity and analyzed.
5-PHENYL-4-CARBOXYL PYRAZOLE

\[ \text{H C} \quad \text{C=COOH} \]
\[ \text{N} \quad \text{C-CeHs} \]
\[ \text{N-H} \]

5-Phenyl-4-carbanilido-pyrazole, 15.5 grams.
Hydrochloric acid (conc.) , 75 cc 

The above mixture was boiled for three hours under a water-cooled condenser. Upon adding several volumes of water, a heavy white precipitate came down immediately. This was filtered off and washed successively with alcohol and ether. The product is slightly soluble in boiling water, crystallizing out as very fine silky needles. It is more soluble in hot ethyl alcohol but not readily so; and is quite insoluble in ether.

Melting point (from alcohol), \( 260^\circ \).
Yield, \( 5.5 \) grams.
### Analysis

<table>
<thead>
<tr>
<th>Sample</th>
<th>Combustion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moist gas,</td>
<td>34.4 cc</td>
</tr>
<tr>
<td>Pressure,</td>
<td>741.5 mm</td>
</tr>
<tr>
<td>Temperature,</td>
<td>20.7°</td>
</tr>
<tr>
<td>Vapor tension,</td>
<td>9.7 mm</td>
</tr>
<tr>
<td>Percent Na,</td>
<td>15.34</td>
</tr>
<tr>
<td>Calculated for C₆H₆O₂Na,</td>
<td>14.89</td>
</tr>
</tbody>
</table>

### Salts of 5-Phenyl-4-Carboxylpyrazole:

(a)

**The Silver Salt:**

Some of the 5-phenyl-4-carboxylpyrazole was treated with nearly enough tenth-normal sodium hydroxide to completely dissolve it on the application of heat. On adding a slight excess of silver nitrate solution, a heavy white precipitate came down. After heating to boiling, the precipitated silver salt was filtered off, washed
with water, dried and analyzed.

**ANALYSIS**

<table>
<thead>
<tr>
<th>Weight of crucible,</th>
<th>4.8300 grams.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight crucible and sample,</td>
<td>5.4715 grams.</td>
</tr>
<tr>
<td>Weight sample,</td>
<td>0.6415 grams.</td>
</tr>
<tr>
<td>Weight crucible and Ag,</td>
<td>5.0669 grams.</td>
</tr>
<tr>
<td>Weight of Ag,</td>
<td>0.2369 grams.</td>
</tr>
</tbody>
</table>

Percent Ag, found, 36.92

Calculated for\( \text{C}_{10}\text{H}_{8}\text{O}_{2}\text{Na} \cdot \text{Ag} \) 36.59

(b)

**THE BARIUM SALT:**

Some 5-phenyl-4-carboxyl-pyrazole, previously dried in the hot-air oven, was heated with a solution of barium hydroxide. Enough of the pyrazole derivative was dissolved in the base to discharge the pink color produced by phenolphthalein. On evaporating to dryness on the water-bath, a smooth glistening scale remained.

**ANALYSIS:**

<table>
<thead>
<tr>
<th>Sample taken,</th>
<th>0.1669</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight BaCO₃ produced,</td>
<td>0.0629</td>
</tr>
<tr>
<td>Percent BaCO₃ found,</td>
<td>39.12</td>
</tr>
<tr>
<td>Calculated for( \text{C}<em>{10}\text{H}</em>{8}\text{O}_{2}\text{Na} \cdot \text{Ba} ) 38.59</td>
<td></td>
</tr>
</tbody>
</table>
THE COPPER SALT:

Some 5-phenyl-4-carboxyl-pyrazole was dissolved in an equivalent of sodium hydroxide. On adding a slight excess of a solution of copper sulphate a bluish-white precipitate came down. This was filtered off, washed with hot water and dried in the oven. The residue, a light-blue powder gave the following analysis:

Sample taken, 0.1178 grams,
Weight of CuO obtained, 0.0214 grams,
Percent CuO found, 18.16
Calculated for (C₆H₆O₆Na)₂Cu) 18.19

REACTIONS ATTEMPTED WITH 5-PHENYL-4-CARBOXYL PYRAZOLE.

(a)

ATTEMPT to ADD METHYL IODIDE

Some of the 5-phenyl-4-carboxyl-pyrazole was placed in a small test-tube. The latter was then drawn out to a fine bore near the mouth and methyl
iodide permitted to run in until the solid was covered. The tube was then fused off and permitted to stand over night. The product isolated was the unchanged pyrazole derivative melting at 260-2°C.

A second tube prepared in a manner similar to the first was heated in boiling water for some time. The product recovered was the unchanged pyrazole derivative melting at 262°C.

(b)

ATTEMPT to form the AMIDE:

A small quantity of 5-phenyl-4-carboxyl-pyrazole was heated for an hour with aniline at 190°. The solid gradually dissolved in the aniline. On cooling, crystals separated. Alcohol was added, the precipitated solid filtered off and washed with alcohol and ether.

Melting point, 260°C.

This is the melting point of the unchanged pyrazole derivative.

Another portion of the pyrazole derivative was heated with aniline in a sealed tube for several minutes at a temperature of 260° to 270°. The
Solid dissolved to a black solution. On standing a few crystals separated. The solid isolated was washed with alcohol and ether.

Melting point, \(260^\circ\). This is the melting point of the original pyrazole derivative.

\[(c)\]

**ATTEMPT to NITRATE:**

Some 5-phenyl-4-carboxyl-pyrazole was treated with concentrated sulphuric acid whereupon it dissolved without charring. An equal volume of concentrated nitric acid was then added. No action was evident. On heating there was no visible action. The solution was permitted to stand over night at room temperature. On diluting with several volumes of water no precipitation occurred. A portion of the solution was neutralized with sodium hydroxide. There was no precipitation but the solution changed to a slight yellow color. The ether extract of this contained a slight oily residue obtained upon evaporation.
EFFECT of HEAT:

About a half-gram of 5-phenyl-4-carboxyl-pyrazole was heated in a test-tube supplied with a delivery tube leading into lime-water. The temperature maintained was slightly above the melting point of the compound. Effervescence rapidly took place at 260° to 270°, carbon dioxide being evolved and the solid changing to a black oil which refused to solidify on cooling. The product of decomposition, 5-phenyl-pyrazole, was prepared in larger quantity and subjected to analysis.

5-PHENYL PYRAZOLE

\[
\begin{array}{c}
\text{H} \\
\text{C} \quad \text{H} \\
\text{N} \quad \text{C-CaHs} \\
\text{N-H}
\end{array}
\]

The oil as prepared above was treated with boiling water and filtered. The filtrate on cooling turned milky but no crystals separated on standing over night at room temperature. On evaporating the filtrate to dryness an oil separated which
formed a syrupy mass on drying. The product was again dissolved in hot water. On cooling the solution the milkiness again appeared but, after standing for thirty hours, a fine, white, crystalline precipitate formed, producing a tough fibrous mass.

Melting point, $77.5^\circ$ to $78^\circ$.

This is the melting point of the 5-phenyl pyrazole described in the literature. (q)

The oil resulting from the heating of five grams of 5-phenyl-4-carboxyl pyrazole was repeatedly extracted with boiling water until everything of an oily consistency was dissolved. The filtrates were united, ice was added, and the resulting mixture permitted to stand. In a short time the pyrazole had separated as a fine white solid. This was thoroughly dried, first in air, finally over calcium chloride.

ANALYSIS COMBUSTION

<table>
<thead>
<tr>
<th>Samples</th>
<th>0.1800</th>
<th>0.1800</th>
<th>0.1797</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moist gas</td>
<td>30.4</td>
<td>34.2</td>
<td>32.6</td>
</tr>
<tr>
<td>Pressure</td>
<td>733.0</td>
<td>725.0</td>
<td>733.5</td>
</tr>
<tr>
<td>Temperature</td>
<td>28.9$^\circ$</td>
<td>28.8$^\circ$</td>
<td>20.7$^\circ$</td>
</tr>
<tr>
<td>Vapor tension</td>
<td>15.4</td>
<td>14.3</td>
<td>9.7</td>
</tr>
<tr>
<td>Percent $N_\text{a}$, found</td>
<td>17.96</td>
<td>19.75</td>
<td>19.77</td>
</tr>
<tr>
<td>Calculated for ((C_7H_9N))</td>
<td>19.51</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5-PHENYL-4-CARBOETHOXY PYRAZOLE

H C. —— C-COOC₆H₅

N

N —— C-C₆H₅

H-H

O-Phenetidylmethylenebenzoylacetecester,

7 grams.

Hydrazine Sulphate,

11 grams.

Sodium Carbonate, anhydrous,

7.2 grams.

Ethyl Alcohol, 95 percent,

75 cc.

The alcohol and the ester were placed in a flask fitted with a water-cooled reflux condenser. The hydrazine sulphate, dissolved in a little water, was neutralized by the addition of the carbonate. The resulting solution was added to the alcohol suspension of the ester. The mixture was heated for six hours over boiling water. The alcohol was then driven off and the remaining liquid evaporated to dryness on the water-bath. The residue was then extracted with hot methyl alcohol, the re-
sulting solution filtered off and allowed to evaporate slowly. White crystals slowly separated from an oily residue. The mixture was dissolved in alcohol, a little acetic acid added, and then much water. On standing, flaky crystals and an oil separated.

Melting point of the crystals, 84° to 85°.
The oil slowly hardened in the cold in contact with dilute alcohol.

Melting point of this, 83° to 86°.
Total yield, 3.9 grams.

REACTION

\[
\text{CeHs-CO} + \text{HNN} \rightarrow \text{COOCeHs} + \text{H2N}
\]

ANALYSIS COMBUSTION

<table>
<thead>
<tr>
<th>Samples</th>
<th>0.2507</th>
<th>0.3017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moist gas,</td>
<td>50.8 cc</td>
<td>56.5 cc</td>
</tr>
<tr>
<td>Pressure,</td>
<td>736.0 mm</td>
<td>736.5 mm</td>
</tr>
<tr>
<td>Temperature,</td>
<td>23.0°</td>
<td>22.2°</td>
</tr>
<tr>
<td>Vapor pressure,</td>
<td>11.1 mm</td>
<td>10.7 mm</td>
</tr>
<tr>
<td>Percent Na found</td>
<td>13.00</td>
<td>13.37</td>
</tr>
</tbody>
</table>

Calculated for (C₆H₁₁N₂O₂), 12.96
HYDROLYSIS
of
5-PHENYL-4-CARBETHOXY PYRAZOLE

A half-gram of 5-phenyl-4-carbethoxy pyrazole was treated with boiling concentrated hydrochloric acid for one hour. On standing, bunches of white needle-like crystals separated. The mixture was reheated for three hours, filtered hot and cooled. No crystals separated as before. The solution was evaporated on the water-bath to one-fourth the original volume. Some oily material separated, doubtless some of the unchanged ester. On diluting the filtrate with water a solid separated in a finely divided condition. This was found to melt with decomposition and effervescence at 260° to 261° to a black oil. This preparation mixed with some of the previously prepared 5-phenyl-4-carboxyl pyrazole melted at 260° to 266°, showing it to be the latter compound.

REACTION

\[
\begin{align*}
HC & \quad C-\text{COOC}_2\text{H}_5 \\
N & \quad \text{C}_2\text{H}_5 \\
N-H & \\
\end{align*}
\]

\[
\begin{align*}
\text{(HCl)} & \\
\end{align*}
\]

\[
\begin{align*}
HC & \quad C-\text{COOH} \\
N & \quad \text{C}_2\text{H}_5 \\
N-H & \\
\end{align*}
\]

\[
\begin{align*}
\text{(H}_2\text{O}) & \\
\end{align*}
\]
ATTEMPTED REACTIONS

(a)

ATTEMPT TO FORM THE HYDROCHLORIDE:

Dry hydrogen chloride was passed into a boiling benzene solution of 5-phenyl-4-carbethoxy pyrazole for a period of two hours. No precipitation occurred. On evaporating the solution, a black oily residue was obtained. This solidified slowly and melted, unpurified, at 75° to 81°. The product was evidently the unchanged pyrazole derivative which, when pure, melts at 84°.

(b)

ATTEMPT TO FORM THE ANILIDE:

A mixture of aniline and 5-phenyl-4-carbethoxy-pyrazole was heated for three hours in an oil-bath at 200°. The mixture was dissolved in alcohol and water added to the resulting solution. On oil settled out resembling the original pyrazole derivative in its impure state.
(c) 

**ATTEMPT to ACETYLATE:**

Some 5-phenyl-4-carbethoxy pyrazole was heated with acetic anhydride. On evaporating the resulting solution, a dark colored oil remained, doubtless the unchanged pyrazole derivative.

(d) 

**ATTEMPT to BENZOYLATE:**

A half-gram of the 5-phenyl-4-carbethoxy-pyrazole was dissolved in pyridine. To this solution a half-gram of benzoic chloride was added and the mixture permitted to stand over night. Transferred to dilute sulphuric acid, an oil separated which on standing formed white crystals in contact with the acid solution. These melt at 84° which is the melting point of the original substance.

(e) 

**ATTEMPT to Add METHYL IODIDE:**

A mixture of 5-phenyl-4-carbethoxy-pyrazole and methyl iodide was confined in a closed tube. After standing for some time and final heating at
100 °C, a black syrupy residue resulted, having the appearance of the original compound in the liquid condition.
THE p-ANISIDIDE
of
5-PHENYL-4-CARBOXYL-
PYRAZOLE.

\[
\text{H} \text{C} \quad \text{CONHH_4CH_3H_5 (p)} \\
\text{N} \quad \text{C-C_6H_5} \\
\text{N-H}
\]

\[\text{p-Anisidomethylenebenzoylacet-p-anisidide,}\]

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrazine sulphate</td>
<td>5.87 grams</td>
</tr>
<tr>
<td>Sodium carbonate (anhydrous)</td>
<td>8.8 grams</td>
</tr>
<tr>
<td>Ethyl alcohol</td>
<td>75 cc</td>
</tr>
</tbody>
</table>

The p-anisidide was placed in a flask containing the alcohol. The hydrazine was dissolved in a small quantity of hot water. To the latter solution the carbonate was added. After effervescence had ceased, the solution was added to the above alcoholic suspension and the mixture digested over boiling water for about four hours. The mixture was then evaporated to dryness on the water-bath, the residue extracted with boiling methyl alcohol.
and the resulting extract diluted with several volumes of water. On standing, long crystals of a brown color developed. These were recrystallized from dilute alcohol (ethyl).

Melting point, 160° to 161°.
Yield, 3.37 grams.

**ANALYSIS**  
**COMBUSTION**

Samples, 0.2546, 0.2199, 0.2110, 0.2005,
Moist gas, 36.0, 31.1, 28.6, 27.7,
Pressure, 723.5, 735.0, 746.0, 753.5,
Temperature, 22.3, 25.4, 23.5, 20.8,
Vapor tension, 10.7, 12.7, 11.4, 9.7,

Percent Na, found, 14.75, 15.43, 15.09, 15.29,
Calculated for C₆H₁₅O₅Na₅, 14.334

The product was recrystallized from dilute alcohol and dried at 100°.

**ANALYSIS**  
**COMBUSTION**

Sample, 0.2033
Moist gas, 27.2
Pressure, 732.0
Temperature, 24.0
Vapor tension, 11.7

Percent Na, found, 14.57
Calculated for C₆H₁₅O₅Na₅, 14.334
HYDROLYSIS:

The p-anisidide of 5-phenyl-4-carboxyl pyrazole, a small quantity, was heated in boiling concentrated hydrochloric acid for two and a half hours. Solution took place slowly. The digested mixture was poured upon ice. A white solid separated.

Melting point, 255° to 256°.

A mixture containing some of this product and some 5-phenyl-4-carboxyl-pyrazole previously prepared was made.

Melting point, 255° to 256°.

Reaction,

\[
\begin{align*}
\text{HC} & \quad \text{C-CONHC}_6\text{H}_4\text{OCH}_3 \\
\text{N} & \quad \text{C-CH}_3 \\
\text{N-H} & + \text{H}_2\text{O} = \\
\text{HC} & \quad \text{C-COOH} \\
\text{N} & \quad \text{C-CH}_3 \\
\text{N-H} & + \text{H}_2\text{N-CH}_2\text{OCH}_3
\end{align*}
\]
THE 6-ANISIDIDE
of
5-PHENYL-4-CARBOXYL-

PYRAZOLE.

\[
\begin{align*}
\text{H C} & \text{C-CONHCH}_2\text{H}_4\text{CH}_3 (o) \\
\text{N} & \text{C-CH}_3 \\
\text{N-H} & 
\end{align*}
\]

- o-Anisidomethylenebenzoylacetyl-o-anisidine, 10.0 grams,
- Hydrazine sulphate, 6.4 grams,
- Sodium carbonate, anhydrous, 5.5 grams,
- Ethyl alcohol, 100 cc.

Two moles of hydrazine sulphate were dissolved in the minimum amount of hot water necessary for solution. To this was added the carbonate, then the alcohol and finally the 6-anisidide.

The mixture was digested over boiling water to the complete solution of the o-anisidide. Time required, six hours. The alcohol was then evaporated and the residue dried over boiling water. The dry residue was extracted repeatedly with boiling methyl alcohol. On partially evaporating the extract,
an oily precipitate formed. Water was added and the mixture allowed to stand. The resulting syrupy settlings, after long standing, solidified to a reddish-brown mass. This was found to be soluble in the following solvents: Ether, alcohol, alcohol and water (1 to 1), boiling water (slightly), benzene, hot gasoline (moderately). The product from gasoline melted at 127°. The whole product was dissolved in alcohol. Ice was added. The solution changed to a 'milky' suspension which gradually deposited a brown syrupy material. This solidified on further cooling.

Melting point, 137° to 138°

Yield, 6.5 grams.

ANALYSIS

COMBUSTION

Sample, 0.3400 grams.

Temperature, 23.8

Pressure, 741.0

Moist gas, 45.66

Vapor tension, 11.0

Percent Na, found, 14.67

Calculated for (C₁₅H₃₀O₀₄Na₂) 14.34
HYDROLYSIS:

Some of the o-anisidine of 3-phenyl-4-carboxyl-pyrazole was heated for ten hours with boiling concentrated hydrochloric acid. Solution took place much less readily than in the case of the analogous 'para' derivative. No solid whatever separated on the addition of water to the digested mixture as occurred in the case of the other derivatives which were hydrolyzed. On evaporation some residue was obtained which melted at about 250°. This may have been some of the hydrochloride of o-anisidine, or it may have been some of the impure 5-phenyl-4-carboxyl pyrazole. At any rate not enough of the material was secured for identification.

Some of the compound was then heated with constant-boiling hydrobromic acid. Solution took place in a half-hour in this case. Needles separated on cooling the solution. These from boiling water, melted at 255°. A mixture containing some of this and some of the acid pyrazole melted at 256° to 257°. The compound was evidently hydrolyzed to the same acid pyrazole which was obtained in each of three other instances.
Anilidomethylenebenzoylacetanilide, 5 grams,
Phenylhydrazine, 1.58 grams,
Alcohol, a few cc.

The above mixture was heated over boiling water for fifteen minutes; partial solution taking place. A little more alcohol and phenylhydrazine was added. Complete solution took place on fifteen minutes further heating. Cooled in ice-water, a yellow solid separated, melting at 144° to a black oil. Solution gives test for aniline. The product was fractionally dissolved in hot alcohol. Each succeeding fraction became lighter in color. The melting point of the crystals from each fraction follows:

<table>
<thead>
<tr>
<th></th>
<th>#1</th>
<th>#2</th>
<th>#3</th>
<th>#4</th>
</tr>
</thead>
<tbody>
<tr>
<td>below 160°</td>
<td>164-5°</td>
<td>164-5°</td>
<td>164-5°</td>
<td></td>
</tr>
</tbody>
</table>

Melting point of anilidomethylenebenzoylacetanilide, 164°. The alcohol was evaporated from all of the
product, more phenylhydrazine and some alcohol were added and the mixture heated again for an hour. The product which separated on cooling was recrystallized from alcohol. Melting point, 164.5°. The cold alcoholic solution and washings were diluted with water acidified with hydrochloric acid. An orange precipitate settled out. This is readily soluble in ethyl alcohol, ether, benzene and glacial acetic acid and slightly soluble in boiling water. The whole product was dissolved in boiling water to remove any phenylhydrazinehydrochloride that might be present and to crystallize the compound.

Melting point, 158° to 140°.

This happens to be the melting point of 1,3-di-phenyl-4-anilidomethylene-5-pyrazolone. The product was dissolved in boiling gasoline. Some solid separated on cooling the gasoline solution.

Melting point, 140°.

On evaporating the filtrate to low volume, some more solid separated.

Melting point, 153°.

The whole product was washed with successive small portions of hot gasoline. The washings became less and less colored. A nearly colorless residue remained:

Melting point, 155° to 157°.
It was recrystallized from hot dilute alcohol.

Melting point, 157° to 158°.

This is the melting point of 1,5-diphenyl-4-carbanilido pyrazole as given in the literature.

The hot gasoline filtrate, highly colored, on cooling and standing, deposited a yellowish-red solid melting near 120°. On further evaporation, some material was obtained melting at 70° to 80°.

A second mixture containing 2.49 grams of anilidomethylenebenzoylacetaanilide and the calculated amount of phenylhydrazine was heated for five hours. The resulting solution was poured into several volumes of water acidified with hydrochloric acid. A brown soft mass at first separated. On addition of ice the mass solidified and a light colored flocculent precipitate separated gradually from the mother liquor. The product was filtered off, dried, washed with boiling gasoline and recrystallized from dilute alcohol.

Melting point, 157° to 158°.

**Attempt to Hydrolyze:**

Some of the above preparation was heated with concentrated hydrochloric acid over boiling water for four hours. The compound dissolved with difficulty in the acid. On cooling the solution
and allowing it to stand, no solid separated. On adding ice-water the solution turned 'milky' at first and finally deposited a heavy curdy precipitate most of which redissolved on stirring leaving only a little granular residue. No precipitation occurred on further dilution. On heating to boiling, a small quantity of flocculent material settled out. Melting point, 150°-155°. Melting point of the original substance, 157° 159°. Melting point of a mixture of the two, 132° 135°. After further purification the products melted as follows:

Unknown product, 150° to 155°.
Original compound, 157° to 159°.
Mixture, 132° to 135°.

Only a small yield of the product was obtained so a second attempt was made as follows:

SECOND ATTEMPT TO HYDROLYZE:

One and one-half grams of 1,5-diphenyl-4-carbonilido pyrazole was heated for several hours with concentrated hydrochloric acid. Complete solution finally took place. On standing, the solution deposited a few tufts of crystals. Filtered. Filtrate was diluted with water to the 'milky' stage and then brought to a temperature of 40° to 50°. The preci-
Pitrate which collected in a curdy mass was filtered off, dissolved in hot water, and the solution allowed to cool. The solid separated as a flocculent precipitate. It was found to be soluble in alcohol. A hot alcoholic solution of the product was diluted with water. The solid separated as gelatinous particles.

Melting point, 154°.
Yield, 0.15 grams.
Test for aniline in solutions obtained above, negative.

THIRD ATTEMPT TO HYDROLYZE:

Some 1,5-diphenyl-4-carbanilido-pyrazole was heated in constant-boiling hydrobromic acid. Solution took place in about an hour. On standing, some crystalline material separated. No further precipitation occurred on diluting the filtrate. On making the filtrate alkaline, a little precipitation took place. The crystalline material obtained was dissolved in alcohol, then reprecipitated by diluting and heating. The reprecipitated solid was dissolved in benzene and the solution allowed to evaporate. A small quantity of a white residue was obtained. Melting point, 175° to 176°. Test for aniline, negative.
FOURTH ATTEMPT to HYDROLYZE:

Some 1,5-diphenyl-4-carbanilido-pyrazole was heated with a solution of one mole of potassium hydroxide in solution for several hours. The filtrate gave a negative test for aniline. The unchanged pyrazole derivative was recovered in practically quantitative yield. Melting point, 160°. Amount of material used, 0.56 grams. Quantity recovered, 0.49 grams. Evidently the compound is not hydrolyzed under the conditions of the experiment.

FIFTH ATTEMPT:

The above recovered material was heated in boiling concentrated hydrochloric acid. The filtrate gave a positive test for aniline. Some material, very small in quantity, was obtained.

Melting point, 134°.

In the above attempts to hydrolyze with hydrochloric acid, hydrolysis doubtless takes place to some extent but the yield of material has been too small for identification.
5-PHENYL-4-CARBANILIDO-OXAZOLE (s)

Anilidomethylenebenzoylacetonilide, 5.0 grams,
Hydroxylaminehydrochloride, 2.0 grams,
Pyridine, 3.0 cc.

To an alcoholic suspension of the anilidomethylene-
benzoylacetonilide were added the pyridine and the
hydroxylaminehydrochloride, the latter in solution
in a little water. The mixture was brought to boil
on the steam-bath and was kept boiling for several hours.
On cooling and standing, tufts of white crystals
separated: This was some of the unchanged anilido
compound melting at 164°. The contents of the flask
were boiled again for several hours. No precipitate
formed now on standing. Addition of ice and water
caused a cloudiness at first followed by the separation
of fine needles. These were separated, dissolved
in hot alcohol and the solution diluted with ice-water.
Crystals separated.

Melting point, 133° to 134°.

Further purified, the melt at 134° to 135°.

This corresponds to the melting point of the oxazole as given in the literature.

**ATTEMPT to HYDROLYZE**

To one gram of 5-phenyl-4-carbanilido-oxazole in a flask were added 75 cc of a solution made by mixing alcohol and concentrated hydrochloric acid in the proportions of 75 cc of the former to 25 cc of the latter. This solution should contain about ten percent hydrogen chloride. The mixture was heated under a reflux condenser in boiling water for two and one-half hours. The solid readily dissolved. On cooling the solution no solid separated. The volume was then reduced about one-half by heating over boiling water. On cooling and standing over night some crystals separated. These were evidently some of the unchanged oxazole melting at 133° to 134°. The crystals were filtered off and the filtrate diluted with ice-water. The solid which separated was found to be slightly soluble in hot water, soluble in cold alcohol and in hot dilute alcohol.
Recrystallized from dilute alcohol and finally from strong alcohol it melted at 135° to 136°. A mixture containing some of this and some of the original substance melted at the above temperature. The filtrate gave a good test for aniline. Evaporated to dryness it gave a residue of 0.2950 grams. 0.4200 grams of the unchanged material were recovered. The residue when dissolved in water gave a strong test for aniline and was evidently composed largely of aniline hydrochloride.

SECOND ATTEMPT to HYDROLYZE:

5-Phenyl-4-carbanilido-oxazole, 1.0 grams,
Alcohol, 50 cc,
Concentrated HCl-solution, 25 cc.

This mixture was heated on the water-bath for ten hours. No precipitation occurred on cooling. Slight precipitation took place on diluting. Evaporated to low volume, the solution gave a good test for aniline. A very small quantity of solid material was obtained on evaporating the solution to dryness. The residue was soluble in water and its solution gave a positive test for aniline. Evidently changes other than merely hydrolytic take place on heating the oxazole with acids.
THIRD ATTEMPT to HYDROLYZE:

A half-gram of the oxazole was heated over boiling water for several hours with a solution containing one molecular equivalent of potassium hydroxide. Practically all of the solid dissolved finally. The filtrate, on acidification, gave a milk-white suspension. The precipitate coagulated on heating. The solid was found to be soluble in hot alcohol but insoluble in hot water. Crystallized from dilute alcohol it melted at 208° to 209°. The product was evidently benzoylcyanacetanilide, \( \text{C}_9\text{H}_8\text{COCH(CN)CONHC}_9\text{H}_5 \), a product which has been shown to be formed when oxazole derivatives of the above type are dissolved in alkali.

The filtrate gave a **positive** test for aniline.

Reaction:

\[
\begin{align*}
\text{H} & \text{C} \quad \text{CONHC}_9\text{H}_5 \\
\text{N} & \quad \text{C} \quad \text{C}_9\text{H}_5 \\
\end{align*}
\] + KOH \rightarrow

\[
\begin{align*}
\text{HC} & \quad \text{CN} \quad \text{CONHC}_9\text{H}_5 \\
\text{C} & \quad \text{C}_9\text{H}_5 \\
\end{align*}
\]
5-PHENYL-4-CARBETHOXY ISOXAZOLE

\[
\begin{array}{c}
\text{H-C} \quad \text{N} \\
\mid \quad \quad \mid \\
\text{O} \quad \text{C-C}_6\text{H}_5 \\
\end{array}
\]

o-Phenetidylmethylenebenzoylacetic ester, 1.0 grs.,
Hydroxylaminohydrochloride, 1 mole.
Pyridine, 1 mole.

To a suspension of the ester in alcohol, were added the pyridine and the chloride, the latter dissolved first in a little water. The mixture was heated in boiling water for four hours. Filtered. The filtrate was poured into dilute sulphuric acid. Added ice to the milky suspension and let stand. Some oil separated.

Preparation of the product on a scale sufficiently large for identification could not be made on account of a lack of supply of the ester-methylene compound.
Anilidomethylenebenzoylacatanilide, 1.0 gms.,
Semicarbazide hydrochloride, 0.5 gms.,
To the methylene compound suspended in alcohol
the hydrochloride, dissolved in a little water,
was added. No apparent action occurred in the
cold. The mixture was heated in boiling water
for six hours. Complete solution failed to take
place. On cooling, some of the unchanged methylene
derivative derivative melting at 164° to 165°
separated. The filtrate gave a negative test for
aniline. Three-fourths of the unchanged methylene
derivative was recovered. The filtrate, diluted,
deposited a few long needles. Melting point,
185°.

Repetition of the method with the substitution
of sodium carbonate for pyridine gave better re-
The following quantities of materials were used:

- Anilidomethylenebenzoylacetanilide, 3.88 gms.
- Semicarbazide hydrochloride, 2.00 gms.
- Sodium Carbonate, (anhydrous), 2.00 gms.
- Alcohol, 100 cc.

The above mixture was digested for six hours. The filtered solution was reduced to one-half its original volume. On dilution with ice-water, crystallization took place. The product was recrystallized from dilute alcohol.

Melting point, 183°.

Re crystallized from hot water it melted at 184° to 185°. Dried at 106°, it gave the following analysis:

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Combustion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samples, 0.2994</td>
<td>0.2980</td>
</tr>
<tr>
<td>Moist gas, 45.4</td>
<td>45.2</td>
</tr>
<tr>
<td>Pressure, 738</td>
<td>738</td>
</tr>
<tr>
<td>Temperature, 25.9</td>
<td>22.3</td>
</tr>
<tr>
<td>Percent Na, found</td>
<td>16.497</td>
</tr>
<tr>
<td>Calculated for C₁₇H₂₀₂Na₂, 18.30</td>
<td></td>
</tr>
</tbody>
</table>

The possibility that all of the methylene derivative had not reacted and that the product may have been contaminated with some of this derivative,
let to the following preparation in which an excess of the semicarbazide was used:—

Anilidomethylenebenzoylacetanilide, 5.00 gms.,
Sodium Carbonate, 5.00 gms.,
Semicarbazide hydrochloride, 6.00 gms.,
Alcohol, 100 cc.

This mixture was digested for several hours. On spontaneous evaporation, a mass of white crystals separated. Melting point of these after partial purification, 180° to 182°. Further work is to be done on this product.
PART II.

FORMAMIDINES.

 METHYLENE DERIVATIVES

 of

 BENZOYL ACETIC ESTER.

 BENZYLPHENYLHYDRAZINE.
DI-PHENYLFORMAMIDINE

\[
\text{N} - \text{C}_6 \text{H}_5 \\
\text{H}_2 \\
\text{N} - \text{C}_6 \text{H}_5
\]

o-Formic ester, 54 grams.
Aniline (redistilled), 75 grams.

The above mixture was heated under a short reflux condenser (air) for three hours at 125° to 150° degrees. On cooling the reaction mixture solidified. The product was recrystallized from strong ethyl alcohol.

Yield, 57 grams.

Reaction:

\[
\text{H}_2 \text{N} - \text{C}_6 \text{H}_5 + \text{C}_2 \text{H}_5 \text{OH} \rightarrow 3 \text{C}_2 \text{H}_5 \text{OH} + \text{H}_2 \text{N} - \text{C}_6 \text{H}_5
\]
FORMAMIDINES

METHENYLDI-O-PHENETIDINE

\[
\begin{align*}
\text{HC} & \quad \text{HNCOH} \\
\text{HNCeH}_4\text{OCeH}_5 & \quad \text{NCeH}_4\text{OCSH}_5
\end{align*}
\]

O-Phenetidine, \quad 25 grams.
o-Formic ester, \quad 10 grams.

The above mixture was heated in an oil bath for four hours at a temperature of 135-40 degrees. A crystalline resulted on standing. This was brought into solution again by heating at 140 degrees. On cooling the product began to crystallize again. On treating with gasoline, a white solid separated. This was washed with gasoline and dried on a porous plate.

Melting point in this condition, \quad 85 degrees.
Twice recrystallized from dilute alcohol, it melted at, \quad 84 to 85 degrees.

Melting point previously reported, \quad 81 degrees.

Yield, \quad 18 grams.
METHENYL-DI-p-ANISIDINE

\[
\begin{align*}
N \text{C}_6\text{H}_4\cdot \text{OCH}_3 \\
H \text{C} \\
H N \text{C}_6\text{H}_4\cdot \text{OCH}_3
\end{align*}
\]

O-Formic ester, 5 grams, 
p-Anisidine, 8.3 grams.

This mixture was heated for eight hours under a short reflux air condenser at 110 to 120 degrees. On cooling, dark-brown crystals separated. The mixture was stirred up with gasoline and filtered. The residue washed first with gasoline, then with ether and dried was light brown in color.

Melting point, 114 degrees 
Yield, 6.4 grams

Reaction:
\[
\begin{align*}
\text{O-C}_6\text{H}_5 & \quad \text{H}_2\text{N-C}_6\text{H}_4\cdot \text{OCH}_3 \quad \text{(p)} \\
\text{H} \quad \text{H} & \quad \text{H} \quad \text{H} \\
\text{O-C}_6\text{H}_5 & \quad \text{H}_2\text{N-C}_6\text{H}_4\cdot \text{OCH}_3 \quad \text{(p)} \\
\text{H} & \quad \text{H} \\
\text{H}_2\text{N-C}_6\text{H}_4\cdot \text{OCH}_3 \quad \text{(p)}
\end{align*}
\]

\[3\text{C}_6\text{H}_5\text{OH} + \]
METHENYL-DI-o-ANISIDINE

\[
\text{H C} \quad \text{H N} \quad \text{C}_6\text{H}_4.\text{OCH}_3 (o)
\]

\[
\text{H C} \quad \text{O-C}_6\text{H}_5 \quad \text{H N} \quad \text{C}_6\text{H}_4.\text{OCH}_3 (o)
\]

o-Formic ester, 13.5 grams,
o-Anisidine, 23 grams.

The mixture was heated at a temperature of 120 degrees for five hours. The product was triturated with gasoline. The gray crystalline product which separated, after being washed with ether and dried, melted at 105 degrees.

Yield, 15.5 grams.

Reaction:

\[
\text{H C} \quad \text{O-C}_6\text{H}_5 \quad \text{H N} \quad \text{C}_6\text{H}_4.\text{OCH}_3 (o) = 3\text{C}_6\text{H}_5\text{OH} + \text{N.C}_6\text{H}_4.\text{OCH}_3 (o)
\]
ANILIDOMETHYLENE
BENZOYL ACETANILIDE.

\[ C_8 H_5 - CO \]
\[ C : CHNH C_6 H_5 \]
\[ CO NH C_6 H_5 \]

Benzoylacetic ester, 12 grams.
Diphenylformamidine, 12 grams.

This mixture was heated for five hours at a temperature of 105° to 110°. The reaction mixture solidified on cooling. The whole was dissolved in hot alcohol. The crystals which separated on cooling and standing were recrystallized from strong alcohol.

Melting point, about 159°.
Yield, 12 grams.
Theoretical yield, 17.9 grams.

The filtrate from the above was diluted with water whereupon some crystals and an oil separated. These crystals melted at 136° as did also a mixture with diphenylformamidine.

A nitrogen determination on some of the 159°-melting product gave a value too high for the ester derivative. Conclusion: the product obtained was the anilide and apparently no ester formation occurred.
under the conditions of the above experiment.

A second mixture of benzoylacetic ester and di-phenylformamidine was heated for nine hours at the temperature of boiling water. Some solid was isolated melting at 162° to 163° showing that the anilide is formed at this temperature also.

A third mixture heated for eight hours at a temperature of 70° to 80° gave no new product. The solid isolated melted at 138° showing it to be the original formamidine. This mixture was then reheated for eleven hours at the above temperature with the formation of a solid melting near 162°. There was no indication of the formation of the ester in any of these attempts.

The product obtained above when purified further by recrystallization from strong alcohol melted sharply at 164°. This is the melting point of the anilide as given by Rüeggeberg.

An analysis, though not required, was made.

**ANALYSIS**

<table>
<thead>
<tr>
<th></th>
<th>KEJELDAHL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samples</td>
<td>0.3934</td>
</tr>
<tr>
<td>N/10 HCl</td>
<td>30.00 cc</td>
</tr>
<tr>
<td>N/10 NaOH</td>
<td>9.05 cc</td>
</tr>
<tr>
<td>N/10 Na</td>
<td>20.95 cc</td>
</tr>
<tr>
<td>Control.</td>
<td>0.45 cc</td>
</tr>
<tr>
<td>Percent Na found</td>
<td>7.29</td>
</tr>
<tr>
<td>Percent Na calculated</td>
<td></td>
</tr>
</tbody>
</table>
o-PHENETIDYLMETHYLENE  
BENZOYL-ACETIC-ESTER.

\[
\text{Ce H}_5 - \text{CO} \\
\text{C} : \text{CH NH CeH}_5 \text{ O CeH}_5 \\
\text{CO OCe H}_5
\]

Benzoyl-acetic-ester, 6.1 grams.  
Di-o-phenetidylformamidine, 10 grams.

This mixture was heated over boiling water for two hours. On cooling, no solid separated. The liquid was found to be soluble in ether and in strong alcohol but insoluble in dilute alcohol. Precipitated from strong alcohol, by the addition of water, the product is a liquid. This liquid solidified and crystallized after standing at a low temperature for some time. It was found to separate as crystals on cooling a hot alcoholic solution.

Melting point from alcohol, 108.

Yield, 3.5 grams.

Another preparation gave a yield of 6.8 grams of the product from 7 grams of the formamidine.
**o-Phenetidylmethylenebenzoylacetic ester.**

(cont.)

**Analysis.**

<table>
<thead>
<tr>
<th></th>
<th>Sample #1</th>
<th>Sample #2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5042</td>
<td>0.5001</td>
</tr>
<tr>
<td>N/10 HCl,</td>
<td>40.00 cc</td>
<td>40.00 cc</td>
</tr>
<tr>
<td>N/10 NaOH,</td>
<td>21.50 cc</td>
<td>23.50 cc</td>
</tr>
<tr>
<td>N/10 Na,</td>
<td>18.50 cc</td>
<td>16.50 cc</td>
</tr>
<tr>
<td>Control,</td>
<td>2.90 cc</td>
<td>2.90 cc</td>
</tr>
<tr>
<td>Net N/10 Na</td>
<td>15.60 cc</td>
<td>13.60 cc</td>
</tr>
</tbody>
</table>

Percent Na found,

|            | 4.33      | 3.80      |

Calculated for C H O₄H, 4.13

**REACTION:**

\[
\begin{align*}
\text{C}_6\text{H}_5 \text{CO} + \text{H}_2 \text{C}_6\text{H}_4 \text{OCaH}_2 \rightarrow \\
\text{C}_6\text{H}_5 \text{COOCaH}_2 + \text{CH}_2 \text{NH} \text{C}_6\text{H}_4 \text{OCaH}_2 \\
\end{align*}
\]
p-Anisidomethylene

\[
\text{Benzoyl-}p\text{-anisidine}
\]

\[
\begin{align*}
\text{C}_{6}\text{H}_{5}\text{CO} \\
\text{C} : \text{CH NH C}_{6}\text{H}_{5} \text{OCH}_{3} (p) \\
\text{CO NH C}_{6}\text{H}_{5} \text{OCH}_{3} (p)
\end{align*}
\]

Benzoylacetic ester, 5 cc
Methenyldi-p-anisidine, 6.7 grams.

In the experiments on this mixture the attempt was made to obtain the ethyl ester of p-anisidomethylene benzoyl acetic acid by heating the material at relatively low temperatures. None of this product, however, was secured.

The above mixture was heated for ten hours at a temperature of 70° to 80°. The solid isolated by stirring some of the mixture with alcohol melted at 117° to 118°. An mixture containing some of the formamidine melted at 117° to 118°. This indicated that no reaction probably had taken place.

The mixture was reheated at the above temperature for eighteen hours. The resulting dark liquid deposited crystals on stirring with alcohol.

Melting point, 195°.
Yield, 2.1 grams.
The residue, a black oily material, was heated at 150° for an hour. A further small yield of the 195°-melting product was obtained from this.

Another mixture of the same proportions of materials as before was heated at the higher temperature, namely, 150°. From six grams of the formamidine there were obtained in this case a yield of 5.87 grams of the product melting at 195°.

The product obtained is p-anisidomethylene-methylbenzoyleacetyl-panisidine, in as much this compound was prepared by Dains and Griffin, having a melting point of 196°.

<table>
<thead>
<tr>
<th>ANALYSIS</th>
<th>K J E L D A H L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samples</td>
<td>0.3613</td>
</tr>
<tr>
<td>N/10 HCl</td>
<td>30.00</td>
</tr>
<tr>
<td>N/10 NaOH</td>
<td>11.95</td>
</tr>
<tr>
<td>N/10 Na</td>
<td>18.05</td>
</tr>
<tr>
<td>Control</td>
<td>0.45</td>
</tr>
<tr>
<td>Percent N₂ found</td>
<td>6.46</td>
</tr>
<tr>
<td>Percent N₂ calculated</td>
<td>6.96</td>
</tr>
</tbody>
</table>
6-ANISIDO METHYLENE
BENZOYL-ACET-o-ANISIDIDE

\[
\begin{align*}
\text{C}_8\text{H}_8 \text{CO} \\
\text{C} : \text{CH} \: \text{NH} \: \text{C}_6\text{H}_5 \: \text{OCH}_3 \: (o) \\
\text{CO} \: \text{NH} \: \text{C}_6\text{H}_5 \: \text{OCH}_3 \: (o)
\end{align*}
\]

Benzoylacetic ester, 13.5 grams.
Methenyl-di-o-anisidine, 18.6 grams.

This mixture was heated for twelve hours at 75° to 90° in an effort to secure the ester derivative. A portion of the mixture was then removed and heated with dilute alcohol. A solid slowly separated from the cooled solution melting at 190° to 192°. The mixture was then heated for six hours at 140° with the view of ascertaining whether a product of higher melting point might be obtained. The mixture was then digested with alcohol. Yellowish crystals separated. Washed with alcohol and then with ether, these melted at 200°. Yield, 4.5 grams. The compound is evidently that described by Ruggenberg, namely, o-anisidomethylenebenzoylacet-o-anisidide. The latter's preparation melted at 199°. The wash-
ings were extracted with ether. The oily residue heated with more of the ester for three hours at 160 further increased the yield of the 200°-melting product by 4.2 grams. Upon recrystallizing the product from benzene it became lighter in color and it then melted at 201° to 202°.

**ANALYSIS**

<table>
<thead>
<tr>
<th>Sample, N/10 HCl</th>
<th>0.5217 grams</th>
</tr>
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<tbody>
<tr>
<td>N/10 NaOH</td>
<td>45.00 cc</td>
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<tr>
<td>N/10 Na₂</td>
<td>18.70 cc</td>
</tr>
<tr>
<td>Control</td>
<td>26.30 cc</td>
</tr>
<tr>
<td></td>
<td>1.00mcc</td>
</tr>
</tbody>
</table>

Percent Na found, 6.79
Percent Na calc for (C₈H₁₃O₄Na) 6.97
DI-m-TOLUIDO METHYLENE
BENZOYLACET-T-m-TOLUIDE.

\[ \text{C}_9\text{H}_8\text{CO} \]
\[ \text{C} : \text{CH NH C}_6\text{H}_5\text{CH}_3 (m) \]
\[ \text{CO NH C}_6\text{H}_5\text{CH}_3 (m) \]

Benzoylacetic ester, 16 cc
Di-m-tolylformamidine, 11.5 grams.

The mixture of the above materials was heated for five hours at 75°. On standing partial crystallization took place. The isolated crystals melted at 118° to 120°. The formamidine melted at 118° to 120°. Evidently no reaction had taken place. The mixture was then reheated for eight hours at the temperature of boiling water. The whole digestion mixture was then dissolved in ether and the resulting solution allowed to evaporate. A mixture of crystals and a syrupy liquid separated. The crystals, washed with ether, melted at 232° to 133°. After long standing, the mixture separated into two layers with the crystalline layer at the bottom. The dark super-
natant layer of syrup was decanted and the crystal-line residue washed with strong alcohol. The product recrystallized white from strong alcohol. It is not readily soluble, even in boiling alcohol.

Melting point, 134°.

Yield, 2.7 grams.

The product was dissolved in hot alcohol and the solution let stand for some time. Long, slender needles separated.

Melting point, 134°.

ANALYSIS

KJELDAHL

Sample, 0.4019 grams

H/10 HCl, 50.00 cc

H/10 NaOH, 26.40 cc

H/10 Na, 23.60 cc

Control, 1.50 cc

Percent Na found, 7.69

Calculated for (C₆H₁₂O₂N₂), 7.58
DI-o-CHLOR-PHENYL
FORMAMIDINE
\[
\begin{align*}
&\text{O}C_6\text{H}_5 \\
&\text{H} \quad \text{H} \quad \text{N} \quad \text{C}_6\text{H}_4\text{Cl} \quad (\circ) \\
&\text{H} \quad \text{C} \quad \text{NHC}_6\text{H}_4\text{Cl} \quad (\circ)
\end{align*}
\]

1-Formic acid, 8 grams.

-o-Chloraniline, 10 grams.

The above mixture was heated for two hours at 160 to 170 degrees. The formation of alcohol under 100 degrees was indicated by the boiling of the mixture. On cooling in ice-water, the reaction mixture solidified. An alcoholic solution of the mass on cooling deposited white crystals. These were re-crystallized from strong alcohol and dried at 120 degrees to remove any alcohol of crystallization that might be present.

Melting point, 140 degrees.

Yield, 7 grams.

Reaction:
\[
\begin{align*}
&\text{O}C_6\text{H}_5 \\
&\text{H} \quad \text{H} \quad \text{N} \quad \text{C}_6\text{H}_4\text{Cl} \quad (\circ) \\
&\text{H} \quad \text{C} \quad \text{NHC}_6\text{H}_4\text{Cl} \quad (\circ)
\end{align*}
\]

ANALYSIS.

<table>
<thead>
<tr>
<th>Samples</th>
<th>KJE LD A H L</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/10 HCl</td>
<td>50.10 cc</td>
</tr>
<tr>
<td>N/10 NaOH</td>
<td>15.10 cc</td>
</tr>
<tr>
<td>N/10 Na</td>
<td>35.00 cc</td>
</tr>
</tbody>
</table>

Na, percent found, 16.95 10.23 10.34

Na, percent calculated, 10.56
D I - o - C H L O R - P H E N Y L  
F O R M A M I D I N E  
H Y D R O C H L O R I D E  

\[
\text{N Ce H}_4 \cdot \text{Cl} \ (o) \\
\text{H C} \quad \text{HCl} \\
\text{NHCe H}_4 \cdot \text{Cl} \ (o)
\]

Dry hydrochloric acid gas was passed into a benzene solution of the formamidine as long as any precipitate formed. A white, finely divided solid separated. This was filtered off and dried in air.

Melting point, 175-78 degrees.

ANALYSIS by TITRATION

Sample taken, 0.4267 grams.
N/10 NaOH, 14.20 cc
Indicator, methyl orange.

Percent HCl, found, 12.10
      calculated, 12.10
BENZYLPHENYLHYDRAZINE

\[
\begin{align*}
\text{C}_6\text{H}_5\text{N} - \text{NH}_2 \\
\text{C}_7\text{H}_7 \\
\end{align*}
\]

Benzaniline, 50 grams.
Sodium Nitrite, 19 "
Sulphuric Acid, conc., 50 "
Alcohol, 625 cc.

The benzaniline was dissolved in the alcohol. To this solution was then added the acid followed by the nitrite in solution in a little water. On standing over night at room temperature, a mass of greenish-yellow crystals had separated. The mixture was poured into about three volumes of water and allowed to stand for several hours. It was then filtered by suction and the product dried in air.

Melting point in this condition, 55° to 58°.
Melting point of pure product, 58°.
Yield, 56 gms.

Reaction:

\[
\begin{align*}
\text{C}_6\text{H}_5\text{NH} + \text{HO-NO} & \rightarrow \text{C}_6\text{H}_5\text{NENO} + \text{H}_2\text{O} \\
\text{C}_7\text{H}_7 & \\
\end{align*}
\]
REDUCTION:

The above benzylphenyl nitrosoamine was dissolved in 350 cubic centimeters of alcohol. To the solution was added an excess of zinc dust (75 gms.) and then gradually with shaking glacial acetic acid until no more heat was generated, and the solution failed to give the Liebermann reaction. The mixture, containing a solution of the product, some white crystals and metallic zinc, was filtered, and the residue washed with boiling alcohol. The united filtrates on cooling deposited a mass of white crystals.

The alcohol was distilled off until the volume of the solution was reduced about three-fourths. On diluting the concentrated solution with water, an oil separated. Evidently the heating had decomposed the acetate. The oil was taken up with ether and the extract dried in contact with solid potassium hydroxide. After driving off the ether, the oil was dissolved in hydrochloric acid, in which it was readily soluble, and then reprecipitated by making the solution alkaline. The reprecipitated oil was then dried as before.

In as much as the oil obtained above was not secured strictly in accordance with the method as described in the literature, a second preparation
was attempted. The quantities of materials used were the same as in the preceding preparation and the procedure was the same up to the point where the alcohol is removed from the digested mixture. At this point, instead of distilling the alcohol, it was removed by gentle heating. No oil separated under these conditions. The mixture was diluted with water and then made alkaline whereupon the oil separated.

**ATTEMPT to CONDENSE:**

Some of the oil from each of the above preparations was heated with o-formic ester for several hours at 150°. No solid separated and there was no evidence of the formation of alcohol. The o-formic ester was practically all recovered by subjecting the mixtures to distillation.

**IDENTIFICATION of the OIL:**

The acetyl derivative was prepared.

Melting point found, 121°.

As given in the literature, 121°.

**CONCLUSION:**

Benzylphenylhydrazine does not condense with o-formic ester under the above conditions.
PART III.

m-DI-BROM-p-TOLUIDINE.

o-BROM-p-TOLUIDINE.

QUINOLINE DERIVATIVES.
0-BROM-P-TOLUIDINE.

Some material, presumably o-brom-p-form-toluid, CH₃.C₆H₅.Br(o)NH₂H₂O (p), was prepared by brominating p-form-toluidine in acetic acid solution. That the product was not the compound supposed but that it was m-di-brom-p-toluidine, was shown by the following work:-

Attempts to hydrolyze the product with the following reagents failed:-

(1) Alcohol containing one-eighth its volume of concentrated hydrochloric acid.

(2) Alcohol and concentrated hydrochloric acid, (1 to 1).

(3) Alcohol and potassium hydroxide (10 to 1). An amount of this solution containing one gram of potassium hydroxide per gram of substance to be hydrolyzed.

(4) Sulphuric acid, (50 percent).

Note: The substance forms a compound with hydrochloric acid melting at 240°.
**Analysis**

<table>
<thead>
<tr>
<th>Samples</th>
<th>0.6300</th>
<th>0.6235</th>
<th>0.5996</th>
<th>0.6079</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/10 HCl</td>
<td>50.10</td>
<td>50.00</td>
<td>50.10</td>
<td>50.10</td>
</tr>
<tr>
<td>N/10 NaOH</td>
<td>26.60</td>
<td>26.39</td>
<td>27.72</td>
<td>27.01</td>
</tr>
</tbody>
</table>

Percent Na, 5.23 5.32 5.25 5.31

Calculated for o-brom-p-form-toluidine, 6.545
Calculated for m-dibrom-p-toluidine, 5.230

The difficulty encountered in attempts to hydrolyze the compound supposed to be the o-brom-p-form toluid led to an attempt to determine the ease of hydrolysis of the compound, p-form-toluidine.

Accordingly some of this compound was heated with a mixture of alcohol and concentrated hydrochloric acid (8 to 1) for several hours. On cooling a mass of crystals separated melting at 240°. The high melting point suggested the probable formation of the hydrochloride of p-toluidine. When a solution of some of this product was made alkaline a substance separated which melted at 45°. This is the melting point of p-toluidine.
BROMINATION of p-form-toluidine in chloroform solution:

p-Form-toluidine, 20 grams, (one mole)
Bromine, 24 grams, (one mole)

Bromine in chloroform was added gradually with agitation to a chloroform solution of the toluidine. A little heat was generated and some gas which fumed with ammonia was evolved. On standing for some minutes the bromine color cleared away. On adding the last portion of the bromine a mass of crystals suddenly separated, doubtless an HBr-salt. Washed with chloroform and dried, the product melted near 200°. Heated in contact with water it decomposes with the production of an oil which solidifies on cooling. Melting point, 70° to 73°.

A mixture made up of the following substances,

(a) Some of the above 70°-73° melting substance,
(b) Some of the product obtained by brominating p-form toluidine in acetic acid,
(c) Some of the product obtained by boiling the latter with fifty percent sulphuric acid,
melted at 75° to 76°. The three substances are evidently the same compound, namely, \( \mu \)-d-brom-p-toluidine.

Yield obtained, 39.6 gms.
Theory, 39.5 gms.

ATTEMPT to ANALYZE the HBr-salt as obtained in the above experiment:
Solutions of the salt in water and in water containing a little alcohol were titrated with standard alkali. In all cases difficulty was experienced on account of fading end-points and the results were in general much lower than the calculated value. Various indicators were used.

The ease with which the salt hydrolyzes suggested the possibility that the product as obtained was a mixture of the salt and the free base. Accordingly, some of the product was hydrolyzed by boiling with water. The liberated base was converted into the hydrochloride by passing dry hydrogen chloride into a benzene solution of the substance.

**ANALYSIS of the HYDROCHLORIDE**

Sample, 0.6577 gms.

N/10 NaOH, 25.88 cc

N/10 HCl, 3.70 cc

Percent HCl found, 12.31

Calculated for

\[
\text{NH}_2\cdot\text{HCL}
\]

\[
\text{Br} \quad \text{Br} \quad \text{CH}_3
\]

12.10
THE FREE BASE.

ANALYSIS

KJELDAHL:

Sample, 0.5083 gms.,
N/10 HCl, 29.99 cc ,
N/10 NaOH, 11.19 cc ,
Percent Na. found, 5.18

Calculated for,  

\[ \text{N\textsubscript{2}H\textsubscript{2}} \]

\[ \begin{array}{c}
\text{Br} \\
\text{CH\textsubscript{3}} \\
\text{Br}
\end{array} \]

5.23

A further indication that the product obtained by brominating in chloroform was a mixture of the free base and its salt is found in the analysis of the product which follows:

ANALYSIS

KJELDAHL

Sample, 0.6163 gms.,
N/10 HCl, 30.06 cc ,
N/10 NaOH, 9.00 cc .
Percent Na found, 4.62

Theory for \[ \text{N\textsubscript{2}H\textsubscript{2}.HBr} \]

\[ \begin{array}{c}
\text{Br} \\
\text{CH\textsubscript{3}} \\
\text{Br}
\end{array} \]

4.65
Theory for,

A mixture of the two would give an intermediate value such as was found.

B R O M I N A T I O N of p-Form-toluid in Water Solution:

p-Form-toluid, 15.5 gms.,
Bromine, 16 gms.

The p-form-toluid was dissolved in alcohol. Ice and water were then added until a milky suspension was produced. To this suspension the bromine was added gradually with constant shaking. The nearly colorless product which separated was filtered off by suction and partially dried in air. It was then dissolved in alcohol and reprecipitated by the addition of ice.

Melting point, 106°.
Recrystallized from boiling water it melted at 106° to 107°.

A N A L Y S I S K J E L D A H L

Sample, 0.3146 gms.,
N/10 HCl, 30.05 cc,
N/10 NaOH, 15.50 cc.
Percent N\(\text{\textsubscript{a}}\) found, \(6.475\)

Calculated for, \(\text{NHCHO}\)

\[
\begin{array}{c}
\text{Br} \\
\text{CH}_3
\end{array}
\]

HYDROLYS of \textit{o-Brom-p-Form-}
\text{ Toluid}: \\
\textit{o-Brom-p-form-toluid}, \ 32 \text{ gms.} , \\
Concentrated HCl-sol., \ 30 \text{ cc} , \\
Alcohol, \ 200 \text{ cc} . \\

The above mixture was boiled for several hours. A crystalline sediment collected. This, it was inferred, was the hydrochloride of \textit{o-brom-p-toluidine}. The alcohol was driven off and the residue made alkaline and subjected to distillation with steam. An oil was obtained. Yield, 18 grams. The product was identified as follows:--

\textbf{Benzoylation}:

With benzoyl chloride the oil formed a white solid. This was crystallized from boiling water.

Melting point, \(147^\circ\) to \(148^\circ\).
This is the melting point of the benzoyl derivative of o-brom-p-toluidine.

**THE HYDROCHLORIDE:**

Dry hydrogen chloride was passed into a benzene solution of the oil until the separation of solid ceased. The white solid was filtered off by suction and dried.

The salt was dissolved in alkali, some alcohol added and the solution titrated with standard acid, using phenolphthalein as indicator:

- Sample: 0.4427 gms.
- N/10 NaOH: 30.81 cc
- N/10 HCl: 10.70 cc
- Percent HCl found: 16.15

Calculated for, \( \text{NH}_2\cdot\text{HCl} \):

\[
\begin{align*}
\text{Br} \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{align*}
\]

**SUMMARY with YIELDS:**

- \( \text{NHCHO} \) 18 gms
- \( \text{NHCHO} \) 32 gms
- \( \text{NH}_2\cdot\text{Br} \) 18.2 gms 73%
The above materials were placed in a liter round-bottom flask and thoroughly mixed. Considerable heat was generated and the mixture changed slowly to a dark-brown solution. The solution was raised to the boiling point and was kept boiling for three hours. On cooling, it was transferred to several volumes of water. This mixture after standing over night was filtered leaving a black residue of small proportions. The filtrate was made alkaline with sodium hydroxide and the voluminous gray precipitate which formed filtered off. This was dissolved in dilute hydrochloric acid and the solution boiled for several hours with animal charcoal. The mixture was filtered while hot, the filtrate made alkaline with ammonia and the re-
Sulting light-gray precipitate collected and dried on the water-bath.

Yield, 382 gms.
Melting point, 149° to 150°.

RE D U C T I O N to p- A M I D O- Q U I N O L I N E

Considerable time was spent in efforts to reduce the nitro-quinoline by various methods and to secure the amino-quinoline in quantity and quality suitable for use in further investigations. The method giving the best results was that by Knueppel which follows:

Iron fillings, 100 parts,
p-Nitro-quinoline, 500 " ;
Alcohol, 8 " ;
MgCl₂, anhydrous, Boneblack, 

(In the following application of the method, ten grams of the amine were used.)

The mixture was brought to boiling under a reflux condenser. To the boiling solution was added gradually in small portions the iron mixed with boneblack. After reduction the mixture was filtered
hot and the residue washed with hot alcohol.

On cooling the combined filtrates, a small quantity of yellow crystals separated. These were filtered off and the filtrate evaporated to dryness over boiling water. The residue, a black oil, hardened to a chocolate colored mass on cooling.

Yield, 7 gms.

Little success was attained in attempts to crystallize this product. The small quantity obtained pure was secured by slow crystallization from water.

Melting point, 114°.
DI-p-QUINOLINE

FORMAMIDINE

\[ \text{N. C}_7 \text{H}_7 \text{N(p)} \]

\[ \text{H}_2 \text{C} \]

\[ \text{NH.C}_7 \text{H}_7 \text{N(p)} \]

p-Aminoquinoline, 10 grams,

O-Formic ester, 5 grams.

This mixture was heated at 110 in a small flask with short reflux condenser for an hour or more. During the heating, a solid gradually separated. This was found to be insoluble in ether, chloroform and benzol. It was washed thoroughly with benzol and dried.

Melting point, 185.

Yield, 7.2 grams.

Color, yellowish-brown.

Structure, non-crystalline.

ANALYSIS

KJELDAHL

N\(_2\), percent found, 17.47, 17.48

calculated for C\(_{9}\)H\(_{10}\)N\(_4\), 18.79

Conclusion: Product is probably the formamidine but not secured sufficiently pure for analysis.
DI-o-QUINOLINE
FORMAMIDINE
HYDROCHLORIDE.

\[
\begin{align*}
\text{N. C}_9\text{H}_8\text{N} (\text{p}) \\
\text{H C} \quad \text{HCl (?)} \\
\text{NH.C}_9\text{H}_8\text{N} (\text{p})
\end{align*}
\]

A portion of the formamidine derivative was dissolved in dilute hydrochloric acid and the resulting solution evaporated to dryness. The residue, a coffee-colored product, is readily soluble in water, giving a yellow solution.

Melting point, decomposes at \(230^\circ\).

Percent HCl by Volhart, \(24.96\)

Calculated for \(\text{C}_{19}\text{H}_{14}\text{N}_4(\text{HCl})_3\), \(26.80\)

Direct titration methods proved unsatisfactory.

Conclusion: The hydrochloride is doubtless formed but not secured sufficiently pure for analysis.
**p-QUINOLIDO-METHYLENE**

**ACETYL-p-QUINOLIDE**

\[
\text{CH}_3\text{CO} \\
\text{C : CHNH}_2\text{C}_7\text{H}_5\text{N (p)} \\
\text{CO.NHC}_7\text{H}_5\text{N (p)}
\]

Di-p-quinoline-formamidine, 3.5 grams.
Aceto-acetic ester, 4.0 grams.

The above mixture was heated in a test-tube with air-condenser for an hour at 115° to 120°. The products dissolved to a dark colored solution. Boiling began at about 120°. On standing, a dark pasty mass was found at the bottom of the tube. This was found to be soluble in ether, alcohol and benzene. The remaining material, a dark-colored liquid, was subjected to distillation. A yellowish liquid came over at 95° to 130°, leaving a dark-brown, pasty residue. Washed with benzol and dried, this melted at 310°. The product dissolved readily in dilute hydrochloric acid to a yellow solution. On neutralizing this solution, a precipitate formed which melted, with decomposition, at 280°. The yield of this product was too small for purification and analysis.

Probable reaction:

\[
\text{CH}_3\text{CO} \\
\text{CH}_2 + \text{H}\rightarrow\text{C} \\
\text{COOC}_7\text{H}_5 \\
\rightarrow \text{HN.C}_7\text{H}_5\text{N (p)}
\]

\[
\text{CH}_3\text{CO} \\
\text{C : CHNH}_2\text{C}_7\text{H}_5\text{N (p)} + \text{H}_2\text{N.C}_7\text{H}_5\text{N (p)} \\
\text{CO.NHC}_7\text{H}_5\text{N (p)}
\]
The relations between the new pyrazole derivatives which were prepared may be expressed graphically as follows:

\[
\begin{align*}
\text{H-C} & \quad \text{C-COOCH}_3 \\
\text{N} & \quad \text{H-C} \\
\text{H} & \quad \text{N-C-CaH}_3 \\
\text{N} & \quad \text{H-C} \\
\text{H} & \quad \text{N-C-CaH}_3
\end{align*}
\]
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(b) Wichelhaus, B. 2, 116 (1869).
(d) Dains and Brown, p. 1153.
(e) Dains and Brown, p. 1155.
(f) " " p. 1156.
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   Reference for 5-phenyl-2 (1)-carboxyl pyrazole not found.
(q) Sjollema, A., 279, 254.
(r) This paper.
(t) A. 227, 361.
(u) A. 510, 75.
It is a pleasant duty in concluding this paper to express my appreciation of Dr. F. B. Dains whose suggestions and patience made the work possible.