Some Reactions of Formamidines

by Otto Oscar Malleis

May 15th, 1913

Submitted to the Department of Chemistry of the University of Kansas in partial fulfillment of the requirements for the Degree of Master of Science

Reaction of the Formamidines with Compounds Containing
Methylene Hydrogen with Special Reference to Di-p-benzyloxy-
diphenylformamidine and Di-p-iodo-diphenylformamidine.

A Thesis Submitted to the Faculty of the Graduate School
of the University of Kansas in Partial Fulfillment of the Re-
quirements.

For

The Degree of Master of Science
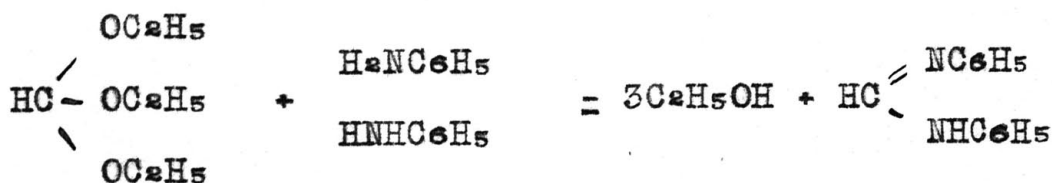

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INTRODUCTION.

Formamidines are substituted formic acids and the simple formamidine is $HC\diagdown\substack{NH \\ NH_2}$. The formamidines used, however, were substituted formamidines which may be obtained by replacing a hydrogen in the amido group and the hydrogen in the imido group by a radicle (aromatic or aliphatic).

The main methods for synthesizing substituted formamidines are:-

    I.- Heating formanilide.

    2.- Action of phosphorous trichloride on a mixture of a
          formanilide and amine.

    3.- The reaction of orthoformic-ester on a primary amine.

$$HC\diagdown\substack{OC_2H_5 \\ OC_2H_5 \\ OC_2H_5} + \substack{H_2NC_6H_5 \\ HNHC_6H_5} = 3C_2H_5OH + HC\diagdown\substack{NC_6H_5 \\ NHC_6H_5}$$

The substituted product in case of aniline is diphenyl-formamidine.

    4.- The reaction of hydrocyanicacid-sesquichloride (2HCN. 3Hcl) with primary amine.

<div align="right">Ber. 35 - 2496</div>

The general types of reactions of the substituted formamidines may be grouped under two heads:-
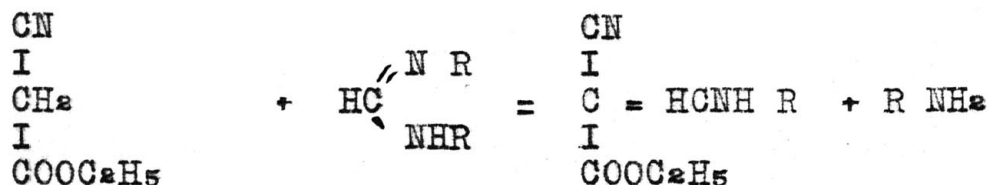
I.- Formation of salts.

    a.- Acid salts as hydrochloride

    b.- Picrates

    c.- Chloroplatinates.

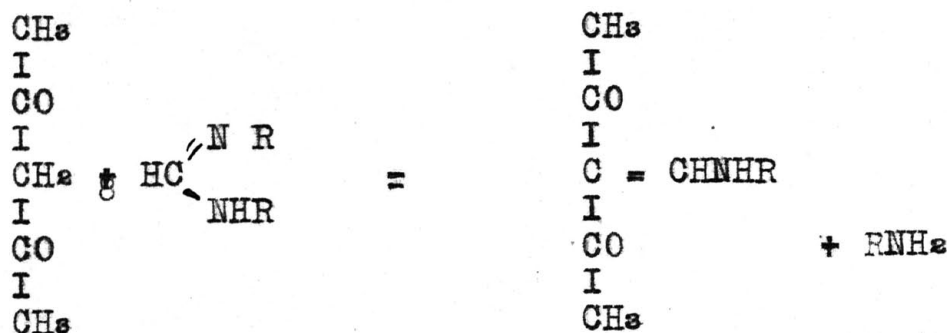2.- Reaction with compounds containing methylene hydrogen.

    a.- Reaction of cyanacetic ethyl ester with a substituted formamidine.
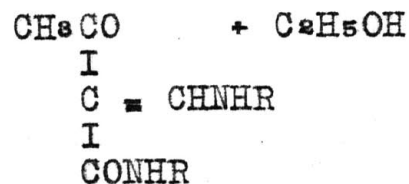
```
CN                      CN
I            ,N R       I
CH2    +  HC<       =   C = HCNH R  + R NH2
I            `NHR       I
COOC2H5                 COOC2H5
```

('R' is an aromatic or aliphatic radicle)

Ber. 35 2496.

    b.- Reaction of acetylacetone with a substituted formamidine.

```
CH3                    CH3
I                      I
CO                     CO
I          ,N R        I
CH2  + HC<        =    C = CHNHR
I          `NHR        I
CO                     CO         + RNH2
I                      I
CH3                    CH3
```

    c.- With a carbethoxy group present a secondary reaction is possible with the free amine formed as is the case with the reaction of aceto-acetic ethyl ester and a substituted formamidine.

```
CH3 CO                                    CH3 CO
  I                                         I
 CH2    +   HC⟨NR          =              C = CHNHR
  I            NHR                          I        + RNH2
 COOC2H5                                   COOC2H5
```

- - - - - - - - -

```
CH3 CO                                    CH3 CO      + C2H5OH
  I                                         I
  C = CHNHR                                 C = CHNHR
  I                                         I
 COOC2H5  +  HNHR                          CONHR
```
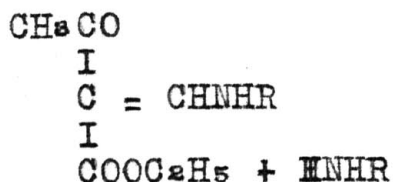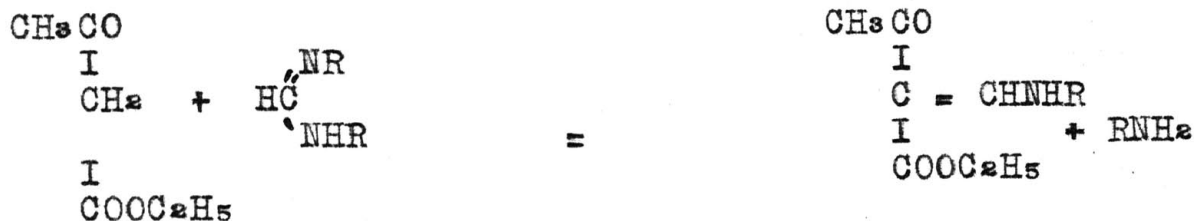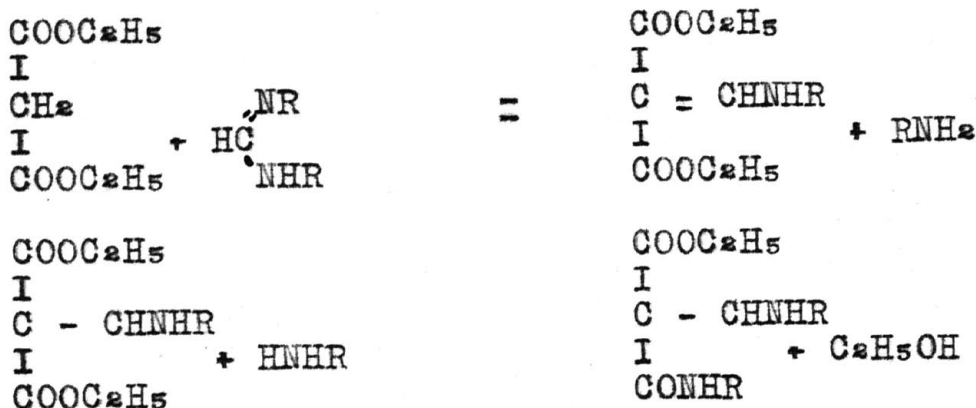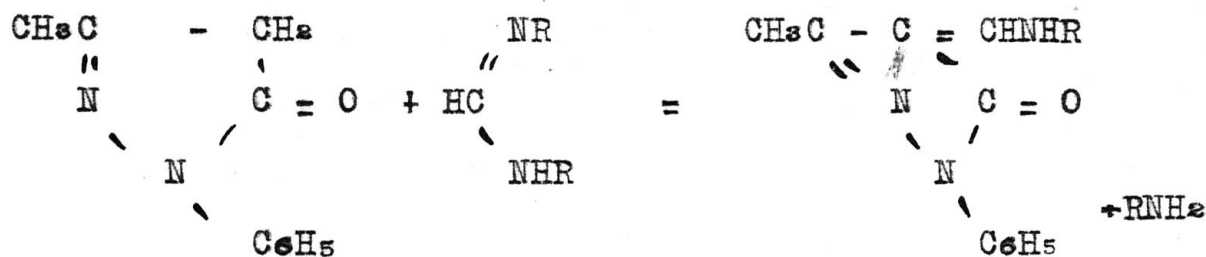
In case of aceto-acetic ethyl ester, it is fairly easy to separate the mono - and di- derivatives. In case of cyanacetic ethyl ester the di- derivative has usually not been obtained.

d.- Reaction of molonic ethyl ester with a substituted formamidine.

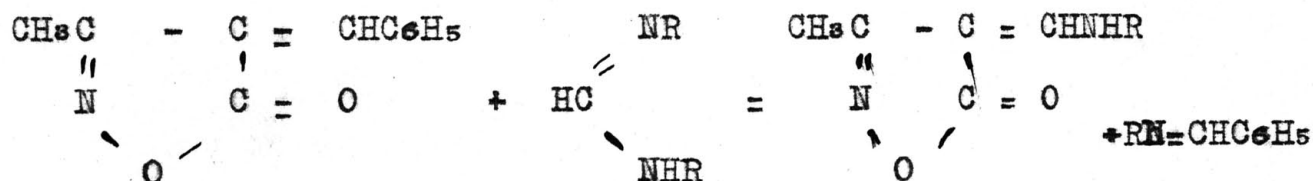It has not been possible to isolate the intermediate or mono-derivative.

```
COOC2H5                                   COOC2H5
  I                                         I
 CH2        NR             =               C = CHNHR
  I    + HC⟨                                I         + RNH2
 COOC2H5    NHR                            COOC2H5
```

```
COOC2H5                                   COOC2H5
  I                                         I
  C - CHNHR                                 C - CHNHR
  I        + HNHR                           I        + C2H5OH
 COOC2H5                                   CONHR
```

e.- Reaction of phenylmethyl-pyrazolone with a substituted formamidine.

$$CH_3C - CH_2 \quad NR \quad CH_3C - C = CHNHR$$
$$\|\quad\quad | \quad\quad \| \quad\quad \|$$
$$N \quad C = O + HC \quad = \quad N \quad C = O$$
$$\backslash \quad / \quad\quad\quad\quad \backslash\quad/$$
$$N \quad\quad NHR \quad\quad\quad N$$
$$\backslash \quad\quad\quad\quad\quad\quad\quad\quad \backslash \quad +RNH_2$$
$$C_6H_5 \quad\quad\quad\quad\quad\quad C_6H_5$$

J.Am. Chem.Soc. 31 - 1148.

f.- Reaction of methylisoxazolon with a substituted forma-midine.

$$CH_3C - C = CHC_6H_5 \quad NR \quad CH_3C - C = CHNHR$$
$$\| \quad | \quad\quad\quad \| \quad\quad \| \quad |$$
$$N \quad C = O \quad + HC \quad = \quad N \quad C = O$$
$$\backslash \quad / \quad\quad\quad\quad \backslash \quad\quad \backslash \quad / \quad +RN=CHC_6H_5$$
$$O \quad\quad\quad\quad NHR \quad\quad O$$

(This brief summary was taken from thesis submitted by Tennyson Meyers in 1912 for degree of Master of Science).

The following is a further study of the synthesis and reactions of certain formamidines, namely:

(p) Amino-phenyl-benzyl ether ((p) $NH_2C_6H_4OCH_2C_6H_5$)

(p) Iodo-aniline ((p) I $C_6H_4NH_2$).

EXPERIMENTAL PART.

Preparation of (p) $NH_2C_6H_4OCH_2C_6H_5$

The Nitro- derivative was first prepared.

(Ann. 224 - 123).

Boil about five hours.

(22 grams potassium hydroxide
(50 grams (p) nitrophenol
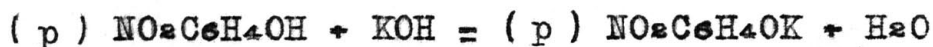(150 Cc. alcohol
(45.5 grams benzylchloride

Distill off the alcohol

Wash with water

Dry on plate

Recrystallize from alcohol.

Reactions:-

(p) $NO_2C_6H_4OH$ + KOH = (p) $NO_2C_6H_4OK$ + H_2O

(p) $NO_2C_6H_4OK$ - $ClCH_2C_6H_5$ = (p) $NO_2C_6H_4OCH_2C_6H_5$ + KCl

Melting Point (M.P.) 106^0.

Yield, over 162 grams from three portions of the above.

Reduction of the nitro- derivative:

(Ber. 34 - 1944).

Boil about three hours.

(5 grams (p) nitro-phenylbenzylether

(5 grams powdered iron

(500 Cc. of 1 % acetic acid solution.

The amine will crystallize out on cooling. Filter and

dissolve in hot alcohol. Pour through filter and add water to filtrate until cloudy and, when cool, the amine will crystallize out.

M.P. 56°

Yield, 125 grams of amine from 160 grams of nitro-derivative or about 80 %.

The Hydrochloride of (p) amino-phenyl-benzyl-ether.

Dissolve the (p) amino-phenyl-benzyl-ether in hot benzene and pass in hydrochloric acid gas, prepared by dropping sulphuric acid on sodium chloride and then passing the resulting gas through sulphuric acid to dry it. The hydrochloride precipitated out as a greyish colored substance.

M.P. 222° - 223°C.

Analysis:-

About .2 gms. of the hydrochloride was boiled with an excess of standard N/IO alkali to split off the Hcl. The excess of alkali was titrated with standard acid.

Initial weight........................... I2.7427

Final weight............................. I2.5589

Weight of Hydrochloride............ .I838

Burette Readings:-

NaOH		Hcl	
46.40	48.98	23.32	39.30
2I.20	46.44	22.3I	23.30
25.20	2.54	I.0I	I6.00

Total NaOH............. 27.74 Cc. Total Hcl.......... I7.0I Cc.

Normality of NaOH = .I028

Ratio of alkali to acid = I.075

$$\frac{(27.74 - (I7.0I \times I.075)) \times .I028 \times .036468}{.I838} = I9.27 \% \ Hcl$$

Theoretical for (p) NH2C6H4OCH2C6H5.Hcl

$$Hcl = \frac{36.468}{235.582} = I9.49 \%$$

Hcl found = I9.27 %

The preparation of benzoyl-p-amino-phenyl-benzyl-ether by the reaction of benzoyl chloride with (p) amino-phenyl-benzyl ether.

Dissolve the (p) amino-phenyl-benzyl ether in alcohol and add potassium hydroxide solution and benzoyl chloride alternately and finally potassium hydroxide in excess.

Crystallized from alcohol in white leaflets.

M.P. 226^0 - 227^0

Reaction:

$C_6H_5COcl + HNHC_6H_4OCH_2C_6H_5 + KOH = C_6H_5CONHC_6H_4OCH_2C_6H_5 + KCl + H_2O$
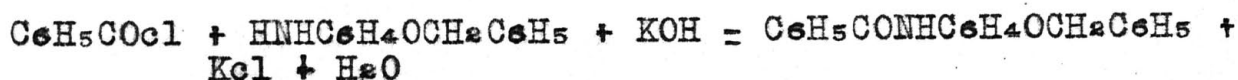
Analysis:

Determination of nitrogen by Kjeldahl method:

Initial weight................... 12.8336

Final weight.................... 12.5824

Weight of substance.......... .2512

Burette Readings:

Hcl			NaOH
45.00	44.88		40.70
.08	44.44		.14
44.92	.44		40.56

Total Hcl........... 45.36 Cc.

Normality of Hcl = .1105

Ratio of acid to alkali = .9297

$$\frac{(45.36 - (40.56 \times .9297)) \times .1105 \times .01401}{.2512} = 4.72 \% N$$

Theoretical for $C_6H_5CONHC_6H_4OCH_2C_6H_5$ or $C_{20}H_{17}NO_2$

$$N = \frac{14.01}{303.146} = 4.84\ \%$$
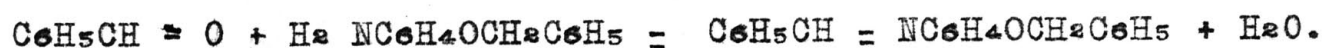
Nitrogen found = 4.72 %

Preparation of benzal-p-amino-phenyl-benzylether by the reaction

of benzaldehyde with (p)-amino-phenyl-benzylether.

Heat molecular quantities slightly on a water bath.

The resulting product crystallizes from gasoline in white

leaflets almost insoluble in hot alcohol.

M.P. 118°

Reaction:

$C_6H_5CH = O + H_2 NC_6H_4OCH_2C_6H_5 = C_6H_5CH = NC_6H_4OCH_2C_6H_5 + H_2O.$

Analysis:

Nitrogen Determination by Kjeldahl method.

Initial weight................ 16.9627

Final weight................ 16.4837

Weight of substance..... .4790

Burette Readings:-

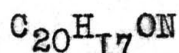| Hcl		NaOH
47.52	32.82	38.04
2.80	32.70	5.80
44.72	.12	32.24

Total Hcl.... 44.84 Cc.

Normality of Hcl = .1105

Ratio of acid to alkali = .9297

$$\frac{(44.84 - (32.24 \times .9297)) \times .1105 \times .01401}{.4790} = 4.82 \% \quad N$$

Theoretical for $C_6H_5CH = NC_6H_4OCH_2C_6H_5$ or,

$$C_{20}H_{17}ON$$

$$N = \frac{14.01}{287.146} = 4.88 \%$$

Nitrogen found = 4.82 %

Preparation of anisal-p-amino-phenyl-benzyl-ether by the reaction of anisylaldehyde with (p) amino-phenyl-benzyl-ether.
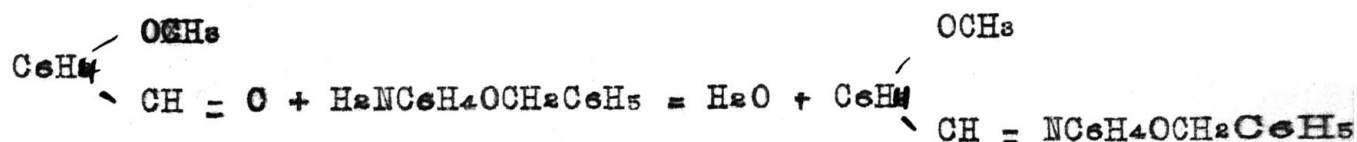
Heat molecular quantities of p-amino-phenyl-benzyl-ether and anisylaldehyde and slight excess on a water bath.

Crystallize from gasolene.

M.P. 150° - 151°.

Fairly soluble in hot gasolene and alcohol and very soluble in chloroform.

Reaction:

$$C_6H_4 \diagup \overset{OCH_3}{\underset{CH = O}{}} + H_2NC_6H_4OCH_2C_6H_5 = H_2O + C_6H_4 \diagup \overset{OCH_3}{\underset{CH = NC_6H_4OCH_2C_6H_5}{}}$$

Analysis:

Nitrogen determination by the Kjeldahl method.

Initial weight................ 11.2966

Final weight................. 10.8600

Weight of substance........ .4366

Burette Readings:

Hcl			NaOH
44.70	46.40		35.61
.10	45.34		.09
44.60	1.06		35.52

Total Hcl.......... 45.66 Cc.

Normality of acid..................... .1105

Ratio of acid to alkali............... .9297

$$\frac{(\ 45.66 - (\ 35.52 \ x \ .9297 \ ) \ ) \ x \ .1105 \ x \ .01401}{.4366} = 4.49 \ \% \ N$$

Theoretical for: $C_6H_4 \overset{OCH_3}{\underset{CH}{<}}$ = $NC_6H_4OCH_2C_6H_5$

$N = \dfrac{14.01}{315.146} = 4.45 \ \%$

Nitrogen found = 4.49 %

Preparation of di-p-benzyloxy-di-phenyl-formamidine.

Heat molecular quantities of (p) amino-phenyl-benzyl-ether and orthoformic ethyl ester + 5 Cc. in excess, on a water bath.
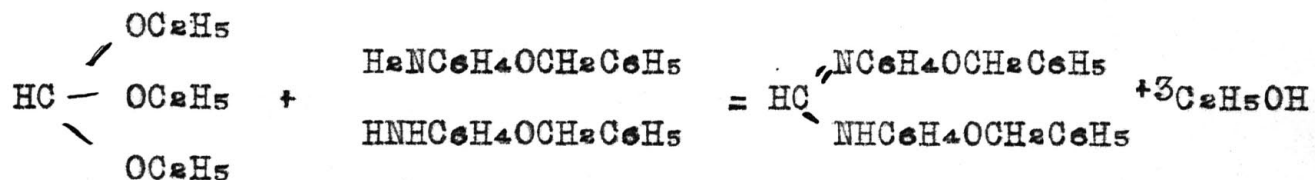
The mixture first melts and then solidifies.

Crystallizes from benzene as a white product.

Soluble in hot chloroform, hot acetone, hot alcohol and hot benzene.

M.P. I53°

Reaction:

$$HC \underset{OC_2H_5}{\overset{OC_2H_5}{-\,OC_2H_5}} + \begin{array}{c} H_2NC_6H_4OCH_2C_6H_5 \\ HNHC_6H_4OCH_2C_6H_5 \end{array} = HC \begin{array}{c} NC_6H_4OCH_2C_6H_5 \\ NHC_6H_4OCH_2C_6H_5 \end{array} + 3C_2H_5OH$$

Yields:

(24 grams (P) amino-phenyl benzyl ether

(24 Cc of orthoformic ester

(I8 grams of formamidine

(I5 grams of (p) amino-phenyl benzyl ether

(I7 Cc of orthoformic ester

(I0 grams of formamidine

(36 grams of (p) amino-phenyl-benzyl ether

(45 Cc of orthoformic ester

(3I grams of formamidine

Average yield about .... 77 %

Analysis:

Nitrogen determination by Kjeldahl method.

	I	II
Initial weight.............	14.4521	14.3331
Final weight..............	14.3331	14.2194
Weight of formamidine..	.1190	.1137

Burette Readings:

	I		II	
Hcl				
44.76		42.45	44.71	43.02
.20		41.88	.92	42.45
44.56		.57	43.79	.57
Correction for alkalinity of water..........	45.13		44.36	
		.37		.37

Total Hcl................ 44.76 Cc   43.99 Cc

NaOH		
28.03		40.40
.04		12.58
27.99		27.82

Normality of Hcl = .06728

Ratio of acid to alkali = 1.290

I
$$\frac{(44.76 - (27.79 \times 1.29)) \times .06728 \times .01401}{.1190} = 7.07 \% \text{ N}$$

II
$$\frac{(43.99 - (27.82 \times 1.29)) \times .06728 \times .01401}{.1137} = 6.89 \%$$

Theoretical for $\quad HC \begin{cases} NC_6H_4OCH_2C_6H_5 \\ NHC_6H_4OCH_2C_6H_5 \end{cases}$ or $C_{27}H_{24}N_2O_2$

$N = \dfrac{28.02}{408.212} = 6.86\ \%$

Nitrogen found : 7.07 %

6.89 %

Preparation of the hydrochloride of di-p-benzyloxydi-phenyl-formamidine

Dissolve the di-p-benzyloxy-di-phenyl-formamidine in hot chloro-
form and while hot, pass in dry hydrochloric acid gas, made by dropp-
ing sulphuric acid on sodium chloride and then passing the resulting
gas through sulphuric acid.

The hydrochloride precipitates out as a slightly bluish-white
product.

This hydrochloride is not very stable and slowly decomposes on
standing.

M.P. 26I° - 262°C.

Analysis:

Could not analyze the salt by boiling with excess alkali and
titrating back with acid.

Heat with pure sodium carbonate in platinum crucible to split
off the Hcl.

Dissolve in water and filter.

Precipitate as silver chloride

Initial weight.................... I5.7462

Final weight..................... I5.3I80

Weight of Hydrochloride..... .4282

Weight of Gooch and Agcl.... I3.5I20

Weight of Gooch............. I3.376I

Weight of Agcl.............. .I359

$$\frac{36.468 \times .I359}{I43.34 \times .4282} = 8.08 \% \text{ Hcl.}$$

Theoretical for: $Hc \underset{NHC_6H_4OCH_2C_6H_5}{\overset{NC_6H_4OCH_2C_6H_5}{<}}$ or $C_{27}H_{25}N_2O_2cl$

$$Hcl = \frac{36.468}{444.6} = 8.20 \%$$

Hcl found $= 8.08 \%$

Preparation of the picrate of di-p-benzyloxydi-phenyl-formamidine.

Dissolve molecular quantities of picric acid and di-p-benzyl-oxy-di-phenyl-formamidine separately in alcohol. Mix and a yellow precipitates forms. Filter. Crystallizes from Acetone.

M.P. 209°C.

Analysis:

Nitrogen determination by a modified Kjeldahl method.

(See Lunge and Klane, page 508)

Initial weight............ II.7550

Final weight.............. II.4998

    Weight of picrate...... .2552

Burette Readings:

Hcl		NaOH
47.58	49.88	32.30
.06	48.46	.I4
47.52	I.42	32.I6

Total Hcl.............. 48.94 Cc.

    Normality of acid.............. .I028

    Ratio of acid to alkali........ .8960

$$\frac{(48.94 - (32.I6 \times .8960)) \times .I028 \times .0I40I}{.2552} = II.36 \% \text{ N.}$$

Theoretical for $HC \begin{subarray}{l} \diagup NC_6H_4OCH_2C_6H_5 \\ \diagdown NHC_6H_4OCH_2C_6H_5 \end{subarray}$ or $C_{34}H_{27}O_9N_5$

$N = \dfrac{70.05}{637.} = I0.99 \%$

Nitrogen found = II.36 %

Preparation of cyanacetic derivatives of di-p-benzyl-oxy-di-phenyl-formamidine.

Heat molecular quantities of di-p-benzyl-oxy-di-phenyl-formamidine and cyanacetic ethyl ester + slight excess for one hour on an oil bath at 125°C.
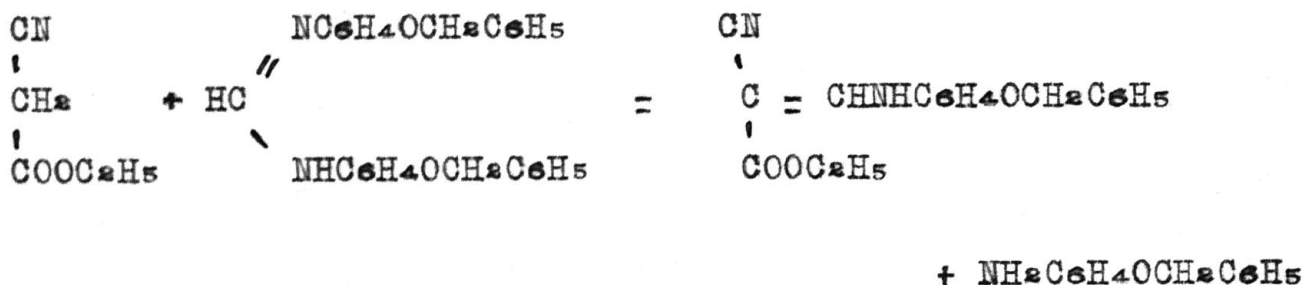
Dissolve the entire product in alcohol and add water acidified with hydrochloric acid to precipitate the cyanacetic derivative. The hydrochloric acid keeps the free amine from separating out.

The cyanacetic derivative is almost insoluble in gasoline; soluble in benzene but does not crystallize on cooling.

Light brown colored product.

M.P. 120°C.

Reaction:

$$CN \quad\quad NC_6H_4OCH_2C_6H_5 \quad\quad CN$$
$$| \quad\quad\quad\quad // \quad\quad\quad\quad |$$
$$CH_2 \quad + \quad HC \quad\quad\quad\quad = \quad C = CHNHC_6H_4OCH_2C_6H_5$$
$$| \quad\quad\quad\quad \backslash \quad\quad\quad\quad\quad\quad |$$
$$COOC_2H_5 \quad\quad NHC_6H_4OCH_2C_6H_5 \quad\quad COOC_2H_5$$

$$+ \; NH_2C_6H_4OCH_2C_6H_5$$

There was no indication of a second or di-derivative being formed by the action of the free amine on the carb.eth-oxy-group. This product may be called p-benzyl-oxy-anilido-methylene-cyan-acetic ethyl ester.

Analysis:

Nitrogen determination by Kjeldahl method.

Initial weight.................. I0.4725

Final weight.................... I0.3349

   Weight of substance......... .I376

Burette Readings:

Hcl		NaOH
46.72	46.86	42.20
.00	46.72	.20
46.72	.I4	42.00

Total Hcl................ 46.86 Cc.

Normality of acid........ .II05

Ratio of acid to alkali.. .9297

$$\frac{(46.86 - (48.00 \times .9297)) \times .II05 \times .0I40I}{.I376} = 8.79 \% \ N$$

Theoretical for

$$\begin{array}{c} CN \\ | \\ C = CHNHC_6H_4OCH_2C_6H_5 \\ | \\ COOC_2H_5 \end{array} \quad \text{or,} \ C_{19}H_{18}N_2O_3$$

$$N = \frac{28.02}{322.I6} = 8.70 \%$$

Nitrogen found = 8.79 %

Make mother liquor alkaline with potassium hydroxide and add benzoyl chloride.

Reaction:

$$C_6H_5COcl + HNHC_6H_4OCH_2C_6H_5 + KOH = C_6H_5CONHC_6H_4OCH_2C_6H_5 +$$

$$Kcl + H_2O$$

Crystallize from alcohol.

M.P. 225°+

Benzoyl-p-amino-phenyl-benzyl-ether results.

This tends to show that the formamidine broke up in the way indicated by the equation, cyanacetic ethyl ester + di-p-benzyl-oxy-di-phenyl-formamidine.

Preparation of the malonic derivative of di-p-benzyl-oxy-di-phenyl-formamidine.

Heat molecular quantities of di-p-benzyl-oxy-di-phenyl-formamidine and malonic ethyl ester + slight excess for one hour on an oil bath at 125°C.
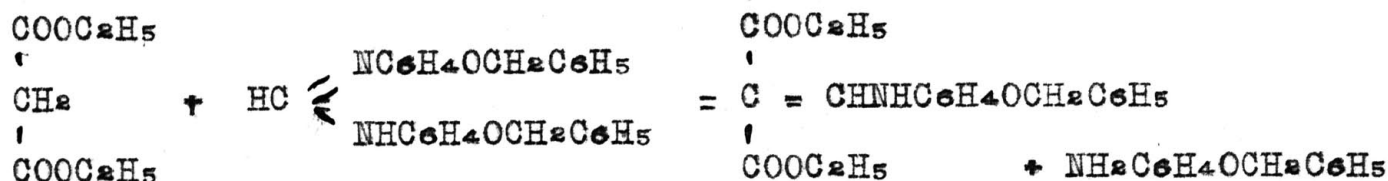
Dissolve the entire product in alcohol and add water acidified with hydrochloric acid to precipitate the malonic derivative. The hydrochloric acid keeps any free amine from separating out.
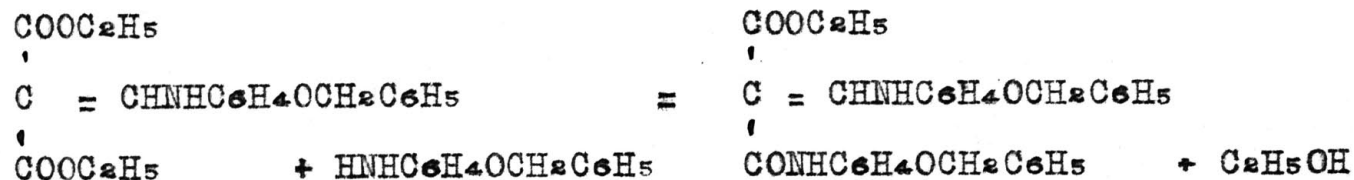
Crystallize from alcohol.

Greyish colored product.

M.P. 131° - 132°C.

Reaction:

$$
\begin{array}{l}
COOC_2H_5 \\
| \\
CH_2 \\
| \\
COOC_2H_5
\end{array}
\quad + \quad HC
\begin{cases}
NC_6H_4OCH_2C_6H_5 \\
NHC_6H_4OCH_2C_6H_5
\end{cases}
=
\begin{array}{l}
COOC_2H_5 \\
| \\
C = CHNHC_6H_4OCH_2C_6H_5 \\
| \\
COOC_2H_5 \quad + NH_2C_6H_4OCH_2C_6H_5
\end{array}
$$

$$
\begin{array}{l}
COOC_2H_5 \\
| \\
C = CHNHC_6H_4OCH_2C_6H_5 \\
| \\
COOC_2H_5 \quad + HNHC_6H_4OCH_2C_6H_5
\end{array}
=
\begin{array}{l}
COOC_2H_5 \\
| \\
C = CHNHC_6H_4OCH_2C_6H_5 \\
| \\
CONHC_6H_4OCH_2C_6H_5 \quad + C_2H_5OH
\end{array}
$$

This product may be called the p-benzyl-oxyanilid of p-benzyl-oxy-anilido-methylene-malonic ethyl ester.

Could not isolate any of the mono-derivatives.

Analysis:

Nitrogen determination by Kjeldahl method.

	I	II
Initial weight.........................	12.6340	12.5047
Final weight..........................	12.5047	12.3667
Weight of substance................	.1293	.1380

Burette Readings:

HCl

I		II	
47.10	33.34	47.32	30.52
.32	32.78	.08	29.84
46.78	.56	47.24	.68

Total HCl.........47.34 Cc ....47.92 Cc.

NaOH

46.00	49.24
.04	2.84
45.96	46.40

Normality of acid....... .1105

Ratio of acid to alkali. .9297

I

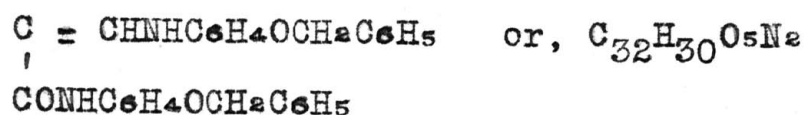$$\frac{(47.34 - (45.96 \times .9297)) \times .1105 \times .01401}{.1293} = 5.54 \% N$$

II

$$\frac{(47.92 - (46.40 \times .9297)) \times .1105 \times .01401}{.1380} = 5.37 \% N$$

Theoretical for $COOC_2H_5$

$C = CHNHC_6H_4OCH_2C_6H_5$ or, $C_{21}H_{23}O_5N$

OC_2H_5

CO
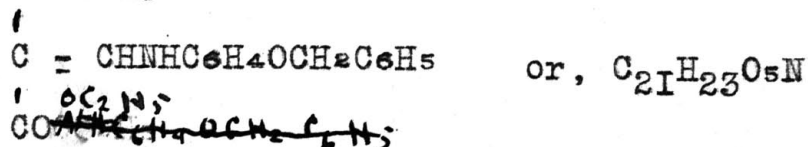
$$N = \frac{14.01}{369.19} = 3.80 \%$$

Theoretical for:

$$COOC_2H_5$$
$$|$$
$$C = CHNHC_6H_4OCH_2C_6H_5 \quad \text{or,} \quad C_{32}H_{30}O_5N_2$$
$$|$$
$$CONHC_6H_4OCH_2C_6H_5$$

$$N = \underline{28.02} = 5.37 \ \%$$

Nitrogen found $= 5.54 \ \%$
$5.37 \ \%$

- - - - - - - - -

Make mother liquor alkaline in potassium hydroxide and heat benzoyl chloride.

Reaction:

$$C_6H_5COCl + HNHC_6H_4OCH_2C_6H_5 + KOH = C_6H_5CONHC_6H_4OCH_2C_6H_5 + KCl + H_2O.$$
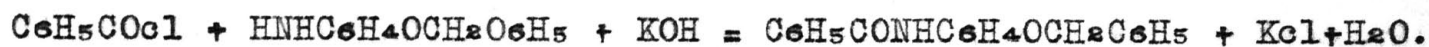
Benzoyl-p-amino-phenyl-benzyl ether is formed.

Crystallize from alcohol.

M.P. $225^{\circ} - 226^{\circ}$

This reaction would tend to show that the formamidine broke up in the way indicated in the equation by the action of malonic ethyl ester on di-p-benzyl-oxy-di-phenyl-formamidine.

The preparation of the aceto-acetic-ethyl ester derivatives of di-p-benxyl-oxy-di-phenyl-formamidine.

Heat molecular quantities of di-p-benzyl-oxy-di-phenyl-formamidine and aceto-acetic-ethyl ester + slight excess one and one-half hours on an oil bath at 120° - 125° C.

Dissolve the entire product in alcohol and add water acidified with hydrochloric acid to precipitate the aceto-acetic derivative. The hydrochloric acid prevents any free amine from precipitating out.
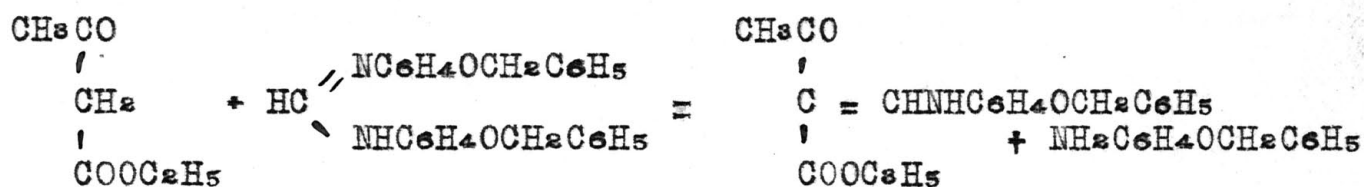
On trying to dissolve the aceto-acetic derivative in gasoline, it was found only part of the product would dissolve. The part soluble in gasoline was found to be the mono-derivative.

Recrystallize from gasoline using as small a quantity as possible.

The mono- derivative is a very light yellow colored substance. M.P. 95° - 96° C.

Reaction:

$$\begin{array}{l} CH_3CO \\ \quad | \\ \quad CH_2 \quad + \quad HC \overset{/\!/\,NC_6H_4OCH_2C_6H_5}{\underset{NHC_6H_4OCH_2C_6H_5}{\diagdown}} \quad = \quad \begin{array}{l} CH_3CO \\ \quad | \\ \quad C = CHNHC_6H_4OCH_2C_6H_5 \\ \quad | \qquad\qquad + NH_2C_6H_4OCH_2C_6H_5 \\ \quad COOC_3H_5 \end{array} \\ \quad COOC_2H_5 \end{array}$$

This product may be called p-benzyl-oxy-anilidomethyleneaceto-acetic ethyl ester.

Analysis:

Nitrogen determination by Kjeldahl method:

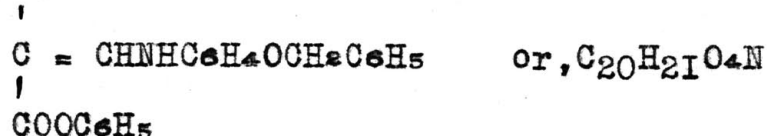Initial weight................. 12.9753

Final weight.................. 12.7918

Weight of substance........ .1835

Burette Readings:

Hcl		NaOH
4I.78	42.50	39.83
.02	42.08	.IO
4I.76	.42	39.73

Total Hcl.................. 42.I8 Cc.

Normality of acid.......... .II05

Ratio of acid to alkali.... .9297

$$\frac{(42.I8 - (39.73 \times .9297)) \times .II05 \times .0I40I}{.I835} = 4.42 \% \ N$$

Theoretical for:

$$\begin{array}{c} CH_3CO \\ | \\ C = CHNHC_6H_4OCH_2C_6H_5 \\ | \\ COOC_6H_5 \end{array} \quad or, C_{20}H_{2I}O_4N$$

$$N = \frac{I4.0I}{339.I8} = 4.I3 \%$$

Nitrogen found = 4.42 %

All the mono-derivative of aceto-acetic derivatives was re-moved by repeated heating with small quantities of gasoline. The part that was still undissolved was dissolved by heating with a small quantity of glacial acetic acid. On cooling this product crystallized out. This product, insoluble in gasoline, was found to be the di- derivative.
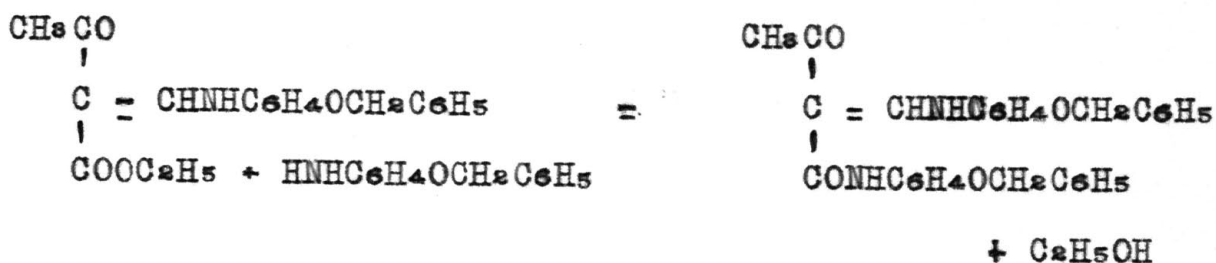
Color, light yellow.

M.P. I64° - I65° C.

This di- derivative is almost insoluble in hot gasoline, alcohol; soluble in hot acetone and benzene.

Reaction:

CH₃CO   CH₃CO

$$C \doteq CHNHC_6H_4OCH_2C_6H_5 \quad = \quad C = CHNHC_6H_4OCH_2C_6H_5$$

$$COOC_2H_5 + HNHC_6H_4OCH_2C_6H_5 \quad\quad CONHC_6H_4OCH_2C_6H_5$$

$$+ C_2H_5OH$$

This product may be called the p-benzyl-oxy-anilid of p-benzyl-oxyanilido-methylene-aceto-acetic ester.

Analysis:

Nitrogen determination by Kjeldahl method.

        Initial weight.......... I4.5392

        Final weight............ I4.3040

          Weight of substance..   .2352

        Burette Readings:

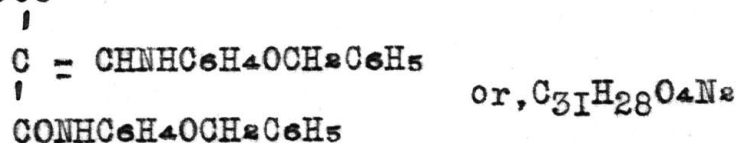| Hcl		NaOH
42.80	43.92	37.I4
.04	43.83	.30
42.76	.I0	36.94

Total Hcl........... 42.86 Cc.

Normality of acid...   .II05

Ratio of acid to alkali.9297

$$\frac{(42.86 - (36.94 \times .9297)) \times .II05 \times .0I40I}{.2352} = 5.6I \% N$$

Theoretical for: CH₃CO

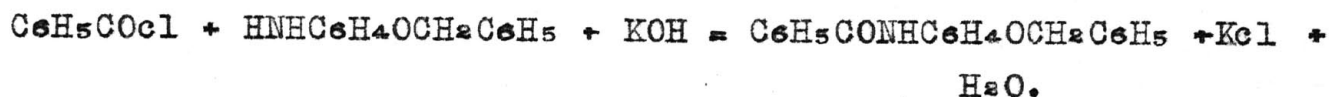$$C = CHNHC_6H_4OCH_2C_6H_5 \quad\quad or, C_{31}H_{28}O_4N_2$$

$$CONHC_6H_4OCH_2C_6H_5$$

$$N = \frac{28.02}{492.24} = 5.69 \%$$

Nitrogen found = 5.6I %

Make the mother liquor alkaline with potassium hydroxide and treat with benzoyl chloride.

Reaction:-

$$C_6H_5COcl + HNHC_6H_4OCH_2C_6H_5 + KOH = C_6H_5CONHC_6H_4OCH_2C_6H_5 + KCl + H_2O.$$

Benzoyl-p-amino-phenyl-benzyl-ether is formed.

Crystallize from alcohol.

M.P. 225° - 226° C.

This reaction shows that the formamidine probably broke up as indicated by the equations.

Preparation of the phenyl-methyl-prazolone derivative of di-p-benzyl-oxy-di-phenyl-formamidine.

Heat molecular quantities of phenyl-methylpyrazolone and di-p-benzyloxydiphenyl-formamidine for one hour on an oil bath at 120° - 125° C.

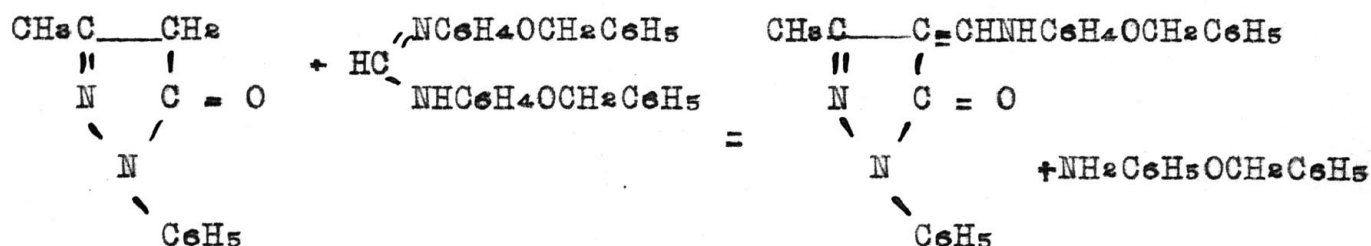Dissolve the entire product in alcohol and precipitate the ~~hydra~~ pyrazolone derivative by adding water acidified with hydrochloric acid. The hydrochloric acid prevents any free amine from coming down.

Crystallize from alcohol.

The pyrazolone derivative comes down as beautiful red needles.

M.P. 181°C.

Reaction:

```
CH3C___CH2                 ,NC6H4OCH2C6H5    CH3C____C=CHNHC6H4OCH2C6H5
   ||   |      + HC                             ||    |
   N   C = O        `NHC6H4OCH2C6H5          N    C = O
    \ /                                    =    \  /
     N                                           N      +NH2C6H5OCH2C6H5
      \                                           \
      C6H5                                        C6H5
```

This product may be called the p-benzyl-oxyanilidomethylene ~~of~~ 1-phenyl - 3-methyl-pyrazalone.

Analysis:

Nitrogen determination by the Dumas method.

Initial weight.................. 4.5855

Final weight.................... 4.4335

Weight of substance......... .1520

Volume of N2................. 16.2 Cc

Temperature................... 27.0°C

Barometer Reading...........741.5 mm.

Tension of water vapor of 50 % KOH solution at $27^{O}C$ is 17.0 mm.
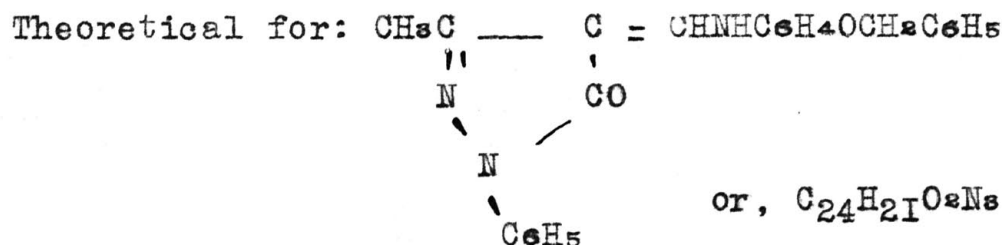
741.5 - 17.0 = 721.5 mm.

From tables, page 95 of Gatteman's "Practical Methods of Organic Ananlysis,

1 Cc of N_2 weighs .0001051 grammes.
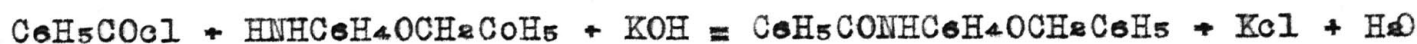
$$\frac{.0001051 \times 16.2}{.1520} = 11.13 \%$$

Theoretical for: CH₃C ____ C = CHNHC₆H₄OCH₂C₆H₅

N
CO
N
C₆H₅

or, $C_{24}H_{21}O_2N_3$

$$N = \frac{42.03}{383.198} = 10.97 \%$$

Nitrogen found = 11.13 %

- - - - - - - - -

Make the mother liquor alkaline with potassium hydroxide and heat with benzoyl chloride.

Reaction:

$C_6H_5COCl + HNHC_6H_4OCH_2C_6H_5 + KOH = C_6H_5CONHC_6H_4OCH_2C_6H_5 + KCl + H_2O$

Benzoyl-p-amino-phenylbenzylether is formed.

Crystallize from alcohol

M.P. $226^{O}C$.

This reaction also shows that the free amine is formed when phenyl-methyl-pyrazolone and di-p-benzyl-di-phenyl-formamidine are heated together.

Preparation of (p) iodo-aniline.

Heat the following mixture on a water bath until the iodine vapors disappear:

22.4 grams aniline

54. " iodine

25. " Calcium carbonate

60. Cc. ether

60. Cc. Water

Allow the ether to evaporate and then distill off the p-iodo-aniline with steam.

Yields from the above proportions:

33;32;37;39;38;36;33;41;34;40 grams.

*Preparation of the benzoyl chloride derivative of p-iodo-aniline.

The p-iodo-aniline was dissolved in alcohol and benzoyl chloride and potassium hydroxide solution were added alternately and finally potassium hydroxide to excess.

Reaction:

$C_6H_5COCl + HNHC_6H_4I + KOH = C_6H_5CONHC_6H_4I + KCl + H_2O$
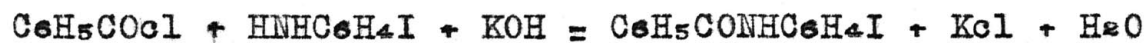
Crystallizes from alcohol as white leaflets.

M.P. $215^\circ - 216^\circ$

This product may be called benzoyl-p-iodo-anilid.

Analysis:

Nitrogen determination by the Kjeldahl method.

Initial weight.............. I4.5085

Final weight............... I4.0I9I

Weight of substance..... .4894

Burette Readings:

Hcl		NaOH
45.I0	45.00	3I.6I
2.30	44.66	.I0
42.80	.34	3I.5I

Total Hcl............ 43.I4 Cc.

Normality of acid.... .II05

Ratio of acid to alkali .9297

$$\frac{(43.I4 - (3I.5I \times .9297)) \times .II05 \times .9297}{.4894} = 4.38 \% \text{ N}$$

Theoretical for:(p) I $C_6H_4NHOCC_6H_5$ or $C_{13}H_{10}ONI$

$N = \dfrac{I4.0I}{323.0I} = 4.34 \%$

Nitrogen found = 4.38 %   *Prepared in I9I2 by Ed.Kohman.

Preparation of the benzaldehyde derivative of (p) iodo-aniline.

Mix molecular quantities of benzaldehyde and p-iodo-aniline. The reaction takes place without being heated.

Dissolve in alcohol and add a little water and, on standing, the benzaldehyde derivative will crystallize as white leaflets.

M.P. $85^{\circ} - 86^{\circ}$ C.

Almost insoluble in hot gasoline or chloroform. Soluble in acetic acid, acetone and benzene.

Reaction:

$$C_6H_5CH = O + H_2NC_6H_4I = C_6H_5CH = NC_6H_4I + H_2O$$

This product may be called benzal-p-iodo-aniline.

Analysis:

Nitrogen determination by Kjeldahl method.

Initial weight...............	I4.7729
Final weight................	I4.I696
Weight of substance......	.6033

Burette Readings:

Hcl		NaOH
45.20	45.I6	38.80
I.92	45.00	I0.80
43.28	.I6	28.00

Total Hcl............. 43.44 Cc.

Normality of acid.... .II05

Ratio of acid to alkali .9297

$$\frac{(\ 43.44 - (28.00 \ x \ .9297)\ )\ x\ .1105\ x\ .01401}{.6033} = 4.48\ \%\ N$$

Theoretical for: $C_6H_5CH = NC_6H_4I$, or, $C_{13}H_{10}NI$

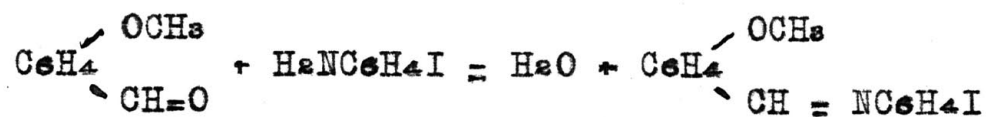$$N = \frac{14.01}{307.01} = 4.56\ \%$$

Nitrogen found $= 4.48\ \%$

Preparation of the anisyl aldehyde derivative of p-iodo-aniline.

Heat molecular quantities of p-iodo-aniline and anisyl aldehyde + slight excess on a water bath for a short time.

Crystallize from alcohol.

M.P. 151°

Reaction:

$$C_6H_4 \underset{CH=O}{\overset{OCH_3}{<}} + H_2NC_6H_4I = H_2O + C_6H_4 \underset{CH=NC_6H_4I}{\overset{OCH_3}{<}}$$

This product may be called anisal-p-iodo-aniline.

Analysis:

Nitrogen determination by Kjeldahl method.

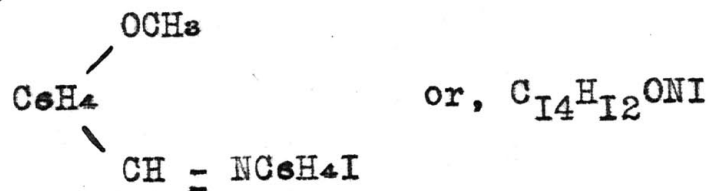Initial weight............ 13.2900

Final weight.............. 13.0614

Weight of substance..... .2286

Burette Readings:

Hcl		NaOH
44.18	45.34	41.24
.02	44.60	.00
44.16	.74	41.24

Total Hcl.............. 44.90 Cc

Normality of acid...... .1105

Ratio of acid to alkali .9297

$$\frac{(\ 44.90 - (41.24 \times .9297)\ )\ \times\ .1105 \times .01401}{.2286} = 4.45\ \%\ N$$

Theoretical for:

$$C_6H_4 \begin{array}{c} OCH_3 \\ \\ CH = NC_6H_4I \end{array} \qquad \text{or,}\ C_{14}H_{12}ONI$$

$$N = \frac{14.01}{337.026} = 4.16\ \%$$

Nitrogen found = 4.45 %
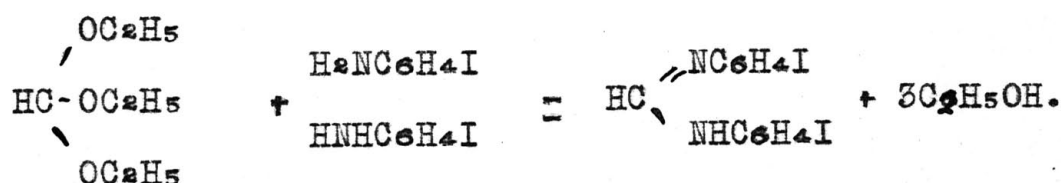
*Preparation of di-p-iodo-di-phenyl-formamidine.

Heat molecular quantities of p-iodo-aniline and ortho-formic-ethyl ester + slight excess on a water bath. The reaction takes place in a short time, forming a solid mass.

A good solvent was not found for di-p-iodo-di-phenyl-formami-dine, so the formamidine was ground in a mortar and washed with gas-oline. By this means a product pure enough to work with was obtained

Di-p-iodo-di-phenyl-formamidine is insoluble in hot gasoline and acetone; slightly soluble in hot chloroform and acetic acid; fairly soluble in hot benzene and hot alcohol.

This formamidine crystallizes best from alcohol but the yield is very poor. The product crystallized from alcohol, is white and melts at 175°C.

Reaction:

$$HC \begin{matrix} OC_2H_5 \\ OC_2H_5 \\ OC_2H_5 \end{matrix} + \begin{matrix} H_2NC_6H_4I \\ HNHC_6H_4I \end{matrix} = HC \begin{matrix} NC_6H_4I \\ NHC_6H_4I \end{matrix} + 3C_2H_5OH.$$

Yield: (120 grams p-iod-aniline
(70 Cc. ortho-formic ester
(108 grams of formamidine.

Analysis:

Nitrogen determination by Kjeldahl method.

Initial weight............ 12.0978

Final weight.............. 12.8014

Weight of substance... .2964

Burette Readings:

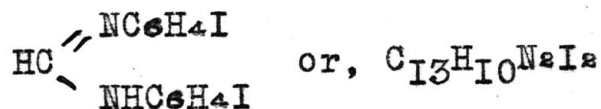| Hcl		NaOH
43.54	44.66	34.90
I.34	44.34	2.09
42.20	.32	32.8I

Total Hcl.......... 42.52 Cc.

Normality of acid.. .II05

Ratio of acid to alkali.9297

$$\frac{(\ 42.52 - (32.8I \times .9297)\ ) \times .II05 \times .0I40I}{.2964} = 6.28 \ \% \ N$$

Theoretical for:

$$HC \underset{NHC_6H_4I}{\overset{NC_6H_4I}{<}} \quad or, \quad C_{I3}H_{I0}N_2I_2$$

$$N = \frac{28.02}{447.94} = 6.26 \ \%$$

Nitrogen found = 6.28 %

* Prepared in I9I2 by Ed.Kohman.

Preparation of the hydrochloride of di-p-iodo-di-phenyl-formamidine.

Dissolve the di-p-iodo-di-phenylformamidine in benzene and pass in dry hydrochloric acid gas made by dropping sulphuric acid on sodium chloride and passing the resulting gas through sulphuric acid. The hydrochloride precipitates out. Filter.

M.P. 248° - 249° C.

Analysis:

Heat the hydrochloride with an excess of standard sodium hydroxide and titrate back with standard acid.

	I		II
Initial weight......	9.7805	....	I0.2894
Final weight	9.68I6	....	I0.I253
Weight of Hydro- chloride.....	.0989	....	.I64I

Burette Readings:

	I			II
NaOH				
	3I.I4	33.I2	30.36	33.67
	.I7	32.94	.I0	33.58
	30.97	.I8	30.26	.09
Total NaOH...........	3I.I5 Cc	....	30.35 Cc	
Hcl				
	26.20		24.29	
	.I8		.20	
	26.02		24.09	

Normality of alkali = .09326
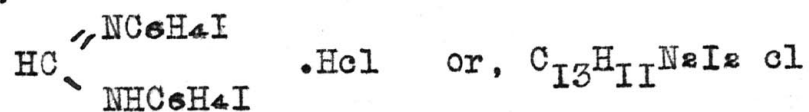
Ratio of alkali to acid= I.II5

I

$$\frac{(3I.I5 - (26.02 \times I.II5)) \times .09326 \times .03647}{.0989} = 7.33 \% \text{ Hcl}$$

II

$$\frac{(30.35 - (24.09 \times I.II5)) \times .09326 \times .03647}{.I64I} = 7.38 \% \text{ Hcl}$$

Theoretical for :

$$HC \overset{NC_6H_4I}{\underset{NHC_6H_4I}{}} \cdot Hcl \quad \text{or,} \quad C_{I3}H_{II}N_2I_2 \text{ cl}$$

$$Hcl = \frac{36.47}{474.46} = 7.53 \%$$

Hcl found = 7.33 %
7.38 %

Preparation of the picrate of di-p-iodo-diphenylformamidine,

Dissolve molecular quantities of picric acid and di-p-iodo-di-phenyl-formamidine separately in alcohol.

Mix. The picrate crystallizes as a dark yellow substance.
Filter.

Recrystallize from cold acetone.

M.P. 226°C.

Analysis:

Nitrogen determination by a modified Kjeldahl method.

(Lunge & Klane, page 508).

Initial weight.............. 5.4770

Final weight................ 5.2943

Weight of picrate......... .1827

Burette Readings:

Hcl			NaOH
46.32	46.76		37.68
.04	46.56		.10
46.28	.20		37.58

Total Hcl.............. 46.48 Cc

Normality of acid...... .1105

Ratio of acid to alkali .9297

$$\frac{(\ 46.48 - (37.58 \times .9297)\ ) \times .1105 \times .01401}{.1827} = 9.78\ \%\ N$$

Theoretical for: $HC\begin{smallmatrix} \nearrow NC_6H_4I \\ \searrow NHC_6H_4I \end{smallmatrix}$ $.C_6H_2(OH)(NO_2)_3$, or, $C_{19}H_{13}N_5\ O_7I_2$
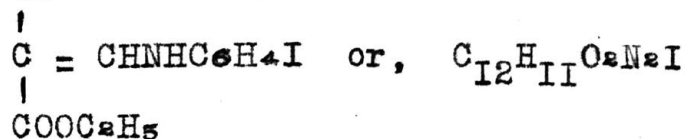
$$N = \frac{70.05}{677.} = 10.35\ \%$$

Nitrogen found = 9.78 %

Total Hcl............ 47.64 Cc.

$$\frac{(47.54 - (41.16 \times .9297)) \times .1105 \times 01401}{.1736} = 8.27 \% \text{ N}$$

Theoretical for:

$$\begin{array}{c} CN \\ | \\ C = CHNHC_6H_4I \\ | \\ COOC_2H_5 \end{array} \quad \text{or,} \quad C_{12}H_{11}O_2N_2I$$

$$N = \frac{28.02}{342.03} = 8.19 \%$$

Nitrogen found $= 8.27 \%$

- - - - - - - - - - - -

Make the mother liquor alkaline with potassium hydroxide
and treat with benzoyl chloride.

Reaction:

$C_6H_5COcl + HNHC_6H_4I + KOH = C_6H_5CONHC_6H_4I + Kcl + H_2O$

Benzoyl-p-iodo-aniline is formed.

Crystallize from alcohol.

M.P. 215°

This reaction shows that the free amine was found when cyanacetic
ethyl ester anddi-p-iodo-diphenylformamidine were heated together.

*Preparation of the malonic derivatives of di-p-iodo-di-phenylformamidine

Heat molecular quantities of di-p-iodo-diphenylformamidine and malonic ethyl ester + slight excess for one hour on an oil bath at 125°C.
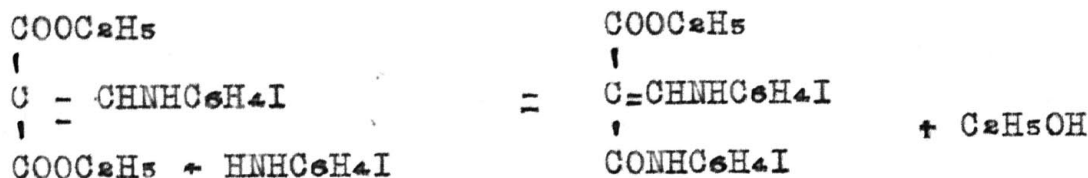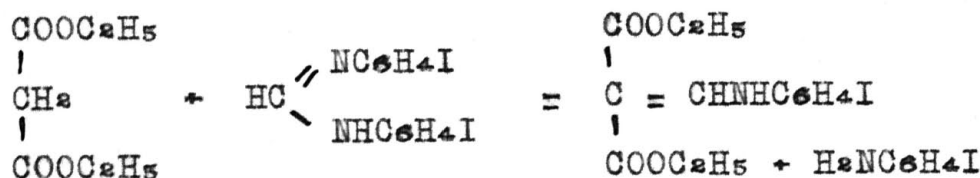
Dissolve the entire product in chloroform and add alcohol to precipitate. The free amine would not precipitate out from this mixture.

The malonic derivative is very soluble in cold chloroform but almost insoluble in alcohol.

M.P. 176° C.

Color, white.

Reaction:

$$\underset{\overset{|}{\text{COOC}_2\text{H}_5}}{\overset{\text{COOC}_2\text{H}_5}{\overset{|}{\text{CH}_2}}} \quad + \quad \text{HC} \overset{\text{NC}_6\text{H}_4\text{I}}{\underset{\text{NHC}_6\text{H}_4\text{I}}{}} \quad = \quad \underset{\text{COOC}_2\text{H}_5 + \text{H}_2\text{NC}_6\text{H}_4\text{I}}{\overset{\text{COOC}_2\text{H}_5}{\overset{|}{\text{C} = \text{CHNHC}_6\text{H}_4\text{I}}}}$$

- - - - - -

$$\underset{\text{COOC}_2\text{H}_5 + \text{HNHC}_6\text{H}_4\text{I}}{\overset{\text{COOC}_2\text{H}_5}{\overset{|}{\text{C} - \text{CHNHC}_6\text{H}_4\text{I}}}} \quad = \quad \underset{\text{CONHC}_6\text{H}_4\text{I}}{\overset{\text{COOC}_2\text{H}_5}{\overset{|}{\text{C}=\text{CHNHC}_6\text{H}_4\text{I}}}} \quad + \text{C}_2\text{H}_5\text{OH}$$

This product may be called the p-iodo-anilid of p-iodo-anilido-methylenemalonic ethyl ester.

No intermediate or mono-derivatives could be isolated.

Analysis:

    Nitrogen determination by the Kjeldahl method.

        Initial weight................... I4.8I89

        Final weight.................... I4.6384

          Weight of substance......... .I805

Burette Readings:

HCl		NaOH
42.04	42.70	39.20
.04	42.50	.I6
42.00	.20	39.04

Total HCl............ 42.20 Cc
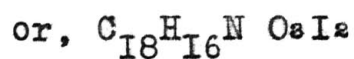
Normality of acid.... .II05

Ratio of acid to alkali .9297

$$\frac{(\ 42.20 - (39.04 \times .9297)\ ) \times .II05 \times .0I40I}{.I805} = 5.I8\ \%\ N$$

Theoretical for:

        $COOC_2H_5$

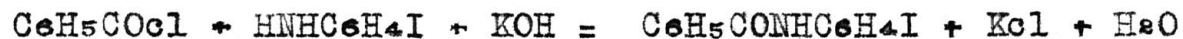 $CCHNHC_6H_4I$ or, $C_{18}H_{16}N\ O_3I_2$

        $CONHC_6H_4I$

$$N = \frac{28.02}{56I.988} = 4.99\ \%$$

Nitrogen found = 5.I8 %

    Make the mother liquor alkaline with potassium hydroxide and treat with benzoyl chloride.

Reaction:

$$C_6H_5COcl + HNHC_6H_4I + KOH = C_6H_5CONHC_6H_4I + Kcl + H_2O$$

Benzoyl-p-iod-aniline is formed.

Crystallize from alcohol.

M.P. 215^0 - 216^0 C.

This reaction shows that the free amine has formed when malonic ethyl ester and di-p-di-phenylformamidine were treated together.

* Prepared, 1912, by Ed.Kohman.

*Preparation of the aceto-acetic ethyl ester derivatives of di-p-iodo-diphenyl-formamidine.

Heat molecular quantities of di-p-iodo-di-phenylformamidine and aceto-acetic ethyl ester + slight excess for one hour on an oil bath at 125° C. Another portion was heated six hours on a water bath.
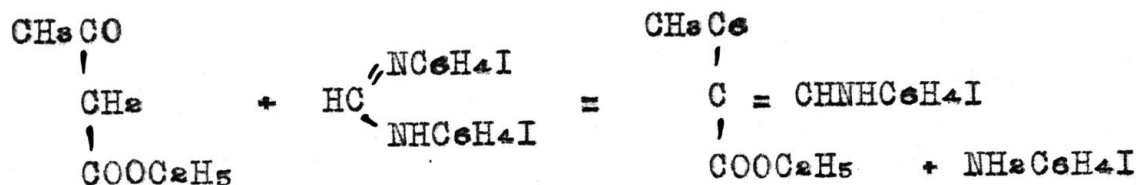
Dissolve the entire product in alcohol and add water acidified with hydrochloric acid to precipitate the aceto-acetic derivatives and at the same time keep any free amine in solution.

Part of this product was insoluble in hot gasoline. The part soluble in hot gasoline crystallized out on cooling as a nearly white product. Recrystallize several times using the smallest quantity of gasoline possible. This product, soluble in gasoline, was found to be the mono- derivative.

M.P. 96° - 97° C.

Soluble in cold chloroform, ether, benzene, acetic acid and hot alcohol

Reaction:

$$
\underset{\substack{|\\ \text{CH}_2\\ |\\ \text{COOC}_2\text{H}_5}}{\text{CH}_3\text{CO}} \quad + \quad \text{HC}\underset{\text{NHC}_6\text{H}_4\text{I}}{\overset{\text{NC}_6\text{H}_4\text{I}}{<}} \quad = \quad \underset{\substack{|\\ \text{C} = \text{CHNHC}_6\text{H}_4\text{I}\\ |\\ \text{COOC}_2\text{H}_5}}{\text{CH}_3\text{C}} \quad + \quad \text{NH}_2\text{C}_6\text{H}_4\text{I}
$$

This product may be called the p-iodo-anilido-methylene-aceto-acetic ethyl ester.

Analysis:

Nitrogen determination by the Kjeldahl method.

	I	II
Initial weight............	13.6563	12.4103
Final weight..............	13.4312	11.8088
Weight of substance...	.2251	.6015

Burette Readings

	I		II	
Hcl				
43.30	43.79	47.20	47.20
2.14	43.33	.10	46.80
41.16	.46	47.10	.40

Total Hcl.......41.62 Cc .... 47.50 Cc.

NaOH	I	II
38.62		34.04
.51		.27
38.11		33.77

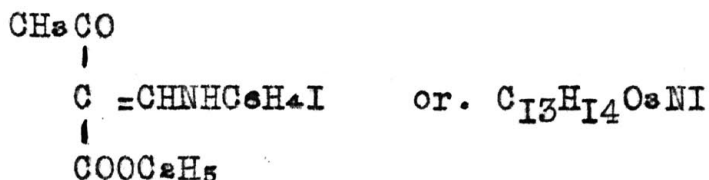Normality of acid............ .1105

Ratio of acid to alkali...... .9297

I

$$\frac{(41.62 - (38.11 \times .9297)) \times .1105 \times .01401}{.2251} = 4.26 \% N$$

II

$$\frac{(47.50 - (33.77 \times .9297)) \times .1105 \times .01401}{.6015} = 4.15 \% N$$

Theoretical for :

$$\begin{array}{c} CH_3CO \\ | \\ C =CHNHC_6H_4I \\ | \\ COOC_2H_5 \end{array} \quad \text{or.} \quad C_{13}H_{14}O_3NI$$

$$N = \frac{14.01}{359.042} = 3.90\%$$
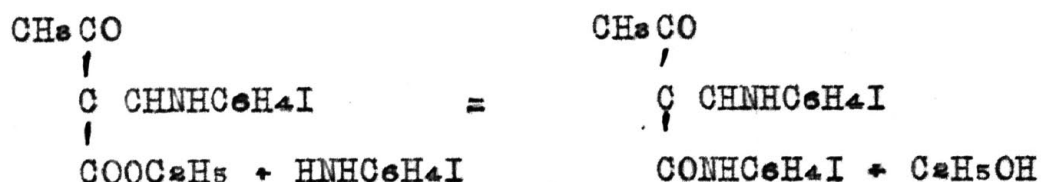
Nitrogen found $= 4.26\%$
4.15%

Dissolve the portion, insoluble in hot gasoline, in chloroform and add alcohol to precipitate the product which was found to be the di- derivative.

M.P. $184^{\circ} - 185^{\circ}$ C.

Soluble in cold chloroform, ether, benzene, acetic acid and hot alcohol.

Color, greyish.

Reaction:

$$\begin{array}{c} CH_3CO \\ | \\ C \ CHNHC_6H_4I \\ | \\ COOC_2H_5 + HNHC_6H_4I \end{array} = \begin{array}{c} CH_3CO \\ | \\ C \ CHNHC_6H_4I \\ | \\ CONHC_6H_4I + C_2H_5OH \end{array}$$

This product may be called the p-iodo-anilid of p-iodo-anilido-methylene-acto-acetic ester.

More di- derivative was obtained from the portion heated on the oil bath than from the portion heated on the water bath.

Analysis:

Nitrogen determination by the Kjeldahl method.

Initial weight................. 12.6996

Final weight.................. 12.3015

Weight of substance........ .3981

Burette Readings:

Hcl   NaOH

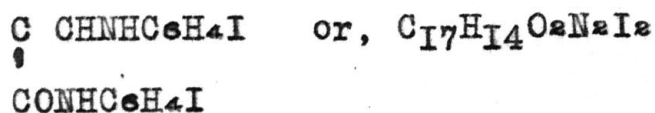45.21   44.04   34.90

.70   43.79   1.18

44.51   .25   33.72

Total Hcl............. 44.76 Cc.

$$\frac{(\,44.76 - (33.72 \times .9297)\,) \times .1105 \times .01401}{.3981} = 5.21\ \%$$

Theoretical for: CH₃CO

C CHNHC₆H₄I   or, $C_{17}H_{14}O_2N_2I_2$

CONHC₆H₄I

$$N = \frac{14.01}{531.972} = 5.27\ \%$$

Nitrogen found = 5.21 %

Make mother liquor alkaline with potassium hydroxide and heat

with benzoyl chloride.

Reaction:-

C₆H₅COCl + HNHC₆H₄I + KOH = C₆H₅CONHC₆H₄I + KCl + H₂O.

Benzoyl-p-iodo-aniline is formed.

Crystallize from alcohol.

M.P. 215° - 216° C.

This reaction shows that the free amine was formed when aceto-acetic ethyl ester and di-p-iodo-di-phenylformamidine were heated together.

*Prepared by Ed.Kohman in 1912.

Preparation of the acetyl-acetone derivative of di-p-iodo-di-phenyl-formamidine.

Heat molecular quantities of di-p-iodo-di-phenyl-formamidine and acetyl acetone + slight excess for one hour on an oil bath at 125°C.
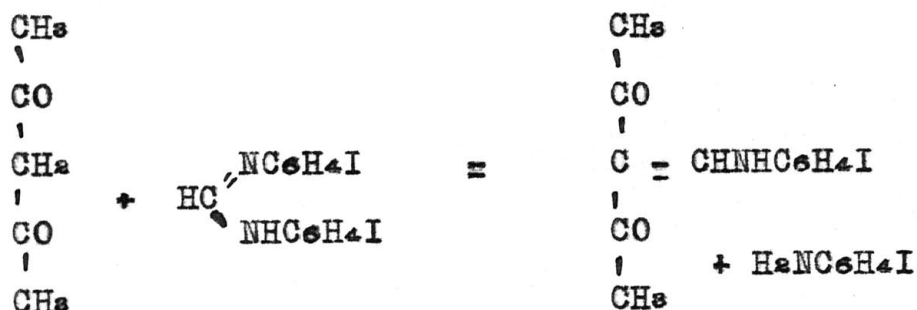
Dissolve the entire product in alcohol and add water acidified with hydrochloric acid to precipitate the acetyl derivatives and, at the same time, to keep the free amine in solution.

Crystallize from alcohol.

M.P. 180° - 181°

Color - very light yellow.

Reaction:

$$
\begin{array}{c}
CH_3 \\
\backslash \\
CO \\
| \\
CH_2 \\
| \\
CO \\
| \\
CH_3
\end{array}
\; + \;
HC \Big\langle \begin{array}{c} NC_6H_4I \\ NHC_6H_4I \end{array}
\; = \;
\begin{array}{c}
CH_3 \\
| \\
CO \\
| \\
C = CHNHC_6H_4I \\
| \\
CO \\
| \qquad + \; H_2NC_6H_4I \\
CH_3
\end{array}
$$

This product may be called the p-iodo-anilido-methyleneacetyl-acetone.

Analysis:

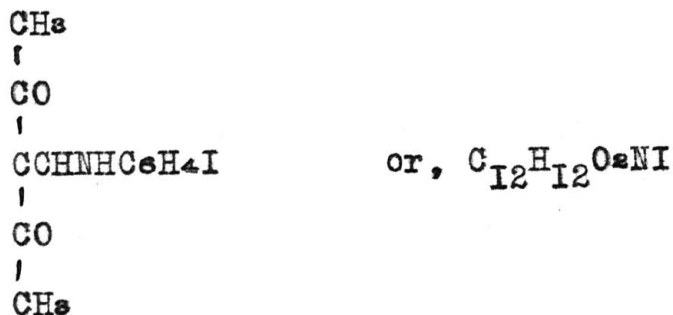Nitrogen determination by the Kjeldahl method.

Initial weight.............. 14.0659

Final weight................ 13.7379

Weight of substance.... .3280

Burette Readings:

HCl		NaOH
44.34	32.44	40.56
.92	31.99	2.76
43.42	.45	37.80

Total Hcl................ 43.87 Cc

Normality of acid....... .1105

Ratio of acid to alkali. .9297

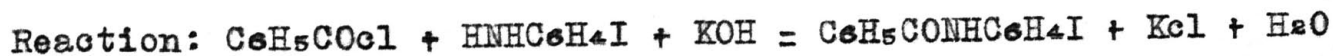$$\frac{(\ 43.87 - (37.80 \times .9297)\ ) \times .1105 \times .01401}{.3280} = 4.12\ \%\ N$$

Theoretical for:

$$
\begin{array}{l}
CH_3 \\
| \\
CO \\
| \\
CCHNHC_6H_4I \qquad \text{or,}\ C_{12}H_{12}O_2NI \\
| \\
CO \\
| \\
CH_3
\end{array}
$$

$N\ =\ \dfrac{14.01}{329.026}\ =\ 4.26\ \%$

Nitrogen found $=$ 4.12 %

Make the mother liquor alkaline with potassium hydroxide and treat with benzoyl chloride.

Reaction: $C_6H_5COcl + HNHC_6H_4I + KOH = C_6H_5CONHC_6H_4I + KCl + H_2O$

Benzoyl - -iodo-aniline is formed.

Crystallize from alcohol.

M.P. 215° +

This reaction shows that the free amine was formed when acetyl acetone and di-p-iodo-di-phenyl-formamidine were heated together.

Preparation of the methyl isoxazalon derivative of di-p-iodo-di-phenylformamidine.

Heat molecular quantities of benzylidinmethylisoxazalon and di-p-iodo-di-phenylformamidine on an oil bath until the mixture melts which was about 140°C. Then lower the temperature to 115°C and heat for about an hour. At higher temperatures decomposition is very liable to take place.
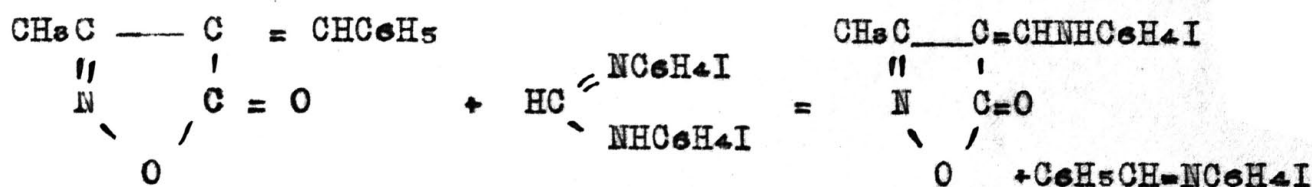
The by-product is soluble in benzene while the isoxazalon derivative is only slightly soluble in benzene . This is the way the two substances were separated.

Crystallize from acetone.

M.P. 208° - 209° C.

Slightly soluble in hot acetic acid and alcohol, fairly soluble in hot acetone.

Reaction:

$$CH_3C \underset{\underset{O}{\overset{N}{\diagdown}\diagup}{\overset{\parallel}{\;}}}{\underline{\quad\quad}} \overset{\mid}{\underset{C=O}{C}} = CHC_6H_5 \quad + \quad HC \overset{\diagup NC_6H_4I}{\underset{\diagdown NHC_6H_4I}{}} \quad = \quad CH_3C \underset{\underset{O}{\overset{N}{\diagdown}\diagup}{\overset{\parallel}{\;}}}{\underline{\quad\quad}} \overset{\mid}{\underset{C=O}{C}} = CHNHC_6H_4I \quad + C_6H_5CH = NC_6H_4I$$

Color - light yellow

Analysis:

Nitrogen determination by Kjeldahl method.

Initial weight.................	10.5740
Final weight..................	10.2460
Weight of substance........	.3280

Burette Readings:

Hcl			NaOH
44.00	31.99		28.14
1.23	31.34		.42
42.77	.65		27.72

Total Hcl........... 43.42 Cc

Normality of acid.... .1105

Ratio of acid to alkali .9297

$$\frac{(\ 43.42 - (27.72 \times .9297)\ ) \times .1105 \times .01401}{.3280} = 8.34 \ \% \ N$$

Theoretical for CH_3C ——— $C = CHNHC_6H_4I$

N   CO

O

or, $C_{11}H_9N_2O_2I$
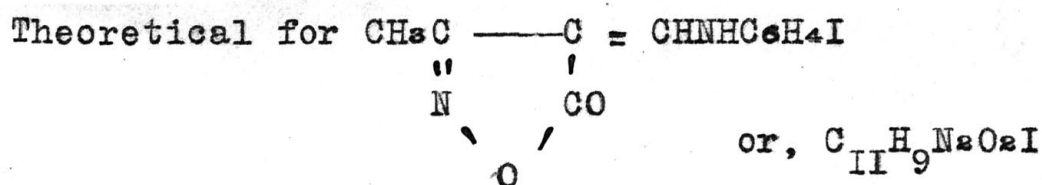
$$N = \frac{28.02}{328.012} = 8.54 \ \%$$

Nitrogen found = 8.34 %

This work was suggested by Dr. F. B. Dains and carried out under his direction.

The author takes this opportunity to express his obligations for the suggestions and guidance in the carrying out of this research.