A STUDY OF A SYNTHESIS OF INDOLE

BY

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of the Requirements
for the Degree of
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Stephen Scala

May 25, 1954

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INDOLE
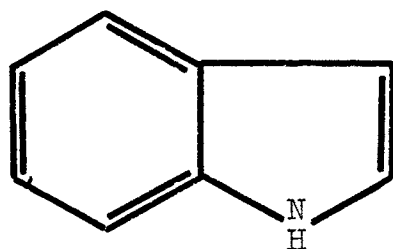
BENZOPYRROLE

1 - BENZAZOLE

C_8H_7N

117.14

M.P. $^{\circ}$C 52.0

BP 253°C at 760 mm

d $\frac{60}{4}$ 1.0643

n $\frac{60}{D}$ 1.609

Picrate M.P.   187°C

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INTRODUCTION

Chemical literature abounds with methods for the synthesis of Indole and its derivatives. Undoubtedly, this is so, because Indole is the parent substance of the historical dyestuff Indigo. This coloring material has been the subject of extensive investigations for many centuries. Early in this century, importance was still placed on Indole Chemistry, but it later gave way to other dyestuffs having different chemical structures. It seems, however, the loss in popularity was to have been short-lived, because of the revitalized interest shown in the chemistry of Indoles since the early 1930's.

It was found that a great number of alkaloids were also derivatives of the Indole nucleus and hence, could enter into a great many syntheses. The amino acid Tryptophan, which has been found to be extremely important to animal nutrition is a derivative of Indole -- as are also many plant hormones.

We also find Indole being used in the perfume industry to enhance such delicate floral imitations as gardenia, lilac and jasmin.

With this very brief introduction to Indole, we will next consider a synthesis of this important substance and still more important intermediate, although the true pleasure lies in being first to synthesize a compound, it would indeed be folly to even imagine being first to try a synthesis of Indole. The author was naive enough earlier in this investi-

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gation to think a new approach was at hand; however, a few hours with the literature cast a new and revealing light on the multitude and variety of synthesis already labored over.

The synthesis first to be investigated in this paper is that using O-amino phenyl-ethyl alcohol as the starting material. By first effecting a dehydration cyclization and then a dehydrogenation of the resulting 2,3- dihydroindole, the desired product is formed. A German patent 606,027 dated November 23, 1934 covers a similar investigation - details of which will be given later.

A second synthesis using 2-Hydroxy ethyl aniline and following the same procedure of cyclization by dehydration, then dehydrogenation, is also the subject of the present investigation, but to a much lesser degree than the first method. Unsuccessful attempts in synthesizing the 2-chloro ethyl aniline impeded any progress that might have resulted from this line of investigation.

In conclusion it might be added, that the present revitalized interest in the chemistry of Indoles, served to give the author sufficient impetus to conduct this minor investigation in what might otherwise be considered a fairly well exhausted topic of chemistry.

SYNTHESIS OF INDOLE

$C_6H_5NHCH_2CH_2Cl$

ALKALINE

HCl

$C_6H_5NHCH_2CH_2Cl$

SO_2Cl

$AlCl_3$

$AlCl_3$

$C_6H_5NHCH_2CH_2OH$

H_2C-CH_2
O

$C_6H_5NH_2$

NAOH
STEAM
DIST.

$O-NH_2C_6H_4CH_2CH_2Cl$

HCl

HCl
130°-140°C

$O-NH_2C_6H_4CH_2CH_2OH$

DEHYDROGENATION
CATALYST HIGH
TEMPERATURE

CAT. HIGH TEMP.
DEHYDRATION-
(DEHYDROGENATION)

REDUCTION

$O-NO_2 C_6H_4CH_2CH_2OH$

HNO_3

$C_6H_5CH_2CH_2OH$

1
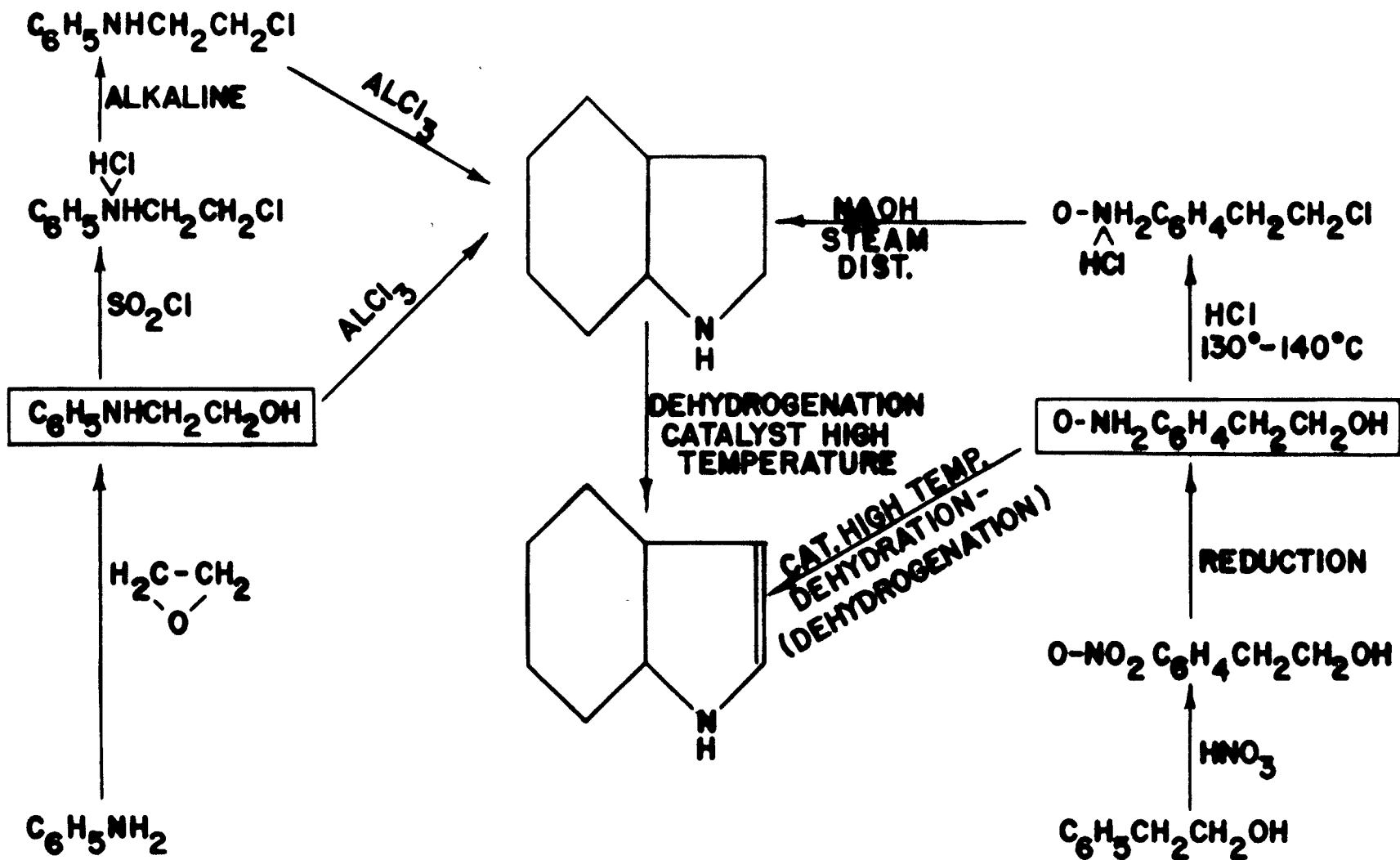
COMPOUNDS AND INTERMEDIATES

Though it was not the purpose of this thesis to undertake the synthesis of all starting materials and intermediates, certain materials were synthesized either because of the unavailability or because of a special interest in the particular synthesis. Mention should be made of the fact that success was not attained in all instances where a synthesis was tried. For example, the replacement of the hydroxyl group with chlorine was unsuccessfully attempted with the compound 2-hydroxy ethyl aniline. Several experiments tried resulted in recovery of the starting material or a product having the appearance of a polymerized mass. These experiments are described in the pages to follow.

Small quantities of other compounds were needed for spectroscopic purposes and in these instances, particular attention was paid to the purity of the material rather than to the resulting yield.

Still in other instances, where a particular starting material required a rather involved or lengthy synthesis, experimental quantities were purchased. However, a literature reference is cited as to a method of synthesis and a synopsis given in this section.

2 - HYDROXY ETHYL ANILINE (1)

This compound is prepared by simply passing ethylene oxide into aniline according to the reaction:

$$C_6H_5NH_2 \quad + \quad H_2C\overset{\displaystyle \diagdown}{\underset{O}{}}CH_2 \quad \longrightarrow \quad C6H_5NHCH_2CH_2OH$$

Mol. Wt. 93   Mol. Wt. 44   Mol. Wt. 137

I   II
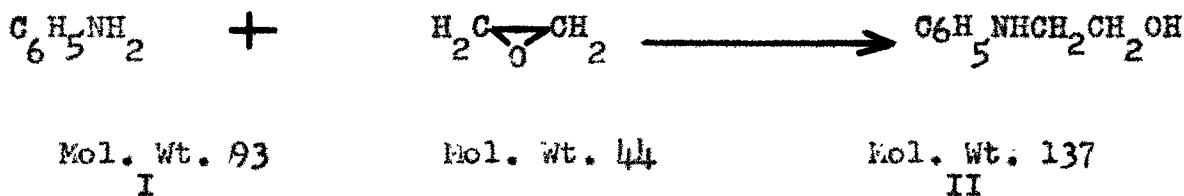
The following procedure was taken from Chemical Abstracts; original reference [9]

> 44 g ethylene oxide passed into 186 g aniline and 35 ml water at 14-16° in 3-4 hrs. At end of reaction, temperature will rise sponteneously to 70-80°C in spite of cooling bath. Distillation yields 78.5% of II b.p. at 19 mm 176°, n $_D^{20}$ 1.5760, d $_4^{20}$ 1.0945, picrate m.p. 124°C.

It was found that upon carrying out the reaction as given above, no product was formed. A second reaction in which the temperature was allowed to rise as the reaction progressed gave the following results:

TIME	TEMPERATURE °C	GRAMS ETHYLENE OXIDE ABSORBED
0	14°C	0
30 mins.	19	-
1 hr. 35 "	32	27
1 " 50 "	34	-
2 " 25 "	39	-
2 " 30 "	45	40
2 " 45 "	52	-
2 " 55 "	67	44 (1 mol.)
3 " 20 "	50	-

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DISTILLATION DATA:

FRAC.	PRESS.	VAP. TEMP.	VOL.	WT.
Aniline	7 mm	61° C	0 ml	
	"	60	20	
	"	60	30	
	"	60	40	
	"	60	50	
	"	60	75	
	"	60	100	102.0 g.
Aniline	"	90	1	
6/17	"	120	2	
C	"	134	4	
Comp. II	"	140	7	
11/17	"	142	11	
	"	143	17	18.4
Comp. II	"	143	0	
	"	143	7	
	"	143	25	27.5
Comp. II	"	143	0	
	"	143	48	51.7
High Boiling Material	"	152	1	
	"	158	2	
	"	185	3.5	4.1
Residue				8.0

Total Aniline recovered
```
102.0                    27.5
  6.5     Comp. II       51.7
108.5 g.                 11.9
                         91.1 g.
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$91.1/137 \times 100 = 66.6 \%$ of theory.

$137/93 \times 100 = 147.2 \%$ theoretical wt. yield on aniline.

$91.1/186-108.5 \times 100 = 117.6 \%$ wt. yield on aniline consumed.

$117.6/147.2 \times 100 = 79.8 \%$ of theory based on aniline consumed.

Comp. II b_7 $143^{\circ}C$, n_D^{20} 1.5771, d_4^{20} 1.0996

2 - CHLORO ETHYL ANILINE

A brief description of the experiments conducted in an attempt to prepare this compound from 2-hydroxy ethyl aniline will be given. The experiments will not be presented in great detail, since the desired compound was never obtained or at least never isolated as such. Because of this failure to prepare 2-chloro ethyl aniline, and also because of lack of time, the synthesis of Indole starting with 2-hydroxy ethyl aniline was not investigated.

Experiment #1 - An attempt to replace the hydroxyl using $SOCl_2$ was tried:

$$C_6H_5NHCH_2CH_2OH + SOCl_2 \longrightarrow C_6H_5NHCH_2CH_2Cl$$
$$\cdot HCl$$

| 137 | 119 | 191 |
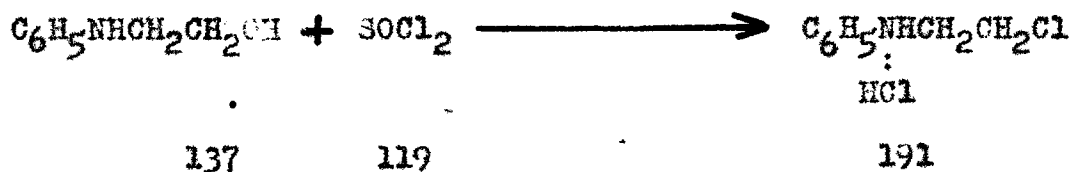
Procedure Used

0.5 mols. of 2-hydroxy ethyl aniline was dissolved in 400 ml toluol and 0.625 mols of $SOCl_2$ added dropwise at 70-85°C over a period of 4 hours. The color during the course of addition of the $SOCl_2$ ranged from brown to dark green and finally black. The dark solid was filtered on a Buchner funnel and washed with toluol - then allowed to suck dry. Final drying was accomplished in an oven at 70°C for 24 hours. The weight of this crude was 99.0 g. When dissolved in 150 g ethyl alcohol at 70°C, cooled and allowed to crystallize, the melting point was 150-153°C. The weight of the crystallized material was 42 g. A second crystallization gave a melting point of 152-155°C.

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Experiment #2 - This experiment was the same as #1 only using a lower reaction temperature. The intention was to make the addition at about 25-30°C, but it was found that a gummy mass separated and adhered to the glass agitator. Stirring became increasingly difficult and could only be relieved by elevating the temperature. Raising the temperature to slightly higher than 35°C gave satisfactory results in this respect. The $SOCl_2$ was added over $2\frac{1}{2}$ hours with the temperature ranging from 35 to 45°C. The cooled reaction was then filtered on a Buchner funnel as before and also completed in the same manner. The recrystallized material weighed 53.7 g and had a melting point of 152°-154°C.

The material from both these experiments was combined and dissolved in water. Sodium carbonate was added until alkaline to litmus. Toluol was then used to extract the released material, and after filtering, the extract was subjected to distillation. The toluol was recovered atmospherically and then a vacuum of 8-10 mm applied. Upon attempting to fractionate the remaining material, a small quantity appeared to sublime, and the rest assumed the appearance of a polymerized mass. The compound seems to be very heat sensitive.

Experiment #3 - An attempt to prepare the 2-chloro ethyl aniline using hydrochloric acid and zinc chloride resulted in recovery of the starting alcohol.

Experiment #4 - An experiment similar to 1 and 2 using ethylene dichloride as the reaction solvent was tried. Using this solvent, it was possible to maintain a low reaction temperature 17-30°C. However, upon completing the experiment it was found that approximately 90% of the original 2-hydroxy ethyl aniline was recovered unchanged.

O-AMINO PHENYLETHYL ALCOHOL (2)

The synthesis of this compound was not undertaken, but a method for its preparation is described from the reference cited.

The method includes first the synthesis of the ortho-nitro phenylethyl alcohol and the subsequent reduction to the amino compound. The nitration of phenylethyl alcohol is carried out in the presence of acetic anhydride, whose ortho-directing effects are well known. Other advantages are the higher nitration temperatures attainable requiring a smaller excess of nitric acid; furthermore and more important, it does not require the isolation of phenylethyl acetate.

$$C_6H_4 \diagup^{NO_2}_{\diagdown CH_2CH_2OH} \qquad I$$
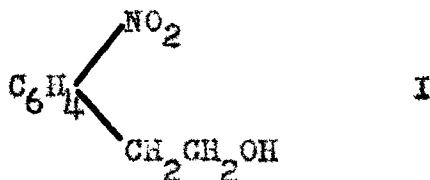
250 cc of phenylethyl alcohol is dissolved in 340 g of acetic anhydride, 1 cc of 66° Be' sulfuric acid is added to the mixture. As soon as the reaction starts, with a considerable generation of heat, the flask is plunged into the cooling mixture. After a certain period of contact, the solution of acetate thus obtained is poured, drop by drop, into a mixture of 625 cc of nitric acid (d = 1.49) and 315 cc of acetic anhydride, the temperature being maintained at 35-40°. The mixture is left standing for an hour and then poured over ice.

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The mixture of nitro acetate is diluted with ether, neutralized with bicarbonate, and dried. After the ether has been removed, the reaction mixture is saponified by refluxing for 3 hours with 500 cc of methyl alcohol containing 2% Hcl, and the solvent is distilled off. The products of four identical operations are poured into water. After standing overnight, the nitrated product solidifies. It is dried and 421 g. of solid para-nitrated alcohol is collected. The liquid mass is distilled under vacuum to separate the poly-nitrated derivatives remaining in solution. 657 g are collected which comes over between 155 and $183°$ at 1.5 mm. It is carefully redistilled of tails which solidify after some time (p-nitro derivatives). We finally obtain 206 g of a pure product, a clear yellow liquid, almost odorless, better tasting, and with the following constants;
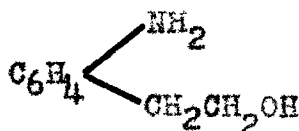
$$b_{1.3} = 144-147°C$$
$$n_D^{22} = 1.5620$$
$$d^{22} = 1.253$$

Yield: Found 43.25%

Calc. 43.26%

$$C_6H_4 \bigg\langle \begin{array}{l} NH_2 \\ CH_2CH_2OH \end{array}$$ II

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The reduction of the ortho-nitro-phenylethyl alcohol was accomplished by means of zinc dust in the presence of $CaCl_2$, a method described in German Patent 83,544 and used successfully by Ferber for the reduction of para-nitro isomer.

Into a liter of hot water containing 20g of dissolved $CaCl_2$ and 200 g of zinc dust in suspension, 50 g of o-nitro phenylethyl alcohol is poured in small portions with stirring, and the mixture refluxed for $\frac{1}{2}$ hour. The zinc is filtered out, washed, the calcium salts precipitated from the filtrate with 20 g of sodium carbonate, filtered again, washed and the water removed under vacuum. Then, disregarding the presence of NaCl, the product is distilled under reduced pressure. Yield 83%. The redistilled product has the following constants:

$$b.p._{3.5} = 147\text{-}148^\circ$$
$$n_D^{19} = 1.5849$$

The product is a viscous, colorless liquid with a weak odor and a bitter aniline taste. It takes on a yellowish tint on exposure to air. It is completely soluble in cold water.

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The ortho-amino-phenylethyl alcohol used in this
paper was obtained by a careful fractionation of a purchased
technical sample. The results of the distillation follow:
charge to Still 189.1 g.

FRAC.	PRESS.	VAP. TEMP.	VOL.	WT.
	9 mm	$94.0^{\circ}C$		
	"	110.0		
#1	"	154.0	20.5 ml	20.4 g
	"	156.0	0	
	"	160.0	5	
	"	162.0	9	
	"	163.0	25	
#2	"	164.0	50	54.7
	"	164.0	0	
#3	"	164.0	54	58.0
	"	164.0	0	
	"	168.0	30	
#4	"	168.0	48	51.4
Residue				4.6

From this fractionation it is determined that the
technical 0-amino phenylethyl alcohol is approximately 75%
pure. Fraction #3 was used exclusively in the experiments
that follow. The constants for this fraction are:

$$b_9 = 164^{\circ}C$$

$$n_D^{20} = 1.5840$$

This material was not needed for any synthesis, but the probability of its being present as a by-product is almost certain. Therefore, a small quantity was prepared in order to obtain an ultraviolet spectrum of the compound.

The material can be readily prepared by dehydration of the o-amino phenylethyl alcohol according to the following reaction:

$$C_6H_4 \underset{CH_2CH_2OH}{\overset{NH_2}{<}} \quad \xrightarrow{K_2CO_3} \quad C_6H_4 \underset{CH = CH_2}{\overset{NH_2}{<}}$$

I   II
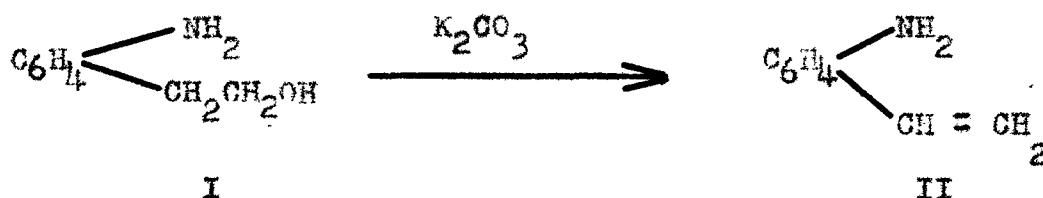
The procedure is to add anhydrous potassium carbonate to the o-amino alcohol and the mixture subjected to distillation under partial vacuum. It was found that the first fraction to come over was high boiling (ie. the b.p. of I), but upon redistillation with potassium carbonate the product collected had the following constants:

$$b_{15} = 102^0$$
$$n_D^{20} = 1.6100$$
$$d_{20}^{20} = 1.0196$$

The constants given in the reference cited had the constants:

$$b_{15} = 104-105$$
$$n_D^{20} = 1.6101$$
$$d_{20}^{20} = 1.0190$$

2,3 DIHYDROINDOLE (?)

The synthesis of this compound according to the reference cited is accomplished by heating the O-amino phenylethyl alcohol with 5 parts, Hcl for 4 hours at 130-140°C. The resulting hydrochloride of $O-NH_2C_6H_4CH_2CH_2$ cl is then neutralized using NaOH and steam distilled yielding the 2,3 Dihydroindole, which is then extracted from the distillate. The constants given are:

$$b_8 = 94.5°C$$

(Hcl salt) m.p. 222-4°C

In the experiment conducted by the author 206 g of O-amino phenylethyl alcohol and 1030 g of conc. HCl were heated in a glass lined auto clave for 4 hours at 140°C. The resulting hydrochloride was neutralized with NaOH and steam distilled. The entire distillate was extracted using benzene, and the crude 2,3 dihydroindole recovered upon evaporation of the benzene. The weight of crude amounted to 58.6 g which yielded 48.4 g of fractionated product having the following constants:

$$b_7 = 91.0°C$$

(HCl salt) m.p. 223°C

The yields obtained are as follows:

$\frac{119}{137}$ x 100 = 86.9% theoretical weight yield

$\frac{48.4}{206}$ x 100 = 23.5% actual weight yield

$\frac{23.5}{86.9}$ x 100 = 27.1% yield on theory

It is believed that the 2,3 dihydroindole can also be prepared from o-amino phenylethyl alcohol dehydration with aluminum chloride. Although the product was not isolated, a brief experiment conducted using aluminum chloride gave the characteristic odor of the 2-3 dihydroindole. Spot tests using P-dimethylamino-benzaldehyde gave the deep orange-yellow precipitate as does dihydroindole.

INDOLE

The synthesis of Indole from O-amino phenylethyl alcohol will be discussed briefly, leaving the experimental details for a later section. Excellent results can be obtained with the above material especially if the 2,3 dihydroindole intermediate is first prepared. The one discouraging consideration is the preparation of the aminoalcohol, which is not very simple as was previously noted.

Indole is prepared by the catalytic dehydration-dehydrogenation at high temperatures, according to the reactions shown schematically on page 1. The reactions can be conducted step-wise by first preparing the 2,3 dihydroindole as cited above. Dehydrogenation of this material gives very good yields of Indole.

It is necessary that the dehydrogenation procede in the presence of a hydrogen acceptor. Benzene was selected for this purpose since cyclohexane does not undergo dehydrogenation very readily. The reaction as conducted in this paper, was carried out atmospherically by passing a benzene solution of the starting material over the heated catalyst - the solution of course is quickly vaporized upon entering the preheating zone. The reaction could have been also conducted in a chrome-vanadium steel vessel in the presence of iodine and benzene at 200^{o}C. (6).

The German Patent 606,027 gives the following examples of the investigation conducted by Dr. Ing. Hanns Ufer and Dr. Wilhelm Brewers:

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Example #1 - Granular bauxite, dehydrated by ignition is moistened with water and 15 g. of water glass solution per liter and then stirred with 100 g of finely divided copper carbonate. The catalyst thus obtained is reduced by subjecting it to a current of hydrogen at 300° for several hours. By passing 50 to 100 g of O-amino phenylethyl alcohol vapor mixed with about 100 liters of nitrogen and 10 liters of hydrogen, at 300°, a reaction product is obtained which outside of small quantities of the unreacted starting material and 2,3 dihydroindole, consists mainly of Indole which can be separated and purified in the usual ways, ie., by steam distillations.

Example #2 - 20 parts by weight of O-aminophenylethyl alcohol is heated with 5 parts by weight of anhydrous zinc chloride in an oil bath. At about 200°, water starts splitting off and a mixture of oil and water distills over. The oil consists of nearly pure 2,3 - dihydroindole. Pure indole can be obtained from this by dehydrogenation according to the British Patent 387,507. In this case the Indole cannot be isolated.

Example #3 - At 300°, 30 g of O-amino phenylethyl alcohol vapor mixed with 180 liters of nitrogen and 30 liters of hydrogen is passed over granular, dehydrated bauxite which is steeped in 30 g of 40° Be' water glass solution. A crude 2,3 dihydroindole is obtained in good yields, which contains a small quantity of indole and O-aminostyrene.

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The second starting material also shown on page 1 is 2-hydroxy ethyl aniline. This compound itself is easily prepared as described by reacting aniline and ethylene oxide. The value of this starting material would lie in being able to go from it to the 2,3 dihydroindole compound and then to procede with the dehydrogenation. It may be possible to accomplish this dehydration-cyclization step by the use of aluminum chloride either directly from the alcohol or by replacement of the hydroxyl with chlorine forming the 2-chloro ethyl aniline and then reacting with aluminum chloride. The possibility of the chloro compound undergoing Friedel-Crafts reaction is of course very great. This line of investigation was abandoned due to poor results in attempting to form the 2-chloro ethyl aniline. Experiments in this preparation were given earlier on pages 6-8.

The equipment used for the high temperature reactions is shown on page 23, and the experimental details given in the section bearing the title "Experimental".

DEHYDROGENATION CATALYST

The nickel on Kieselguhr catalyst used in the experimental section was prepared according to the method of Atkins, Richards and Davis (6). The method of preparation is also described in Reactions of Hydrogen by Adkins (8). The preparation is as follows:

58 g of Baker and Adamson or Mallinckrodt c.p. nickel nitrate hexahydrate $Ni (NO_3)_2$ $6H_2O$ dissolved in 80 ml dist. H_2O was ground for thirty to 60 minutes in a mortar with 50 g of nitric acid washed Kieselguhr (ex. Johns Manville "Filter Cil") until the mixture was apparently homogenous and flowed as freely as a heavy lubricating oil. It was then slowly added to a solution prepared from 34 g Mallinckrodt c.p. ammonium carbonate mono-hydrate $(NH_4)_2 CO_3 H_2O$ and 200 ml of dist. H_2O. The resulting mixture was filtered with suction, washed with 100 ml of water in two portions, and dried overnight at$110^{o}C$. The yield was 66 g. Just before use from 2 to 6 g of the product so obtained was reduced for 1 hr. at $450^{o}C$ in a stream of hydrogen passing over the catalyst at a rate of 10-15 ml/min. The catalyst was then cooled to room temperature and transferred in a stream of H_2 to the reaction vessel, which had been filled with CO_2.

In using this catalyst in a reaction tube such as was used in this experiment, obviously, does not require performing the last step in which the catalyst was cooled and transferred.

The catalyst was fixed on silicon carbide (Grit #10) in the case of the catalyst already described and also the one whose description follows:

CU - ZNO - Bi_2O_3 catalyst

Stir 560 g of basic cupric carbonate and 700 ml of 28% ammonium hydroxide together until well mixed. Then add into this mixture, slowly, a well blended mixture of 175 g zinc carbonate and 40 g bismuth oxide. The entire mixture is then well blended. The mixture is then coated on the silicon carbide (enough for 1-2 liters) and spread out to dry. When completely dried, the clusters are broken apart and the catalyst charged to the reaction tube.

The catalyst is activated by passing a slow current of hydrogen through the catalyst bed at $400^{\circ} - 450^{\circ}C$.
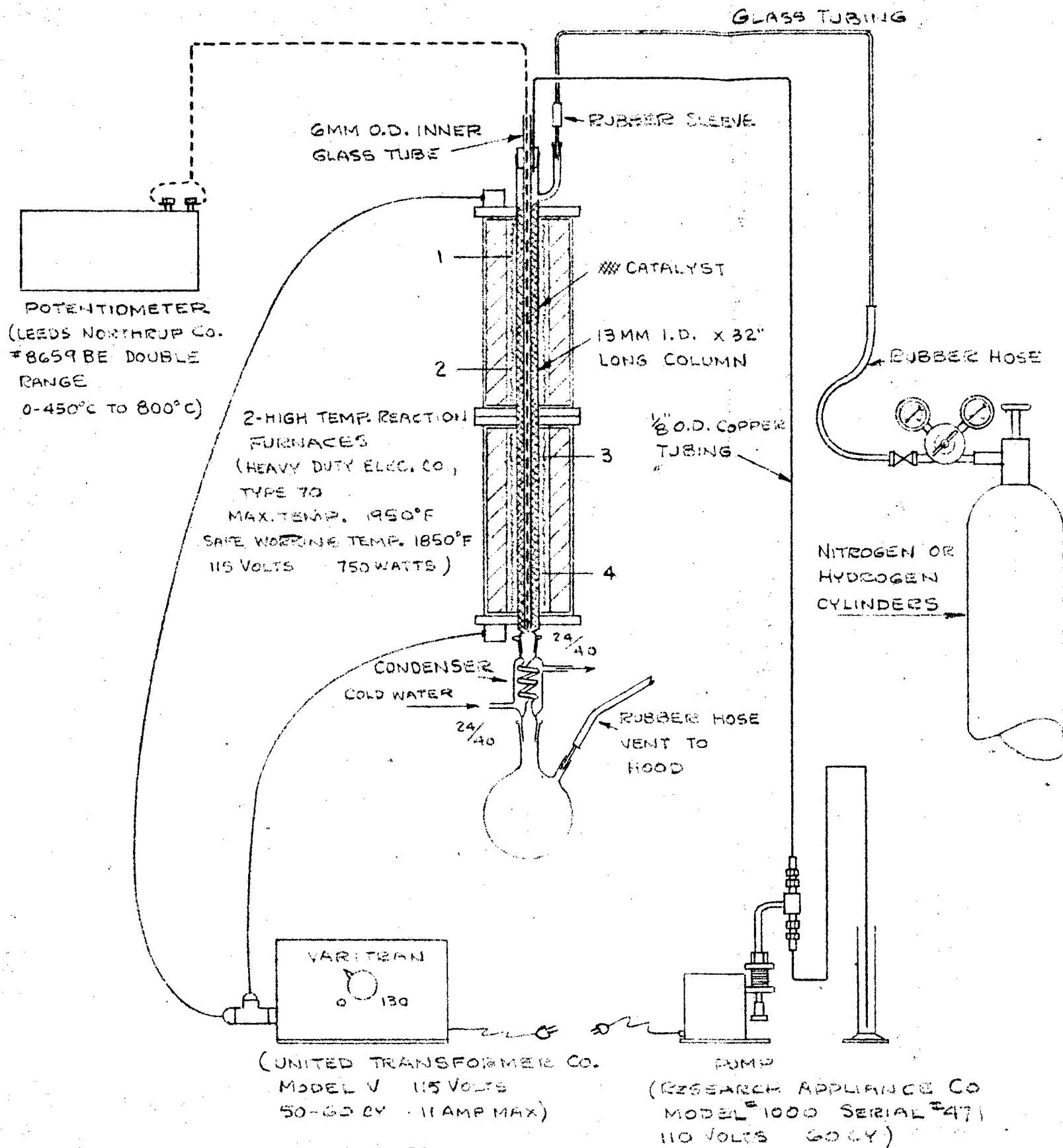
EQUIPMENT

The equipment used in obtaining the experimental data is shown on page 23. It is believed, the auxiliary equipment is adequately labeled so that its description need not be undertaken in detail. The temperature was measured by means of an Iron-Constantan Thermocouple, which was inserted in a glass tube having one end sealed. The thermocouple could be raised or lowered to measure the temperature at any point of the reactor tube. This glass tube is shown by dotted lines in the drawing.

The furnace itself was perhaps the poorest piece of equipment assembled. Temperatures at the points 1,2,3 and 4 were not uniform to a satisfactory degree - in fact, it was decided to use the top furnace (points 1-2) as a pre-heating zone, with the catalyst occupying only the lower furnace. The reactor-tube space above the catalyst was filled with helices and the thermocouple placed midway between points 3 and 4 for all the experimental runs. It is to be noted, that the temperature recorded in this manner was fairly close to the average of points 3 and 4.

When activating the catalyst, the rubber sleeve was connected as shown in the drawing - the excess hydrogen being vented to the hood. After activation, the rubber sleeve is replaced with a rubber stopper and feeding of the solution started.

The calibration curve shown on page 24 is for the Corson - Cerveny Micro-Bellows Pump. The curve as drawn applies only to benzene, but a correlation can be obtained for other liquids with no great difficulty.

REACTION FURNACE

GLASS TUBING

6MM O.D. INNER GLASS TUBE

RUBBER SLEEVE

POTENTIOMETER
(LEEDS NORTHRUP CO.
#8659 BE DOUBLE
RANGE
0-450°C TO 800°C)

CATALYST

13MM I.D. X 32" LONG COLUMN

2-HIGH TEMP. REACTION
FURNACES
(HEAVY DUTY ELEC. CO.
TYPE 70
MAX. TEMP. 1950°F
SAFE WORKING TEMP. 1850°F
115 VOLTS   750 WATTS)

RUBBER HOSE

1/8" O.D. COPPER TUBING

NITROGEN OR HYDROGEN CYLINDERS

1
2
3
4

24/40

CONDENSER
COLD WATER

24/40

RUBBER HOSE VENT TO HOOD

VARITRAN

0   130

(UNITED TRANSFORMER CO.
MODEL V   115 VOLTS
50-60 CY 11 AMP MAX)

PUMP
(RESEARCH APPLIANCE CO
MODEL #1000 SERIAL #471
110 VOLTS   60 CY)

23

CORSON-CERVENY MICRO-BELLOWS PUMP
CALIBRATION WITH BENZENE

TURNS ON ADJUSTING NUT

MI/HR

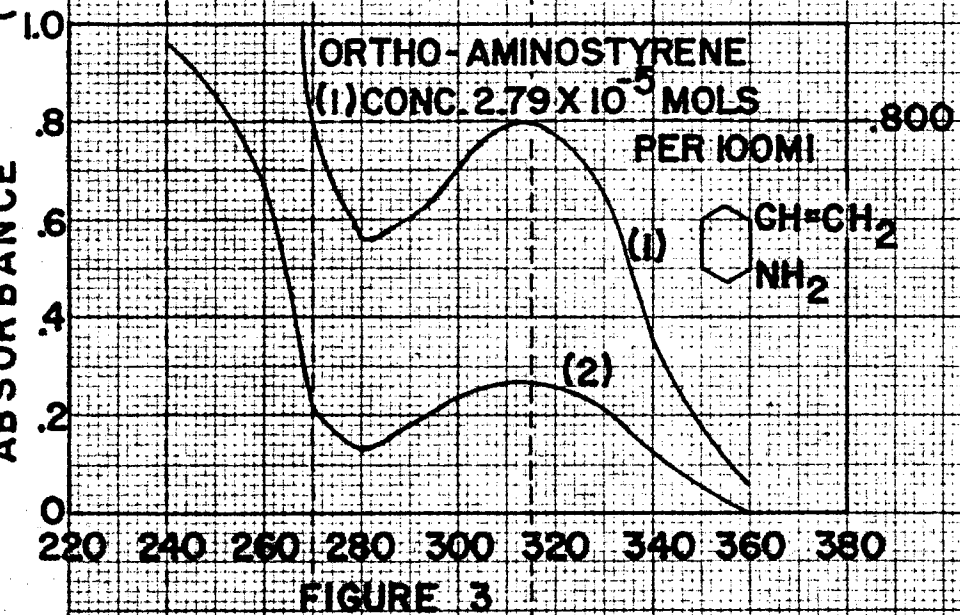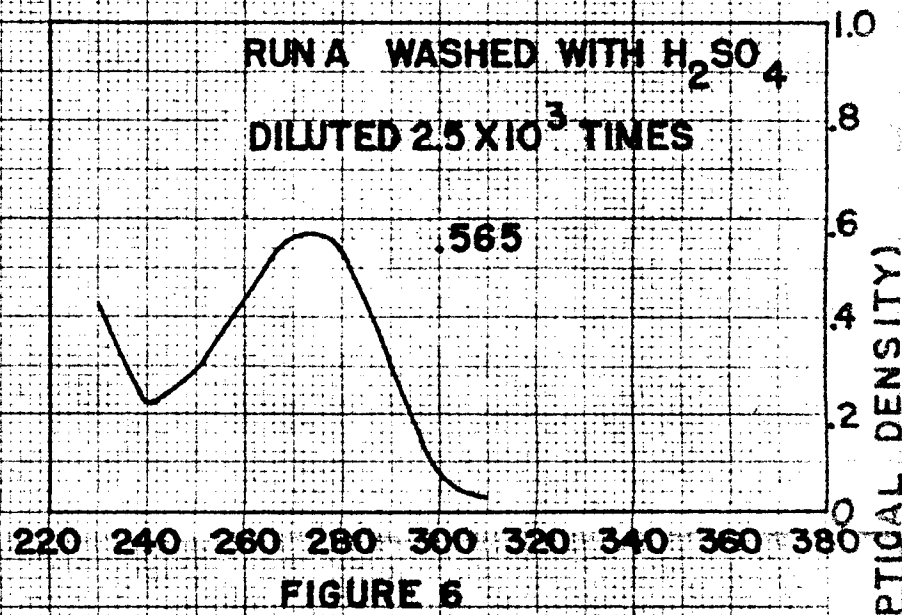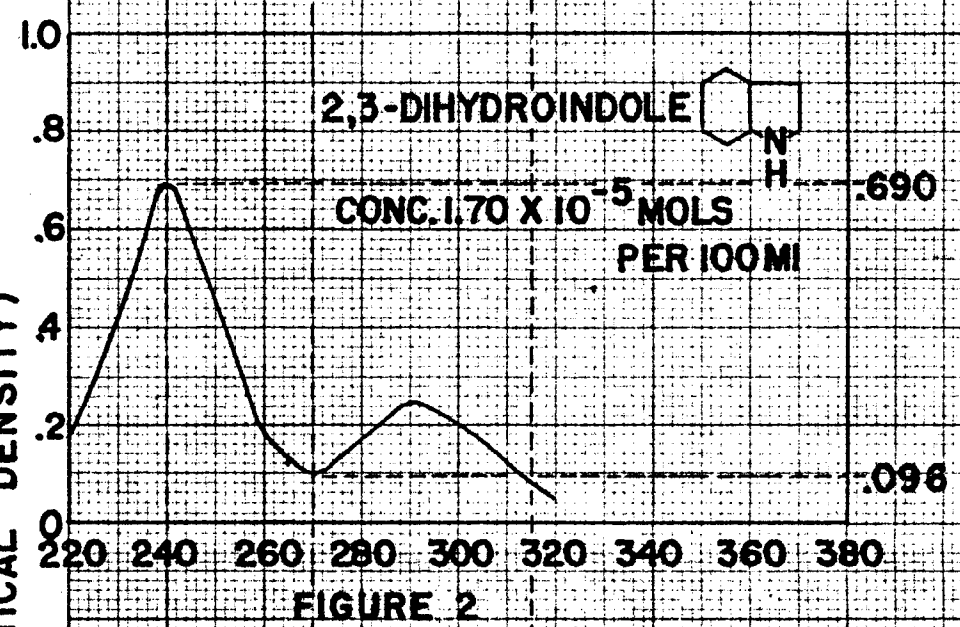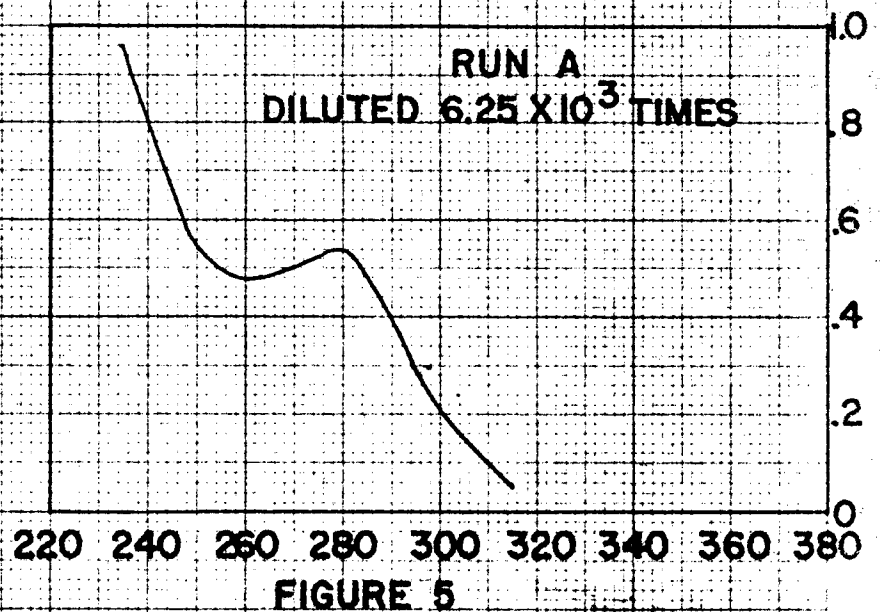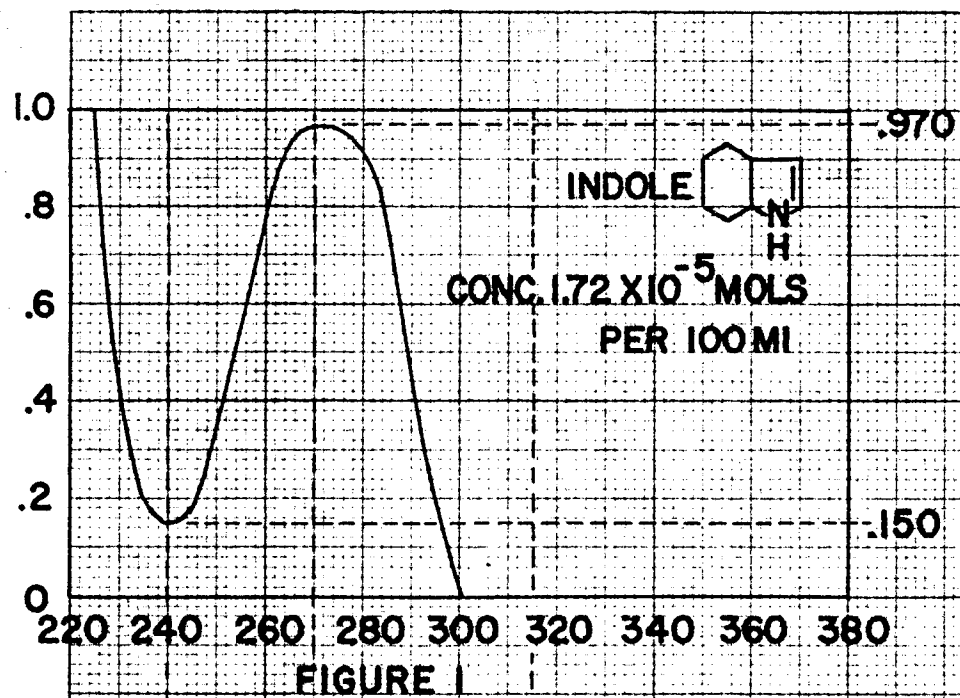0 100 200 300 400 500 600 700 800 900 1000 1100 1200 1300 1400
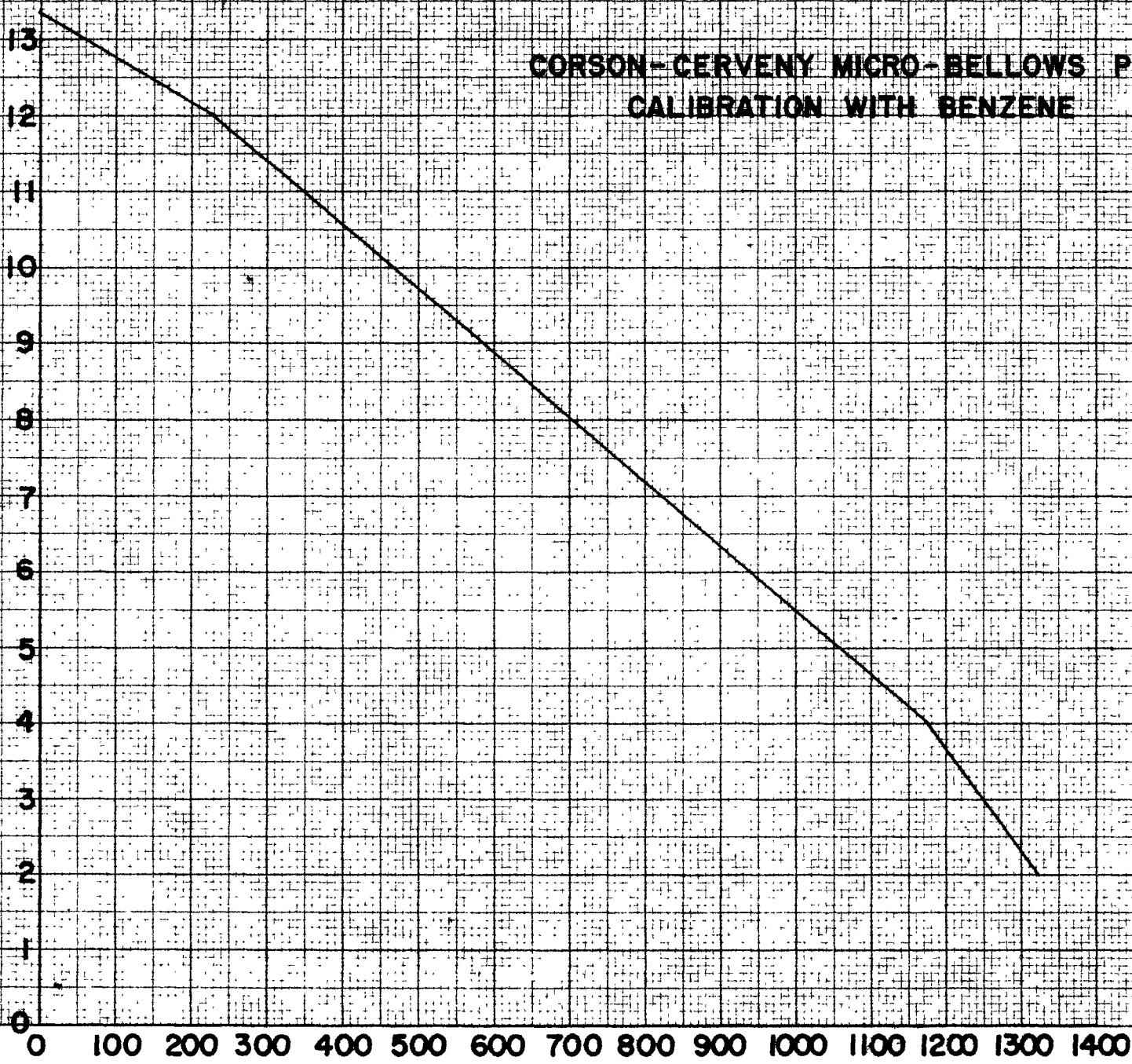
ULTRAVIOLET METHOD OF ANALYSIS

The simplicity of the absorption law (Beer-Bouguer Law) which states that absorbance is linear with concentration, and that absorbances of various components in a mixture are additive, makes this method of analysis particularly adaptable for the type of study undertaken in this paper. For materials that deviate from linearity, it becomes necessary to apply calibration curves of concentration versus absorbance or to apply correction factors. These deviations are usually traceable to interaction between solute molecules or between solvent and solute molecules.

The following relationship is used to analyze for an absorbing component in a mixture of non-absorbing compounds:

$$\frac{O.D..of\ comp.\ in\ mixture}{unknown\ conc.} = \frac{O.D.\ of\ pure\ comp.}{conc.\ of\ pure\ comp.\ used\ to\ obtain\ spectrum}$$

The analysis of two or more mutually interfering components requires the simultaneous solution of an equal number of equations. The method will not be described here, since it requires that all the components of a mixture be known. The nature of the experiments conducted precludes the knowledge of such information to a large degree. Secondly, it is desirable that all the components behave linearly - another condition which is only partly fulfilled. Reference to figures 1-4 will show the spectra of the desired product Indole - together with that of the starting material 0-amino phenylethyl alcohol and also two highly

FIGURE 1 — INDOLE, CONC. 1.72 X 10⁻⁵ MOLS PER 100 MI; .970; .150

FIGURE 2 — 2,3-DIHYDROINDOLE, CONC. 1.70 X 10⁻⁵ MOLS PER 100 MI; .690; .096

FIGURE 3 — ORTHO-AMINOSTYRENE (I) CONC. 2.79 X 10⁻⁵ MOLS PER 100 MI; .800

FIGURE 4 — ORTHO-AMINO-PHENYLETHYL ALCOHOL, CONC. 1.68 X 10⁻⁵ MOLS PER 100 MI; .678; .080

FIGURE 5 — RUN A DILUTED 6.25 X 10³ TIMES

FIGURE 6 — RUN A WASHED WITH H₂SO₄ DILUTED 2.5 X 10³ TIMES; .565

FIGURE 7 — RUN D DILUTED 1.25 X 10⁴ TIMES

FIGURE 8 — RUN D WASHED WITH H₂SO₄ DILUTED 1.25 X 10⁴ TIMES

ABSORBANCE (OPTICAL DENSITY)

WAVELENGTH IN MILLIMICRONS

probable by-products namely, 2,3 dehydroindole and O-amino styrene.

The method of application found most useful and giving results of satisfactory accuracy, was to wash each furnace run with sulfuric acid to eliminate interfering impurities. However, it could not simply be assumed that such a procedure was adequate without some measure of proof. The success of the method can be readily recognized from the brief discussion to follow:

Figure 5 shows the spectrum of experimental run A. Figure 6 shows the same experimental run washed with sulfuric acid. It is clearly observed, that the spectrum of figure 6 is resolved by the acid wash into the characteristic curve of Indole (figure 1). Another run D, is shown in figure 7, and below in figure 8 is shown the same run washed with acid. Here, we have another situation wherein, the acid washed material does not result in a spectrum characteristic of Indole. The material was later isolated and its melting point proved, of course, that it was not Indole. One can readily conclude from these examples, that the latter result could hardly be used as a quantitative means ie., without recourse to simultaneous solution - which again is not applicable as previously noted. The first example, in which the washed material resulted in a spectrum characteristic of Indole, could be used for quantitative results. Following the outline of the exact procedure used, will be given an
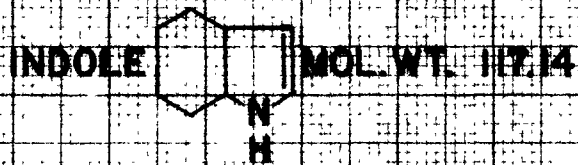
illustration of the entire method of analysis:

PROCEDURE FOR CONDUCTING TEST

1. The solvent used in all solutions subjected to spectroscopic examination was ethyl alcohol (benzene free-pure grade).

2. The wavelength used in preparing the standard curve (figure 9) is 270 millimicrons, which is seen in figure 1 to be that of maximum absorbance.

3. Dilutions of all samples were made to give absorbance readings of from .2 to .9, being the preferred working range for quantitative analysis.

4. Since benzene is used as a diluent, its presence must be eliminated because of the error incurred if allowed to remain. It is to be noted, that this evaporation of benzene is conducted in a test tube in which is placed a 1 ml. sample of the particular run and does not present a serious problem.

5. The washing procedure using 15% sulfuric acid is of course carried on prior to measuring the 1 ml. aliquot three acid washes of equal volume and a single water wash were found to be adequate. Care must be exercised to not allow evaporation of benzene during the washings by keeping the separatory funnel stoppered.

6. The residue from the 1 ml. aliquot on evaporation, has a small amount of ethyl alcohol added to it and the evaporation allowed to procede once again. This measure is to insure the complete removal of benzene.

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The residue thus obtained is then dissolved in ethyl alcohol and made up to 100 ml in a volumetric flask. This solution with one further dilution in most cases, is ready for spectroscopic analysis.

7. The instrument used for all measurements was the Beckman Du Quartz Spectrophotometer.

FIGURE 9

FIGURE 10   FIGURE 11   FIGURE 12

COMPOSITION SHOWN BELOW DILUTED 6.25×10^3 TIMES

SAME COMPOSITION DILUTED 6.25×10^3 TIMES WASHED WITH 5% H_2SO_4

(1) SAME COMPOSITION WASHED WITH 10% H_2SO_4
(2) WASHED WITH 15% H_2SO_4 & CONCENTRATION OF SOLUTION 2.5 TIMES GREATER THAN (1) (2.5×10^3)

.596
.220
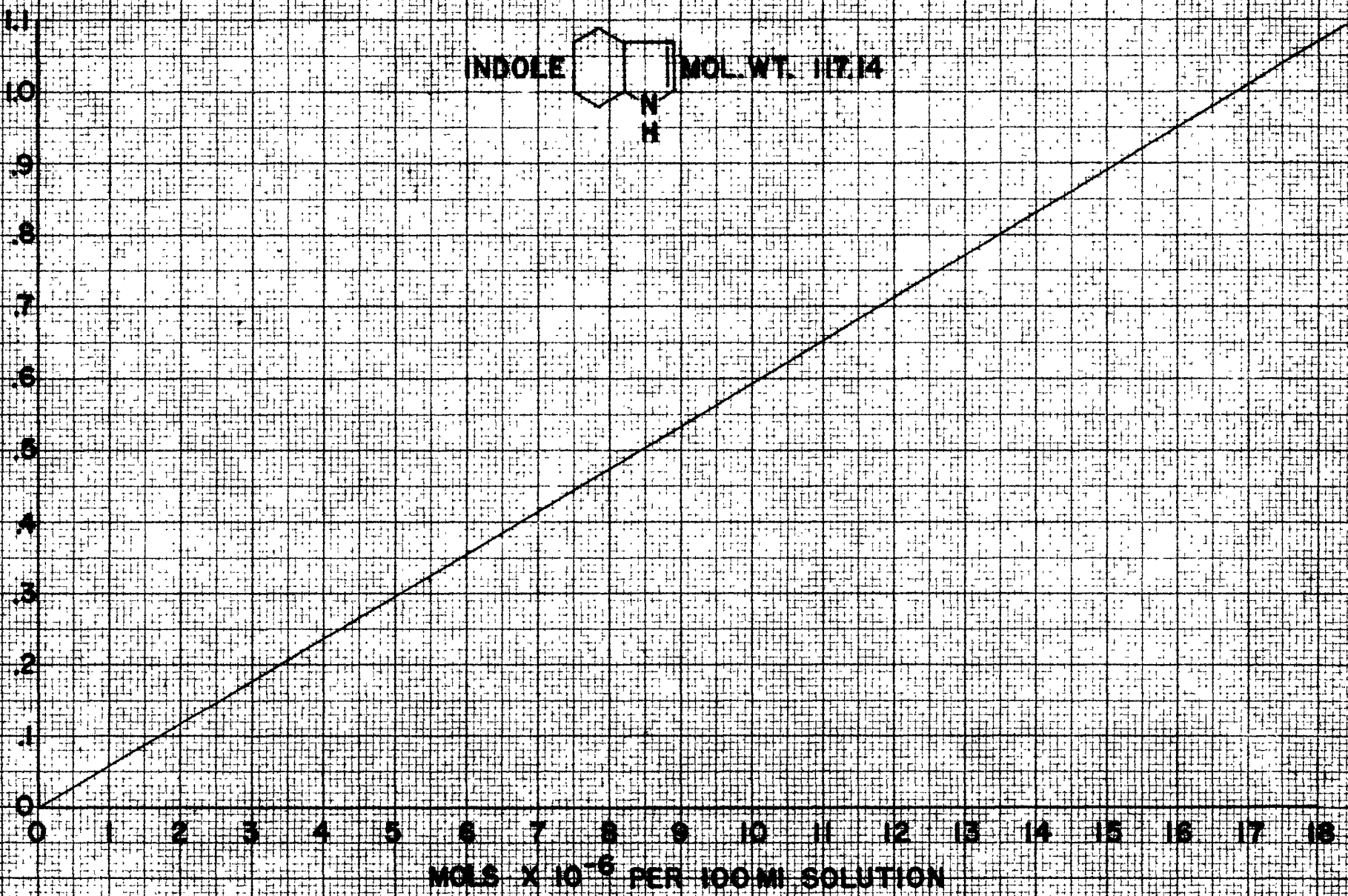
ABSORBANCE (OPTICAL DENSITY)
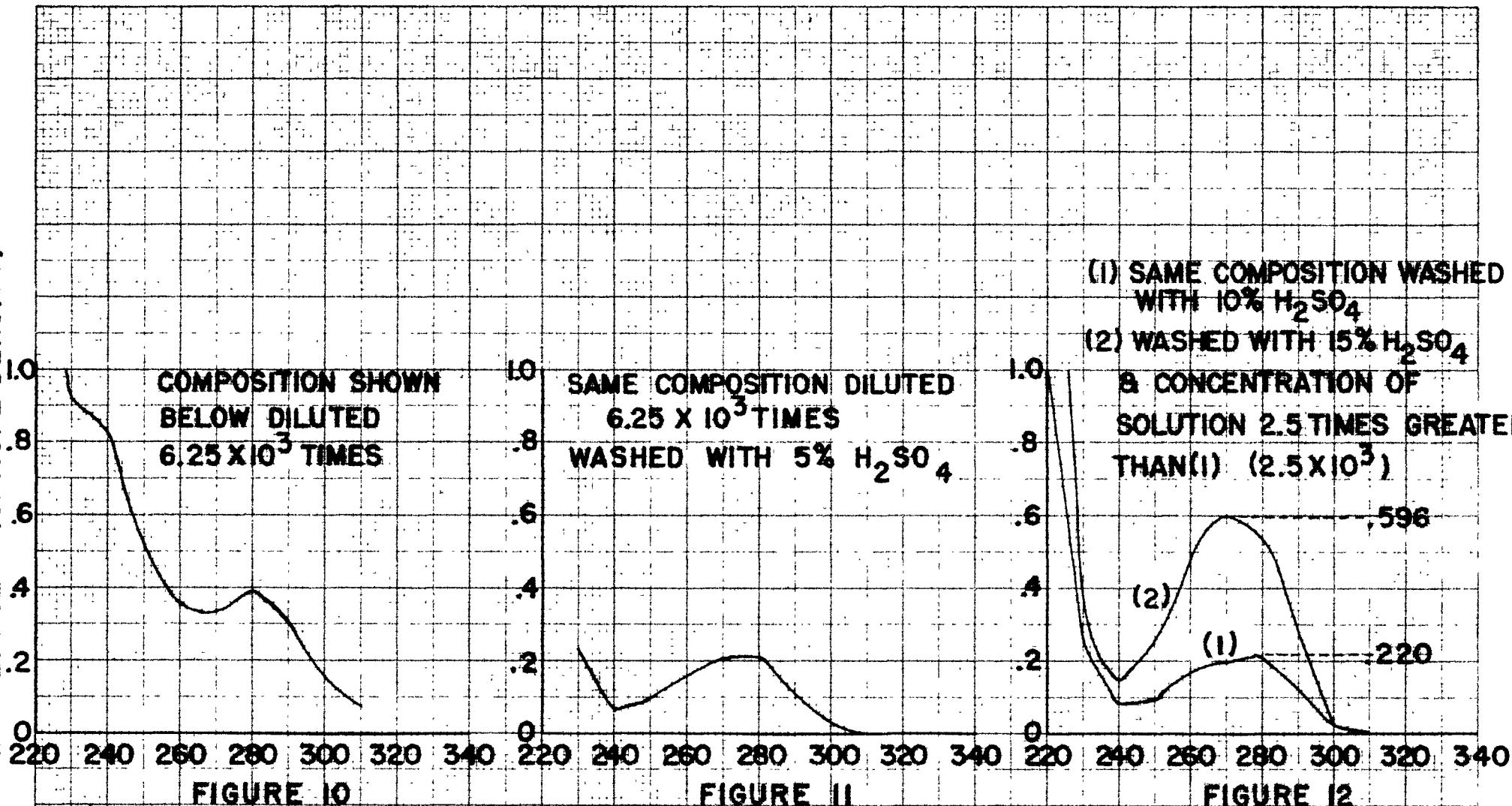
WAVELENGTH IN MILLIMICRONS

INDOLE	6.208×10^{-3} MOLS
ORTHO-AMINO STYRENE	2.709×10^{-3} MOLS
DIHYDROINDOLE	4.358×10^{-3} MOLS
ORTHO-AMINO PHENYLETHYL ALCOHOL	11.363×10^{-3} MOLS

RUN B
DILUTED 125 X 10³ TIMES

—470

220 240 260 280 300 320 340 360 380

FIGURE 13

RUN C
DILUTED 125 X 10² TIMES

—472

220 240 260 280 300 320 340 360 380

FIGURE 14

RUN F
DILUTED 125 X 10² TIMES

—.247

220 240 260 280 300 320 340 360 380

FIGURE 15

RUN H
DILUTED 5.00 X 10² TIMES

—.770

220 240 260 280 300 320 340 360 380

FIGURE 16

RUN I₂
DILUTED 625 X 10² TIMES

—585

220 240 260 280 300 320 340 360 380

FIGURE 17

RUN M
DILUTED 125 X 10⁴ TIMES

—314

220 240 260 280 300 320 340 360 380

FIGURE 18

RUN R
DILUTED 2.5 X 10³ TIMES

—410

220 240 260 280 300 320 340 360 380

FIGURE 19

RUN S
DILUTED 2.5 X 10³ TIMES

—280

220 240 260 280 300 320 340 360 380

FIGURE 20

ABSORBANCE (OPTICAL DENSITY)

ABSORBANCE (OPTICAL DENSITY)

WAVELENGTH IN MILLIMICRONS

<u>ULTRAVIOLET ANALYSIS OF KNOWN MIXTURE</u>

The mixture subjected to the analysis is given below:

Indole - - - - - - - - - - - - - - - - -6.208 x 10^{-3} mols.

O-amino styrene - - - - - - - - - - - 2.709 x 10^{-3} "

2,3 dihydroindole - - - - - - - - - - 4.350 x 10^{-3} "

O-amino phenylethyl alcohol - - - -11.353 x 10^{-3} "

This mixture was dissolved in 125 ml of benzene and approximately 10 ml portions washed with different concentrations of sulfuric acid.

Figure 10 shows the spectrum of the mixture, unwashed with sulfuric acid, but conducted according to the procedure outlined for the test. Figure 11 shows the mixture washed with 5% acid. Figure 12 the spectrum resulting from the mixture being washed with 10% and 15% acid, curves 1 and 2 respectively. 15% sulfuric acid was found to be mo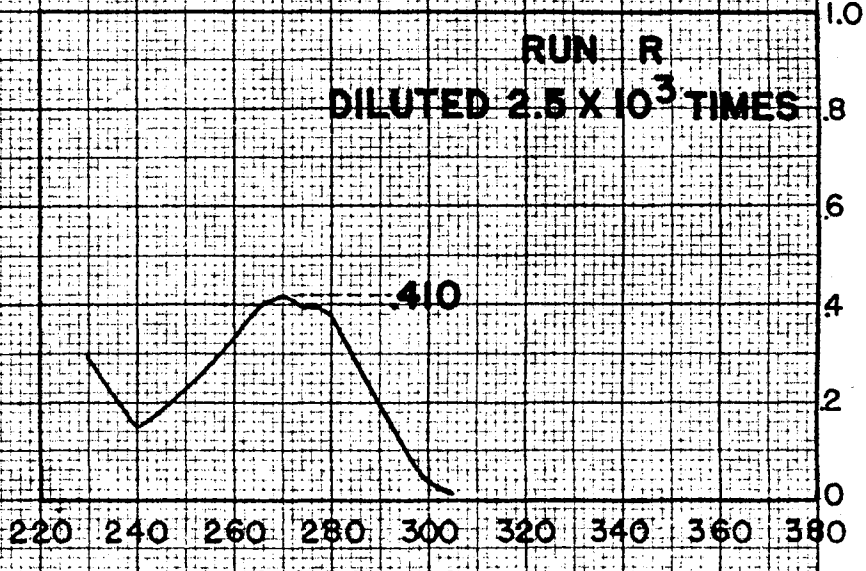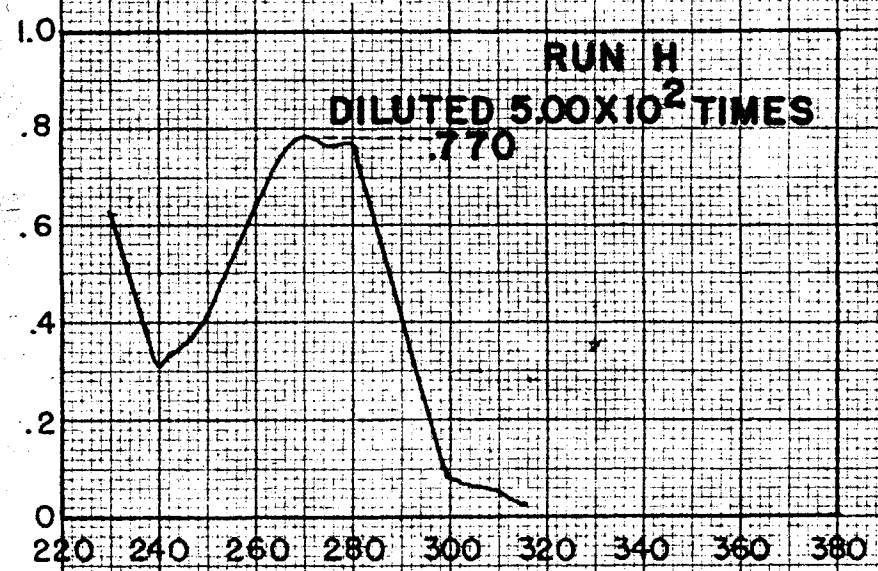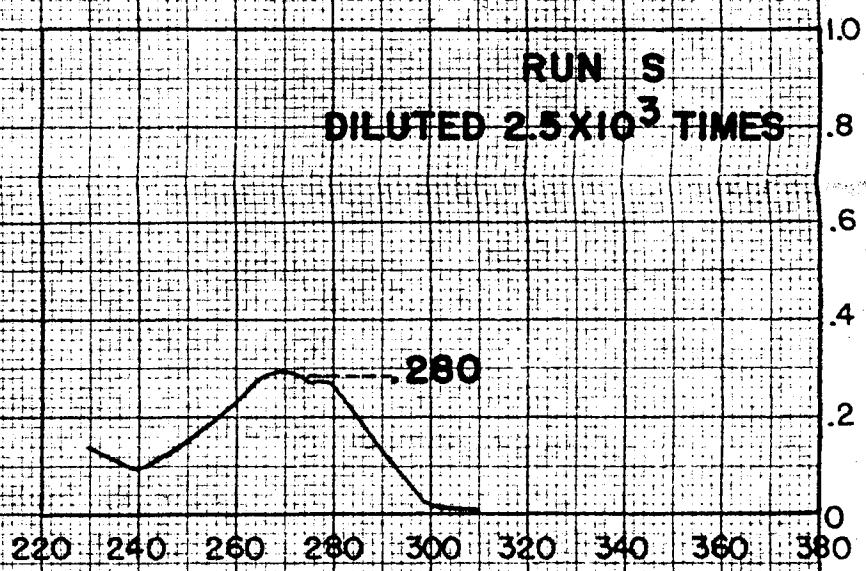st effective, but either the 5% or 10% acid could also have been used. The more important reason in obtaining curve 2 figure 12, was to work with a more concentrated solution having its maximum absorbance in the range of .2 to .9.

<u>CALCULATION OF MOLS OF INDOLE</u>

absorbance (optical density) at 270 Mu = .596

from figure 9, .596 = 10.05 x 10^{-6} mols/100 ml

final dilution 25 ml hence, $\frac{1}{4}$ x 10.05 x 10^{-6} mols/25ml

dilution factor (ie. final dilution subjected to spectroscopic examination) was 2.5 x 10^{3} then:

Indole = $\frac{10.05 \times 10^{-6}}{4}$ x 2.5 x 10^{3} = 6.275 x 10^{-3} mols.

It can be seen from this result, that with reason-
able care, reliable analysis can be obtained.

ULTRAVIOLET SPECTRA DATA (O.D.)

Indole (Fig. 1)		2,3 Dihydro-indole (Fig. 2)		O-amino Styrene (Fig. 3)		O-amino phenyl ethyl alcohol (Fig. 4)	
Mu	O.D.	Mu	O.D.	Mu	O.D.	Mu	O.D.
220	1.540	220	.198	220	2	220	.400
225	1.520	225	.287	230	2	230	.595
230	.410	230	.445	240	2	235	.678
240	.150	240	.690	250	2	240	.625
250	.397	250	.455	260	1.560	245	.466
260	.735	260	.180	265	1.270	250	.287
265	.924	270	.096	270	.780	260	..083
270	.970	280	.168	280	.560	270	.087
280	.928	290	.243	290	.600	280	.140
290	.441	300	.207	300	.700	285	.159
300	0	310	.118	305	.760	290	.155
		320	.006	310	.795	300	.100
				315	.800	310	.038
				320	.760		
				330	.580		
				340	.355		
				350	.175		
				360	.065		

ULTRAVIOLET SPECTRA DATA   (O.D.)

Wavelength Mu	Run A (Fig.5) unwashed	Run A (Fig.6) acid washed	Run D (Fig.7) unwashed	Run D (Fig.8) acid washed
220	1.720	1.800	.792	.500
230	1.020	.430	.610	.335
235	.960	-	.700	.432
240	.806	.222	.742	.520
250	.530	.287	.735	.610
260	.472	.467	.538	.455
268	.500	-	.382	.292
270	.505	.565	.348	.255
280	.540	.560	.235	.120
290	.390	.305	.144	.042
300	.202	.055	.082	.012
310	.100	.025	.050	.004
315	.055	.020	.025	0
320	-	-	.018	-

DATA: OPTICAL DENSITY VS. MOLS x 10^{-6} per 100 ml sol.(Fig. 9)

Standard solution of Indole in ethyl alcohol

.2140 g/100 Ml

Stock solution 1.5 ml of standard solution per 100 ml

solution or:

.00321 g/100 Ml

Dilutions	Conc. G/100 Ml	O.D.	mols x 10^{-6}
1. Stock Sol.	.00321	1.430	27.4
2. 80 Ml stock/100 ml	.00289	1.180	24.7
3. 60 Ml stock/100 ml	.00193	.980	16.5
4. 40 Ml stock/100 ml	.00128	.650	10.9
5. 20 Ml stock/100 ml	.00064	.322	5.5

ULTRAVIOLET SPECTRA OF KNOWN COMPOSITION MIXTURE (O.D.)

Wavelength Mu	Unwashed (Fig. 10)	Washed 5% H_2SO_4 (Fig. 11)	Washed 10% H_2SO_4 (Fig. 12 (1))	Washed 15% H_2SO_4 (Fig.12) (2)
220	1.620	1.080	1.08	2
230	.920	.235	.257	.352
235	.918	.119	.120	.184
37	.898	.097	.107	.162
240	.836	.078	.082	.151
250	.518	.097	.090	.255
260	.353	.163	.164	.476
265	.336	.193	.193	.563
270	.333	.204	.208	.596
275	.354	.205	.202	.578
280	.390	.210	.208	.586
290	.307	.120	.125	.296
300	.147	.020	.022	.017
310	.078	.007	.010	0
315	.057	.004	.010	0
320	-	-	-	-
330	-	-	-	-
340	-	-	-	-

ULTRAVIOLET SPECTRA DATA   (O.D.)

Mu	Run B (Fig. 13)	Run C (Fig. 14)	Run F (Fig. 15)	Run H (Fig. 16)
220	1.80	1.66	1.70	1.900
230	.334	.582	.405	.630
235	.205	.428	.355	.460
237	.192	.391	.337	.341
240	.178	.260	.200	.314
250	.248	.302	.246	.404
260	.396	.402	.244	.642
265	.454	.446	.245	.742
270	.470	.472	.247	.770
275	.468	.470	.245	.765
280	.470	.480	.243	.764
290	.262	.312	.202	.416
300	.055	.132	.134	.078
310	.025	.066	.076	.042
315	.017	.050	.060	.035

ULTRAVIOLET SPECTRA DATA   (C.D.)

Wavelength Mu	Run I (Fig. 17)	Run M (Fig. 18)	Run R (Fig. 19)	Run S (Fig. 20)
220	1.85	1.45	1.78	1.37
230	.418	.205	.298	.173
235	.273	-	-	-
237	.253	-	-	-
240	.240	.110	.148	.090
250	.320	.162	.208	.142
260	.498	.252	.337	.221
265	.570	.300	.388	.265
270	.585	.314	.410	.280
275	.584	.301	.395	.272
280	.582	.306	.395	.274
290	.330	.155	.198	.137
300	.085	.025	.025	.018
310	.037	.022	.015	.012
315	.028	.016	.010	.008

EXPERIMENTAL: HIGH TEMPERATURE - FURNACE RUNS

The data assembled on the following page gives all the necessary starting materials and conditions of the individual runs through the high temperature apparatus shown on page 23. The optical densities, on which the final calculations were based, were all obtained from complete spectra data. The actual data is assembled in tables on pages 31 to 36. The curves representing this data are shown in figures 1 - 20. A brief description of the experimental procedure follows:

The starting material, dissolved in benzene, is placed into a graduated cylinder into which is also placed the tube connected to the suction side of the Corson pump. The catalyst is placed in the center reactor tube and properly activated as described in the preparation of the catalyst. The Corson pump is then started and the reactants delivered to the catalyst tube, noting the temperature and duration of run (the pump must be primed). After the run is completed, 25 ml of benzene is added to the cylinder and fed in as before, in order to drive out any entrapped vapors. The final volume is brought to 125 ml and washed with 15% H_2SO_4, followed by water. 1 ml of the washed run is evaporated in a test tube and the analysis conducted as previously described on page 27.
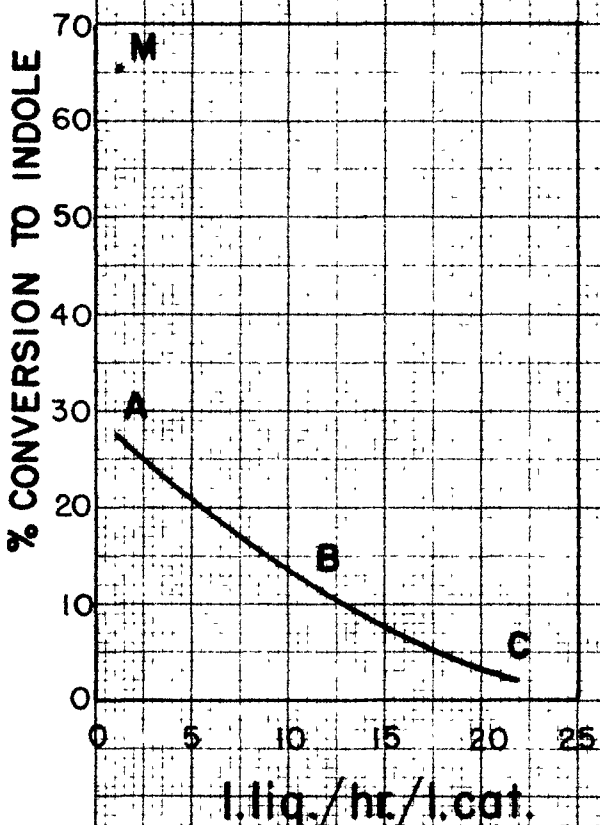
EXPERIMENTAL DATA AND RESULTS

VARIABLE INVESTIGATED	EXPERIMENTAL RUN	STARTING MATERIAL		CONCENTRATION OF STARTING MATERIAL IN BENZENE DILUENT		CATALYST (VOL.33MI-.033L)		CORSON-CERVENY MICRO BELLOW PUMP		SPACE VELO-CITY	VARITRAN				OPTICAL DENSITY	VOLUME OF SOLUTION ANALYZED [+]	% CONVERSION TO INDOLE
		O-AMINO PHENYL ETHYL ALCOHOL	2,3 DIHYDROINDOLE	GRAMS PER 100 MI	MOLS PER 100 MI	Cu-ZNO-Bi_2O_3	NICKEL ON KIESELGUHR	SETTINGS (TURNS ON ADJUSTING NUT)	FEED RATE MI/HR	l.liq/hr/l.cat.	SETTING	REACTION ZONE TEMPERATURE °C	FINAL VOLUME OF EXPERIMENTAL RUN – INCLUDES 25 MI FROM FURNACE – BENZENE USED AS CHASER	DILUTION FACTOR OF SOLUTION SUBMITTED TO SPECTROSCOPIC ANALYSIS			
CONTACT TIME	A	X		3.00	2.187×10^{-2}	X		13	75	2.27	63	415	125	2.5×10^3	.565	25	27.1
CONTACT TIME	B	X		3.00	2.187×10^{-2}	X		10	435	13.20	63	415	125	1.5×10^3	.470	25	11.3
CONTACT TIME	C	X		3.00	2.187×10^{-2}	X		7	775	23.50	63	415	125	1.25×10^2	.472	50	2.3
TEMPERATURE	D	X		3.00	2.187×10^{-2}	X		13	75	2.27	90	550	125	1.25×10^4	.255	25	SEE RUN D CALCULATIONS
TEMPERATURE	E[*]	X		3.00	2.187×10^{-2}	X		13	75	2.27	63	415	125	2.5×10^3	.565	25	27.1
TEMPERATURE	F	X		3.00	2.187×10^{-2}	X		13	75	2.27	36	260	125	1.25×10^2	.247	50	1.2
CONCENTRATION	G[*]	X		3.00	2.187×10^{-2}	X		13	75	2.27	63	415	125	2.5×10^3	.565	25	27.1
CONCENTRATION	H	X		2.25	1.640×10^{-2}	X		13	75	2.27	63	415	125	5.00×10^2	.770	50	19.8
CONCENTRATION	I	X		1.50	1.093×10^{-2}	X		13	75	2.27	63	415	125	6.25×10^2	.585	25	14.2
STARTING MATERIAL	M		X	3.0054	2.522×10^{-2}	X		13	75	2.27	63	415	125	1.25×10^4	.314	25	65.6
CATALYST	R		X	3.0317	2.544×10^{-2}		X	13	75	2.27	63	415	125	2.5×10^3	.410	25	16.9
CATALYST	S	X		3.0886	2.252×10^{-2}		X	13	75	2.27	63	415	125	2.5×10^3	.280	25	13.2

[*] IDENTICAL WITH A

[+] FIGURE 9 BASED ON MOLS PER 100 MI SOLUTION

EXPERIMENTAL RESULTS

FIGURE 21

% CONVERSION TO INDOLE

l.liq./hc/l.cat.

FIGURE 22

TEMPERATURE °C

FIGURE 23

% CONVERSION TO INDOLE

STARTING MATERIAL IN BENZENE
DILUENT MOLS X 10^{-2} PER 100ML
SOLUTION
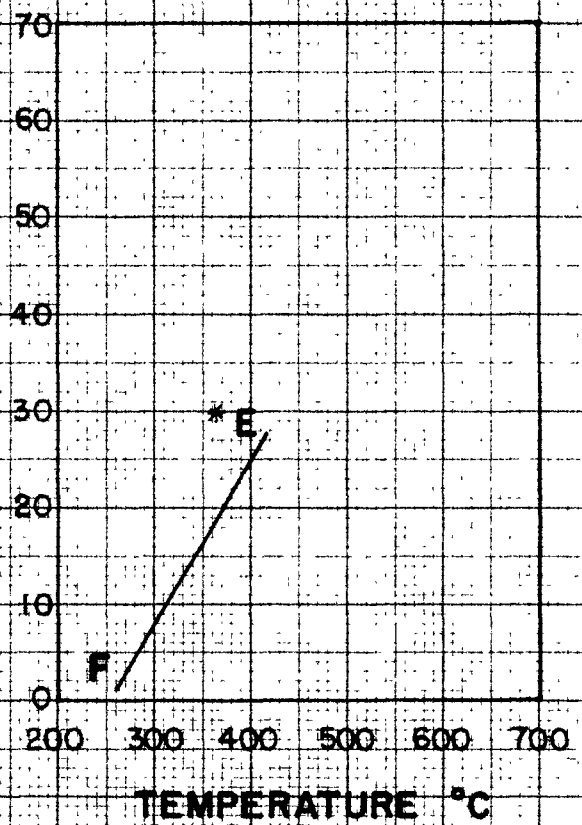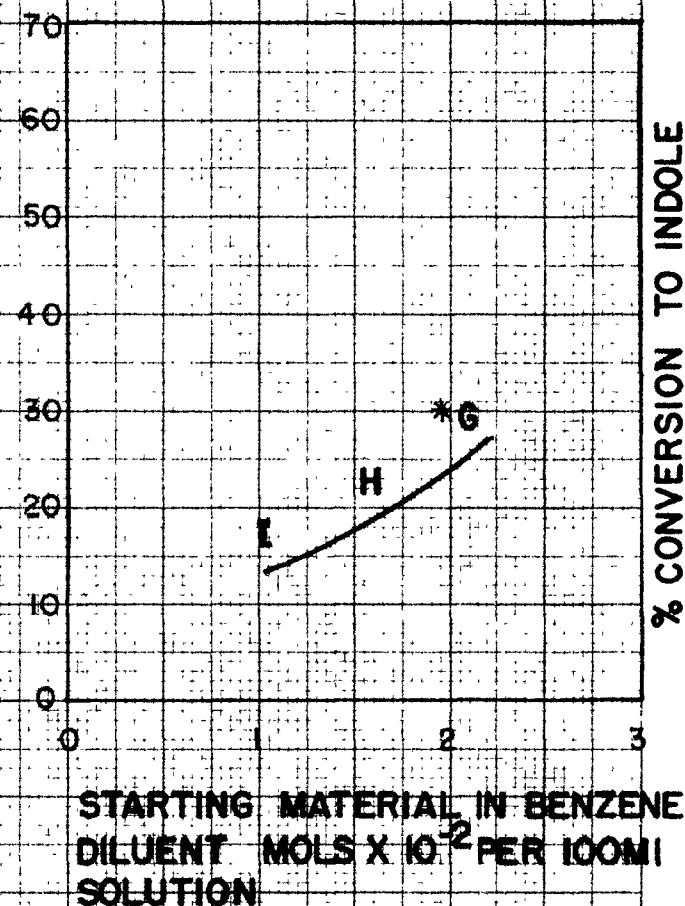
*E & G IDENTICAL WITH A
M, CONDITIONS IDENTICAL WITH A EXCEPT 2,3 DIHYDROINDOLE
USED AS STARTING MATERIAL

CALCULATIONS

<u>RUN A:</u>

O.D. .565 = 9.5 x 10^{-6} Mols./100 ml sol. (from Fig. 9)

Final measurement made on 25 ml sample.

Hence: $\dfrac{9.5}{4}$ x 10^{-6} = 2.375 x 10^{-6} mols/25 ml

Multiplying by dilution factor

$(2.375 \times 10^{-6})(2.5 \times 10^{3}) = 5.94 \times 10^{-3}$ mols

PERCENT CONVERSION:

$$\dfrac{5.94 \times 10^{-3}}{2.187 \times 10^{-2}} \times 100 = 27.1\%$$

<u>RUN B:</u>

O.D. .470 = 7.9 x 10^{-6} mols/100 ml sol.

Final measurement made on 25 ml sample.

Hence: $\dfrac{7.9}{4}$ x 10^{-6} = 1.975 x 10^{-6} mols/25 ml sol.

Multiplying by dilution factor

$(1.975 \times 10^{-6})(1.25 \times 10^{3}) = 2.47 \times 10^{-3}$ mols

PERCENT CONVERSION:

$$\dfrac{2.47 \times 10^{-3}}{2.187 \times 10^{-2}} \times 100 = 11.3\%$$

<u>RUN C:</u>

O.D. .472 = 8.0 x 10^{-6} mols/100 ml sol.

Final measurement made on 50 ml sample.

Hence: $\dfrac{8.0}{2}$ x 10^{-6} = 4.0 x 10^{-6} mols/50 ml sol.

Multiplying by dilution factor

$(4.0 \times 10^{-6})(1.25 \times 10^{2}) = 5.0 \times 10^{-4}$ mols

PERCENT CONVERSION:

$$\dfrac{5.0 \times 10^{-4}}{2.187 \times 10^{-2}} \times 100 = 2.3\%$$

CALCULATIONS RUN D

In this run, where the furnace temperature was 550°C, the principle material formed was not Indole. This can be readily seen by referring to figure 8 in which appears the spectrum of the acid washed material. In this instance, the characteristic Indole curve did not result as was the case with all the other runs. Figure 7 shows run D prior to acid washing. The material formed in this run was isolated and showed a melting point of 67.5 to 69°C and upon crystallizing from Methanol 69.5°C. The identity of this material was not established.

The procedure used to isolate the compound was briefly as follows:

A known volume of the benzene solution was washed with 15% H_2SO_4, as discussed in the method of analysis. The benzene is then evaporated, leaving a residue which should be crude indole and soluble in hot heptane. However, it was necessary to use methanol as a solvent for this residue - it is to be noted that indole recrystallizes very nicely from heptane. The heated methanol solution was treated with a small amount of darco and filtered. The crystallized product gave the melting range of 67.5 to 69°C and upon recrystallizing had a melting point of 69.5°C as was previously cited.

CALCULATIONS

RUN F:

$$O.D. \quad .247 = 4.2 \times 10^{-6} \text{ mols/100 ml sol.}$$

Final measurement made on 50 ml sample.

Hence: $\dfrac{4.2}{2} \times 10^{-6} = 2.1 \times 10^{-6}$ mols/50 ml sol.

Multiplying by dilution factor

$$(2.1 \times 10^{-6})\ (1.25 \times 10^{2}) = 2.63 \times 10^{-4} \text{ mols}$$

PERCENT CONVERSION:

$$\dfrac{2.63 \times 10^{-4}}{2.187 \times 10^{-2}} \times 100 = 1.2\%$$

RUN H:

$$O.D. \quad .770 = 13.0 \times 10^{-6} \text{ mols/100 ml sol.}$$

Final measurement made on 50 ml sample.

Hence: $\dfrac{13.0}{2} \times 10^{-6} = 6.5 \times 10^{-6}$ mols/50 ml sol.

Multiplying by dilution factor

$$(6.5 \times 10^{-6})\ (5.00 \times 10^{2}) = 32.5 \times 10^{-4} \text{ mols}$$

PERCENT CONVERSION:

$$\dfrac{32.5 \times 10^{-4}}{1.64 \times 10^{-2}} \times 100 = 19.8\%$$

RUN I:

$$O.D. \quad .585 = 9.9 \times 10^{-6} \text{ mols/100 ml sol.}$$

Final measurement made on 25 ml sample.

Hence: $\dfrac{9.9}{4} \times 10^{-6} = 2.475 \times 10^{-6}$ mols/25 ml sol.

Multiplying by dilution factor

$$(2.475 \times 10^{-6})\ (6.25 \times 10^{2}) = 15.45 \times 10^{-4} \text{ mols}$$

PERCENT CONVERSION:

$$\dfrac{15.45 \times 10^{-4}}{1.093 \times 10^{-2}} \times 100 = 14.15\%$$

CALCULATIONS

RUN M:

$$O.D. \ .314 = 5.3 \times 10^{-6} \text{ mols/100 ml. sol.}$$

Final measurement made on 25 ml sample.

Hence: $\dfrac{5.3 \times 10^{-6}}{4} = 1.325 \times 10^{-6} \text{ mols/25 ml sol}$

Multiplying by dilution factor

$$(1.325 \times 10^{-6})(1.25 \times 10^{4}) = 1.66 \times 10^{-2} \text{ mols}$$

PERCENT CONVERSION:

$$\dfrac{1.66 \times 10^{-2}}{2.522 \times 10^{-2}} \times 100 = 65.6\%$$

RUN R:

$$O.D. \ .410 = 6.9 \times 10^{-6} \text{ mols per 100 ml sol}$$

Final measurement made on 25 ml sample.

Hence: $\dfrac{6.9 \times 10^{-6}}{4} = 1.725 \times 10^{-6} \text{ mols/25 ml sol}$

Multiplying by dilution factor

$$(1.725 \times 10^{-6})(2.5 \times 10^{3}) = 4.31 \times 10^{-3} \text{ mols}$$

PERCENT CONVERSION:

$$\dfrac{4.31 \times 10^{-3}}{2.544 \times 10^{-2}} \times 100 = 16.9\%$$

RUN S:

$$O.D. \ .280 = 4.75 \times 10^{-6} \text{ molsper 100 ml sol}$$

Final measurement made on 25 ml sample.

Hence: $\dfrac{4.75}{4} \times 10^{-6} = 1.187 \text{ mols/25 ml sol}$

Multiplying by dilution factor

$$(1.187 \times 10^{-6})(2.5 \times 10^{3}) = 2.97 \times 10^{-3} \text{ mols}$$

PERCENT CONVERSION:

$$\dfrac{2.97 \times 10^{-3}}{2.252 \times 10^{-2}} \times 100 = 13.2\%$$

CONCLUSIONS

1. The important intermediate 2,3 dihydroindole can easily be prepared from the starting material O-amino phenyl-ethyl alcohol. Although the yield obtained was only 27.1% in the experiment conducted in this paper, the reference cited claimed almost "quantitative results". This compound could also be synthesized using $ZNcl_2$ as the dehydrating agent (see example 2 page 17) and possibly aluminum chloride.

2. Yields of Indole are much higher when starting with 2,3 dihydroindole than with O-amino phenylethyl alcohol - ie., the catalyst performs only a dehydrogen-ation.

3. The CU-ZNO-Bi_2O_3 catalyst is more effective than the Ni on Kieselguhr.

4. Although optimum conditions were not obtained, higher concentrations of starting material, higher temperatures (to 415^{o}C), and relatively long contact periods tend to favor the reaction. Note: At 550^{o}C Indole was not formed but a product having a melting point of ca. 69^{o}.

5. Benzene seems to be a suitable solvent for the reactant material as far as hydrogen acceptance is concerned. However, while 2,3 dihydroindole is very soluble; O-amino phenylethyl alcohol is only soluble to the extent of approximately 4 g per 100 ml benzene.

6. Ultraviolet analysis offers a very sensitive and accurate means of evaluation.

APPENDIX

An experiment in which 0-chloro aniline was reacted with ethylene oxide, under the same conditions used with aniline (see page 3), resulted in no conversion to the corresponding amino alcohol. This is undoubtedly due to the reduction in basicity of the amino group when ortho to chlorine.

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