# UNIVERSITY OF CINCINNATI

May 18 1934

*I hereby recommend that the thesis prepared under my supervision by* Gordon Coleson Harrold

*entitled* I Attempt to prepare 2-fluorene-phenyl-nitromethane. II Preparation of α naphthyl-diazomethane.

*be accepted as fulfilling this part of the requirements for the degree of* Doctor of Philosophy

*Approved by:*

Francis E Ray

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Form 668—G. S. and Ed.—1M—7-31

# I. ATTEMPTS TO PREPARE 2-FLUORENE-PHENYL-NITRO-METHANE.

# II. PREPARATION OF α NAPHTHYL-PHENYL-DIAZO-METHANE.

A dissertation submitted to the

Graduate School
of the University of Cincinnati

in partial fulfillment

of the

requirements for the degree of

DOCTOR OF PHILOSOPHY

1934

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# ACKNOWLEDGMENT

The author wishes to express his sincere appreciation for the invaluable aid and kindly encouragement rendered during the course of this investigation by Dr. F. E. Ray, at whose suggestion and under whose direction this research was undertaken.

## HISTORICAL

The discovery of isomerism may be taken as the achievement responsible for the development of our structure theory. It is certain that the attempt to form graphic and spatial pictures of the various compounds was directly due to the various kinds of isomerisms. Pasteur, in 1861, laid the foundations of stereo chemistry by his work on tartaric acid. Pasteur(1)stated that the phenomena of optical activity was due to the arrangement of atoms in right and left hand spirals, or at the corners of a tetrahedron. He emphasized the fact that the one configuration was the non-superimposable mirror image of the other, owing to the absence of some symmetry properties in their arrangements, or as he expressed it, the existence of a certain dis-symmetry. He explained that it was the special geometrical properties of the molecules as wholes that were the determining properties. Wislicensus(2) and Kekule(3)also proposed to explain some cases of optical activity by means of a tetrahedral spatial model.

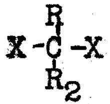
Van't Hoff(4) and LeBel(5) accounted for the isomerism of optically active compounds and geometric isomers by means of explanations based on spatial tetrahedral models which have proved to hold true in every case investigated up to comparatively recent times. They showed that the isomerism could be explained on the basis of four different radicals attached to one carbon atom. If these radicals were arranged around the carbon atom, not in one plane, but in various different planes, it was shown that two modifications could be had for every asymmetric carbon atom. These two modifications are not identical as they cannot be superimposed. Van't Hoff described the phenomena by placing the carbon atom at the center and the radicals at the corners of a tetrahedral figure.

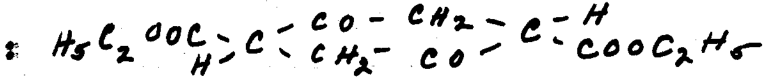
It was shown by LeBel(6) in the case of forty derivatives of active amyl compounds that should any two of the radicals be the same, then the asymmetry of the molecule is destroyed and no optical activity exists.

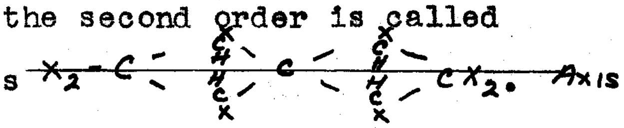
We are not limited, however, to an asymmetric carbon atom as our test for asymmetry. LeBel was correct in stating that when we have an asymmetric carbon atom, we can have optical activity, and that such asymmetry is destroyed when we do not have four different groups attached to the carbon atom. We may nevertheless have asymmetric carbon atoms and no optical activity, as discussed later under second order axis symmetry.

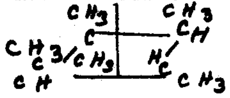
So it is, that later developments have shown Pasteur's thesis; that optical activity is due to the dissymmetry of the molecule as a whole rather than to any special circumstance, is the only tenable universal hypothesis. While Van't Hoff and LeBel performed valuable service in developing the special case of the asymmetric carbon atom, there is no question but that the asymmetric carbon atom is only a special manifestation of a larger phenomena.

There are several possibilities. With one asymmetric carbon atom we may have an equal mixture of the two optical antipodes. Thus, the resultant mixture is inactive. If we have more than one asymmetric atom, we have the possibility of internal compensation, that is, two asymmetric carbon atoms with equal and opposite rotations in the same molecule. It is also possible to have asymmetry with or without optical activity in those cases characterized as psuedo asymmetric. That is, those cases where we have three or more carbon atoms in odd numbers, with the ends identical. The central carbon atom appears symmetrical because of the identical group on each end. If these end groups are arranged in reverse orders the view from the central carbon will be unsymmetrical.

In those cases where we have a plane or point of symmetry we never have optical activity. We may have either a vertical or a horizontal plane cutting a molecule in two reflection parts. Thus  $X-\overset{R}{\underset{R_2}{C}}-X$ can be cut by a plane so that reflection images identically the same may be formed.

In the case of a point of symmetry we may have a compound such as :  $\begin{matrix}H_5C_2OOC\\H\end{matrix}>C<\begin{matrix}CO-CH_2\\CH_2-CO\end{matrix}>C<\begin{matrix}H\\COOC_2H_5\end{matrix}$ , which has a center of symmetry, i.e. a line drawn from any group through the center of the molecule will intersect an identical group on the opposite side. No activity results in this case.

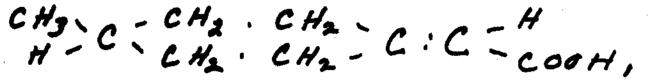
With axes of symmetry, however, we may or may not have optical activity. When a compound is axially symmetrical, no free rotation about the axis can give two enantiomorphous forms which coincide. This form of symmetry is called that of the first order, and is not sufficient to render the compound inactive. The axis of the second order is called a mirror axis. A good example is 

When we have an alternating axis of symmetry, we have an axis of the second order, or better still a mirror axis. In this case we may have asymmetry but no activity. Should we rotate any chosen group through 90°, we will find a similar group occupying the exact spot where the mirror image of the chosen group would appear to be. It must be here noted that we may have asymmetric carbon atoms with no activity. For example, we have the compound 

with asymmetric carbon atoms, yet no optical activity has been found.

The question then arises as to whether we would have optical activity if we had a compound with three different groups attached to a carbon atom; one with a double bond and the other two with single bonds. It was pointed out by Van't Hoff(7) that allylene derivatives of the type:- $\begin{matrix}R_1\\R_2\end{matrix}{>}C{:}C{:}C{<}\begin{matrix}R_3\\R_4\end{matrix}$ could exist in enantimorphous forms. For if $R_1$ and $R_2$ lie in one plane the groups $R_3$ and $R_4$ lie in another plane. It appears as though we have no asymmetric carbon atom, but this appearance is false if we accept Marsh's(8) definition of an asymmetric carbon atom. He defines an asymmetric carbon atom as one which, when replaced in a space formula by its mirror image, gives rise to a space formula different from the original one. This is essentially what Pasteur(1) stated in more general terms, i.e. the asymmetry of the molecule as a whole.

As a matter of fact, a cyclic modification,

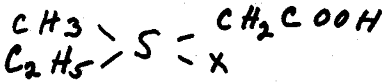


$$\begin{matrix} CH_3 \\ H \end{matrix} > C < \begin{matrix} CH_2 \cdot CH_2 \\ CH_2 \cdot CH_2 \end{matrix} > C : C < \begin{matrix} H \\ COOH, \end{matrix}$$

of the allylene type of asymmetry was prepared by Pope and Perkin(9) and resolved by Perkin, Pope and Wallach(10).

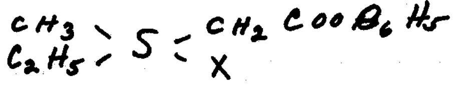
When we consider the ethylene series, we are limited by the classical considerations to cases wherein no asymmetric carbon atom exists, and since the atoms of carbon lie in the same plane no asymmetry exists and hence we have no optical activity. Geometrical isomerism is exhibited if we have different groups, R and R' on the two carbon atoms. Various attempts (11) (12) to show that the groups arrange themselves at the corners of a tetrahedron instead of on one plane failed, thus tentatively proving that all atoms lie in the same plane.

We have, however, other evidence in the work on the quadrivalent sulphur compounds. Pope and Peachy(13) resolved the camphor-sulphonate and bromo-camphor sulphonate of methyl-ethyl thetine,



$$\begin{matrix} CH_3 \\ C_2H_5 \end{matrix} > S < \begin{matrix} CH_2COOH \\ X \end{matrix}$$

and Smiles(14) resolves the same salt of phenyl ester of methyl-ethyl-thetine,



$$\begin{matrix} CH_3 \\ C_2H_5 \end{matrix} > S < \begin{matrix} CH_2COOC_6H_5 \\ X \end{matrix}$$

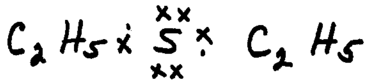
These compounds and analagous selenium compounds retained activity when in the form of camphor sulphonate, picrates, and chloro-platinates. Therefore, they all had an ionized linking and the authors above mentioned, showed that activities did not disappear when these compounds were ionized. This would seem to show that the groups $R_1$, $R_2$ and $R_3$, occupying three points of the tetrahedron can retain their positions even though the fourth point is occupied only by an electrical charge.

Kenyon and Philips(15), et al, resolved the sulphinic esters $O=S{<}^{OR}_{C_6H_4CH_3}$, $O=S{<}^{OR}_{C_6H_4C_2H_5}$, unsymmetrical sulphoxide(16), $O=S\,\underline{-CH_3}\;C_6H_4COOH$ and the sulphilamines(17) $C_7H_7\cdot SO_2\cdot N \longleftrightarrow S{<}^{CH_3}_{C_6H_4COOH}$; all of these latter compounds owe their activity to three groups around the sulphur atom along with an electrical charge. This is also true of selenium compounds which were found to be optically active. Now this asymmetry is impossible according to classical theory if we write the formula ${}^{R_1}_{R}{>}S=O$, for we will find the three groups in one plane and will have super-imposable mirror images. Since optical activity is present we must have some difference in the oxygen to sulphur linkage. This means that the fourth place in the tetrahedral model is occupied, not by a radical, but by an electrical charge, that is, the positive charge is localized on the central atom so that the formula may be represented as ${}^{R'}_{R}{>}S^{+}-\bar{O}$. This representation does not violate any of the conventions, and fully represents the fact that we have non-superimposable mirror images. Before going on to further developments it may be profitable to trace the electronic conceptions which are used to explain the linking of those types of compounds which have a double bond and which still exhibit optical activity.

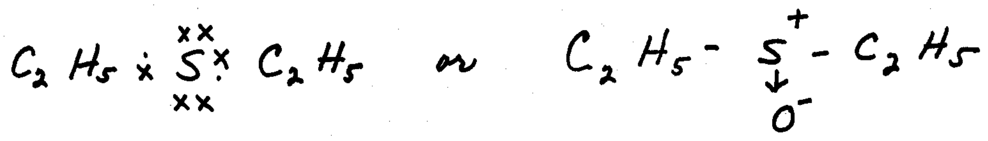
G.N. Lewis(18) assumed that the cause of chemical combination is the tendency of electrons to form stable arrangements such as exist in the inert gases. His advance consisted mainly in suggesting that two electrons could be shared between two atoms so that they could count toward the stability of both of the atoms. If we assume such sharing we can explain non-ionized linkages by the Lewis theory. Kossel(19) explained that elements with too many electrons for stability could completely give up the excess to atoms that had too few, and thus give an electrically neutral molecule. Lewis explained "co-valency" or the non-ionizable linkages while Kossel's work explained "Electro valency" or ionizable linkages.

The first of these two types of linkages, co-valent (or shared electron) linkage, can arise in two ways: (1) one electron is contributed by each atom. This is normal co-valence in which the co-valence is limited in number by the periodic group of the atom. (2) Both electrons are contributed by the same atom. In this, coordinate valence, the valencies are not dependent on the periodic group to which the atom belongs. We also have a combination of these two which is called a semi-polar linkage in which the elements are united by both a co-valent link and a polar link. With this type of semi-polar linkage we have a polar compound, as is shown by dipole moment and parachor measurements. The linkage is polar in the sense that a physicist uses the word polar, i.e. having an unbalanced electric charge even though no ions are formed.

Examples of these linkages may be taken from the sulphur compounds since they were mentioned previously. Thus, sulphur can only form two normal co-valences as in the compound diethyl sulfide $(C_2H_5)_2S$ , because these co-valences give sulphur the full valency group of eight; i.e.,



$C_2H_5 \overset{\cdot}{\times} \overset{\times\times}{\underset{\times\times}{S}} \overset{\times}{\cdot} C_2H_5$ , since sulphur itself has six valence electrons. Now the crosses in the illustration, sometimes called lone pairs, can form co-valences of the second kind by sharing these pairs with atoms of oxygen which need two electrons to make a stable octet; i.e.,



$$C_2H_5 \overset{\cdot}{\times} \overset{\times\times}{\underset{\times\times}{S}} \overset{\times}{\cdot} C_2H_5 \quad \text{or} \quad C_2H_5 - \underset{\overset{\downarrow}{O^-}}{\overset{+}{S}} - C_2H_5$$

These coordinated links enable the sulphur atom to increase its co-valency from two to four.

These examples show that we have two criteria of stability; I. The nuclear charge on the atom must be satisfied. This can be done in two ways; (a) Each free electron balances one nuclear charge. (b) Each pair of shared electrons balances one nuclear charge.

II. An octet of electrons about an atom gives a stable configuration. Each shared or unshared electron contributes equally toward this octet.

In the example given the link between the sulphur and oxygen is a semi-polar double bond. We have the sulphur contributing one of its lone pairs of electrons to the oxygen atom which has only six electrons and which by accepting two from the sulphur forms a stable octet about the oxygen. The sulphur, however, gains one positive charge for the oxygen accepted. Thus we have a co-valence, arising in the second way and called a coordinate link and a polar bond between the oxygen and sulphur. This makes for the greatest stability as the sulphur atom has also completed its octet.

As mentioned before we have three co-valent sulphur in $\begin{matrix} R1 \diagdown \\ R2 - \end{matrix} \overset{+}{S} - \overset{-}{O}$ and it was postulated that divalent carbon could be regarded as three co-valent with a structure C X in which the carbon is the acceptor and not the donor. If the aliphatic nitro salt has the following formula; $\left.\begin{matrix} R_1 \diagdown \\ R_2 \diagup \end{matrix} C^{-} \rightleftharpoons N^{+} \begin{matrix} = O \\ \diagdown\, {}^{-}O \end{matrix}\right]^{-} Na^{+}$ , with a semi-polar double bond between the carbon and the nitrogen the compound should be asymmetrical. This may also be written; $\left.\begin{matrix} R' - \\ R_2 - \end{matrix} \underset{-}{C} : \underset{+}{N} \begin{matrix} = O \\ \diagdown\, O \end{matrix}\right]^{-} Na^{+}$

A similar structure would be needed to explain any optical activity in the diazo compounds; i.e., $\begin{matrix} R1 \diagdown \\ R2 \diagup \end{matrix} C \rightleftharpoons N \equiv N$. The formula $\begin{matrix} R_1 \\ R_2 \end{matrix} \underset{\cdot\cdot}{C} : N : : : N$ being needed to explain the activity due to a semi-polar link between the carbon and nitrogen.

As has been pointed out by Fry(20) many chemists do not care to use the electronic terminology in its present state of confusion, preferring to use simply the + and - notation. This confusion was largely caused by G.N. Lewis's(21) interpretation of the physicists terms polar and non-polar. His lists of typical polar compounds include both typical electro-valent compounds such as potassium chloride, and co-valent compounds such as the alcohols. His non-polar materials, though all are co-valent, some are non-polar as the parafins or benzene; i.e., they have no dipole moment; and others, as chloroform, are polar according to the physical meaning. Inasmuch as a tremendous literature is being built up using the electronic terminology the explanations were included in that language even though it may seem cumbersome at the present time.

## GENERAL PURPOSE OF INVESTIGATION

Our task has been to collect evidence concerning the aliphatic nitro compounds and the aliphatic diazo compounds which would lead to some conclusion concerning the structures of these compounds.

Part A is concerned with attempts to prepare an optically active aci-nitro compound.

Part B is concerned with the preparation of the a-naphthol phenyl diazo methane, with the view of ascertaining whether or not there is optical activity in an aliphatic diazo compound.

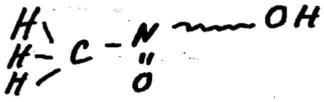
## PART A

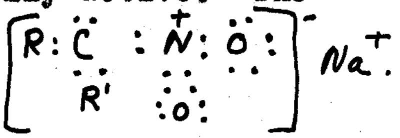
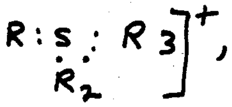
## HISTORICAL INTRODUCTION TO THE NITRO COMPOUNDS

The aliphatic nitro compounds were first prepared by V. Meyer(22) in 1872. His method of treating an alkyl halide with silver nitrite was found(23) to give an acidic radical. He assumed the structure to be $R \underset{M}{C} H\ NO_2$, where M = metal. A. Michael(24) showed that the metallic derivative of the nitro compounds was attached to an oxygen atom as $CH_2 = \underset{O}{N}-O-Na$. Neff (25) (26) showed that these derivatives could be regarded as salts of the hypothetical acid $CH_2 = \underset{O}{N}-O-H$.

Holleman(27), Hantzsch and Schultze(28), and Konowalow(29), proved this view to be correct by isolating the isomeric derivatives. Thus phenyl nitro methane was isolated in both its isomeric forms, generally represented by $C_6H_5\ CH_2NO_2$ for the stable neutral form and $C_6H_5\ CH = \underset{O}{N}-OH$ for the labile form.

Hantzsch(30), who called the labile compound the aci-form of the nitro compound, proved its structure by means of conductivity experiments. The gradual loss of conductivity of the aci-form showed the equilibrum existing between the true nitro compound and its labile isomer.

Baudisch(31) indicated that the greater activity of the aci-form was due to the different linkings between the nitrogen and the Oh group; i.e.,  $\begin{array}{l}H\diagdown \\ H-C-\underset{\underset{O}{\|}}{N}\sim OH \\ H\diagup\end{array}$ in alkaline solution.

The next important development was made by Kuhn and Albrecht(32) when they converted an optically active solution of 2-nitro butane into the solution of the salts of the aci form which were also optically active. The results were explained by the formula  This form is much like the sulfonium ion , previously described.

Shriner and Young(33) similarly prepared solutions of the optically active salts of 2-nitro octane. This work did not decide the question of the constitution of the aci-form, as the work was done in solution and no pure compounds isolated so that impurities might be responsible for the observed rotations.

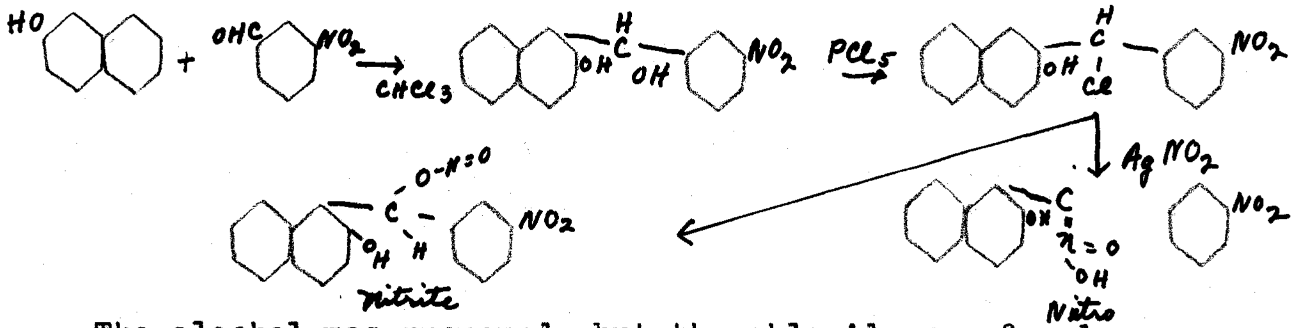
Shriner and Parker(34) prepared an optically active cyclo 2-nitro-4-methyl hexanone, but could not decide whether the activity was due to the carbom in the 2 or the 4 position.

While Shriner and Young started with optically active materials, Mills and Cole(35), recently reported that they had succeeded in resolving phenyl-cyannitro-methane, $C_6H_5CH(CN)NO_2$, by means of the brucine salt, into its optical antimers. The sodium salt gave a strongly active solution but lost this activity on the addition of excess mineral acid.

## DISCUSSION OF THE WORK ON NITRO COMPOUNDS

Since previous work had been done in solution and no compound isolated, and since optically active materials were used to begin with, it was clear that the resolution from an inactive aci-nitro compound would prove the existence of a semi-polar bond between carbon and nitrogen.

It was proposed that we start with the preparation of beta-naphthol-meta-nitro-benzal alcohol; then substitute a chlorine atom for the hydroxyl group, and subsequently by the use of silver nitrite prepare the nitro compound which in turn was to be resolved.



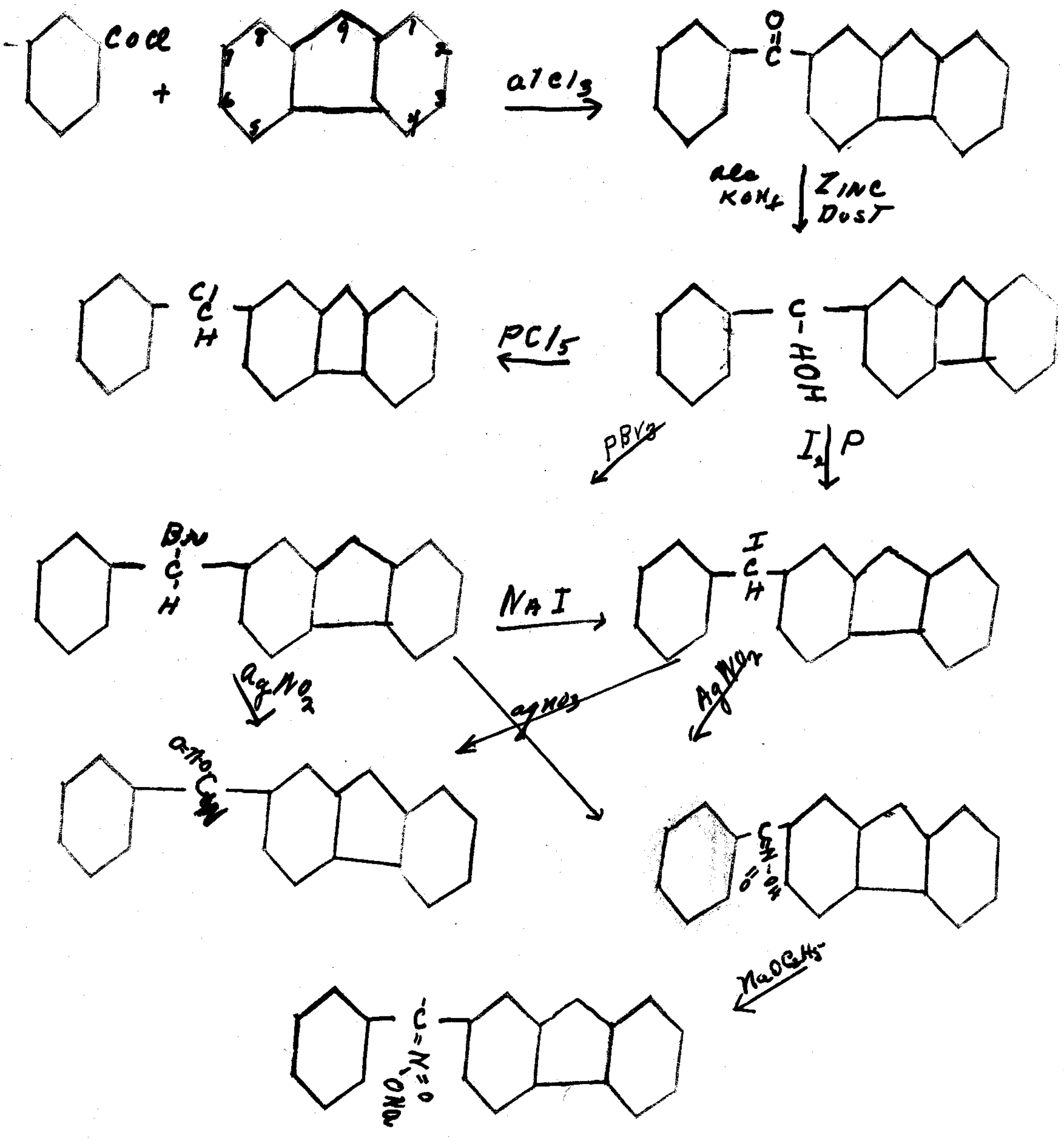
The alcohol was prepared, but the chloride was found to be decomposed into the m-nitro-benzal chloride when chlorination was attempted. While the methylation of the naphtholic group might have prevented this decomposition, it was decided that the fluorene group would be more useful.

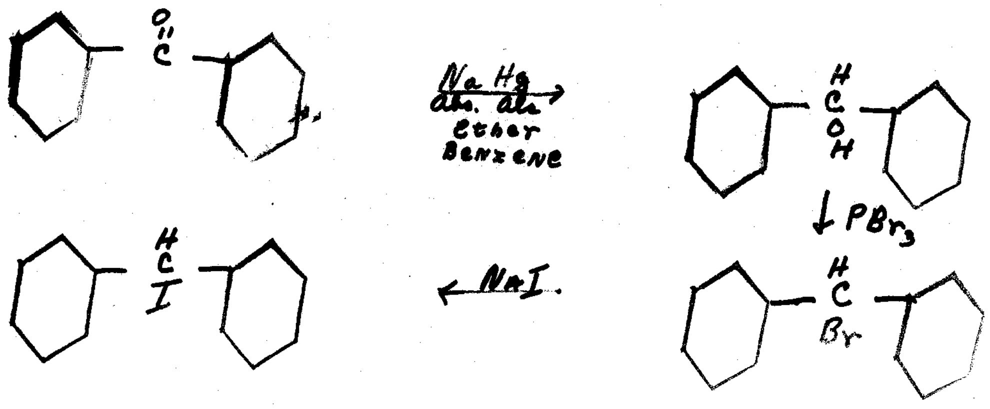
2-Fluorene-phenyl-ketone was prepared by the Friedel Crafts synthesis. The ketone was reduced to 2-fluorene-phenyl-carbinol. This secondary alcohol had not been previously prepared.

The alcohol was next converted to the chloride by phosphorous penta chloride, but the chloride was found to be unsuited to the formation of the nitro compounds because it was unreactive towards silver nitrite. We converted the alcohol to the bromide by the use of phosphorous tribromide. We attempted the preparation of the nitro compound. However, the reaction did not take place readily in the cold, and on heating decomposition took place. This was the experience of Holleman(36) in working on similar compoumds. The analysis of the material produced showed that we obtained only 18% of the nitro and nitrite compounds together. It was impossible to isolate the pure nitro compound from material containing such a small percentage. Therefore it was decided that we prepare the iodide, since Hantzsch(37) had found that better yields were obtained through the use of iodides.

It was found that the best method of preparation was that in which the dry 2-fluorene-phenyl-bromo-methane was treated with anhydrous sodium iodide in a non-oxidizing medium. Even under these conditions the iodide was found to be present in less than seventy percent. The preparation of the nitro compound using iodide in solution gave a mixture of materials which contained only a trace of the nitro compound. While the problem was solvable it was not feasible, due to the time which might be required and the research was abandoned inasmuch as large quantities of

## CHART OF REACTIONS IN PART A





nitro compound would be needed in order to attempt resolution of the unstable form.

In order to provide checks on the V. Meyer method for our type of compound, we prepared from benzophenone the bromide and the iodide. The iodide was found too unstable for use; in the presence of traces of air or moisture decomposition took place quite rapidly.

## CONCLUSIONS

It has been shown that the best method of preparing the iodides is that in which all moisture and oxidizing influences were removed. While this method was not refined it gives promise of being successful, in which case preparation of the nitro compounds under anhydrous conditions should be possible. The following new compounds were prepared:

1. 2-Fluorene-phenyl-carbinol.
2. 2-Fluorene-phenyl-chloro-methane.
3. 2-Fluorene-phenyl-bromo-methane.
4. 2-Fluorene-phenyl-iodo-methane.

The diphenyl-iodo-methane was prepared as a solid. The only reference in the literature states that a liquid thought to be the iodide compound was prepared.

## EXPERIMENTAL WORK ON NITRO COMPOUNDS

### A. PREPARATION OF β-NAPHTHOL-META-NITRO-BENZAL ALCOHOL

Commercial B-naphthol was recrystallized by means of hot alcohol. Mp. 121°C. Six and one-tenth grams of meta nitro benzaldehyde was condensed with 5.8 grams of B-naphthol in 300 c.c. chloroform for one hour and forty minutes.

It was filtered through a hot water filter and the chloroform was distilled off leaving a solid condensation product. The material formed was soluble in alcohol. Yield 80% - Mp. 91°C.

Some material was prepared using petroleum ether as a solvent. The yields were very poor in this case.

### B. CHLORINATION OF B-NAPHTHOL-m-NITRO PHENYL CARBINOL

Phosphorous Pentachloride was used as a chlorinating agent with ether as a solvent. Ten per cent. excess phosphorous pentachloride was used.

Twenty nine and seven-tenths grams of B-naphthol-m-nitro phenyl carbinol with 22.5 grams phosphorous pentachloride in 500 c.c. ether were heated over a water bath and stirred continuously for four hours. Yield 15 grams of product or 50% of theory after the ether was distilled off. Mp. 57-63°C.

#### 1. Analysis of compound.

The compound was analyzed for chlorine by The Parr bomb method. Used $Na_2O_2$ of fifteen times the weight of sample; dissolved residue in $HNO_3$(dil.) and precipitated as AgCl with $AgNO_3$.

Anal.Subs. (a).5000g. : AgCl, .6793g.
(b).5000g. : AgCl, .6782g.
(c).8000g. : AgCl,1.1523g.
(d).5000g. : AgCl, .6770g.

Calc'd. for $C_{17}H_{12}O_3NCl$; (a) Cl, 11.3 Found:(a) 33.6
(b) 33.58
(c) 35.
(d) 33.2

Theoretical Possibilities

I 

34.41% Cl M.P. 65°C.

II 

21.84% Cl M.P. 56°C.

It was concluded that chlorination produced decomposition leading to the formation of m-nitro-benzal chloride, I. The methylation of the nap~~t~~holic group might have prevented this decomposition. However, this compound was not useful in furthering this research and was abandoned.

## II.A. 2-FLUORENE-PHENYL-KETONE

1. Crude fluorene was recrystallized from glacial acetic acid after boiling for half an hour with bone black and filtering through a hot water funnel.

Proportions:

100 grams Fluorene
250 c.c. Glacial acetic
20 grams bone black

M.P. of material 106-112°C.

This brown product was then recrystallized from hot ethyl alcohol. Yield 70 grams = 70%. M.P. 114°C.

2. The Friedel Grafts reaction was followed in making the ketone. Attachment was to the 2 position of the fluorene as Fortner(38)(39)(40) showed.

Fifty-five grams of recrystallized fluorene was placed in a liter R.B. Flask with three necks. Attached to the flask was a mercury seal stirrer, dropping funnel, and a reflux condenser with tubing leading outside to remove hydrogen chloride fumes. 350 c.c. of anhydrous carbon bisulfide and 49 grams of anhydrous aluminum chloride were quickly added and 50-75 c.c. of carbon bisulfide used to wash the flask.

This prevents the air from oxidizing and moistening the aluminum chloride.

Thirty nine c.c. of commercial benzoyl chloride was placed in the dropping funnel with about 80 c.c. of carbon bisulfide acting as a dilutent. (Benzoyl chloride does not need to be freshly distilled; the undistilled gave about the same results.

The material was stirred for about ten minutes after which time the benzoyl chloride was added drop by drop. If one was careful about the addition of the benzoyl chloride no cooling was needed. Care must be taken however that no excess unreacted benzoyl chloride accumulates in the reaction flask. The reaction was controlled by observing the heat evolved and testing the gas from the reflux condenser with ammonium hydroxide.

After all the benzoyl chloride has been added, the mixture was refluxed for about four hours on a water bath. The mixture was then cooled and poured into a beaker of cracked ice containing 10-20 c.c. of hydrochloric acid to change any unconverted aluminum chloride. Heat was generated in large quantities in this process. The solid reddish brown mass was placed, along with the liquid, in a steam distillation flask and carbon bisulfide removed. The solid was drained free of water and dried. The brown porous mass was recrystallized from alcohol. Mp. 122°C. The yields averaged 61.5% based on the fluorene used and the recrystallized product obtained, melting at 122°-124°C. Fortner(38) gave 122°C. for the 2-fluorene phenyl ketone.

This average yield includes several runs using petroleum ether as a solvent. This solvent gave very poor yields under all conditions tried. For the method as given using carbon disulphide the yields averaged 73% including the original trial runs which were not as good as the latter when the yields often went up to 85%.

## B. PREPARATION OF 2-FLUORENE-PHENYL-CARBINOL

Various quantities of reagents were tried in reducing the above mentioned ketone to the corresponding secondary alcohol by means of zinc dust and alcoholic KOH. The best yields were obtained from the process described below.

1. One hundred and ten grams of ketone was dissolved in 1000 c.c. of alcohol and 40 grams of a concentrated aqueous solution of potassium hydroxide was added. Then from 200 to 250 grams of zinc dust was placed in the flask and the materials refluxed for seven or eight hours. Mild refluxing is recommended. After this the hot alcoholic solution was decanted from the zinc, filtered, and poured into a small quantity of water. This liquid was then treated with water until the solid white alcohol precipitated out.

The mother liquor on addition of more water gave another quantity of alcohol purer than the first crop. This was recrystallized from ethyl alcohol and dried;

the method gave 80-90% yields of a product melting at 116°C.

As this compound was not described in the literature, an analysis was necessary.

Using the regular combustion method for carbon and hydrogen the following results were obtained:

Anal. Calc'd for $C_{20}H_{16}O$: C, 88.24; H, 5.88.
Found: C, 87.24; H, 5.82
87.08; 5.99
87.54; 5.97
87.60; 5.91
87.68; 5.90

Molecular weight determined by the freezing point method using benzene as a solvent gave an average value of 264. Mol. wt. Calc'd: 272. Found: 263. Found: 265. M.P. 116°C. (uncorr.) M.P. of ketone 124.5°C. The compound was found to be very soluble in alcohol, ether, benzene, chloroform, and less soluble in methyl alcohol. It was only slightly soluble in water.

### II C. PREPARATION OF FLUORENE-PHENYL-CHLOR-METHANE

A small quantity of chloride was prepared by the use of phosphorous pentachloride in ether solution. The compound precipitated from the solution in a fairly pure state. M.P. 78°C. Yield 80%.

It was found however, that the chlorides were not suitable for use in making the nitro compounds with silver nitrite because the chlorine was too firmly held to permit reaction to take place in the cold and on heating the nitro compound decomposed.(27)

## D. PREPARATION OF THE 2-FLUORENE-PHENYL-BROMO-METHANE

Twenty-seven grams of the previously prepared alcohol, 10% excess phosphorous tribromide, and 200 c.c. of ether were stirred vigorously for half an hour. During this time the bromide precipitated out as it is sparingly soluble in ether. After about two hours the reaction was complete. Better results were obtained by adding phosphorous tribromide drop by drop, over a period of one hour. Yield 78%. Both of the above mentioned compounds were very soluble in acetone and chloroform but less though appreciably soluble in ether, benzene, and alcohol. M.P. 84.5C.

Analysis of the 2-fluorene-phenyl-bromo-methane by means of the Parr bomb and Pringsheim's(41) method.

Anal. Calc'd for $C_{20}H_{15}Br$: Br, 23.85.
Found: Br, 23.7.
" Br, 23.68
" Br, 23.5
" Br, 23.72

The molecular weight was found using benzene as a solvent and determining the lowering of the freezing point.

Mol. Wt. Calc'd: 335. Found 328.
" 325.

## E. PREPARATION OF 2-FLUORENE-PHENYL-NITRO METHANE

Victor Meyer's(22) method was followed in this preparation. Three and four-tenths grams of 2-fluorene-phenyl-bromo-methane was dissolved in about 20 c.c. of benzene. Then 2.0 grams of silver nitrite (freshly prepared by the method described below) was added and the material put away in a closed vessel.

The silver nitrite was prepared by allowing a saturated solution of potassium nitrite to react with a warm solution of silver nitrate. The yellow silver nitrite rapidly crystallized and was washed with distilled water.

With the above procedure and proportions a series of reactions were carried out with the conditions varying in one respect or another, i.e.:

1. Reacted in the cold for two weeks.
2. Reacted over a water bath at 60°C for ten hours.
3. Reacted at the boiling point of benzene for eight hours.

When the temperature was raised it was found that decomposition took place, as evidenced by the color (reddish brown) and the odor of the fumes coming off. This was the experience of Holleman(42) in working on similar compounds.

Reactions were also run in the cold with larger quantities of silver nitrite added. Excesses were added ranging from 25% to 1000%, in an effort to send the reaction nearer to completion.

Another series of reactions were run in which catalysts were used under varied conditions. Platinous Bromide and platinic bromide were used, as was platinum metal, aluminum and zinc. No one of these materials under lowering or raising of the temperature, increased the reaction enough to be noted in the product. The volume of solvent used seemed to have little effect on the reaction.

The best product obtained from any of the reactions was gummy and not distincly crystalline. This was obtained by filtering off the benzeneliquid from the silver bromide and evaporating the benzene at room temperature.

The material was treated with sodium hydroxide to get the sodium salt of the aci-form, but the sodium hydroxide did not react with this compound. Potassium hydroxide was tried but separation of the nitro and nitrite forms could not be effected with this reagent as the potassium salt evidently did not form. When sodium methylate was used complete solubility was obtained in some cases and partial solubility in others. This however, could be shown to be the case when absolute alcohol was used, so that we did not necessarily have the sodium salt of the aci-form. In a few trials some aci-form was obtained, as was shown by the fact that on eliminating the methyl alcohol and dissolving the solids in water, some of the solid did dissolve and on treatment with acid gave an oily material which floated on the surface of the water.

The gummy material which was collected was analyzed for nitrogen by the Dumas method. A nickel tube was used in conjunction with an electric furnace; instead of the glass tube, gas fired equipment. Carbon dioxide was generated by the action of CP hydrochloric acid on boiled marble chips. The samples analyzed were made by the action of silver nitrite on the 2-fluorene-phenyl-bromo-methane. They included both the nitrite and nitro compound, since no separation had been effected.

(a) Anal. subs., .4000g. $N_2$, 3 c.c. Bar. (uncorr.)749 m.m.
Temp. (corr.) 27°C.

(b) Anal. Subs., .4000g. $N_2$, .8 cc Bar. 748 m.m.
Temp. 28°C.

(c) Anal. Subs., .4000g. $N_2$, 2.7 c.c. Bar. 748 m.m.
Temp. 27°C.

Calc'd for $C_{20}H_{15}O_2N$: N, 4.65. Found: (a) N, .87.
(b) N, .23.
(c) N, .77.

Since it was impossible to prepare the nitro and nitrite mixture in any pure condition; the above analysis would indicate a mixture containing only 18.7% of nitro and nitrite compound together; it was decided that attempts should be made to prepare the 2-fluorene-phenyl-iodo-methane, inasmuch as better yields of nitro compounds had been obtained by other investigators(37) when using the iodide compounds in place of chlorides or bromides.

This yield must be the best possible since the method yields a larger percentage of the nitrite compound than it does of the nitro form.

## F. PREPARATION OF 2-FLUORENE-PHENYL-IODO-METHANE

The methods used in attempting to prepare 2-fluorene, phenyl iodo-methane were divided into three classes:

1. Methods using phosphorous, both red and yellow in various solvents and under various conditions, with iodine and fluorene-phenyl-carbinol.
2. Methods in which sodium iodide was used with a solvent, in order to replace the bromine in 2-fluorene-phenyl-bromo-methane by iodine.

3. Methods in which sodium iodide was used to replace the bromine in the fluorene phenyl bromo-methane, under such conditions the water was excluded from the reaction.

F.
1. (a) RED PHOSPHOROUS REAGENT

Six grams of iodine, 15 grams of red phosphorous and ten grams of 2-fluorene-phenyl-carbinol were mixed with 50 c.c. of ether. The mixture was heated for two hours and then allowed to stand over night. The ether solution was then filtered to remove the phosphorous compound and the excess phosphorous, and the filtrate was treated with sodium thiosulfate in water solution to remove the excess iodine. The solutions were separated and the ether solution dried with calcium chloride (Anhydrous) to remove the moisture. The dried ether was filtered from the calcium chloride and evaporated at room temperature. The resultant compound was a yellow, gummy solid which could not be made to crystallize from ether, ether and petroleum ether, alcohol, alcohol and water, benzene, chloroform or acetone. The melting point was about 90° to 95°C. with decomposition.

The yellow substance was very soluble in chloroform, acetone, ethyl acetate, ether, and benzene. It was slightly soluble in methyl alcohol, and methyl alcohol and water. No difference in solubility in hot solution was noted so purification by this method was not feasible.

F.
1. (b)

The same proportions of materials were used, and the procedure was identical except that the reaction proceeded six hours instead of two hours. The result was a yellow gum with a melting point of 90° to 95°C. with decomposition. The gum was solid but not crystalline.

F.
1. (c)

The same procedure as before was used except that the reaction continued for a period of twelve hours. The ether solution was not evaporated but the solid was precipitated out with alcohol and petroleum ether. This solid was not crystalline. M.P. about 80° with decomposition. The petroleum ether did not precipitate out the solid very well, but when alcohol was added and the mixture heated to drive off the ether, we obtained a yellow material, globular in form but not definitely crystalline when examined under the microscope. A powder resulted when the mass was crushed but this powder was not crystalline.

Attempts were made to purify this material with absolute alcohol and while a small amount of compound dissolved in the cold and a greater amount dissolved on heating, the differential was not large enough for test purposes. Solids precipitated out in a gummy mass instead of in crystalline form. Some of the material was white and some yellow. The white material was more definitely crystalline than the yellow. The melting points were 74° to 78° for the white form and 90° to 94° with decomposition for the yellow form.

F.
1. (d)

Several attempts were made using carbon bisulfide as a solvent. This solvent was used because the iodine as well as the alcohol dissolved in it. The procedure described in I(a) was followed except that the time of reaction was three hours. We found that washing the carbon bisulfide solution with sodium thiosulphate extracted the excess iodine from the solution, and the dark red color disappeared leaving a colorless white liquid. However, on standing this condition was changed inasmuch as the solvent grew darker with the passing of time. Usually the solution became a very dark red color in ten minutes. Ether, alcohol, or petroleum ether could be used for precipitating the solid from the carbon bisulfide. A greenish, black solid resulted. The melting point was from 74° to 78°C.

Other attempts were made with carbon bisulfide as solvent and the procedure as described in 1(a) but with varying times of reaction. Trials were made in which the times of reaction were: 3, 6, and 12 hours. One trial was made in which the reaction was heated gently for forty-eight hours over a hot plate. The results were all the same as in the first attempt.

F.
1. (e)

Trials were made as in 1(a) except that a trace of yellow phosphorous was added. On standing, with alcohol added to the ether solution, a yellow gummy material with a M.P. of 90° to 94°C. with decomposition,and a white solid with M.P. of 78°C. separated out. With the above methods and longer periods of reaction: 3, 6, and 12 hours, the resultant materials were identical with those first obtained.

F.
1. (f)

Trials were made using glacial acetic acid, with proportions the same as in 1(a) and the procedure identical except that the solid was precipitated from solution. The reaction proceeded eight hours. The solution, after treatment with sodium thiosulfate, was treated with excess water. A precipitate formed but not in large quantities. This white material was so finely divided that it could not be made to separate out. It may have been sulphur from the sodium thiosulfate.

Other trials were made in which the solution was finally treated with just enough water to cause cloudiness. Eventually a little partially crystalline material came out. This material had a melting point of 78° to 88°C. but did not give a conclusive test for iodine.

Attempts were made to freeze out any water present after collecting the gum from the solution in ether, but no crystalline material was obtained on evaporating the ether to small volume.

F.
1. (g)

Trials were made in which no solvent was used but the iodine, phosphorous, and secondary alcohol were melted together.

Ten grams of the secondary alcohol, 3.8 grams of iodine and .4 of a gram of red phosphorous were melted over an oil bath. Evolution of iodine fumes took place and vigorous action was evidenced by the bubbling and increased temperature exhibited. The procedure was altered in that the secondary alcohol was first melted, then phosphorous added, and the iodine added from time to time. This run proceeded for six hours, leaving at the end of that time a heavy gum. This gum was treated with water to destroy the excess phosphorous trichloride, decanted, and the water layer treated with ether and sodium thiosulfate. The gum was treated with ethyl alcohol. Iodine came out as was shown by the color but no appreciable part of the gum dissolved. Ether was then added to the gummy material and most of it dissolved. The ether solution was treated with sodium thiosulfate in water and separated from the water layer. Both ether layers on evaporation yielded a gum. More material was obtained from the solid residue portion.

Other trials were made at 71°C. and 90°C.; the procedure otherwise being the same. The results were the same as in the previous determination. Attempts to recrystallize the gum all failed. Alcohol, ether, acetone, chloroform and benzene were used as crystallizing agents. The material was boiled with bone black as in the other attempted repurification.

F.
1. (h)

Using the above methods trials were run in which a trace of yellow phosphorous was used, and also pure yellow phosphorous in place of the red phosphorous. The evaporation of the ether left a gum which became solid on treating with alcohol. When carbon bisulfide was added a green solution resulted. One portion of ether solution which was allowed to evaporate very slowly was found to have crystal-like masses interspersed in the gummy material. It was impossible to separate or dry these crystals, however much the type of solvent varied.

Anal. Subs., 0.2000g.: AgI, .0306g.
Calc'd for $C_{20}H_{15}I$; I, 33.2. Found: 8.38.

The materials resulting from the reaction in sections (g) and (h) were found to be very soluble in: chloroform, xylol, benzene, carbon bisulfide, and ethyl acetate; moderately soluble in glacial acetic acid and acetone; slightly soluble in petroleum ether, methyl alcohol, ethyl alcohol and absolute alcohol, both hot and cold.

When these materials obtained from the reactions mentioned were treated with sodium to get qualitative tests for iodine, many of them showed no iodine and others gave inconclusive tests for iodine. These materials from glacial acetic acid and carbon bisulfide as solvents, gave tests for iodine in every case. The material prepared by methods (g) and (h) gave some fair tests for iodine though in one or two cases no conclusion could be reached as to whether iodine was present in the compound or not. It was deemed advisable to try other methods or preparation in which water was excluded as hydrogen iodide probably reverses the reaction and in water, hydrogen iodide is almost sure to be formed. These methods, then, were found very unsatisfactory for the production of this type of iodide.

F.
2. (a)

The first reactions in which 2-fluorene-phenyl-bromo-methane were treated with sodium iodide were ones in which a solvent was used.

2-fluorene-phenyl-bromo-methane, melting at 84°C. when recrystallized from alcohol, was used in this reaction. Sodium iodide was made anhydrous by drying in the oven at 110°C. Acetone was treated with calcium chloride and sodium sulfate to make it anhydrous. Sodium iodide was dissolved in anhydrous acetone to make up a 15% solution by weight. 2-fluorene-phenyl-bromo-methane was dissolved in 30 c.c. of acetone. Both of these solutions were colorless. However, on adding a solution containing the bromo-methane, a yellow color appeared which changed to a brownish red color in a very short time. After about ten minutes sodium bromide appeared and the color change ceased, indicating the end of the reaction, or the equilibrium point. After separating the sodium bromide, the acetone solution was evaporated leaving a crystalline material. The crystalline material was green in color. On air drying this material a green powder was obtained which on further exposure to the air turned reddish brown and finally a dark yellow. The paper on which the powder lay was discolored as if free iodine had attacked it. M.P. 80°C.

Iodine vapor could be discerned when melting points were taken.

Anal. Subs., 0.2000g. AgI, .0262: .0185: .0146: .0339.
Calc'd for $C_{20}H_{15}I$: I, 33.2. Found: 7.1
Found: 5.0
Found: 4.1
Found: 9.0

Attempts were made to precipitate the iodide compound from the acetone solution using alcohol, petroleum ether, ether, carbon bisulfide, and water. With all these materials a gum or a gummy semi-solid was produced.

F.
2. (b)

Further experimentation with the use of petroleum ether and ether as solvents lead to the production of a yellow powder instead of the green powder produced when acetone was slowly evaporated. This yellow powder, however, when treated with sulphuric acid gave a test for iodine. M.P. 80°C. Analysis of this powder using the Parr bomb method and precipitation as silver iodide is as follows:

Anal. Subs., 0.2000g. AgI, .0460g
Calc'd for $C_{20}H_{15}I$: I, 33.2. Found: 12.2.

F.
2. (c)

Further attempts were made with the above mentioned method in which the time of heating was varied from two to twelve hours. The products in all cases were the same as mentioned above.

F.
2. (d)

When the acetone solution was evaporated in a current of nitrogen gas a greyish powder resulted. On trying to analyze this it became exposed to air enough to change color to a yellow powder.

Anal. Subs., 0.2000g. AgI, .0461g.
Calc'd for $C_{20}H_{15}I$: I, 33.2. Found: 12.3.

F.
3. (a) ACTION OF ANHYDROUS SODIUM IODIDE ON MELTED 2-FLUORENE PHENYL BROMO METHANE

The temperature was kept below 50°C. and five grams of solid sodium iodide sifted onto ten grams of the bromo compound. Melting took place as soon as a small amount of sodium iodide had been added and a violent evolution of purplish, violet vapor took place. Finally, after about ten minutes, a brownish green vapor came off. This vapor probably was BrI. The solid mass was extracted with water, separated from the water and dried. The product was a greenish black crystalline mass. The melting point seemed to be about 190°, but decomposition was evident as the temperature was raised. The Test for iodine indicated that large quantities of that element was present.

When the reaction was carried out at 70°C. and 90°C. the results were identical with those above.

Anal. Subs., 0.2000g. AgI, .05019
Calc'd. for $C_{20}H_{15}I$; I, 33.2. Found: 17.78.

One run was made in which the air was excluded and nitrogen used as the gaseous medium. This also gave a greenish black crystalline product.

Anal. subs., 0.2000g. AgI, .0828
Calc'd. for $C_{20}H_{15}I$; I, 33.2. Found: 23.1.
Found: 20.9.

F.
3. (b)

Recrystallization was attempted with the product obtained using an atmosphere of nitrogen but the same difficulties encountered before were at hand to complicate the process.

The material was found to be very soluble in chloroform, carbon disulfide and benzene. It was slightly soluble in ethyl alcohol and almost insoluble in petroleum ether and anhydrous ethyl ether. On dissolving in benzene and precipitating out with petroleum ether, green crystals were formed, and the liquor turned pink. When the benzene was decanted and evaporated, a green gummy mass was formed. M.P. 190° to 195°C. with decomposition. The crystalline material also melted at this temperature. Treatment with alcohol gave a brownish liquid and a crystalline material with a melting point of 190° to 195°C.

Purification with benzene and precipitation with petroleum ether gave some gum and some green powder. This green powder had the following analysis:

Anal. Subs., 0.2000g. I, .0427g.
Calc'd. for $C_{20}H_{15}I$: I, 33.2. Found: I, 21.4.

F.
3. (c)

The indications were that the 2-fluorene-phenyl-iodo methane decomposed in air and that the iodide may be prepared pure by excluding water and air, but that it is so unstable under normal conditions as to preclude its use as a means of forming nitro compounds. A special technique would have to be used to do any special work in this direction.

G.
1.

## SUMMARY OF THE ANALYSES OF THE VARIOUS PREPARATIONS OF IODO METHANE

Analysis of material prepared in F1(h),--8.38% iodine
" " " " " F2(a),7.1,5.6,4.0,9.2.
" " " " " F2(b),12.2, 11.9.

These preparations were not anhydrous.

Analysis of material prepared according to the directions in F(3): (greyish black powder). 17.78%I.

Analysis of material prepared according to F3(b)
Iodine 21.4%

Analysis of material prepared according to F3(a) with nitrogen as a gaseous medium. Iodine 23.1, 20.9%.

## H. PREPARATION OF METHYL-PHENYL-CARBINOL.

Since the nitro compound, methyl-phenyl-nitromethane had been prepared,(43) it was deemed advisable to try and prepare this compound by the procedure applied to the fluorene compounds.

One hundred and twenty grams of acetophenone in five hundred c.c. of alcohol were refluxed with two hundred grams of zinc and forty grams of potassium hydroxide for three and one-half hours, then decanted and precipitated with water. On drying a white compound resulted which had a melting point of 110°C. This was the pinacone, as methyl-phenyl carbinol would have been a liquid boiling at 202-204°C. We therefore prepared the methyl-phenyl-carbinol by Bachmans(44) modification of Goldsmith's method of reduction by sodium amalgam in anhydrous solution.

### Preparation of Sodium Amalgam.

Two Hundred and Sixty grams of mercury were placed in a pyrex test tube and covered with sixty-five c.c. of toluene. The toluene was heated to boiling and five grams of sodium added in small pieces. After cooling, the solid mass was wiped with a clean towel after breaking up into pieces.

The prepared sodium amalgam was placed in a five hundred c.c. pyrex flask. Ten grams of aceto-phenone in one hundred c.c. of anhydrous benzene, one hundred c.c. of anhydrous ether and twenty c.c. of absolute alcohol were then added. The whole mass was shaken for twenty minutes, during which time the solution changed to a yellow color, then to a bluish grey, and then back to a clear colorless solution. Heat was evolved during this period of the reaction and the mercury became completely liquid. The solution and mercury were poured into a separatory funnel partially filled with water and the mercury was drawn off. The residue was acidified and the benzene, ether layer drawn off. When the benzene and ether had been dried and evaporated the residue was found to be a thick liquid. This material was distilled with the following results:

1/2 c.c. came over from 130°-203°C.
5 c.c. came over from 203-205°C.
2 c.c. came over from 205-218°C.

Inasmuch as acetophenone boils at 202-203°C. and methyl-phenyl-carbinol boiled at 202-204°, this work was abandoned as it would not do to have impure materials, and the preparation of the pure carbinol involved excessive difficulty.

## I. PREPARATION OF DIPHENYL CARBINOL

The diphenyl-nitro-methane having been prepared(45), it was decided that we attempt its preparation by V. Meyer's method.

One hundred and five grams of diphenyl ketone was dissolved in one and one-tenth liters of alcohol and refluxed for three and one-half hours in the presence of two hundred grams of zinc dust and forty grams of potassium hydroxide. The product was obtained, after decanting off the alcohol, by adding water to the alcoholic solution until it became turbid. The compound crystallized out in white solid flakes melting at 66°. Our material was recrystallized from alcohol to give a product with a melting point of 67.5°. Bodroux(46) found the value of 68° for the melting point.

## J. PREPARATION OF DIPHENYL-BROMO-METHANE

This compound has been prepared(47) by the action of bromine on diphenyl-methane. The melting point was 45°C, and the boiling point 186°C.

Ten grams of diphenyl carbinol was placed in 100 c.c. of anhydrous ether and three and one-half grams of phosphorous tribromide was added drop by drop. The solution was stirred quite vigorously during this addition. Then water was added to destroy the excess phosphorous tribromide, the ether solution was separated and dried. The compound was crystallized from the ether solution. M.P. 36-38°. When this compound was recrystallized from ether using enough petroleum ether to start turbidity, a compound melting at 45° was obtained.

## K. PREPARATION OF DIPHENYL-IODO-METHANE

The only references concerning this compound refer one to the Journal of Russian Physical Chem. 43, 1841, (1911.)but the abstract in the Chem. Zentrallblatt, (I) 1614, (1912) only mentions a scheme in which the compound is presumably formed. However, no constants were given. It is doubtful that this compound has been isolated.

Ten grams of diphenyl-bromo-methane was melted at 40° with six grams of anhydrous sodium iodide. As melting took place evidence of vigorous action was observed in the form of iodine fumes and evolution of quantities of heat. The material was extracted with benzene. When the benzene was evaporated a black partially crystalline residue was left. M.P. 90°C. with decomposition.

## L. DIPHENYL-NITRO-METHANE

The mixture of diphenyl-iodo-methane with silver nitrite in benzene gave a gum which showed only traces of nitrogen when the gum was decomposed.

## M. 2-FLUORENE PHENYL-NITRO-METHANE FROM THE IODIDE.

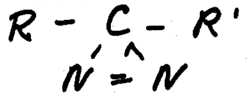
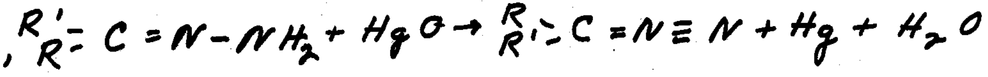
The procedure previously described under Section E was followed.

The product was a sticky gum which could not be purified by the use of solvents. Some nitrogen was evolved on treating with concentrated sulfuric acid but the results were not encouraging enough to warrant an analysis for nitrogen.

# PART B

## HISTORICAL INTRODUCTION TO THE OPTICALLY ACTIVE ALIPHATIC DIAZO COMPOUNDS.

The aliphatic diazo compounds were discovered by Curtius.(48) Diazo-ethyl ester, $N_2CHCOOC_2H_5$, the first of the series to be prepared, was obtained by the action of nitrous acid on glycocoll ester hydrochloride. The reaction had been extended to cover other -amino esters and also similar compounds, as -amino cyanides, - amino ketones, and -amino imides.

Curtius(49) assigned to the diazo compounds the structure  $R-C(N=N)-R'$. This structure was accepted for about twenty years until Angeli(50) suggested that the structure might be  $^{R}_{R'}{>}C=N\equiv N$. After Staudinger(51) showed that the diazo compounds could be obtained by the oxidation of hydrazones,  $^{R'}_{R}{>}C=N-NH_2+HgO\rightarrow{}^{R}_{R'}{>}C=N\equiv N+Hg+H_2O$ Thiele(52) again brought forward the open chain structure as more logical for these compounds. Hantzsch(53), from a study of the absorption spectra of diazo-methane, supported the Curtius structure. Darapsky and Prabhakar(54) studied the reduction of diazo-acetic-ethyl ester and from their results they concluded that the Thiele-Angeli structure was correct. Forster and Caldwell(55) studied the action of the Grignard reagent on diazo compounds and stated that their results could best be explained on the Thiele-Angeli structure. Staudinger(56) with his co-workers carried out a very thorough investigation of the reactions of the aliphatic diazo compounds. He attempted, without success, to isolate isomeric diazo compounds, one of which he expected to have the Curtius formula and the other the Thiele-Angeli formula. More recently Langmuir(57) has assigned to diazo-methane an open chain structure based on Lewis' octet theory.

It would seem that the true structure of the aliphatic diazo compounds is not definitely determined. The reactions which they undergo can be explained equally well by means of either Curtius or the Thiele-Angeli formula.

In 1915 Levene and LaForge(58) made an observation which pointed to the formation of a diazo compound as an intermediary phase in the process of transformation of glucosaminic-acid-ethyl ester into anhydro-ethyl ester.

This observation was: that if one started with an optically active amine and treated it with nitrous acid, there was formed an hydroxy-compound, which was still optically active. If there was an intermediate compound formed in the reaction, it too must be optically active because an optically active compound could not be formed from one that is not active itself. The inter-mediate compound was thought to be the diazo compound.

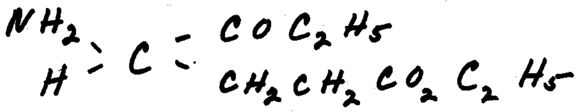
Levene(59) has suggested the possibility of electromers in these intermediate aliphatic diazo compounds. He has presented as evidence for their existence the conversion of certain hexosaminic acids into the corresponding anhydrosugar acids without racemization of the carbon atom bearing the amino group.

In a previous paper(60) it was shown that the benzal derivative of the ethyl ester of one of the hexosaminic acids gave a diazo compound on treatment with nitrous acid. This fact has, apparently, been considered as evidence that in replacement of an aliphatic amino group by an hydroxyl group the diazo compound is an intermediate product. Walden,(61) Fischer(62) and others had also shown that almost any optically active amino acid gave an active hydroxy acid on treatment with nitrous acid. However, no diazo compound has been prepared from an α amino acid, although such compounds can be obtained in a more or less pure condition from almost any of the α amino esters. These facts make it appear doubtful if the diazo compound is an intermediate in the replacement of an amino group by a hydroxyl group when the free amino acid is treated with nitrous acid.

In 1920 Levene and Mikeska(59) undertook to test the existence of optical isomerism in the aliphatic diazo compounds. These authors obtained rotations of plus 1.27° and 1.00°, but as they worked entirely with solutions of the diazo compounds their work was not regarded as conclusive.

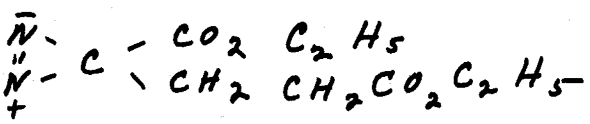
In 1922 Chiles and Noyes(63) succeeded in preparing six active compounds. The first compound obtained was diethyl-diazo-glutarate.

I.

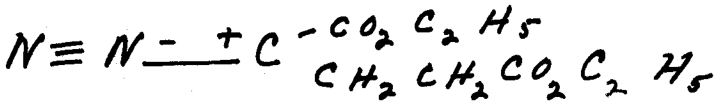


$$\begin{matrix} NH_2 \\ H \end{matrix} > C < \begin{matrix} COC_2H_5 \\ CH_2CH_2CO_2C_2H_5 \end{matrix}$$

II. The Curtius formula



III. The Angeli-Thiele formula



$$N\equiv \overset{-}{N}-\overset{+}{C}\begin{matrix}-CO_2C_2H_5\\ CH_2CH_2CO_2C_2H_5\end{matrix}$$

The only pure diazo esters prepared in this work were obtained by the Curtius method and purified by the vacuum distillation of the thoroughly washed and dried crude samples. The following active diazo esters were prepared.

| | |
|---|---|
| Diethyl-alpha-diazoglutarate, | 0.85° to 1.86° |
| Dimethyl-alpha-diazoglutarate, | 0.89° |
| Diethyl-alpha-diazosuccinate, | 1.23° |
| Ethyl-alpha-diazo-n-caproate, | -1.89° |
| Ethyl-alpha-diazo-n-caproate, | +1.84° |
| Ethyl-alpha-diazo-isocaproate, | -1.52° |

These diazo esters upon treatment with dilute sulphuric acid all gave a mixture of an unsaturated ester and an hydroxy ester with the same direction of rotation as the amino esters and diazo esters from which these were prepared, and of the same order of magnitude as the diazo ester.

The rotation of the diazoglutaric esters prepared could not, according to the authors, be due to the presence of the amino ester, as this product was specifically tested for by the Van Slyke nitrous acid method, after treatment with dilute acid to destroy the diazo ester, and the total amount of nitrogen obtained calculated as the amino ester.

The amounts obtained were negligible; moreover, the amino ester gave only a normal increase in rotation when added to the diazo ester. The rotation could not be due to the presence of an hydroxy ester as the rotations of the hydroxy ester, prepared by treatment of the amino ester with nitrous acid so as to decompose the diazo esters without isolation, were of the same order as those of the diazo esters. The rotation could not be due to the hydroxy acid as this compound in the first place is levorotary.

The arguments which have been advanced in the case of the glutaric esters were applied to all the other diazo esters prepared.

The rotation of the active diazo compounds obtained was so small that some critics thought that it might be due to impurities which were not removable from such unstable substances. Noyes and Kendall(64) attempted to secure a compound with a higher rotary power and also compounds that could be purified by crystallization. They obtained such compounds from both cis and transamino-camphonanic acid. Since these compounds contained two asymmetric carbon atoms, it was necessary to secure the diazo compound from both forms in order to establish the optical activity of the diazo group.

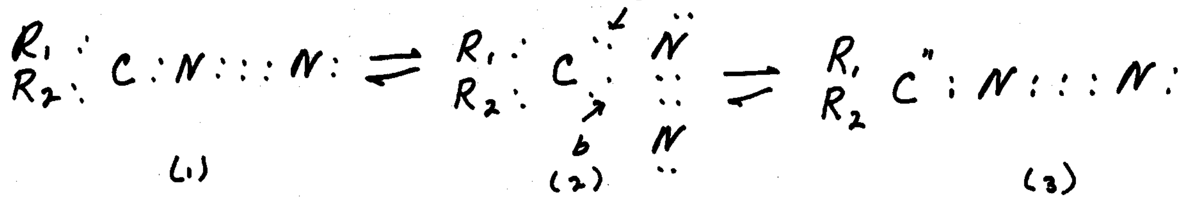
These authors obtained a crystalline compound by treating the nitroso-anhydride of cis-aminocamphonanic acid with sodium methylate at -20°. The values obtained for the specific rotation of the diazo compound varied considerably, due probably to the gradual decomposition of the compound in ether solution. Their average specific rotation was +409° from the cis-aminocamphonanic acid.

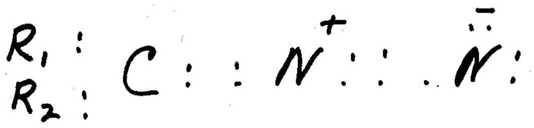
In order to decide definitely whether this high rotation was due in part to the diazo group or entirely to the <u>other</u> asymmetric carbon atom, they attempted to obtain the diazo from the isomeric trans form. They obtained the trans diazo compound by use of Werners reaction; the treatment of a nitroso derivative of disubstituted alkyl urea with alkali.

Both the cis and the trans compounds were dextro rotary and had approximately the same rotation which precluded any decision as to the activity of the carbon attached to the diazo group.

Additional evidence was contributed by Ray,(65) who obtained different products of decomposition from the cis camphonanic acid, thus showing that the two forms are different. The diazo compounds of the trans and cis form were prepared and decomposed under identical conditions, and the decomposition products studied. Direct evidence was obtained that the two compounds differ.

Ray offers the view that the ring and chain formulas represent tautomeric modifications that exist in equilibrium. He points out that this would account for the ease with which the active form racemizes.



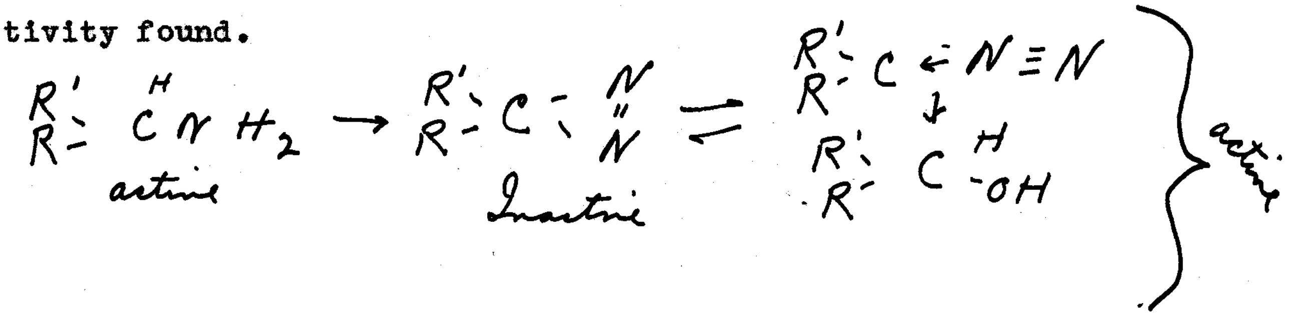


IV

The transition from the ring to the chain form may occur by a fission in the ring at either point (a) or at point (b). When the carbon-nitrogen bond breaks, the carbon must retain both electrons, for if both electrons went with the separating nitrogen, this nitrogen would be negative, the nitrogen adjacent to the carbon positive, and the compound optically inactive (form IV). If one of the electrons forming this severed carbon-nitrogen bond went with the carbon and the other with the nitrogen, neither the carbon nor the remote nitrogen would have a complete octet.

If the ring II opens at (a) then form III will result, while if fission occurs at (b), form I will be obtained. The carbon retaining the electrons being negative and the remote nitrogen positive, the free electrons on the nitrogen adjacent to the carbon will shift and occupy a place between the two nitrogen atoms. All atoms have completed octets in this interpretation.

Weissberger and Haase(66) have recently advanced the view that when a compound of the type $\begin{matrix}R'\\R\end{matrix}\!>\overset{H}{C}-NH_2$ is diazotized, giving rise to $\begin{matrix}R'\\R\end{matrix}\!>C<\begin{matrix}N\\ \|\\ N\end{matrix}$ which is inactive, and $\begin{matrix}R'\\R\end{matrix}\!>C=N\equiv N$ which may or may not be active, enough of the alcohol is formed to account for all the activity found.



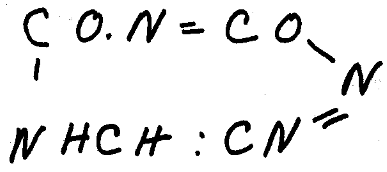
Weissberger and Haase pointed out that the action of sodium nitrite and hydrochloric acid on diethyl-aspartate led in all cases to dextro rotatory products. Decomposition of the products with dilute acids caused evolution of less than the calculated amount of nitrogen and did not affect the specific rotation. The optical activity was unaffected by catalytic hydrongenation of the product in the presence of colloidal palladium. This, the authors pointed out, was evidence that the optical activity was not due to the ethyl diazosuccinate, but was caused by an impurity.

The possible presence of diethyl-d-malate harmonized approximately with the deficit of nitrogen and the optical activity of the product and, if this was accepted, the production of d-bromosuccinic acid by treatment of the diazo-ester with hydrogen bromide in diethyl oxide would lose validity as evidence of optically active diazo-ester.

The authors further point out that, since l-aspartic acid is converted by nitrous acid into i-malic acid, the exact nature of the impurity would be uncertain.

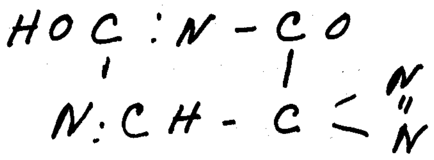
Weissberger and Bach(67) have isolated a diazo compound of diethyl ester of succinic acid. This was obtained in a crystalline form from solution at -24°. The diazo compound was inactive, but the mother liquor was active to a small amount. This was due to the diethyl-melate which was formed in the reaction, as pointed out by Weissberger and Haase(66).

Johnson, Baudisch and Hoffman(68) have diazotized amino-uracil and obtained the diazo product as the anhydride, for which they give either of the formulas to.



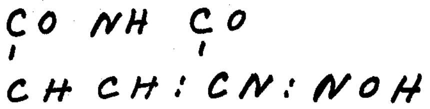
$$\begin{array}{l} CO.N=CO\diagdown \\ | \qquad\qquad\qquad N \\ NHCH:CN\diagup\!\!= \end{array}$$

or



$$\begin{array}{l} HOC:N-CO \\ \quad | \qquad\quad | \qquad N \\ N:CH-C \lessgtr \, \| \\ \qquad\qquad\qquad\quad N \end{array}$$

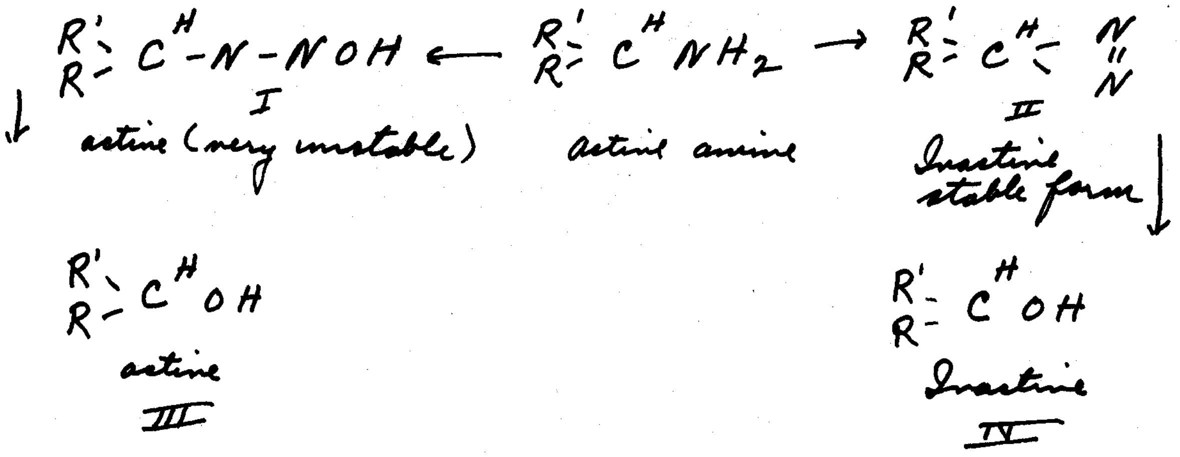
Angeli(50) obtained a diazo uracil but gave the following formula to it:



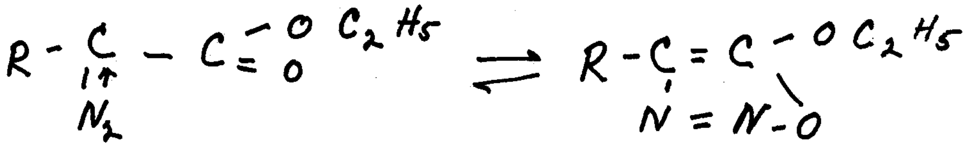
$$\begin{array}{l} CO \quad NH \quad CO \\ | \qquad\qquad\quad | \\ CH \;\; CH:CN:NOH \end{array}$$

Johnson, Baudisch and Hoffman think that whether I or III is formed depends on the H-ion concentration. These views are similar to those of Weissberger.

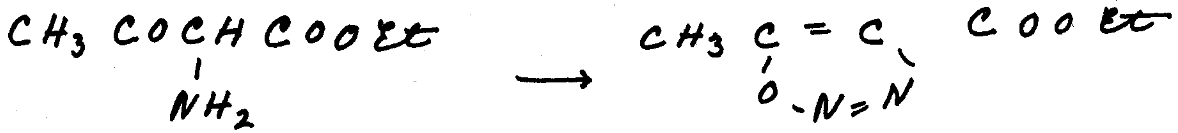
In his most recent paper Weissberger(69) gathered the existing data but refrained from endorsing any one structure though he tacitly assumes the ring structure to be the correct one. His results lead him to believe that any activity is due to the alcohol, III, formed from the active but unstable diazonium derivative, I, as follows:



It is suggested that the work on the diazo esters infers the possibility of an inactive ring structure due to the keto group present in those compounds. We may have



in addition to the inactive diazo compound,  To eliminate this possibility a compound containing no keto group is necessary. The type of ring compound postulated above is similar to the diazo anhydrides of Wolff (70):



It appears as though Shriner's (33) explanation as applied to the active aci-nitro compound is much the same as Ray's (65) explanation of the diazo compounds, for Shriner assumes the possibility of tautomerism between the active and inactive forms. Whether the active forms predominates in the diazo compound or in the sodium salt of the aci-nitro compound is yet to be determined. The evidence is not complete enough to say which conclusions are true.

## STATEMENT OF PURPOSE

This research has for its purpose the preparation, if possible, of an optically active diazo compound. Accordingly the preparation of the alpha-naphthyl-phenyl-diazo-methane in optically active form was undertaken.

This compound should be stable due to the negative substituent and we should be able to give some indication as to whether $R_1R_2C \mathrel{\substack{- \\ \leftarrow}} N_2$ or $R_1R_2C \mathrel{\substack{- \\ \searrow}} \begin{matrix}N\\ \| \\ N\end{matrix}$ is formed. This diazo then should decide whether Weissberger's view of the formation of optically active materials through the intermediate unstable diazonium compound is correct or not.

# THE SCOPE OF THE EXPERIMENTAL WORK ON THE OPTICALLY ACTIVE DIAZO COMPOUNDS.

The general plan of attack on this problem may be summarized as follows:

(1) The preparation of the alpha-naphthyl-phenyl ketone.

(2) The formation of the oxime from the ketone.

(3) The reduction of the oxime to the amine.

(4) The resolution of the amine into its active antipodes.

(5) The preparation of the active urethane.

(6) The diazotization of the urethane leading to the formation of the optically active alpha-naphthyl-phenyl-diazo-methane.

The alpha-naphthyl-phenyl ketone was prepared according to the method of Crucarevic and Merz(71). This method gave only 65% yields, even though the mother liquor was recrystallized. It was noticed that if one redistilled the impure oil a product with a melting point of 56-59° was obtained. Since the alpha-naphthyl-phenyl-methane has a melting point of 58.6°C., it is reasonably sure, either that the distillation over a free flame, or the condensation reaction, forms a large quantity of the hydro-carbon in this method.

The oxime was found to be very difficult to prepare by the ordinary methods. There is to be found in Betti and Poccianti's(72) work, records of several investigators who had incorrectly reported the oxime in the literature. Thus

Kegel(73), had reported a melting point of 140-142°C. and Cailles(74) a melting point of 95°C.

The oxime was prepared by Betti and Poccianti in both the syn and anti forms. The one with the melting point of 127°C. and the other with a melting point of 161°C. Kegel, by heating the ketone in alcohol at 110° with hydroxylamine hydrochloride, had evidently prepared a mixture of these two forms. Cailles ' material was evidently unchanged ketone. A modified method was finally evolved which gave 80-85% yields.of a pure product melting at 127°C. It was also noted that Betti and Poccianti produced the compound melting at 161°C. from a neutral solution. Since we used barium carbonate, we had very close to a neutral solution, but our product was mainly the form melting at 127°C. This may have been due to the use of pressure in Betti and Poccianti's method. If that were the case, it would indicate that the compound melting at 161°C. has a smaller molecular volume than that melting at 127°C.

For the reduction of the oxime to the amine, several methods were tried. The method finally adopted was the one used by Betti and Poccianti(75) with minor modifications. This method consisted in reducing the oxime at 60-70°C. for eighteen hours with zinc dust and acidic alcoholic solution. Then the amine hydrochloride was treated with alkali and extracted with ether.

Among the other methods described in the experimental part was one which gave very good results. This method suggested by Dr. Ray and Dr. Farnau, from a cursory search of the literature,does not appear to have been used for the reduction of this type of compound. The method consisted in reducing the oxime in ether solution with aluminum amalgam. The advantages are that an 80% yield of amine is obtained in a dry state, and it eliminates the formation of the hydrochloride, acetate and other salts which have to be neutralized and extracted with a solvent, with the consequent loss of the product desired. It also eliminates such controversies as that between Betti and Poccianti(74) and Bourke and Leefhalen(76) as to the constitution of the amine. Betti and Poccianti proved that Bourke and Leefhalen had prepared the acetate with a melting point of 120°C. rather than the free amine which had a mälting point of 56-59°C.

Betti and Poccianti's method was further modified inasmuch as it was found unnecessary to distill the amine after extraction with ether. It was found that the material,distilled at 225°C. at 12-13 mm., gave the same results as the undistilled material. They had to distill the material because they used calcium chloride to dry the extracted solutions, and this caused a crystalline mass to be formed. When anhydrous sodium sulfate was used, the amine remained as an oil on driving off the ether and on standing crystallized out as the impure amine with a melting point of from 49-57°.

The resolution was completed using a modification of Berlingozzi's(77) method. Alcoholic solutions of alpha-naphthyl-phenyl-amino-methane and tartaric acid were mixed at 16-18°C. and the crystalline material was filtered off after about 50% of the total crystallization had taken place.

Berlingozzi(77) states that the l-amine-d-tartrate is soluble in alcohol, and the d-amine-d-tartrate is only slightly soluble. This is contrary to our experience as both forms dissolve in alcohol in small quantities. He also states that the d-form is dissolved in boiling water, the l-form being insoluble. This also has not been our experience. All the racemic material goes into solution in boiling water, with the exception of a very small amount, and this residue by its activity was found to be the pure d-form. But unless large quantities of water are used and very slow crystallization is resorted to, the racemic form crystallizes out. The racemic amine-tartrate was accordingly resolved by slow crystallization from dilute aqueous solution. The tartrate of alpha-napthyl-phenyl-amino-methane was converted to the urethane,using chlor-ethyl carbonate as a reagent.

In an early experiment the urethane in ether was treated with $N_2O_3$ and the solution washed with ice cold sodium bicarbonate solution. A copious evolution of gas took place and alpha-napthyl-phenyl-carbinol was obtained. These compounds are evidently too unstable for this treatment.

When the active urethane in ether, cooled to -60°C., was treated with $N_2O_3$, the nitrous acid washed out with ice cold water, and the ether solution dried by freezing out the water, a yellow solution of the nitroso compound was formed. The dry ethereal solution on treatment with sodium methylate gave an orange-red solution of the diazo compound. This solution after further washing gave a pink-red ether solution which decomposed under certain conditions, as the temperature approached -20°C., and even at lower temperatures gave off a slow stream of nitrogen gas. However, the compound was reasonably stable when room temperature was approached gradually, and a sample was kept for three days at room temperature.

This diazo compound had a specific rotation of 10.08° while the decomposition product had a specific rotation of 7.91°.

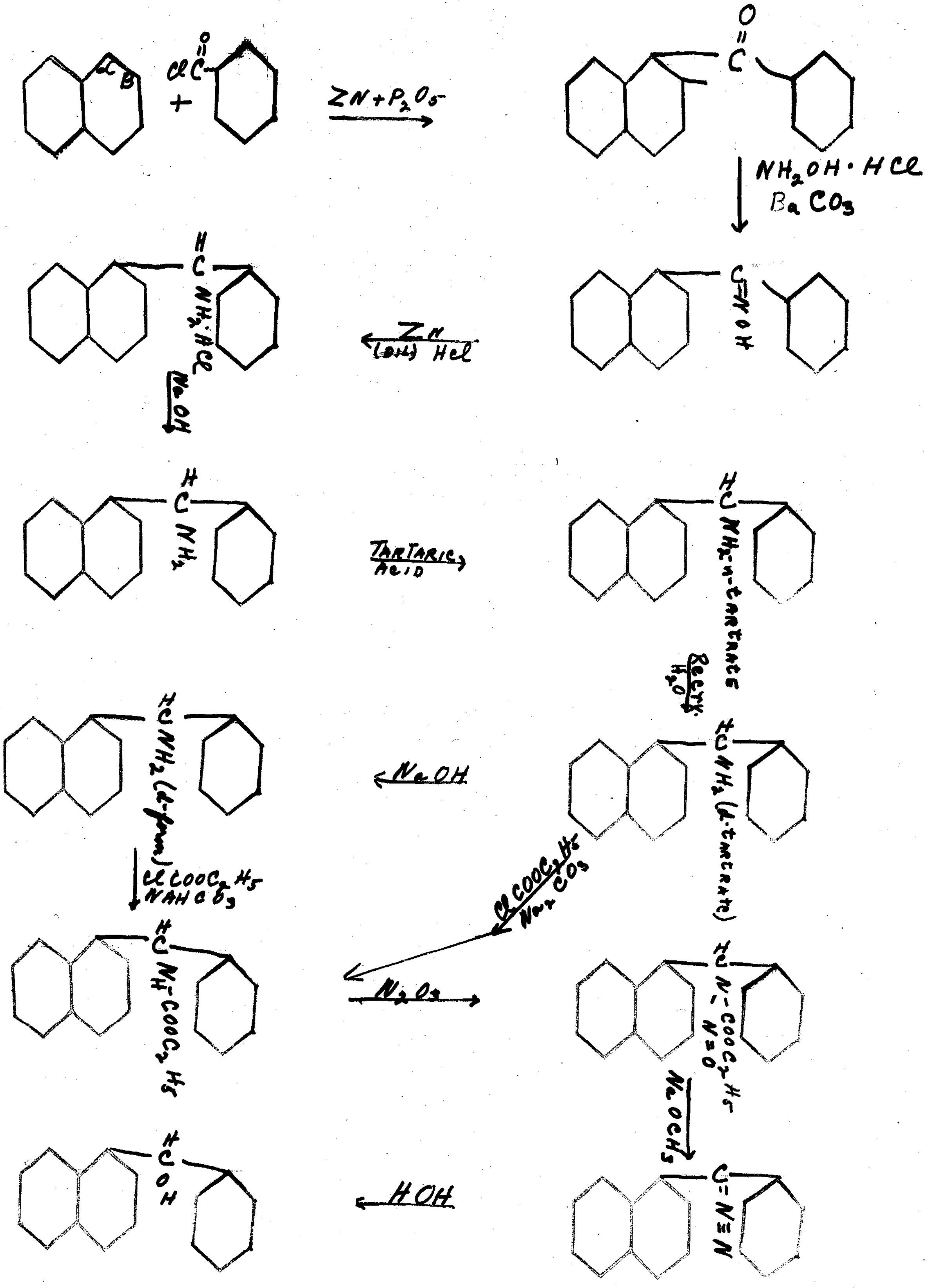
# CONCLUSION

In view of the assertion of Weissberger that the rotation of aliphatic diazo compound is due to impurities, we cannot draw final conclusions until this compound is prepared in a solid crystalline state. (At room temperatures this compound is an oil, but it may be noted that all the compounds prepared in this investigation have first come down as oils and on careful treatment have become crystalline.) After the first crystalline material was formed they invariably went into the crystalline state.

We can definitely state that from the optically active amine we have prepared the optically active urethane; then through the intermediate nitroso compound we have prepared the optically active diazo, which, however, was not crystalline but in the form of an oil. The decomposition products were also found to be active. The problem of optical activity in aliphatic diazo compounds cannot be said to be solved, but we have found a compound more stable than any hitherto prepared, suitable for this type of investigation. This compound exhibits a great deal more activity than the compounds prepared by other investigators and should, when crystallized, definitely decide whether or not activity in aliphatic diazo compounds is due to impurities or to the diazo compound.

It is well to emphasize that this compound is relatively simple, and is not open to the sort of criticism leveled at compounds containing keto groups or other radicals capable of easy reactions. There is only one asymmetric carbon atom in place of two or more as has been the case with several of the compounds which have been prepared. Therefore, we are forced to conclude that the rotation in our compound is due either to impurity or to the diazo grouping. The relatively large rotation coupled with the slightly lower rotation of the decomposition product leads to the belief that purification will not remove all of the activity. The rotation should be larger rather than smaller than the present values indicate because the d-amine used did not have the highest rotation obtainable; in fact, only two-thirds of the total rotation obtainable from the purest resolved compound.

## CHART OF REACTIONS IN PART B



# PART B

## EXPERIMENTAL WORK ON DIAZO COMPOUND

### PREPARATION OF α-NAPHTHYL-PHENYL KETONE

This compound was prepared according to the method of Grucarevic and Merz.(71)

One hundred grams of naphthalene and eighty grams of benzoyl chloride were refluxed for four hours. Several pieces of mossy zinc, weighing not more than one gram, and a trace of phosphorous pentoxide were added to catalyze the reaction. When the evolution of hydrogen chloride ceased, the reaction was completed. It was found that the best yields were obtained when the temperature was held at from 175 to 195°C; the highest temperature being maintained at the end of the reaction. The dark red-brown fluid was then distilled over a direct flame. An air condenser was found to be a satisfactory means of cooling the vapor. The first fraction was made up of excess naphthalene. After the temperature had reached 340°C., a dense yellow oil came over. This yellow oil was the pure product, but if better yields were desired, the distillation was continued until a light yellow vapor was evolved. After the discharge of the yellow oil, we had a dark red oil appearing; this is mainly the alpha ketone with some beta ketone present. The total distillate weighed about one hundred and forty grams. It was mixed with eighty c.c. of ether and ten c.c. of ethyl alcohol and then set aside to evaporate and crystallize. If undisturbed, colorless prismatic crystals separated out from a heavy oily medium. These prisms were mostly the alpha ketone. A yield of sixty grams was obtained. The mother liquor gave further crystals on standing one or two days after it was treated with more ether and alcohol so that the total yield was 65% of alpha-naphthol-phenyl ketone with a melting point of 75.5°. Betti and Poccianti(75) found a melting point of 75.5° for this compound.

Recrystallization from alcohol separated the alpha ketone from the beta ketone which stayed in the oily mother liquor. It was found that some ether had to be present when recrystallizing the compound in order to keep the beta form of the ketone in a liquid condition, as alcohol alone would solidify the whole mass.into a crystalline conglomeration. The result of using alcohol alone was the formation of a mixture melting at 55 to 63°. This mixture was very difficult to purify.

The method of Rousset,(78) provided another way of separating the alpha from the beta ketone. This method consisted of treating a benzene solution of the mixed product with picric acid to precipitate out the beta ketone. The alpha ketone was then recrystallized from alcohol after the benzene solution was evaporated. The beta ketone recovered from the picrate melting at 82°C. Rousset(78) gives a melting point of 82°C. for the beta ketone.

The alpha and beta ketones may also be separated by a method devised by G. Reddelieu(79) in which he used pyridine as the medium of separation.

It should be mentioned that if the mixed ketone from the distillation is disturbed after treating with ether and alcohol, or if too much alcohol is added, the mixture almost immediately crystallizes into a solid yellow mass. It was more difficult to purify this material than the material obtained by slow crystallization. The usual results was a larger yield of impure material. The melting point of this was 65 to 73°C. even after several recrystallizations.

## PREPARATION OF THE ALPHA-NAPHTHYL-PHENYL-KETOXIME

Some material was prepared by Betti and Poccianti's(75) method using a glass Carius tube, heated in an oil bath.

Five grams of ketone was dissolved in twenty-five c.c. of ethyl alcohol. Two grams of hydroxylamine hydrochloride and six c.c. of 20% sodium hydroxide were added and the solution was sealed in a glass tube. After heating for eight hours from 130 to 140°C. the tube was opened and washed out with alcohol. The solution was then made turbid with water. After some time a crystalline compound was filtered off. The melting point was from 125- to 145°C. On successive recrystallizations from alcohol (12 times) the pure syn-compound melting sharply at 127°C. was obtained. Yield 40%. Betti and Poccianti report a melting point of 127°C.

This method was modified in order that larger quantities might be prepared. Therefore, a number of attempts were made using an autoclave made of iron, with a capacity of one and one-half liters. The quantities of material were varied so that the hydroxyl-amine hydrochloride was present up to 400% excess. The quantity of solvent, alcohol, was varied from just enough to dissolve the constituents to 1300 c.c. for 50 grams of ketone. With each variation in concentration of the reaction, the times of heating were varied from three hours to forty-eight hours. Runs were made at 3, 9, 15 and 48 hours. In addition runs were made under the above mentioned varied conditions but with the temperature at 90 to 100°, 130 to 140°, 170 to 180°. The pressures using an ammonia gauge varied from 60 lbs. per square inch to 400 lbs. at the highest temperature and with the largest quantity of hydroxyl-amine hydrochloride and alcohol in the bomb. Invariably the contents of the bomb proved to be an oil, or an alcoholic solution which yielded an oil and gave no crystalline material when treated with water, extracted with ether or other solvents such as benzene. In some few cases crystalline material was eventually separated but it proved to be unreacted ketone with a melting point of 75°. Tests were made using pyridine as a solvent, but these tests were also unsuccessful. Tests were also run using a porcelain-lined bomb. This method was also unsuccessful. Betti and Poccanti(72) mention using sodium carbonate as the means of liberating the amine. They, however, carried this reaction out under reduced pressure and used small amounts of ketone, so that this method was not useful in making large quantities of the oxime. This method gave a compound with a melting point of about 120°.

The method finally adopted involved the use of barium carbonate in neutral alcoholic solution, at atmospheric pressure. Twenty grams of alpha-naphthyl-phenyl ketone was dissolved in two hundred and fifty c.c. of ethyl alcohol. Ten grams of hydroxyl amine hydrochloride was dissolved in fifteen to twenty c.c. of water and twenty grams of pulverized barium carbonate was then added. This mixture was heated in an oil bath at 60 to 70° for seventy-two hours. At the end of this time the solution was filtered and the liquid treated with water until turbid. On standing a few hours, a white crystalline compound separated out. The melting point was about 127°C. The yield, including the material recovered from the mother liquor, was

80% or better. While the oxime in the melting point tube liquified at about 127°C., it did not become clear until about 138°C. indicating that some of the modification melting at 161° was present. Indeed, Betti and Poccianti(72) show that the form melting at 127° is gradually transformed on heating, into the form melting at 161°. This is no bar to the use of either form or a mixture, as both readily reduced to the same amine. Our first trial runs produced materials melting from 115 to 145°C. When pure ketone was used, however, the melting point was consistently 127° or above and never more than 161°C., indicating that only oxime was present. The oxime did not need recrystallization, but after two, and sometimes three crops of crystals were gathered, the mother liquor was treated with a large volume of water and the gummy semi-crystalline mass which resulted was again treated with hydroxylamine hydrochloride as previously described. In this way, the average yield of the oxime was raised to 84%.

This method gives promise of converting ketones into oximes in cases where potassium or sodium alkalis prove to be too strong. The net result of the use of barium carbonate is a nearly neutral solution, whereas other neutralizing substances generally leave the solution definitely alkaline. A distinct advantage is gained in that the oxime is sufficiently pure without further recrystallization when using the method just described. Only three recrystallizations produced a compound melting sharply at 127°C.

The method used by Betti and Poccianti required many more recrystallizations to produce a pure substance. One difference noted is that this method produces a compound melting at 127°C. from a solution that is neutral at all times. They state that the modification melting at 161° is produced in a neutral solution. Their method, of course, involves the use of high pressure and this may have had some effect on the compound. This may indicate that the compound melting at 161° has a smaller molecular volume.

## PREPARATION OF THE HYDROCHLORIDE OF ALPHA-NAPHTHYL-PHENYL AMINO-METHANE.

The procedure of Betti and Poccianti(75) was used in this investigation with several modifications.

Fifteen grams of the alpha-naphthyl-phenyl ketoxime was dissolved in 200 c.c. of ethyl alcohol. Sixty c.c. of six normal hydrochloric acid was added and forty grams of zinc dust sifted into the solution. Instead of refluxing, this solution was heated at 60 to 70° for eighteen hours. The solution was then decanted from the zinc and treated with water until milky in appearance. Better results were later obtained by pouring the decanted liquid into one-fourth of its volume of hydrochloric acid. After the first material had been filtered off, another 100 c.c. of water was added and a white flocculent mass settled out. The amine hydrochloride turned brown on drying and if heated in the oven, a small amount of black tar speckled the powdery mass. This, however, is easily removed. The compound melts at 275° to 278°C. Yield 85%.

## PREPARATION OF THE ACETATE OF ALPHA-NAPHTHYL-PHENYL-AMINO-METHANE.

Ten grams of oxime dissolved in 200 c.c. of ethyl alcohol was reduced with two hundred and fifty grams of 2½% sodium amalgam in glacial acetic acid (20 c.c.). After heating for eight hours a compound was precipitated from the alcoholic solution having a melting point of 120°C. This was the acetate of the amino-methane previously prepared by Betti and Pocciantі.(75)

Bachman's(44) modification of Goldsmith's method of reduction with sodium amalgam in anhydrous ether, benzene, and absolute alcohol was also used. Here the amine itself was formed instead of the salt of the amine. Good results were not obtained in this case; perhaps the reason for the lack of results was the fact that the reaction was kept at too low a temperature.

## REDUCTION WITH ALUMINUM AMALGAM

The direct reduction of the oxime to the amine was successfully effected using aluminum amalgam in ether solution. Five grams of oxime was dissolved in forty c.c. of ether and two grams of aluminum amalgam was added. After three days at room temperature the ether solution on evaporation yielded four grams of alpha-naphthyl-phenyl-amino-methane on further treatment with tartaric acid gave the alpha-naphthyl-phenyl-amino-methane tartrate with a melting point of 190 to 200°C. with decomposition. Since this compound was described by Berlingozzi(77) as giving the same melting point, it was concluded that the method gave the proper product. This method gave a good yield and was very satisfactory when the aluminum amalgam was made with care. Kincaid(80) gives a good detailed description of a method of preparation of the aluminum amalgam.

## ISOLATION OF ALPHA-NAPHTHYL-PHENYL-AMINO-METHANE.

Ten grams of amine hydrochloride was treated with sufficient sodium hydroxide to make the resulting viscous liquid definitely alkaline. This solution was extracted six times with ether and the ether dried over anhydrous sodium sulfate. The ether was evaporated, leaving a light brown oil which became partially crystalline on standing. M.P. 54 to 59°C. Berlingozzi(77) reported 56-59°C.

## PREPARATION OF THE ALPHA-NAPHTHYL-PHENYL-AMINO-METHANE TARTRATE

The procedure of Berlingozzi was followed in this preparation. Eight grams of alpha-naphthyl-phenyl-amino-methane was dissolved in five hundred c.c. of 95% ethyl alcohol and mixed quickly at 18°C. with a solution of five and one-half grams of d-tartaric acid dissolved in 50 c.c. of ethyl alcohol. After standing for about fifteen minutes small crystals were observed in the solution. After one hour a fractional precipitate was separated and again after three, five and twelve hours. Some of this crystalline material was air-dried. The melting point was 195° to 205°C. Yield 90%. Resolution resulted as follows: three grams of material in one hundred c.c. of ether gave alpha + .904°. The specific rotation was +30.1°. This resolution was obtained from the above tartrate which was neutralized to give the free amine.

## D-TARTRATE OF D-ALPHA-NAPHTHYL-PHENYL-AMINO-METHANE

Five grams of the racemic tartrate was boiled with fifty to eighty c.c. of ethyl alcohol. While the D-form was soluble, the L-form was more soluble. The residue was treated with two hundred c.c. of boiling water to dissolve the D-form: the L-form was soluble in water, though Berlingozzi stated that it was not soluble. On cooling, shiny crystals separated from the solution. After drying in the oven,one and one-half grams of the D-form was obtained. The melting point was 198° to 205°C. which checked with that melting point obtained by Berlingozzi.(77)

The rotation obtained from 0.56 grams of material dissolved in one hundred c.c. of benzene was +0.65° in a 2 dm. tube. The specific rotation was $(a)_D^{20} = +59.0°$.

The alcoholic solution containing the L-form and mixed crystals was put aside for future use.

## HYDROCHLORIDE OF THE D-ALPHA-NAPHTHYL-PHENYL-D-AMINO-METHANE

One gram of d-tartrate of the alpha-naphthyl-phenyl-d-amino-methane was treated with enough sodium hydroxide to make the solution alkaline, extracted four times with ether, and the ether dried over sodium sulfate. The ether was evaporated at room temperature, leaving a powdery solid. This material was treated with ten c.c. of normal hydrochloric acid and allowed to stand for six hours. A white crystalline powder settled out. This powder was dissolved in alcohol and gave a specific rotation $(a)^{20}_{D} = -49.1°$. The melting point was found to be 275 to 283°C.

Berlingozzi(77) got $(a)^{15}_{D} = +63°$ for the d-amine and $(a)^{15}_{D} = -53°$ for the d-hydrochloride.

## PREPARATION OF $\alpha$ NAPHTHYL-BENZYL URETHANE

Five grams of d-tartrate of $\alpha$ naphthyl-phenyl-d-amino-methane were added to thirty-five c.c. of ether. Two and one-half grams of chlor-ethyl-carbonate and four grams of anhydrous sodium carbonate were then added. The mixture was refluxed for one hour and then set aside at room temperature for two days. The mixture was again refluxed for one hour and the ether layer filtered off. On evaporation a crystalline solid settled out. The yield was three grams, or 67%. The compound melted at 99-103°C. and had a specific rotation of about +5.0°. The conclusion was drawn that the tartrate had not been completely resolved.

Later preparations of the active urethane resulted in compounds having rotations up to +28.0° with the purest active d-amine obtained. The recrystallized inactive urethane had a melting point of from 99-101°. The recrystallized d-form melted sharply at 104-105°C.

The specific rotation of +28.0° for the urethane was obtained while using a d-amine with the rotation of +43.2°.

## PREPARATION OF THE $\alpha$ NAPHTHYL-PHENYL-D-DIAZO-METHANE.

Five grams of urethane with a specific rotation of +28.0° was dissolved in seventy c.c. of anhydrous ether. This solution, in a dry two hundred c.c. test tube, was placed in a Dewar flask containing a carbon dioxide snow and ether mixture. Then dried $N_2O_3$ was passed into the solution for five hours. During this time a yellow precipitate formed but disappeared as the concentration of $N_2O_3$ became greater. Then the temperature was raised to -20.0°C. and the excess nitrous acid washed out with ice water. The color of the solution changed from a very deep black red to yellow. The water was separated from the ether solution by freezing and filtering the ether solution through a filter stick. Excess sodium methylate was added to the dry ether solution and the mixture allowed to react at -20.0°C. for two hours. At the end of this time the solution was orange in color and contained a precipitate. This solution was washed three times with ice water to remove all the sodium hydroxide, sodium nitrite, and methyl alcohol. The ether solution became a decided pink-red as the impurities were washed out. This ether solution was dried as before mentioned at -80.0°C. One noticed a violent bubbling of gas as the ether was filtered off from the ice. This decomposition could have been avoided if the filter stick had been immersed in solid carbon dioxide. On cooling the ether solution to -20°C. the evolution of nitrogen gradually ceased even though a steady stream of air was being used to evaporate off the ether. It was also noted that pink crystals formed on the filter paper at temperatures below -20°C.

After evaporation to a small volume, a residue of a red oil was obtained. This was diluted with ether to ten c.c. and the rotation taken. Due to the intense red color, sufficient light could not be sent through the solution, and while there appeared to be strong rotation, dilution was necessary in order to determine this rotation accurately. Two and one-half grams of the diazo dissolved in one hundred c.c. of ether gave a plus rotation of .27°. This corresponds to a specific rotation $(a)^{20}_{D} = +10.08°$.

This pink-red liquid was then evaporated and the residue decomposed over a steam bath. The resulting product of a concentration of 2.4 grams in one hundred c.c. of ether gave a rotation of .19°. This corresponds to $(a)^{20}_{D} = +7.91°$.

A previous experiment carried out without precautions as to keeping the solutions dry and cold resulted in a yellowish-white solid which on recrystallizing from alcohol gave a white crystalline material with a melting point of 86°C. This corresponded to the value, 86.5°C. given for the alpha-naphthyl-phenyl-carbinol.(81)

Another experiment in which the nitroso was first prepared in ether solution and then by passing dried nitrogen gas through the solution resulted in partial decomposition probably because the evaporation took place at room temperature. This material when treated with sodium methylate and the resulting product isolated, gave a red liquor and white crystals. The red liquor on standing over night solidified and became yellow in color. This material gave nitrogen to the extent of 20% of the theoretical value. Since the nitrogen was collected over concentrated potassium hydroxide and none of the bubbles were absorbed, we did not have the urethane. The melting point was 85°C. with partial decomposition.

## GENERAL CONCLUSIONS

## PARTS A AND B

We have prepared the following new compounds:

1. 2-Fluorene-phenyl-carbinol.
2. 2-Fluorene-phenyl-chlor-methane.
3. 2-Fluorene-phenyl-bromo-methane.
4. 2-Fluorene-phenyl-iodo-methane.
5. Racemic and d-form of alpha-naphthyl-benzyl-urethane.
6. Racemic and d-form of alpha-naphthyl-phenyl-diazo methane.

While the optically active aliphatic aci-nitro compound was not prepared due to the difficulty in obtaining the iodide compound, that difficulty was eliminated and the path cleared toward a further investigation on the subject.

A diazo compound was prepared having optical activity. The decomposition product also had activity in a slightly lesser degree.

While the question of optical activity in aliphatic diazo compounds was not definitely settled, the nature of the compound prepared gives definite indications that a solution will be effected by crystallization and purification of this compound.

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