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I hereby recommend that the thesis prepared under my supervision by Steve Palinchak

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Approved by:

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THE ALIPHATIC NITRO GROUP:
ITS STRUCTURE AND PROPERTIES

A dissertation submitted to the
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by

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HISTORICAL DEVELOPMENT

A. Preparation of Aliphatic Nitro Compounds

As early as 1868 Fettig(1) prepared nitromesitylene with fuming nitric acid. Later Biedermann and Ledoux(2) prepared nitromesitylene by gradually adding a mixture of equal volumes of mesitylene and acetic acid to a mixture of equal volumes of fuming nitric and acetic acids.

In 1872, V. Meyer(3) prepared the first nitroparaffin, namely nitropentane, by the distillation of silver nitrite and pentyl iodide. In the same year, Kolbe(4) prepared nitromethane by reacting potassium nitrite and potassium chloracetate.

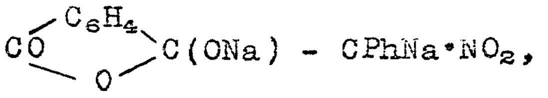
$$CH_2ClCO_2H + KNO_2 \longrightarrow [CH_2(NO_2)CO_2H] \longrightarrow CH_3NO_2 + CO_2 .$$

This method was later modified by Priebish(5) and in 1908, by Steinkopf(6). Two years later, V. Meyer(7) prepared nitromethane by heating methyl iodide and silver nitrite.

$$CH_3I + AgNO_2 \longrightarrow AgI + CH_3NO_2$$

Beilstein and Kurbatow(8) prepared mononitrocyclohexane by nitration of petroleum.

In 1885, S. Gabriel(9) prepared a compound, $C_{15}H_{10}N_2O_6$, by treating benzylidenephthalide with nitrous acid. This compound with dilute alkali gave



$CO\langle{}^{C_6H_4}_{O}\rangle C(ONa) - CPhNa \cdot NO_2$, which on acidification produced phenylnitromethane and phthalic anhydride. Phenylnitromethane was later prepared by the action of silver nitrite on benzylic chloride by Holleman(10).

By prolonged heating at 130°-140°C of a hydrocarbon with dilute nitric acid in a sealed tube Konowaloff(11) prepared some higher aliphatic nitro compounds. He reported that normal hexane or octane gave dinitrocompounds. However, Worstall(12) showed that primary nitrocompounds are also formed and that normal heptane is easier to nitrate than normal hexane. With decane 30% of the mono-nitro derivative may be obtained with fuming nitric acid.

Bamberger(13) prepared nitromethane by oxidizing methylamine by use of Caro's reagent. He gave the following steps for the reaction:

$$CH_3NH_2 \longrightarrow [CH_3NHOH] \longrightarrow CH_2 = NOH \longrightarrow CH_2 = NOOH \longrightarrow CH_3NO_2$$

He also prepared phenylmethylnitromethane by oxidation of the corresponding oxime.(14).

By reacting sodium, potassium or barium salts of ethyl sulphuric acid with the nitrites of alkali metals or alkaline earth metals, Ray and Neogi(15) prepared nitromethane.

Walden(16) prepared nitromethane by using a dilute solution of potassium nitrite and dimethylsulphate.

$$CH_3OSO_2OCH_3 + KNO_2 \longrightarrow CH_3OSO_2K + CH_3NO_2.$$

Steinkopf and Kirchoff(17) also prepared it from sodium nitrite and the sodium salt of chloroacetic acid.

Bewad(18) prepared primary, secondary and tertiary nitroparaffins by reacting zinc alkyls and chloro- or bromonitroparaffins.

In 1908, W. Wislicenus and A. Endres(19) found that ethyl nitrate would condense in the presence of sodium ethylate with compounds containing a reactive methylene group to give the sodium salt of the acid form of the nitro compound.

$$EtONO_2 + NaOEt + C_6H_5CH_2CO_2Et \quad 2EtOH + C_6H_5C{:}(NO\cdot ONa)CO_2Et$$

Recent methods for the preparation of aliphatic nitro compounds have been developed alongvapor phase nitration. Hass, Hodge and Vanderbuilt(20) have prepared with some success primary aliphatic nitro compounds of low molecular weight by passing gaseous paraffins over hot concentrated nitric acid.

By a new direct method, T. Urbanski and Slon(21) have obtained eighty percent yields of nitro compounds. Their method consisted in heating the hydrocarbon vapors, paraffinic or polymethylenic, at temperatures above 100° with nitrogen tetraoxide. Mixtures of mono and dinitro derivatives were obtained.

H. B. Hass(22) gives in detail means by which nitro compounds, prepared by vapor phase nitration, can be converted into a number of derivatives. Some of these are: nitroalcohols, nitroglycols, nitroalkanetrials, amines, hydroxamic and carboxylic acids, substituted amines and chloronitroparaffins.

A number of the methods given here for the preparation of the mono-nitro compounds can also be applied in preparation of dinitro derivatives, similarly for tri- and tetranitro compounds. Von Braun and Sobecki(23) by applying V. Meyer's Method(3) prepared dinitrocompounds of $NO_2(CH_2)_nNO_2$, from the corresponding diiodo- derivatives and silver nitrite when n is greater than three.

Chattaway(24) prepared trinitro- and tetranitromethane by the action of nitric acid (D = 1.53) on acetic anhydride. Equimolar quantities were mixed and mixture was allowed to stand for several days.

In conclusion, the method of Wislicenus(19), the condensation of an aliphatic hydrocarbon containing an active methylenic group with ethyl nitrate is presence of potassium ethylate, was found both simple and satisfactory. A detailed description of this method with certain modifications will be discussed thoroughly in the experimental part of this thesis.

B. Chemical Reactions of Aliphatic Nitro Compounds

The reactions of aliphatic nitro compounds can be divided into two types, that of reduction and salt formation. Reduction can be affected by a wide variety of reagents. The nature of the reagent and conditions under which reduction takes place governs the products that are produced. Since, this thesis will deal largely with the structure of the nitro group, it will suffice to give only a brief historical summary of the different methods for reduction. A more detailed discussion will be devoted to reactions which deal with the constitution of the nitro group.

1. Reduction - Nitro compounds can always be reduced to primary amines. They can also be sometimes reduced to nitroso compounds, hydroxylamines, oximes, azoxy compounds, azo compounds and hydrazo compounds. Most of these reactions have their chief practical importance in the field of aromatic chemistry.

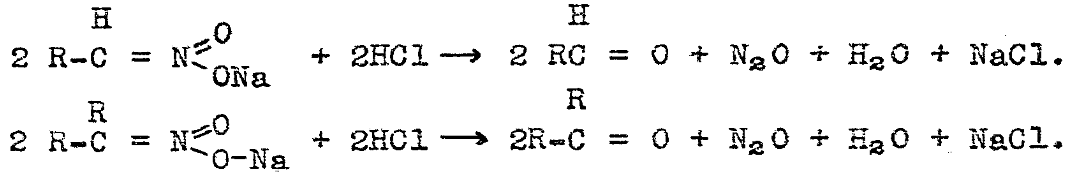
Primary amines can be produced from nitro compounds by the use of tin and hydrochloric acid, stannous chloride and hydrochloric acid, zinc and hydrochloric acid and iron and hydrochloric or acetic acid.

β-hydroxylamines can be produced by the reduction of nitroparaffins with stannous chloride and hydrochloric acid as first shown by Lübin(25) and later by Hoffman and V. Meyer(26). Pierron(27) prepared β-hydrylamines by electro-reduction at room temperature of nitroparaffins in an alcoholic solution containing sulphuric acid. Other methods consist of the use of aluminum amalgam on a moist etheral solution by H. Wislicenus(28), use of zinc amalgam by Bomberger and M. Knecht(29). Lapworth and Pearson(30) and R. D. Haworth and Lapworth(31) made use of sodium sulphide, hydrochloric acid, calcium chloride and ammonium chloride as a reducing medium. Recently an electrolytic reduction of aliphatic nitro compounds has been developed by V. Bruckner, A. Kramli, and E. Vinkler(32).

2. Salt formation - The action of alkali upon aliphatic nitro compounds was first studied by P. Friese(33). He investigated the action of alcoholic sodium hydroxide upon nitromethane and obtained the sodium salt of nitromethane, a white crystalline powder.

Victor Meyer in 1894(34) obtained the sodium salt of nitromethane by the use of sodium ethylate upon nitromethane.

Similarly, Nef(35) obtained the sodium salt of nitromethane by adding sodium to an ethereal solution of nitromethane and evaporating to dryness. He found that, when a cold aqueous solution of a salt of a nitroparaffin was decomposed by dilute cold hydrochloric acid, the nitroparaffin was only regenerated to a small extent. The greater part of the nitro paraffin decomposed into nitrous oxide and an aldehyde or ketone depending on whether it was a primary or secondary nitrocompound.



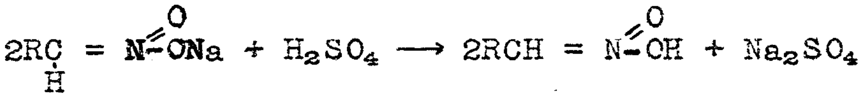
$$2\ \text{R-}\overset{\text{H}}{\text{C}} = \text{N}\begin{smallmatrix}=\text{O}\\ -\text{ONa}\end{smallmatrix} + 2\text{HCl} \longrightarrow 2\ \text{R}\overset{\text{H}}{\text{C}} = \text{O} + \text{N}_2\text{O} + \text{H}_2\text{O} + \text{NaCl}.$$

$$2\ \text{R-}\overset{\text{R}}{\text{C}} = \text{N}\begin{smallmatrix}=\text{O}\\ -\text{O-Na}\end{smallmatrix} + 2\text{HCl} \longrightarrow 2\text{R-}\overset{\text{R}}{\text{C}} = \text{O} + \text{N}_2\text{O} + \text{H}_2\text{O} + \text{NaCl}.$$

This indicated that the salt was of a different constitution than the original nitro compound, for if both had the same structure, the original nitro compound should have been totally regenerated. With dilute sulphuric acid he found the following reaction took place in almost quantitative yield:

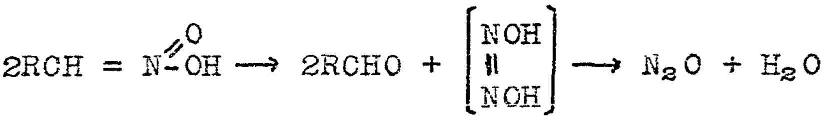
$$2\text{RCH} = \text{N:O}\cdot\text{ONa} + \text{H}_2\text{SO}_4 \longrightarrow 2\text{RCHO} + \text{N}_2\text{O} + \text{H}_2\text{O}$$

He gave the following as the probable mechanism for the reaction:



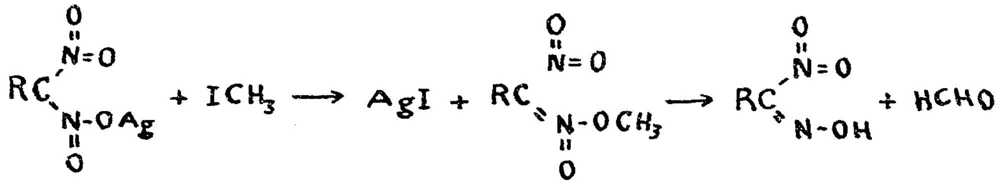
$$2\text{R}\underset{\text{H}}{\text{C}} = \overset{\text{O}}{\overset{\|}{\text{N}}}\text{-ONa} + \text{H}_2\text{SO}_4 \longrightarrow 2\text{RCH} = \overset{\text{O}}{\overset{\|}{\text{N}}}\text{-OH} + \text{Na}_2\text{SO}_4$$

Decomposition then occurred forming an aldehyde and an intermediate compound which decomposed into nitrous oxide and water:

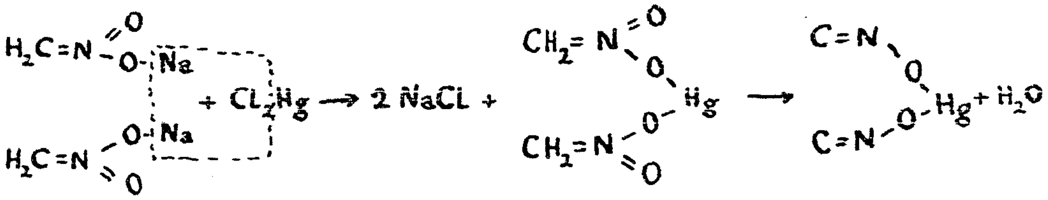


$$2\text{RCH} = \overset{\text{O}}{\overset{\|}{\text{N}}}\text{-OH} \longrightarrow 2\text{RCHO} + \left[\begin{matrix}\text{NOH}\\ \|\\ \text{NOH}\end{matrix}\right] \longrightarrow \text{N}_2\text{O} + \text{H}_2\text{O}$$

Nef also found that by the action of methyl iodide upon the silver salt of dinitromethane ethyl nitrolic acid and formaldehyde were formed.

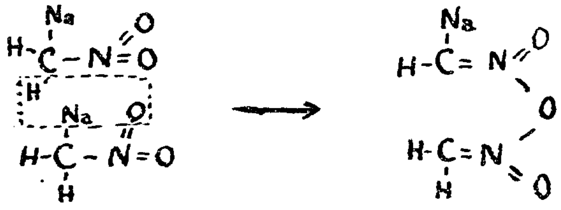


When he treated the sodium salt of nitromethane with aqueous mercuric chloride, mercuric fulminate was formed.

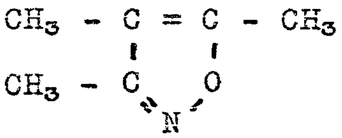


Through the use of these reactions, Nef showed that the sodium salt of nitromethane was $CH_2 = N\begin{smallmatrix}\nearrow O\\ \searrow ONa\end{smallmatrix}$ and not $CH_2Na-N\begin{smallmatrix}\nearrow O\\ \searrow O\end{smallmatrix}$.

In 1876 Lecco(36) discovered that if nitromethane is heated with sodium ethylate, a light brown powder, the sodium salt of methazonic acid, was obtained. On the supposition that the sodium salt of nitromethane was $\underset{Na}{\underset{|}{CH_2}}-N\begin{smallmatrix}\nearrow O\\ \searrow O\end{smallmatrix}$ he proposed the following mechanism for the preparation of the salt of methazonic acid.



It was found by Dunstan and Dymand(37) that if nitromethane was allowed to stand with a strong aqueous solution of potassium carbonate that the mixture became yellow and potassium hydrogen carbonate separated out. On heating the mixture two layers separated. The upper layer yielded methyl cyanide while the lower gave a nitrite, ammonia and trimethyl-isoxazole,



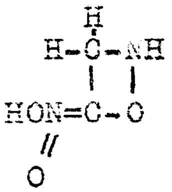
He also found that warm aqueous sodium or potassium hydroxide upon nitromethane gave a nitrite, trimethylisoxazole, ammonia, acetic acid and some resin. The ammonia and the acetic acid came from $CH_3-C\equiv N$ which was first formed. Alcoholic sodium or potassium hydroxide gave trimethylisoxazole, an aldehyde, nitrite and a brown resin. Calcium hydroxide gave no action but dry ammonia at 0°C gave $C_2H_5NO_2\cdot NH_3$, which now would be formulated $CH_3CH=N\genfrac{}{}{0pt}{}{\nearrow O}{\searrow ONH_4}$.

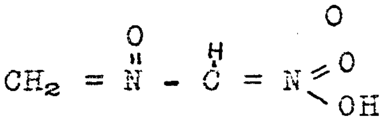
Concentrated aqueous ammonia heated in a sealed tube at 110°-120°C with nitromethane gave ammonium nitrite, acetonitrile and trimethyl-isoxazole. Aqueous ammonia or potassium carbonate with nitromethane gave a nitrite, hydrocyanic acid and methazonic acid.

Dunstan also found that alkali on primary nitropropane at 100° gave trimethyl-isoxazole, ethyl cyanide and nitrous acid. Secondary nitropropane in a sealed tube with aqueous sodium hydroxide at 115° gave acetone, nitrous acid, hydroxylamine and a cyanide.

Dunstan and Goulding(38) obtained the sodium and ammonium salts of methazonic acid. They also postulated a mechanism to explain the preparation of methazonic acid and trimethyl-isoxazole. They based their mechanism on Nef's formula of the sodium salt of nitromethane but the mechanism was long and involved.

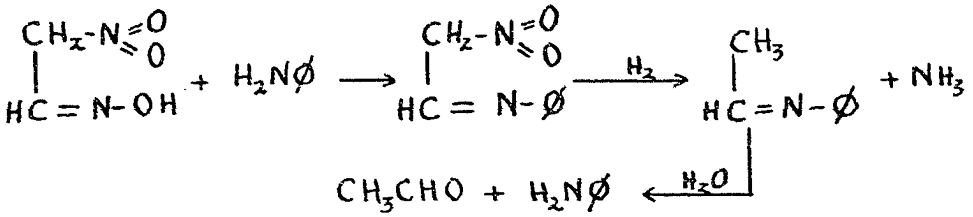
For this reason, Scholl(39) attacked Dunstan's formula for methazonic acid,



and gave  $CH_2 = \overset{\overset{O}{\|}}{N} - \overset{H}{C} = N\genfrac{}{}{0pt}{}{\nearrow O}{\searrow OH}$ as the structure for the acid.

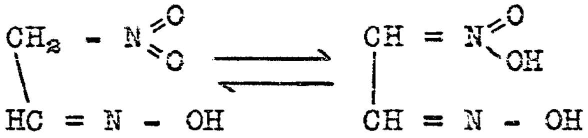
Meister(40) and Steinkopf(42) found that the free methazonic acid could be obtained from its sodium salt if treated with sulfuric or hydrochloric acid.

Meister(42) made an intensive study of the acid. He reacted it with aniline, chloraniline and phenylhydrazine and then showed that the acid still contained a primary nitro-group since it gave the nitrolic test with nitrous acid. On reduction of the methazonic acid-aniline compound, ammonia split off and the resulting anil on hydrolysis gave acetaldehyde and aniline, indicating a carbon to carbon linkage in methazonic acid.



This eliminates Scholl's formula and is evidence in favor of Dunstan's.

Meister also postulated that methazonic acid may tautomerize to another form.



Hantzsch(43) confirmed this by means of spectral analysis.

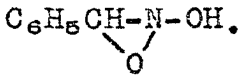
In 1935, Fry and Treon(44) found that three-normal sodium hydroxide with nitromethane gave ammonia, sodium carbonate and water while one-normal produced methazonic acid.

C. Aci-Nitro Compounds

1. Preparation and Properties

- S. Gabriel and M. Koppe(45) found that if phenylnitromethane is heated with fuming hydrochloric acid at 150°C it decomposes into benzoic acid and hydroxylamine. When it is treated with alcoholic soda it forms crystals. These crystals Gabriel supposed to be due to the sodium derivative of phenylnitromethane. If the sodium derivative is treated with bromine phenyldibromonitromethane is formed. Iodine in place of bromine produced C_7H_5NO. Indications pointed to a dimolecular compound, $(C_7H_5NO)_2$.

In 1891 V. Meyer(46) found that if iodomethylene is treated with silver nitrite an oil is produced which forms with sodium ethylate an explosive white salt. Iodoallyl when treated in the same manner yielded a very explosive salt having the formula, $CH_2 = CHCH{=}NO_2Na$. This salt on acidification gave nitropropylene, a light mobile oil, volatile with ether vapors. Treatment of the salt with benzenediazonium sulphate gave a crystalline azo derivative, $CH_2 = H\ CH = N - \overset{O\searrow}{ON} = N - C_6H_5$. Ethylene bromide also yielded an oil when boiled with silver nitrite which formed an explosive salt with sodium ethylate.

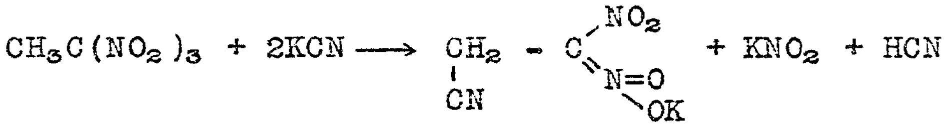
Hantzsch and Schultze(47) studied the properties of phenylnitromethane after preparing it by adding silver nitrite to an ethereal solution of benzylic iodide at 0°. From its salt they found that acetic or carbonic acid produced an oil. With mineral acids at not too high a temperature it gave a white crystalline compound, melting at 74-76°. These were transformed into an oil when heated to boiling in an ethereal or alcoholic solution. A similar change took place if the crystals were allowed to stand in contact with hydrochloric acid or in benzene solution. The crystals dissolved in alkali carbonates with no evolution of carbon dioxide and gave the ferric chloride color test. The authors suggested the following formula for the compound,  $C_6H_5CH{-}N{-}OH$ (with O bridging CH and N). They called it an isonitro-compound. Now it is called an *aci*-nitro-compound or a nitronic acid.

In the same year Konawaloff(48) prepared a number of *aci*-or *iso*nitro-compounds which he called the "labile" forms. *Aci*-ω-nitromesitylene was obtained by the action of dilute sulphuric acid on the sodium salt of ω-nitromesitylene (xylylnitromethane). Needle-like crystals were obtained from benzene which were soluble in sodium carbonate and gave a color reaction with ferric chloride. The *aci*-form was fairly stable in ice-cold water. On standing it readily converted to an oil which was a mixture of the stable nitro form, labile *aci*-nitro form and an aldehyde.

He found that diphenylnitromethane yielded an aci-form which gave a color reaction with ferric chloride and was soluble in sodium carbonate. At ordinary temperatures it decomposed to benzophenone, benzophenoneoxime and the stable nitro form. The aci-form was stable at low temperatures and in an ethereal solution.

Konowaloff also obtained an aci-form of phenylisopropylnitromethane. He found that nitromononaphthene and secondary nitroisoamyl yield liquid aci-forms while phenylethylnitromethane gave a well crystalline aci-isomer.

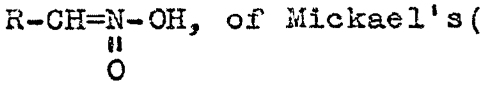
In 1906, Meisenheimer and Schwartz(49) obtained a compound, $\mathrm{EtOCH_2C{-}\underset{\searrow OK}{\overset{NO_2}{N}}{=}O}$, when trinitroethane, $\mathrm{CH_3\underset{H}{C}\begin{matrix}\nearrow NO_2\\ - NO_2\\ \searrow NO_2\end{matrix}}$, was treated with potassium ethylate. Methyl-β-β - dinitro-propionate with methyl alcoholic potash gave a mono potassium derivative. When a methyl alcoholic solution of trinitroethane was treated with an alkaline solution of hydroxylamine a quantitative yield of potassium *aci*-dinitroethane was obtained. They, also, found that if trinitroethane was treated with potassium cyanide that it added on in the following fashion:



$$\mathrm{CH_3C(NO_2)_3 + 2KCN \longrightarrow \underset{CN}{\underset{|}{CH_2}} - C\begin{matrix}\nearrow NO_2\\ \searrow\!\!\searrow N{=}O\\ \quad\ \searrow OK\end{matrix} + KNO_2 + HCN}$$

After the discovery of *aci*-nitro compounds, many workers studied their properties in order to elucidate upon their structure.

Nef and Jones(50) after studying the properties of some *aci*-nitro compounds criticized the ring formula, $\mathrm{R{-}\underbrace{CH{=}N}_{O}{-}OH}$, suggested by Hantzsch and Schultze(47) and gave



the unsaturated formula, $R\text{-}CH=\underset{\underset{O}{\parallel}}{N}\text{-}OH$, of Mickael's(51) as the correct one.

In 1899, Hantzsch and Veit(52) presented a thorough summary of the properties of *aci*-nitro compounds. They found that the normal compound of nitromethane gave no acid reaction, yielded solutions of low conductivity and gave no color reaction with ferric chloride.

They found that the sodium salt of *aci*-nitromethane, when acidified with hydrochloric acid, gave a transient, red coloration with ferric chloride. An aqueous solution of the barium salt decomposed gradually to give nitrous acid, hydroxylamine, formaldehyde or formoxime, formic acid and hydrocyanic acid.

Hantzsch and Veit found that bromonitromethane gave no color with ferric chloride and was a non-electrolyte. The sodium salt, however, gave an intense red coloration with ferric chloride which persisted for sometime when the solution was acidified. The salt decomposed into the normal form about as rapidly as the salt *aci*-nitromethane. It also decomposed into hydrogen bromide and nitrous acid. The dibromo compound behaved similarly to that of the monobromide.

Although they found that in the case of nitroethane the *aci*-compound was more stable than the *aci*-nitromethane, it was not able to be isolated. The sodium salt in presence of excess acid decomposed into hyponitrous acid and an aldehyde.

Nitropentane, the above authors found, also formed a salt with alkali which gave with ferric chloride a red coloration. This coloration also appeared in freshly acidified solution.

They found that the ammonium salt of phenylnitromethane could be precipitated from a solution containing the aci-nitro compound but not from that containing the nitro compound. The salt reacted with phenylcarbimide and phosphorous pentachloride but they isolate no products. The sodium salt on titration with hydrochloric acid became neutral very slowly due to the great stability of the aci-phenylnitromethane. The aci-compound decomposed to give benzoldehyde and nitrous oxide.

Hantzsch and Veit were able to keep aci-paranitrophenylnitromethane in a dessicator for about a day before it lost its reaction to ferric chloride. However, they found it was stable in solution. It was most stable in chloroform, less stable in benzene, ether and alcohol and the least stable in water. Excess alkali on the aci-form decomposed it to sodium nitrite and a probable stilbene derivative.

Aci-nitroacetophenone was found to be a stronger acid than benzoic. Its dissociation constant was found to be, 0.0063. The aci-form was stable in solution. Isonitroacetone yielded a neutral sodium salt which did not color a solution of potassium iodide and starch. It decomposed rapidly even at 0°. It was a good electrolyte but did not give constant conductivity.

Hantzsch and Veit also found that the monopotassium salt of aci-dinitromethane was neutral. It gave no color with ferric chloride. The free aci-form was about eight times as strong as acetic acid. Its dissociation constant at 0° was 0.0143, at 25°, 0.0264. 1-1 dinitroethane differed from dinitromethane and resembled nitromethane in its properties. The conductivity of a mixture of the potassium salt and hydrochloric acid in equivalent quantities fell after about fifteen minutes at 0°C to that of potassium chloride in solution. Titration with hydrochloric acid showed results similar to nitromethane.

In 1900 Holleman(53) found that tertiary nitro-compounds were not acidic. Also, in a nitro compound where the hydrogens were replaced by bromine atoms, the nitro compound lost its acidic characteristics.

It was found by Steinkopf and Jurgens(54), that when a suspension of the sodium salt of aci-nitroethane in a large volume of ether was treated with excess hydrochloric acid and the solution evaporated rapidly, after removal of the sodium chloride present, colored chloronitrosoethane was obtained. If, however, the volume of ether was small and an excess of hydrochloric acid was avoided, ethyl nitrolic acid was formed. The formation of this acid was probably due to the action of nitrous acid produced by the reaction of the intermediately formed NOCMeHOH; on unchanged nitroethane.

In cases where nitro compounds had other strongly negative groups attached, such as nitroacetic acid and nitroacetonitrile, they reported that there was no blue coloration when heated with acids. Therefore, here no decomposition to aldehyde and nitroxyl took place.

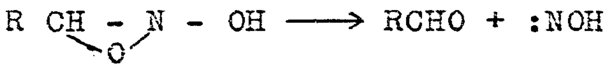
ω - nitro-acetophenone when treated with hydrochloric acid in an ether solution gave ω-chloro-ω-oximinoacetophenone without the formation of a colored nitroso compound as an intermediate.

Aci-phenylnitromethane only slowly developed a blue coloration on treatment with acids which gradually disappeared with the formation of benzhydroxamic acid. Aci-phenylnitromethane contains a feeble negative phenyl group, and, therefore, should occupy an intermediate position between a nitro compound with saturated groups and a nitro-compound with a more negative unsaturated group such as ω-aci-nitroacetophenone. For this reason the reaction is gradual.

Hantzsch and Schultze(47) found that all the aci-nitro compounds that were tested and their salts gave a sky-blue coloration when they were suspended in ether and treated with a current of hydrochloric acid or acetyl chloride.

Hantzsch and Veit(52) found that a solution of the sodium salt of nitromethane and concentrated acid formed an intense red color which appeared at the moment of neutralization but disappeared with excess acid. They thought this indicated the formation of  $\underset{NO_2}{CH} = N{-}OH$. They also found that the sodium salt of nitroethane with hydrochloric acid gave a blue characteristic coloration of the <u>aci</u>-nitro compounds which they thought was probably due to ethyl nitrolic acid that was formed.

Steinkopf and Jurgens(54) using Hantzsch's ring formula postulated the formation of hydroxamic chlorides as due to the decomposition to the corresponding aldehyde and nitroxyl.



These then combined to form a nitroso alcohol.

$$RCHO + :NOH \longrightarrow RCH(NO)OH$$

The nitroso alcohol then combined with hydrochloric acid forming a chloronitroso compound which is transformed into hydroxamic acid.

$$RCH(NO) + HCl \longrightarrow \underset{\text{Blue}}{RCHClNO} \longrightarrow R{\cdot}CCl{:}NOH$$

These reactions would take place only if there were no negative groups present. If negative groups were present, they would stabilize the compound and cause the splitting to take place thus:

hydroxamic acid.

On the other hand, Nametkin(55) criticized Steinkopf and Jurgens support of Hantzsch's ring formula. He laid stress on the unsaturated character of the nitro compounds in their reactions with halogens, halogen hydroacids and oxidation with dilute permanganate. Nametkin and Pozdnjakova(56) found that oxidation of secondary nitrocompounds with dilute potassium permanganate (between 1-2%) gave quantitative yields of the corresponding ketones. Nitrocyclohexane gave 97% yield of cycohexanone and nitrofluorene gave a 96% yield of fluorenone.

Such oxidation would be difficult to explain by Hantzsch's formula while by the use of Michael's unsaturated formula(51), Nametkin(55) gave the following mechanism:

$$=C=NO-OK \longrightarrow =C(OH)\cdot NO(OH)(OK) \longrightarrow$$

$$=C=O + KNO_2 + H_2O$$

Another argument presented in favor of unsaturation is the behavior of primary nitroparaffins on acidification where transitory nitroso compounds and hydroxamic acid were obtained.

$$CHR = NO-OH \longrightarrow RCH{:}O + {:}NOH \longrightarrow$$

$$RCH(OH)\cdot NO \longrightarrow RC(OH){:}NOH$$

when the nitrogroup is accompanied by a negative group, the intermediate formation of the nitroso compound does not take place since there is no blue or green color change.

$$RCH{:}NOOH + HCl \longrightarrow RCHCl\ NH(OH){:}O \longrightarrow$$

$$RCHCl{\cdot}N(OH)_2 \longrightarrow RCCl{:}NOH$$

Where a halogen acid is used and there is slight stability the loss of water may take place before rearrangement. A nitroso compound would then be formed as an intermediate

$$CHR : NO.OH \longrightarrow CHRCl : NH(OH) :O \xrightarrow{-H_2O}$$

$$CHRCl.NO \longrightarrow CRCl{:}NOH$$

Interpretations in analogous manner can be given for the formation of halogen substituted nitro products, nitrolic acids and nitroles. Nametkin showed that there was no need for ring formula for Nef's reaction(35) can be explained without the use of a ring structure.

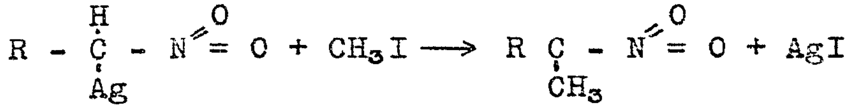
$$:C{:}NO{\cdot}OH + H_2O \longrightarrow :C(OH){\cdot}NH(OH){:}O + H_2O \longrightarrow$$

$$:C(OH)_2 + :NOH + H_2O$$

It is interesting to note here that Hantzsch(57), while studying the absorption spectra of a number of nitro compounds, finally arrived at the conclusion that the unsaturated structure was the more probable one.

2. Alkylation of *Aci*-Nitro Compounds - The term alkylation usually refers to the treatment of the sodium, potassium or silver salt of the nitro compound with an alkyl halide. There are two possible types of alkylations. The *aci*-ion would be expected to produce O-alkylation which would yield a nitronic ester, while the carbonion should produce C-alkylation, forming a secondary or tertiary nitro compound.

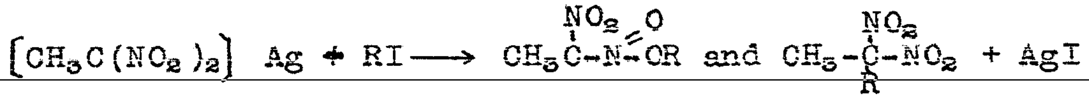
$$R - \overset{H}{C} = \overset{O}{N} - OAg + CH_3I \longrightarrow R - \overset{H}{C} = \overset{O}{N} - OCH_3 + AgI$$



$$R - \underset{Ag}{\overset{H}{C}} - \overset{O}{N} = O + CH_3I \longrightarrow R\ \underset{CH_3}{C} - \overset{O}{N} = O + AgI$$

Studies have shown that both types of alkylation occur.

Nef(35) alkylated 1-1 dinitroethane and obtained both O- and C-alkylation while Dieden(58) only reported C-alkylation.

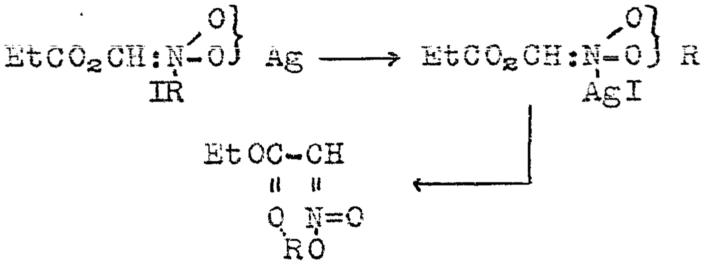


$$[CH_3C(NO_2)_2]\ Ag + RI \longrightarrow CH_3\overset{NO_2}{C}-\overset{O}{N}-OR \text{ and } CH_3-\underset{R}{\overset{NO_2}{C}}-NO_2 + AgI$$

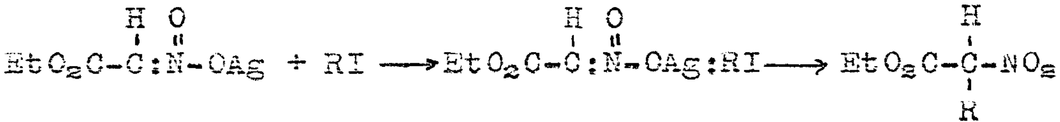
Ratz(59) upon treatment of silver nitromalonamide with methyl iodide obtained O-alkylation while Ulpiani (60) reported only C-alkylation in the case of ammonium nitromalonic ester.

Steinkopf in 1923,(61) found that the silver salt of ethylnitroacetate and methyl iodide at 0° formed ethyl α-nitropropionate and ethyl nitroacetate-*aci*-methyl ether, $EtCO_2CH:NO_2Me$. The later was a colorless liquid which gave a red coloration with ferric chloride. With concentrated hydrochloric acid at 70° formaldehyde and *aci*-nitroso-acetic acid was obtained. Ethyl iodide yielded nitro-butyrate and ethyl nitroacetate-*aci*-ethyl ether. The *aci*-nitro ethers were quite stable and did not show any tendency to undergo isomerization to C-alkyl derivatives.

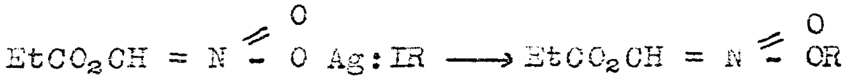
If the silver salt was added to the alkyl iodide at -20° it dissolved immediately to give a deep brown solution. This color disappeared rapidly, giving place to a white opalescence and silver iodide precipitated. At -60° no action took place until the solution was warmed, then, the silver salt dissolved and the solution turned brown and finally became colorless. The mechanism for the reaction was given as:



A new mechanism based on modern theories, can also be shown where the RI adds directly to the compound and then rearranges in two ways.

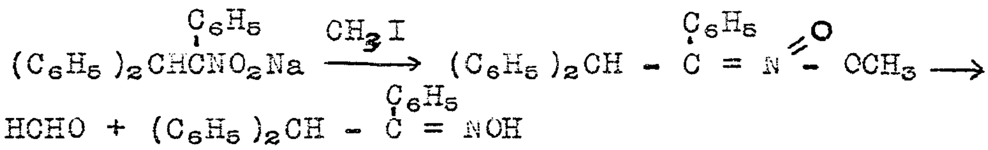
(1) 

$$EtO_2\overset{H}{C}-\overset{O}{C}:N-OAg + RI \longrightarrow EtO_2\overset{H}{C}-\overset{O}{C}:N-OAg:RI \longrightarrow EtO_2C-\underset{R}{\overset{H}{C}}-NO_2$$

(2) 

$$EtCO_2CH = N\begin{smallmatrix}\diagup\!\!\diagup O\\ -\ O\end{smallmatrix}\ Ag:IR \longrightarrow EtCO_2CH = N\begin{smallmatrix}\diagup\!\!\diagup O\\ -\ OR\end{smallmatrix}$$

Kohler and Stone(62) obtained no evidence for C-alkylation when they treated sodium triphenylethane with methyl iodide. The product was an oxime indicating O-alkylation to the intermediate nitronic ester followed by decomposition of the nitronic ester to the oxime and an aldehyde



$$(C_6H_5)_2CH\overset{C_6H_5}{C}NO_2Na \xrightarrow{CH_3I} (C_6H_5)_2CH-\overset{C_6H_5}{C}=N\begin{smallmatrix}\diagup\!\!\diagup O\\ -\ OCH_3\end{smallmatrix} \longrightarrow HCHO + (C_6H_5)_2CH-\overset{C_6H_5}{C}=NOH$$

Nenitzescu and Isacescu(63) obtained fluorenone oxime by alkylation of potassium 9-nitrofluorene. Later they isolated the intermediate methylnitronic ester. The silver salt of 2-bromo-9-nitrofluorene also undergoes O-alkylation to produce the nitronic ester. They also claim that the sodium salt of phenyl=aci=nitromethane gave, when treated with acyl chlorides, the acyl derivative of hydroxamic acid, $C_6H_5C(OH):N-O\ Ac$.

Wieland and Hochtlen(64) however, reported the C-alkylation of phenylnitroacetonitrile by treatment of the silver salt with diphenylbromomethane or triphenylchloromethane.

In 1935 Arndt and Rose(65) investigated the manner of alkylation in several different types of nitro compounds. The following compounds were investigated, phenylnitromethane, p-bromophenylnitromethane, ω-nitroacetophenone, ethyl nitroacetate, methyl nitromalonate and p-toluene sulphonylnitromethane. The last compound was used because the methylene group carrying the nitro group is strongly acidic but no conjugated system is possible.

They found that the aci-forms of phenylnitromethane and p-bromophenylnitromethane reacted vigorously with diazomethane to give the nitronic esters. The corresponding normal compounds showed no visible reaction with diazomethane, but are slowly transformed into the same nitronic esters obtained from the aci-form. In these cases, they assumed a possible tautomerism of the nitro to the aci-form although the equilibrium is too slight to be detected with ferric chloride but which, on account of its strong acidity, can react with diazomethane. Such a tautomerism these authors claimed would not exist with ethyl nitroacetate and p-toluenesulphonylnitromethane. These compounds they claimed gave no enolic reactions, but they reacted vigorously with diazomethane, yielding nitronic esters. They then considered the difference between sulphonyl ketones, which they claimed do not enolise, and the β-ketones, which enolize considerably, and assumed that if there was spontaneous desmotropy in the reaction of ethyl nitroacetate and toluenesulphonylnitromethane that it should be detected by ferric chloride. These authors, therefore, considered the formation of nitronic esters from ethyl nitroacetate and toluenesulphonylnitromethane as due to indirect methylation.

It seemed that these authors failed to consider the fact that ethylnitroacetate is similar to acetoacetic ester which does enolize. It is very likely that under the conditions of the experiment that ethyl nitroacetate showed enolization and therefore underwent direct methylation to the enol group.

Nitromalonic ester, they found, showed, in alcoholic solution, a feeble enolic reaction which they thought was probably due to small enolization of the carbonyl ester. However, diazomethane reacted with it vigorously, yielding almost quantitatively under all conditions the nitronic ester. ω-nitroacetophenone showed a much stronger enolic reaction. It reacted with diazomethane to give an oil which contained a probable mixture of two-thirds nitronic ester and one-third enolic ester. This indicated that there is enolization of both the nitro group and the ester group.

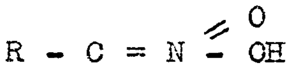
Arndt and Rose, therefore, concluded that the nitro group was different from the nitronic group and that methylation of the nitro group to give a nitronic ester may be either direct or indirect.

Thurston and Shriner(66) found that methyl iodide on silver phenylnitroacetonitrile at 0° produced the nitronic ester.

$$C_6H_5\overset{CN}{C} = N\overset{\nearrow O}{-}OAg + CH_3I \longrightarrow C_6H_5\overset{CN}{C} = N\overset{\nearrow O}{-}OCH_3 + AgI$$

Treatment of the silver salt of phenylnitroacetonitrile with benzyl chloride produced a very unstable nitronic ester which could not be isolated since it immediately decomposed into benzylnitrileoxime and benzaldehyde.

From the following reactions it seems that alkylation of the aci-nitro compound can take place in two ways; C- and O- alkylation. In most cases, O- alkylation was the prevalent reaction. This again pointed to the unsaturated structure for the aci-nitro compounds.



$$R - C = N\genfrac{}{}{0pt}{}{\diagup\!\!\!\diagup O}{- OH}$$

D. Physico-Chemical Properties.

1. Conductivity - In 1899 Hantzsch and Veit(52), while studying some of the properties of *aci*-nitro compounds, noticed that a mixture of equivalent quantities of nitromethane and barium hydroxide showed a decrease in conductivity during fifteen minutes at 0°. This they claimed indicated that the base was gradually neutralized by the acid-form of nitromethane. When they reversed the process and treated the barium salt with an equivalent of hydrochloric acid, they found that the conductivity fell after about fifteen minutes to that of the value of barium chloride in solution.

When the nitro compound was treated with barium hydroxide, at the moment of mixing there was conductivity due only to the base barium hydroxide. As some of the nitro form of nitromethane was changed to the *aci*-form, this aci-form then neutralized the barium hydroxide. This proceeded until finally the conductivity was due only to the barium salt of the *aci*-form.

In the reverse process, the reaction was not so simple, for there was more than one change taking place. On mixing the hydrochloric acid with the barium *aci*-nitromethane the conductivity was due to the hydrochloric acid and the barium salt. The hydrochloric acid then reacted with the barium salt to form barium chloride and the *aci*-nitro compound. The conductivity then was due to these two substances. The *aci*-nitromethane then changed into free nitromethane which has no conductivity; the final conductivity being due only to the barium chloride.

Hantzsch and Veit(52) studied the neutralization effect of nitroethane by conductivity measurements. With nitroethane and sodium hydroxide neutralization took about forty minutes at 0° and three minutes at 25°. The fall of conductivity on neutralization of the barium salt with hydrochloric acid at 35°C took about two days.

In 1927, Branch and Jaxon-Deelman(67) also studied the effect of neutralization on conductance. They expressed the conductivity of aci-nitro acid in terms of the final solution. This was obtained by subtracting the final conductivity from the measured conductivity and dividing this result by the final conductivity. This value was proportional to the concentration of the negative ion of the aci-nitro compound assuming that mobility of the ions was negligible during the experiment since the solution was very dilute and the total conductivity never changed more than forty percent. The curves for a number of reactions were plotted and the rates of decrease of conductivity were found to diminish at first and then after some time they were observed to become proportional to the conductivities and remain thus.

This, according to Branch and Jaxon-Deelman, indicated that at first two simultaneous reactions took place followed by a simple reaction which is in accordance with the views of Hantzsch and Veit(52).

2. Absorption Spectra - Baly and Desch(68) found that nitromethane and nitroethane gave a shallow absorption band at 3600A° when examined in a tenth-normal alcoholic solution. When one equivalent of sodium ethylate was added, the band was removed. But, it was found that if the solution containing nitromethane was allowed to stand over night and then diluted that a new band developed at 3300A°. The alkaline solution containing nitroethane remained unchanged for many days. Baly and Desch, hence, concluded that monnitroparaffins show a small, but distinct, absorption band.

About the same time, Hedley(69) while making similar studies, came to the conclusion that mononitroparaffins only exhibited a continuous absorption. This absorption was increased with the addition of alkali, but no band was produced.

Zelinsky and Rosanoff(70) studied the ultraviolet absorption spectra of a number of nitro compounds. With nitromethane the absorption increased considerably in passing from the free nitro to the sodium salt. With nitroethane there was selective absorption which changed to a continuous spectra on the formation of the sodium salt. β-nitropropane acted similar to the others having a maximum at 3600A°. ω-nitropropane was found to have a greater general absorption in the free state and a more selective absorption as a sodium salt. The maximum was at 3500A°. However, a yellow color was formed on the addition of sodium ethylate and the increased absorption was thought to be due to the formation of this color.

Tetranitromethane was found to have a large selective absorption, the maximum being at 2975A°. ω-nitrophenylmethane gave curves similar to the primary nitrocompounds. The maximum absorption was at 3465A°. With ω- nitrocyclohexylmethane selective absorption only occurred with its salts. The maximum absorption was at 3440A°. The free nitro compound showed a marked general absorption. Free nitrocyclohexane showed two absorption bands at 3500 and 3720A°. Its salts showed a general absorption. Similar curves were found for 1-nitro-1-methylcylcopentane.

The above authors found that the introduction of other nitro groups caused an increase in general absorption along with a greater selective absorption. Hedley(69) claimed that this was due to the formation of a quinoid structure. Baly and Collie(71), explained this as due to the residual valence of the nitro group.

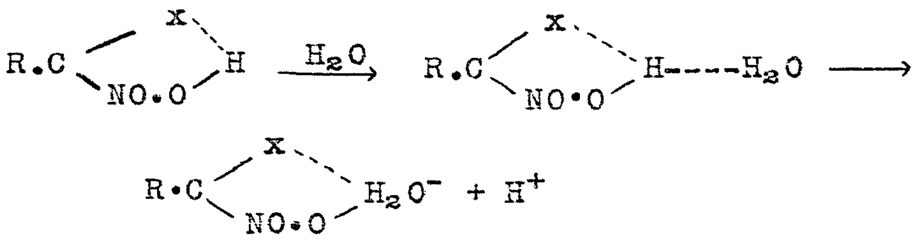
Zelinsky and Rosanoff then came to the conclusion that there should be no difference in the general character between the absorption curves of the mono- and dinitro aliphatic compounds. This conclusion was contrary to the results of Hedley who found no selective absorption for nitromethane.

Hantzsch and Voight(72) disagreed with the conclusion arrived at by Zelinsky and Rosanoff. They claimed that Zelinsky and Rosanoff overlooked the fact pointed out by Baly that a solution of nitromethane is not stable and forms nitroacetaldoxime which is a conjugated *aci*-nitro compound and shows selective absorption.

Hantzsch and Voigt came to the conclusion that true nitro groups show weak selective absorption at high concentrations of about one-hundredth normal. The simple *aci*-groups show weak general absorption. The introduction of further $-NO_2$ groups or other unsaturated negative groups scarcely influenced the absorption of true nitro compounds but increased enormously that of the *aci*-nitro-compounds. This absorption, also, differed fundamentally in the character and the strength of absorption from that of the simple *aci*-nitro compound.

Hantzsch and Voigt based this conclusion on some of their own spectrometrical work(73). They found that there were three forms in the nitro compounds. First, there was the true nitro compound or group which gave a feeble selective absorption, a flat band at 3413A°. Secondly, there was the *aci*-group $- C:N\genfrac{}{}{0pt}{}{=O}{\diagdown OH}$ which gave weak general absorption. This group was present in the salts of the nitro compounds. Finally when this *aci*-group was connected with another negative group, it portrayed strong selective absorption. This group they called the conjugated *aci* nitro.

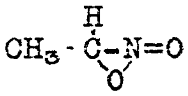
They explained that the strong selective absorption may be due to ionization of a ring-form of the nitro compound.



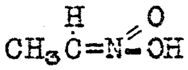
x = a negative group such as NO_2, ^-CN, COOH, etc.

They also indicated that conjugation of this sort gave stability to a compound. For instance, fulminuric and nitrobarbituric acid cannot be converted to the true nitro compound by use of sulphuric acid.

Although there is a disagreement between authors as to absorption, all indications show that the free nitro and the aci-form have different structures. The possible structures that can be represented are those of Hantzsch(47) and Mickael's(51) for the aci-form.



$CH_3\text{-}\overset{H}{C}\text{-}N{=}O$



$CH_3\overset{H}{C}{=}\overset{\quad O}{N}{-}OH$

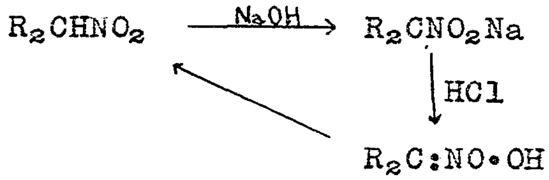
Auwers and Harres(74) in their study of spectrochemical groups found that there was no support for a three ring formula.

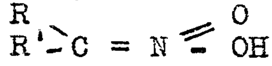
In 1930 Shriner and Young(75) found that the absorption curve for optically active d-2-nitro-octane was different from that for its sodium salt in the visable spectra.

The views presented show there is no definite agreement among the authors as to absorption of aci-nitro compounds. It must also be noticed that in all cases the aci-form was studied as a metallic salt. It, therefore, seems possible that the change in absorption from the normal nitro compound to the aci-form was not due to tautomerism but due to salt formation.

It was found by Lowry and Desch(85) that intramolecular changes were not always accompanied by selective absorption. They found that if nitro-camphor was converted to the aci-form that no characteristic band appeared, but if the sodium salt was made, a characteristic band appeared which did not change with excess alkali. This work indicated that both the normal nitro and aci-form should have similar absorption spectra. However, a final test will come only, when the absorption of a number of stable, aci-forms has been studied.

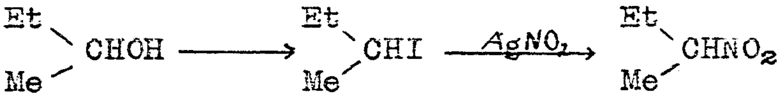
3. Optical Activity - Thus far it has been shown from the many reactions presented that primary and secondary nitro compounds have salt-forming properties. These salts on acidification may yield the original nitro compound or the aci-form which may tautomerize to give the original form.



The aci-form of a secondary nitro compound may be represented by the structure,  $\begin{matrix}R\\R'\end{matrix}\!>C=N\!\begin{matrix}\nearrow O\\ \searrow OH\end{matrix}$, as suggested by Mickael(51). In such a compound the group,

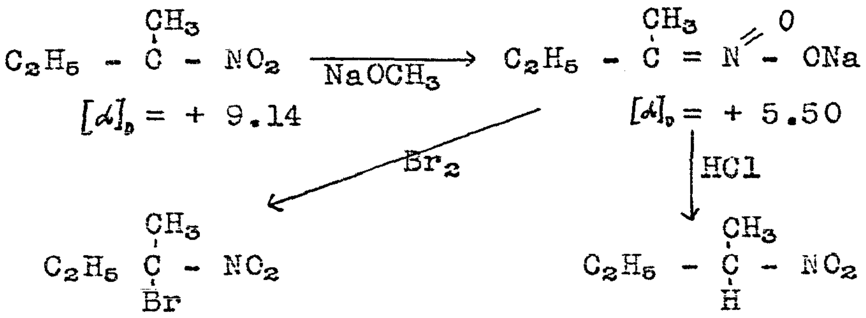
$\rangle C = N \langle$, and the four atoms directly attached to it would lie in a single plane. However, the discovery by Kuhn and Albrecht(76) that optically active methylethylnitromethane retained its activity when converted into its salt seemed to indicate that the symmetrical structure was not correct.

Kuhn and Albrecht prepared methylethylnitromethane in both laevo and dextro rotatory forms from optically active secondary butyl alcohol.



$$\begin{matrix}Et \\ Me\end{matrix}\rangle CHOH \longrightarrow \begin{matrix}Et \\ Me\end{matrix}\rangle CHI \xrightarrow{AgNO_2} \begin{matrix}Et \\ Me\end{matrix}\rangle CHNO_2$$

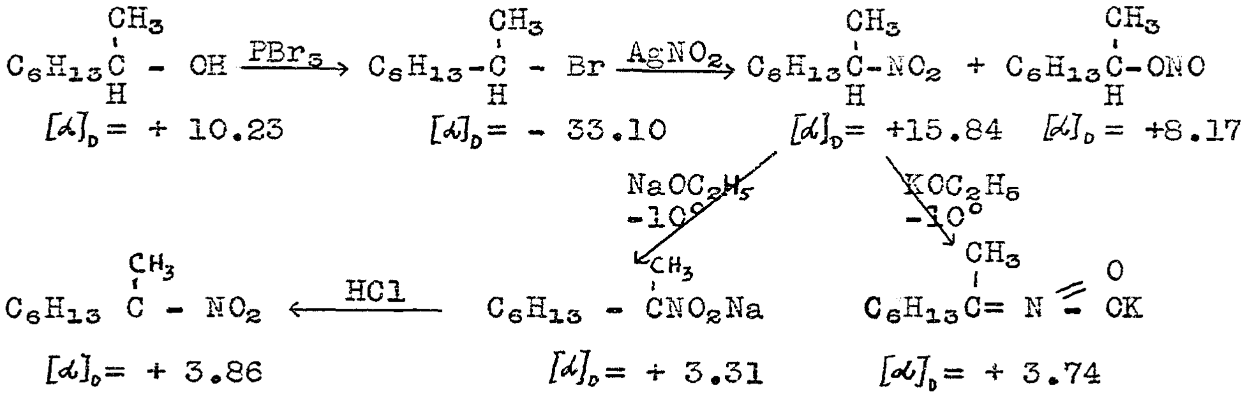
They then studied the effect of salt formation on the activity of the nitro compound. They found that if to the methyl alcohol solution of the active nitro compound aqueous caustic soda was added in excess the activity was completely destroyed. If the alkali was not in excess, the activity was incomplete due to incomplete salt formation. Now, if they added a methyl alcohol solution of sodium or potassium methylate to the solution of the nitro compound, the activity remained. This activity was shown not to be due to incomplete salt formation by adding an excess of sodium methylate or by diluting with water and extracting with ether. There was no decrease in activity in either case. If the free nitro compound was present, it was removed with the ether extract and so rotation must have been due to the salt alone. Bromination of the active product produced the optically active 2-bromo-2-nitrobutane.



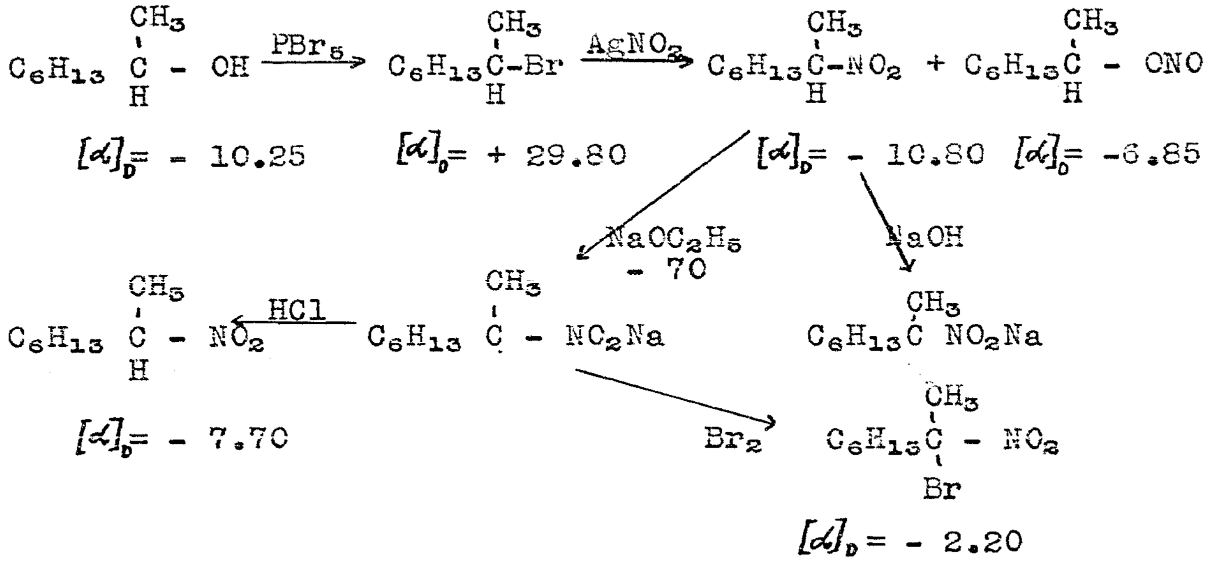
Addition of a large amount of ether to the alcoholic solution, containing the active salt, gave a white solid. This white solid gave an active solution when dissolved in cold methyl alcohol. Analysis of the salt showed it not to be the pure salt. It contained a high content of sodium indicating the presence of sodium methylate.

These results were confirmed by Shriner and Young in 1930, (77). The results of their experiments are represented by the following charts. Nitro-octane was used as the active nitro compound.

Dextro Series



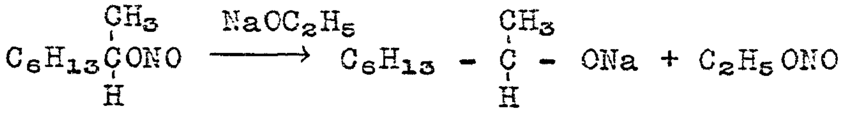
Levo Series



Shriner and Young found that if equivalent amounts of the nitro compound and sodium ethylate were mixed, a constant rotation was immediately attained and remained constant over a period of twenty-four hours. The use of two equivalents of sodium ethylate gave the same rotation as one equivalent. This indicated a complete conversion to the salt and that the activity was not due to unreacted nitro compound.

The nitro compound was regenerated from the sodium salt. This regenerated compound had a rotation lower than the original nitro compound, 24% in case of dextro at -10° and 71% in case of levo at -70°. Therefore, the sodium salt must have been active in order to regenerate some active nitro compound. With potassium ethylate, they found the results to be the same as with sodium ethylate. This they claimed, indicated that the rotation was due to the negative aci-ion since the metal had no particular effect on the rotation. Treatment of the *l*-sodium salt with bromine gave *l*-2-bromo-2-nitro-octane which was also active.

Shriner and Young checked the possibility that the active nitrite, formed in the preparation of the active nitro compound, may have had an effect on the observed rotations. The *d*-octyl-2-nitrite was, therefore, treated with sodium ethylate. The rotation on mixing was observed to be + 3.46 and on standing had slowly increased to + 6.00. With two equivalents the rotation was similar except it took a shorter time for the attainment of an equilibrium value. They assumed this change of rotation as due to the saponification of the nitrite.

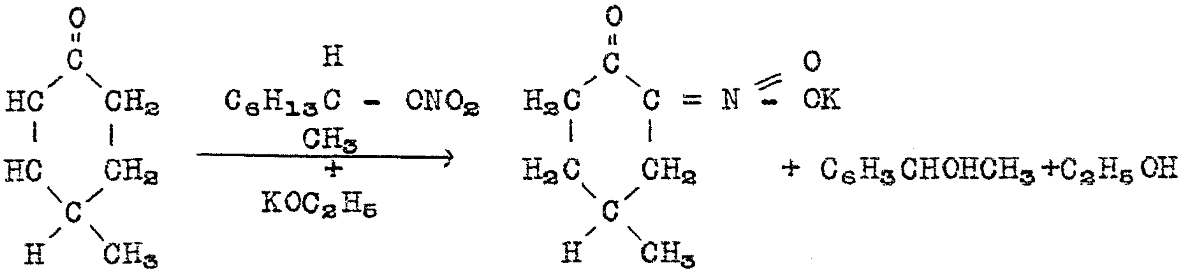


$$C_6H_{13}\underset{H}{\overset{CH_3}{C}}ONO \xrightarrow{NaOC_2H_5} C_6H_{13} - \underset{H}{\overset{CH_3}{C}} - ONa + C_2H_5ONO$$

Their results indicated that the nitrite behaved differently from the nitrocompound when treated with sodium ethylate.

Attempting to prove more conclusively that an aci-nitro group led to an optical active configuration, Shriner and Parker(78) reacted 4-methylcycohexanone with d-2-octyl nitrate.in the presence of potassium ethylate. They found that the dextro potassium salt of 2-nitro-4-

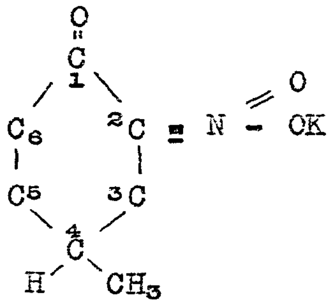
methyclcyclohexanone precipitated out.



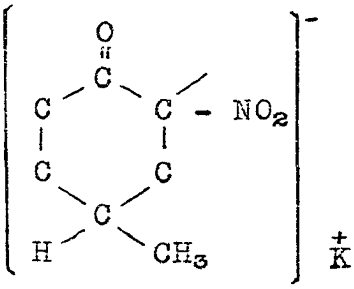
d-2-nitro-4-methylcyclohexanone.

Similarly 4-methylcyclohexanone gave with *l*-2-octyl nitrate the levo potassium salt. The solid active potassium salts were isolated and analyzed eliminating the possibility of the activity being due to some other active substance in the reaction. Both of the salts racemized in about an hour.

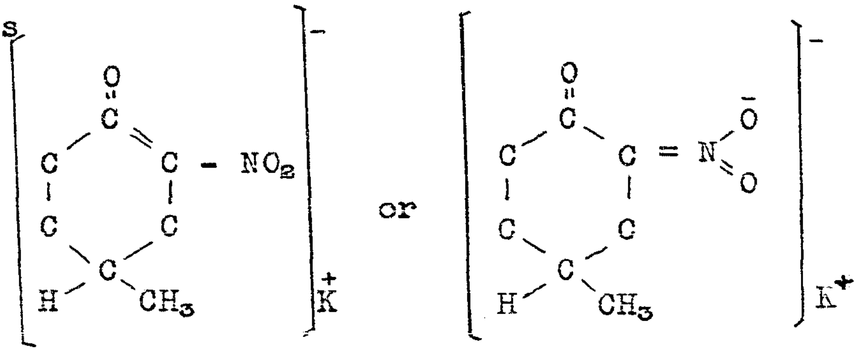
According to the authors, it would be difficult to explain racemization if the activity were due to carbon atom four.



However, if the compound had the following structure,



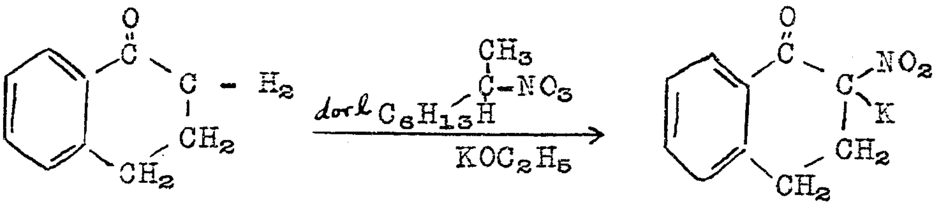
it could tautomerize to give either one of the following compounds,



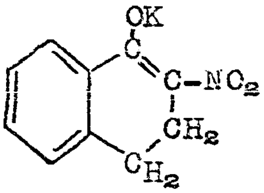
which would lead ro racemization. Such a tautomeric shift, according to the authors should not destroy the activity if due to carbon four but would if it were due to carbon two.

By carrying out the same reaction on cyclohexanone, they found that an active potassium <u>aci</u>-nitro salt was formed which racemized in about an hour. However, the product was difficult to isolate, gave poor yields and was hygroscropic. For this reason, no correct analysis for nitrogen or potassium was obtained.

In order to eliminate the possibility of the 4-asymmetric carbon atom and yet get a stable substance for analysis, Horne and Shriner(79) treated α-tetralone with d and l-2-octyl nitrates in the presence of potassium ethylate. They found that potassium salts of β-nitro-α-tetralone were obtained which were inactive in every case.



The reaction was carried out at 40, 22 and 0° with no active salts forming. Immediate treatment of the potassium salt with acid gave free β-nitro-α- tetralone optically inactive. No aci-form was produced. For this reason, Horne and Shriner thought the compound that was formed on nitration was



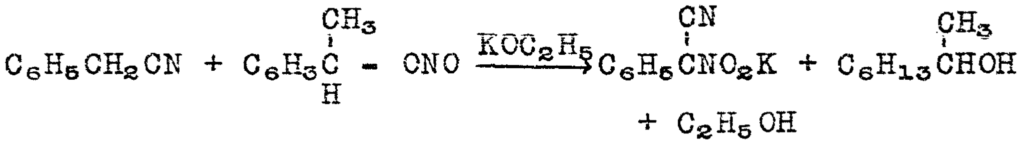
In 1935, Thurston and Shriner(80) reported a partial asymmetric synthesis which was performed by treating 2-bromofluorene with both *d*-and *l*-2-octyl nitrate in the presence of potassium ethylate. The *d*-2-octyl nitrate gave a potassium salt which had an actual rotation of + 0.06± 0.01° and + 0.05± 0.01 for two independent preparations. The *l*-2-octyl nitrate gave a potassium salt of very low specific rotation, $[\alpha]_D = -1.71°$. The salts recemized rapidly. Immediate treatment of the *d*-potassium salt with acid gave 9-aci-nitro-2-bromofluorene which was optically inactive.

It is possible that the results of Shriner could have been easily in error for the actual rotations were small enough to be within the experimental error (0.05 ± 0.01°). This error could have been easily due to impurities.

Mills(81) reported the resolution of phenylnitroacetonitrile by means of its brucine salt and converted the brucine salt into an optically active sodium salt.

Attempts to confirm this work by Thurston and

Shriner(66) have been unsuccessful. They, therefore, attempted to obtain optically active salts by means of an asymmetric synthesis. Treatment of phenylacetonitrile with *d*- or *l*-octyl nitrate in presence of potassium ethylate gave potassium salts which were inactive.



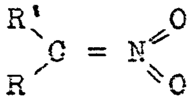
$$C_6H_5CH_2CN + C_6H_3\overset{CH_3}{\underset{H}{C}} - CNO \xrightarrow{KOC_2H_5} C_6H_5\overset{CN}{C}NO_2K + C_6H_{13}\overset{CH_3}{C}HOH + C_2H_5OH$$

The reaction was repeated several times with changes in temperature, the ratio of reactants and order of addition of the reactants, but in no case did the salts show any activity.

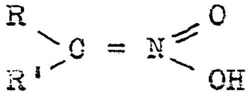
OBJECTIVE

The results presented in the historical section of this thesis indicated that there are three possible forms of aliphatic nitro compounds, namely, the normal nitro form, I, the aci-form, II, and the conjugated aci-form, III.

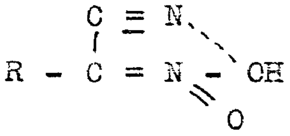
I.



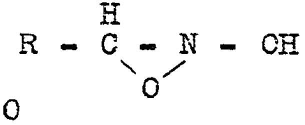
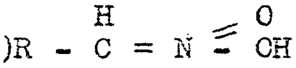
II.



III.



That an aci-form, II, does exist has been shown by the salt forming properties of the normal nitro form, I. Stable aci-forms also have been isolated and converted to the nitro form. Reactions, conductivity and absorption spectra of the salt of the nitro form showed the aci-form to be different in structure from the nitro form, I.

For this aci-form, II, two structures have been proposed, that of Hantzsch(47)  $R - \underbrace{\overset{H}{C} - N}_{O} - CH$ and that of Mickael(51)  $R - \overset{H}{C} = N \begin{matrix} = O \\ - OH \end{matrix}$

IV

V.

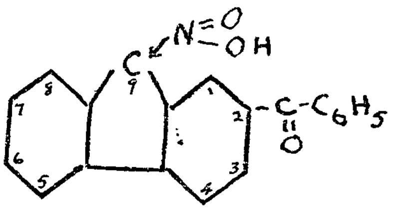
The reactions of the aci-nitro compounds were more readily explained by the use of structure, V, so the ring structure of Hantzsch was discarded even by himself.

It would, therefore, seem that the $>C = N<$ group of the aci-form would lie in one plane, But the discovery by Kuhn and Albrecht(76) and the confirmation by Young and Shriner(77) that optical activity existed in such an ion indicated that the structure was non-planar. Although, not conclusive, results have been reported which indicated that the *aci*-nitro ion portrayed optical activity. Therefore, to show conclusively the structure of the *aci*-nitro ion, it is necessary to isolate its optical forms. Shriner and his co-workers tried to do this by means of an asymmetric synthesis. They, however, obtained no conclusive results, although, they had indications of an optically active *aci*-ion. They were also unable to isolate any of their products because of the instability of the *aci*-nitro compound.

If optical activity does exist in the aliphatic nitro group, it should be possible to resolve an inactive *aci*-nitro compound into its optical antimers. Mills(81) has reported the resolution of phenylnitroacetonitrile by means of its brucine salt. However, his work has never been confirmed. He gave no details of his experimental work and has not mentioned it in any of his subsequent publications.

I, therefore, undertook to prepare a stable *aci*-nitro compound and by means of optically active resolving agents to resolve the inactive compound into its optical antimers.

The compound chosen for study was 9-aci-nitro-2-benzoylfluorene.



Such a compound is stable due to the negative groups that are present. The phenylene group is negative and the benzoyl group increases the negativity and gives stability to the compound.

The preparation and attempted resolution of potassium 9-aci-nitro-2-benzoylfluorene has been discussed in a previous thesis(86).

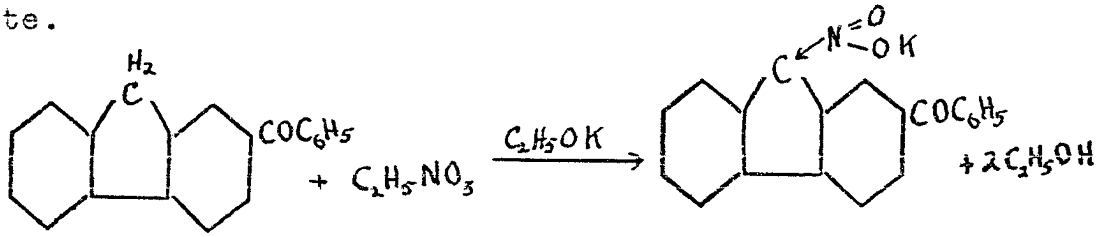
In the present work definite evidence has been obtained for the isolation of an optically active form of 9-aci-nitro-2-benzoylfluorene.

First, a detailed discussion of the preparation and composition of the active brucine 9-aci-nitro-2-benzoylfluorene will be given. Second, a discussion of attempts to isolate a second diastereoisomer and also an active aci- or potassium aci-form of the nitro compound will be presented. Thirdly, a discussion of the effects of solvents on the racemization and decomposition will be discussed, and finally the extension of Wislicenus' condensation(28) to other nitro compounds will be presented.

PROCEDURE and RESULTS

A. 9-aci-nitro-2-benzoylfluorene

Potassium 9-*aci*-nitro-2-benzoylfluorene was prepared by Wislicenus' condensation(28). 2-Benzoylfluorene was condensed with ethyl nitrate in the presence of potassium ethylate.



An atmosphere of nitrogen was found effective in eliminating the presence of by-products formed by oxidation.

The free *aci*-nitro-2-benzoylfluorene was obtained by acidification of aqueous solution of the potassium salt with cold, dilute hydrochloric acid. Acidification of a hot solution resulted in an oil which crystallized on cooling. The composition of the crystals was not determined.

The 9-*aci*-nitro-2-benzoylfluorene was soluble in ether. If concentrated hydrochloric acid was added in excess to an ethereal solution containing the *aci*-form, an oil immediately separated which turned to a gum. There was no blue color produced as was noticed by Hantzsch(47) in his study of *aci*-nitro compounds. On standing, the ether evaporated, leaving behind light yellow crystals. The melting point of the crystals showed it to be different from the *aci*-form.

B. Brucine 9-*aci*-nitro-2-benzoylfluorene

1. *Preparation and Composition* - Brucine 9-*aci*-nitro-2-benzoylfluorene crystallized out of an alcoholic solution when equivalent quantities of potassium 9-*aci*-nitro-2-benzoylfluorene and brucine hydrochloride were mixed together. The salt crystallized out in greenish-yellow crystals which had a specific optical rotation of about +75° in chloroform and +70° in pyridine. The rotation of the salt varied for several independent preparations from +75 to 76°. Brucine in chloroform has a specific rotation of -116.25° while that of brucine hydrochloride is -17.82.

If the method of preparation was varied so that one equivalent of potassium 9-*aci*-nitro-2-benzoylfluorene was treated with two equivalents of brucine hydrochloride, the yield was about ninety[redacted] percent of the theoretical. However, the specific rotation of the salt was only about 55° as compared to 70° when equivalent quantities were used. When an equivalent of potassium 9-*aci*-nitro-2-benzoylfluorene was treated with an equivalent of brucine and an equivalent of brucine hydrochloride, the yield was about sixty percent of the theoretical and the specific rotation was about +75°.

These results seemed to indicate two possibilities. The possibility that two equivalents of brucine hydrochloride were necessary to react with an equivalent of potassium 9-*aci*-nitro-2-benzoyl-fluorene to form a brucine salt containing one equivalent of the *aci*-form to two equivalents of the brucine ion. The second possibility was that the potassium 9-aci-nitro-2-benzoylfluorene and brucine hydrochloride reacted in equivalent quantities and the yield of fifty percent was due to the crystallization of one diastereoismer of 9-aci-nitro-2-benzoylfluorene. If this were the case, then, where two equivalents of brucine hydrochloride were used, both diastereoismers precipitated out together, causing the low rotation in the case of this brucine salt. The excess brucine hydrochloride has a salting-out effect which causes the second diastereoismer to crystallize out along with the first. The effect of the mixture of the two diastereoisomers causes the lowering in rotation of the brucine salt.

If the brucine 9-aci-nitro-2-benzoylfluorene was dissolved in chloroform and then treated with aqueous sodium hydroxide, the yellow salt of sodium 9-aci-nitro-2-benzoylfluorene precipitated. By calculating the amount of aci-form from the sodium salt produced, the percentage of aci-form in the brucine 9-aci-nitro-2-benzoylfluorene was found to be 38.49 while the calculated was 41.85. The low result was due to the solubility of the sodium salt in the solution.

The brucine 9-aci-nitro-2-benzoylfluorene, after treatment with sodium hydroxide, was extracted with benzene and the rotation was determined in the polarimeter. In two determinations, the specific rotations on the basis of the amount of brucine that should have been present were

-96.61 and -86.38. The specific rotation of pure brucine in benzene is -102°.

Hydrogen and carbon combustion analysis also indicated that the brucine salt was in ratio of one *aci*-nitro to one brucine-ion. It also showed that one molecule of ethyl alcohol was coordinated with the brucine salt. The calculated values for carbon and hydrogen for a one to one *aci*-nitro and brucine molecule is 72.77% and 5.50% respectively; with ethyl alcohol of coordination the values are 71.50% and 5.96%. An average of six determinations gave for carbon 71.84% and for hydrogen 5.93%.

The brucine 9-*aci*-nitro-2-benzoylfluorene was also prepared using n-butyl alcohol as a solvent. The color of this salt was slightly different from that of the brucine 9-*aci*-nitro-2-benzoylfluorene, the former being a bright greenish-yellow while the latter was a dull yellow-green. The specific rotation of the brucine 9-*aci*-nitro-2-benzoylfluorene which was prepared in n-butyl alcohol was found to be +66 as against +75 in the case of the brucine salt prepared from ethyl alcohol. It was also noticed that the light was absorbed to a greater extent in the case of the brucine salt with n-butyl alcohol and the rotation was difficult to read.

Treatment of the brucine salt containing n-butyl alcohol with dilute hydrochloric acid and then oxidation with potassium dichromate yielded the odor of butyric acid;

thus indicating the presence of n-butyl alcohol of coordination.

Carbon and hydrogen combustion analysis of this salt gave low results for hydrogen. Calculated for carbon, 71.99%; for hydrogen, 6.26%; found for carbon, 71.92%; for hydrogen 5.56%. The low results for hydrogen were interpreted as due to the backward diffusion of water in the combustion tube.

The brucine 9-aci-nitro-2-benzoylfluorene is a stable compound which has no definite melting point. It will not hydrolyze when treated with water. This property was used to rid the salt of potassium chloride which crystallized out along with the brucine salt.

The foregoing results indicated that one diastereoisomer of 9-aci-nitro-2-benzoylfluorene crystallized out of the alcoholic solution. Therefore, several attempts were made to isolate the other diastereoisomer. The alcoholic solution from which the first set of crystals was obtained, yielded no active substance when cooled to -10°C. The product obtained from the alcoholic solution was 2-benzoylfluorenone.

It was found that if a mixture of equivalent quantities of potassium 9-aci-nitro-2-benzoylfluorene and brucine hydrochloride were mixed in hot alcohol that four sets of crystals could be obtained at different temperatures. The specific rotation of the crystals varied from +69 to

+43°. The total amount that crystallized out was 57.4% of the theoretical. The alcoholic solution that remained had a specific rotation of +5.5°.

These results indicated that the fourth set of crystals was a mixture of both diastereoisomers, hence the low specific rotation. The mother liquor contained the remainder of the second diastereoisomer which had a low positive specific rotation.

2. The Potassium Salt from active Brucine 9-*aci*-nitro-2-benzoylfluorene - Brucine 9-*aci*-nitro-2-benzoylfluorene was found to yield the potassium 9-*aci*-nitro-2-benzoylfluorene when treated with potassium hydroxide or potassium ethylate and the 9-*aci*-nitro-2-benzoylfluorene when treatedwith cold, dilute hydrochloric acid. In every case, where either the potassium salt or the free *aci*-form was isolated, they were found to be inactive. However, the effect of acid or basic solutions on the salt led to some interesting results.

It was found that if brucine 9-*aci*-nitro-2-benzoylfluorene was treated with anaqueous solution of potassium hydroxide a specific rotation of -51.33° was obtained on the basis of the free brucine present.

If, however, alcoholic potassium hydroxide was used the original specific rotation, rotation on mixing, was -65.02° at 23°C on the basis of free brucine. At the end of about four hours, the specific rotation had changed to -75.6°. The rotation became constant after the end of thirty hours at -82.87. Free brucine in alcoholic potassium hydroxide under the same conditions had a specific rotation of -83.54.

Such a change in rotation could only be due to two factors. One, that it took thirty hours for the potassium hydroxide to react with the brucine salt, and two, that a potassium salt was formed from the brucine salt which had a definite specific rotation, hence, the rotation was due to the brucine plus that of the potassium salt. The potassium salt then racemized slowly and finally the rotation was only due to that of brucine alone. This latter seemed to be the case, for in the case of aqueous potassium hydroxide, the value became constant almost immediately showing that the reaction with the brucine salt took place at once. This rotation then indicated that the potassium salt, formed in the alcoholic solution, was active.

It was found also that if the brucine 9-aci-nitro-2-benzoylfluorene was dissolved in the least possible amount of chloroform and a saturated solution of potassium acetate in anhydrous n-butyl alcohol was added that a negative rotation was assumed. This rotation then changed slightly towards the positive, reached a maximum and then changed towards the neagative. The actual rotation at the moment after mixing was -1.70°; after an hour and fifteen minutes, it had changed to -1.56° and finally became constant after about sixty-four hours at -1.65°. It was noticed that when the rotation began to change from -1.56 to -1.65 that the potassium salt of 9-*aci*-nitro-2-benzoylfluorene began to precipitate. This potassium salt when removed from the solution was inactive.

The change in rotation from -1.70 to -1.56° offered difficulty in interpretation. The only suggestion that can be offered is that the reaction took about three hours to come to equilibrium. The later change from -1.56 to -1.65° can be easily explained. The potassium salt while in solution was active, hence, the rotation was due to the potassium salt and brucine acetate. As soon as the alcohol of coordination was removed, the salt racemized or decomposed and precipitated out, causing a change in rotation.

Analysis of the salt for potassium showed it to be potassium 9-*aci*-nitro-2-benzoylfluorene. Calculated for potassium was 11.05%; found, 10.99%.

If the brucine 9-*aci*-nitro-2-benzoylfluorene was dissolved in a saturated solution of potassium acetate and anhydrous n-butyl alcohol, the rotation remained at a constant value. There was no change in rotation. Attempts to precipitate out the potassium salt were unsuccessful. The addition of chloroform or ether only precipitated out the potassium acetate. The specific rotation of the brucine salt in the saturated potassium acetate solution on the basis of amount of free brucine present had a specific rotation of -86.64 while free brucine under the same conditions has a specific rotation of -88.37. In one attempted there was an indication that the solution changed from an actual rotation of -.36 to -.43 but this could not be confirmed by other runs.

When a suspension of brucine 9-*aci*-nitro-2-benzoylfluorene was treated with dilute hydrochloric acid, the pale-yellow 9-*aci*-nitro-2-benzoylfluorene precipitated out. This *aci*-form showed no activity. This was the case also when the precipitation was performed at about -10°C.

In glacial acetic acid, however, brucine 9-*aci*-nitro-2-benzoylfluorene gave an actual rotation of +0.11 which changed to -0.08 after thirty minutes. The specific rotations accordingly were +5.54° and -4.04°. The specific rotation of brucine in glacial acetic acid is -6.00°. This indicated that the *aci*-form was active but racemized readily to the inactive form.

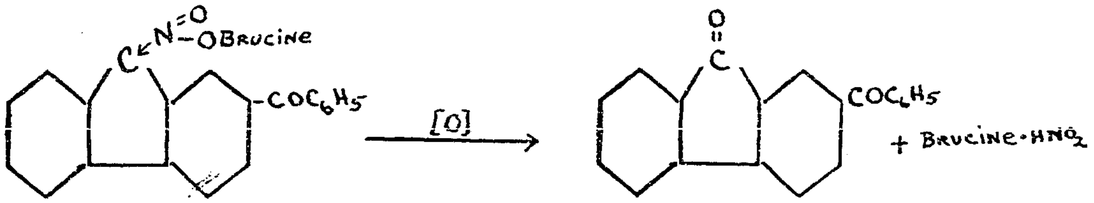
These results indicated that one diastereoisomer was obtained and that the potassium or *aci*-forms are only active for a short time in solution and soon racemize to an inactive form.

3. *Mutarotary Effect of Brucine 9-aci-nitro-2-benzoylfluorene*. - It was noticed, that when brucine 9-*aci*-nitro-2-benzoylfluorene was dissolved in chloroform the rotation was not constant. This change at first was very

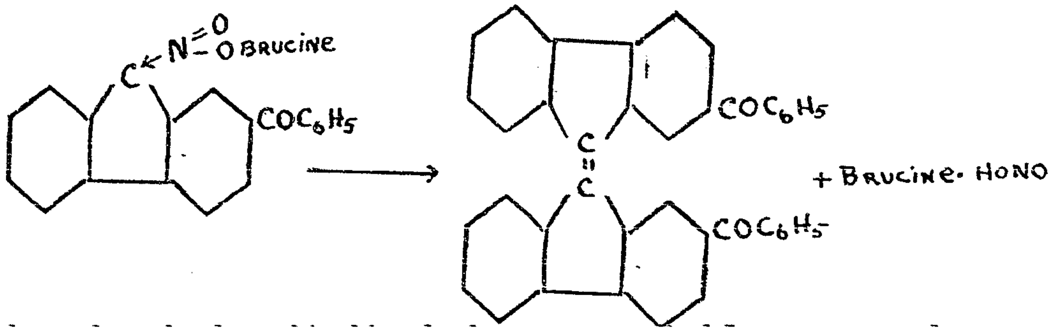
rapid and then gradually decreased. The value changed from a high positive value to a high negative value.

The time was plotted against the log of the concentration, one over the concentration and one over the concentration squared but in no case was a straight line obtained, but the slope of the curves in all three cases were similar.

On the basis of these results, it, therefore, seemed that the change in rotation was not due to any one effect but to two or more simultaneous reactions. If one looks at the structure of brucine 9-aci-nitro-2-benzoylfluorene, one will see that several simultaneous reactions can take place. First, assuming that the brucine salt is a diastereoisomer, it may racemize. Second, the salt may mutarotate, for brucine salts have been shown by Adams(82), McKenzie(83), Kenyon(84) and others to mutarotate in chloroform. Thirdly, the brucine salt may decompose. Due to air oxidation brucine hydronitrite, 2-benzoylfluorenone and potassium nitrite may result.



It also may decompose to give brucine hydronitrite and a dimolecular compound.



Then brucine hydronitrite being an unstable compound may decompose to give brucine and nitrous oxide which would add another effect. Finally, the alcohol of coordination present may be oxidized to acetic acid by the nitrous acid. The acetic acid may then combine with brucine to form brucine hydroacetate. The final rotation seemed to indicate that brucine acetate was an end product.

It has been shown previously in this thesis that the brucine 9-*aci*-nitro-2-benzoylfluorene crystallizes out of ethyl alcohol with a molecule of ethyl alcohol of coordination and out of n-butyl with a molecule of n-butyl alcohol of coordination. The salts obtained from these two solvents should act differently when dissolved in chloroform. The n-butyl alcohol, being a heavier molecule than ethyl alcohol, would be expected to break away from the brucine salt more readily and, therefore, the decomposition of the brucine salt would be expected to be more rapid. A study of the rotations of the two salts in chloroform showed this to be so.

Rotation of Brucine 9-*aci*-nitro-2-benzoylfluorene with Ethyl Alcohol of Coordination in Chloroform.

Solution I. (Curve I)

Brucine salt(0.5020 g.) in 25 cc. of chloroform.
Temperature 23°.
Length of polarimeter tube two decimeters.

Time in hours	Reading	Zero Reading	α	$[\alpha]_D^{23}$
0	0.47	3.50	+3.03	75.75
0:05	0.83	3.50	+2.67	66.76
0:10	0.93	3.50	+2.54	63.51
0:20	1.03	3.50	+2.47	61.76
0:30	1.09	3.50	+2.41	60.26
0:45	1.15	3.50	+2.35	58.76
1:00	1.19	3.50	+2.31	57.76
1:30	1.28	3.50	+2.22	55.51
2:30	1.43	3.50	+2.07	51.76
4:45	1.60	3.50	+1.90	47.51
8:00	1.67	3.50	+1.83	45.76
23:00	2.24	3.50	+1.26	31.51
31:15	2.44	3.50	+1.06	26.51
47:00	2.69	3.50	+0.81	20.25
72:00	3.09	3.50	+0.41	10.25
95:00	3.36	3.50	+0.14	3.50
143:00	3.81	3.50	-0.31	-7.75
169:00	3.91	3.50	-0.41	-10.25
217:00	4.20	3.50	-0.70	-17.50
293:00	4.45	3.50	-0.95	-23.75
389:00	4.61	3.50	-1.11	-27.75
485:00	4.77	3.50	-1.27	-31.76

Solution II

Brucine salt(0.3946 g.) in 25 cc. of chloroform.
Polarimeter tube two decimeters.
temperature = 23°C.

Time in hours	Reading	Zero Reading	α	$[\alpha]_D^{23}$
0:00	1.15	3.53	+2.38	+75.39
0:25	1.68	3.53	+1.85	+58.60
0:55	1.79	3.53	+1.74	+55.11
2:20	2.00	3.53	+1.53	+48.46
21:20	2.65	3.53	+0.88	+27.87
67:40	3.57	3.53	-0.04	- 1.27
119:20	3.98	3.53	-0.45	-14.23
142:30	4.14	3.53	-0.61	-19.32
165:20	4.36	3.53	-0.83	-26.29
199:00	4.40	3.53	-0.87	-27.55

Solution III

Brucine salt(0.3985g.) in 25 cc. of chloroform.
Temperature 23°C
Polarimeter tube two decimeters.

Time in hours	Reading	Zero reading	$[\alpha]$	$[\alpha]_D^{23}$
0:00	1.10	3.53	+2.43	+76.22
0:25	1.62	3.53	+1.91	+59.91
0:55	1.75	3.53	+1.79	+56.15
2:20	1.91	3.53	+1.62	+50.82
21:20	2.70	3.53	+0.83	+26.03
67:40	3.61	3.53	-0.08	- 2.51
119:20	4.00	3.53	-0.47	-14.71
142:30	4.24	3.53	-0.71	-22.27
165:20	4.42	3.53	=0.89	=27.92
199:00	4.50	3.53	-0.97	-38.31

Rotation of Brucine 9-*aci*-nitro-2-benzoylfluorene with n-Butyl Alcohol of Coordination in Chloroform.

Solution I, (Curve II)

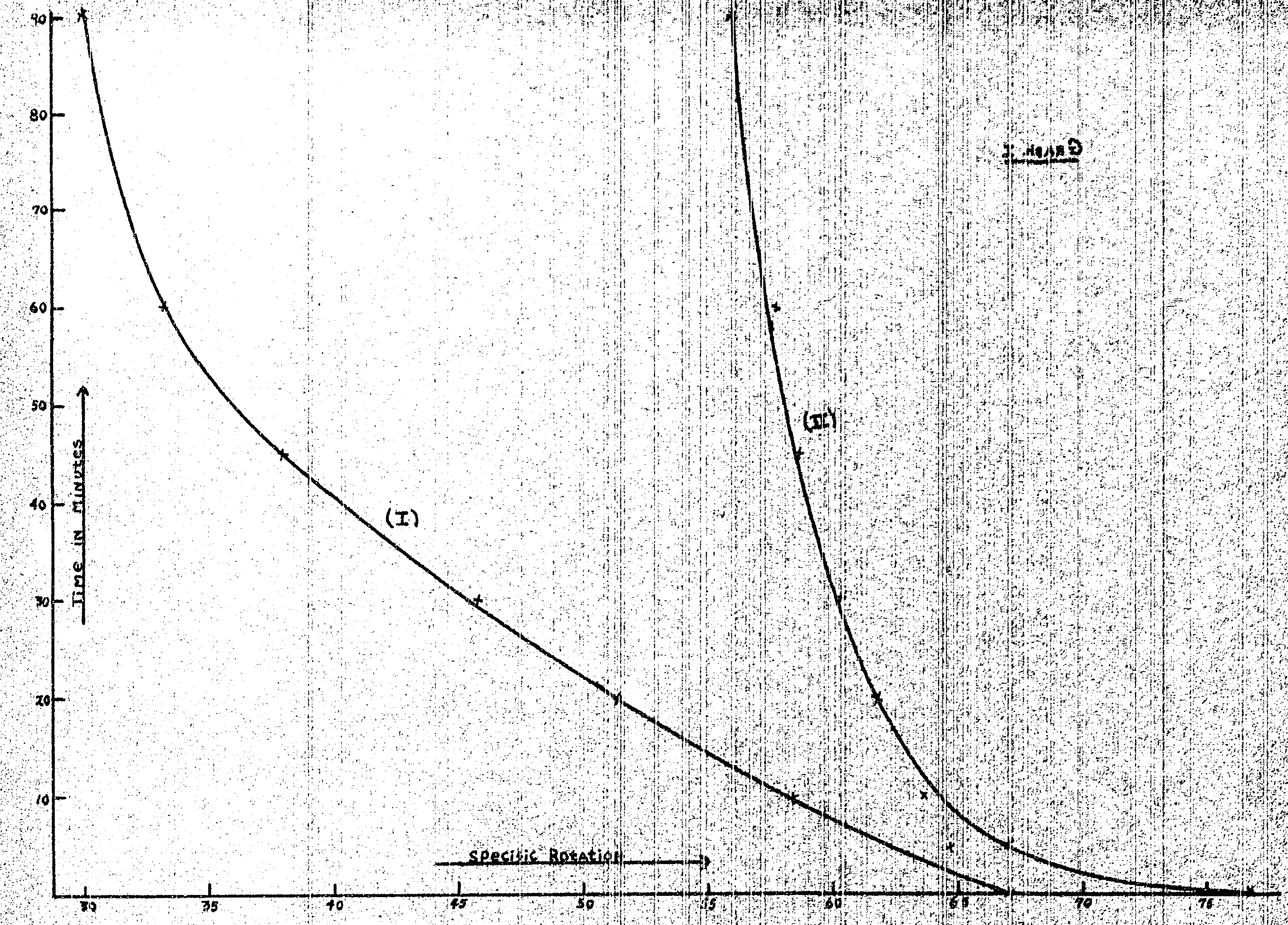
Brucine salt (0.1584 g.) in 25 cc. of chloroform.
Temperature 23°.
Length of tube, polarimeter, two decimeters.

Time in hours	Reading	Zero reading	α	$[\alpha]_D^{23}$
0:00	2.64	3.48	+0.84	+66.89
0:05	2.66	3.48	+0.82	+64.71
0:10	2.74	3.48	+0.74	+58.38
0:20	2.83	3.48	+0.65	+51.29
0:30	2.90	3.48	+0.58	+45.76
0:45	3.00	3.48	+0.48	+37.87
1:00	3.06	3.48	+0.42	+33.13
1:30	3.10	3.48	+0.38	+29.96
2:00	3.14	3.48	+0.34	+26.83
3:00	3.23	3.48	+0.21	+16.57
6:30	3.32	3.48	+0.16	+12.63
47:53	3.75	3.48	-0.27	-21.30
73:36	3.88	3.48	-0.40	-31.56
121:58	3.94	3.48	-0.46	-36.29
269:17	4.01	3.48	-0.53	-41.82
293:57	4.00	3.48	-0.52	-41.03

Solution II

Brucine salt (0.2070) in 25 cc. of chloroform.
Polarimeter tube two decimeters.
Temperature 23°C.

Time in hours	Reading	Zero reading	α	$[\alpha]_D^{23}$
0:00	2.40	3.50	1.10	+66.42
0:05	2.47	3.50	1.03	+62.19
0:10	2.61	3.50	0.89	+53.74
0:20	2.72	3.50	0.78	+47.10
0:30	2.80	3.50	0.70	+42.27
0:45	2.84	3.50	0.66	+39.85
1:00	2.88	3.50	0.62	+37.44
1:20	2.90	3.50	0.60	+36.23
2:20	2.96	3.50	0.54	+32.60


GRAPH I
(I)
(II)
Time in Minutes
Specific Rotation
90
80
70
60
50
40
30
20
10
30
35
40
45
50
55
60
65
70
75

The two curves here presented show the specific rotation plotted against time for the first few hours. It can be seen that the salt containing the n-butyl alcohol of coordination(I) begins with an initial specific rotation of about +66 while that with the ethyl alcohol(II) is +75. The curve for the n-butyl alcohol of coordination(I) shows a rapid change in rotation for the first few hours which then gradually decreases. The ethyl alcohol curve(II), however, shows a very rapid rotational change for the first few minutes which gradually tapers off.

If conditions are selected so that both diastereoisomers are present and alcohol of coordination absent, there should be a difference in the initial rotation and the mutarotary effect. These conditions were obtained by mixing equivalent quantities of potassium 9-aci-nitro-2-benzoylfluorene with brucine hydrochloride in chloroform. The potassium chloride formed was filtered before the solution was placed in the polarimeter tube.

It was found that the initial rotation of this mixture was different from that of the brucine salt crystallized in 50% yield from alcohol. Three independent determinations gave specific rotations of +59.20°, +52.88°, and +56.11°. The active brucine salt from alcohol in chloroform had a specific rotation of about +75.

The change of rotation in chloroform for the three different mixtures is given in the following tables.

Mutarotary effect of a mixture of one equivalent of potassium 9-*aci*-nitro-2-benzoylfluorene with one equivalent of brucine hydrochloride in chloroform.

Solution I

Potassium 9-*aci*-nitro-2-benzoylfluorene(0.3280) and 0.4 of a gram of brucine hydrochloride were weighed into a 25 cc. volumetric flask. Chloroform was added and the solution was filtered directly into a two decimeter polarimeter tube.

Temperature - 23°

Amount of brucine salt formed was (0.6588 grams)

Time in hours	Reading	Zero reading	α	$[\alpha]_D^{23}$
0:00	1.92	3.48	+1.56	59.20
0:05	2.05	3.48	+1.43	54.26
0:10	2.12	3.48	+1.36	51.60
0:20	2.17	3.48	+1.31	49.72
0:30	2.22	3.48	+1.26	47.82
0:50	2.32	3.48	+1.16	44.02
1:20	2.37	3.48	+1.11	42.12
2:20	2.60	3.48	+0.88	33.39
3:35	2.84	3.48	+0.64	24.29
19:35	3.92	3.48	-0.44	-16.70
48:45	3.96	3.48	-0.48	-18.22
73:00	3.96	3.48	-0.48	-18.22
121:40	3.96	3.48	-0.48	-18.22

Solution II

Potassium 9-<u>aci</u>-nitro-2-benzoylfluorene (0.3280) mixed with 0.4000 g. of brucine hydrochloride in 25 cc. chloroform. Rotation in two decimeter tube at 23°. Amount of brucine salt formed was 0.6588.

Time in hours	Reading	Zero reading	α	$[\alpha]_D^{23}$
0:00	0.70	3.48	2.78	52.88
0:10	0.70	3.48	2.78	52.88
0:30	0.76	3.48	2.72	51.75
2:25	0.98	3.48	2.50	47.55
19:00	1.82	3.48	1.66	31.58
91:10	3.25	3.48	0.23	4.38
137:15	3.75	3.48	-0.27	-5.14

Solution III

Amounts of salts and conditions same as in Solution II.

Time in hours	Reading	Zero reading	α	$[\alpha]_D^{23}$
0:00	0.53	3.48	2.95	56.11
0:10	0.68	3.48	2.80	53.27
2:00	0.82	3.48	2.66	50.60
18:45	1.87	3.48	1.61	30.63
91:00	3.67	3.48	- .19	- 3.62
137:00	4.50	3.48	-1.02	-19.40

The change for each solution is different. The initial rotation is about the same for each one, but the time for each to become constant and the final rotation are different. However, the important and interesting factor is that the initial rotation is less than that of the brucine salt which was crystallized from alcohol. This indicates that potassium 9-_aci_-nitro-2-benzoylfluorene and brucine hydrochloride in chloroform give, as might be expected, both diastereoisomers of brucine 9-_aci_-nitro-2-benzoylfluorene, while slow crystallization from alcohol gives but one.

It is important to note here the fact previously mentioned (page 46) that when the brucine 9-_aci_-nitro-2-benzoylfluorene was prepared from one equivalent of potassium 9-_aci_-nitro-2-benzoylfluorene and two equivalents of brucine hydrochloride, 90% of the salt precipitated out (both diastereoisomers). The rotation of this salt is similar to that of the simple mixture of potassium 9-_aci_-nitro-2-benzoylfluorene and brucine hydrochloride in chloroform.

Mutarotatory effect of brucine 9-*aci*-nitro-9-benzoylfluorene prepared from two equivalents of brucine hydrochloride and one equivalent of potassium *aci*-nitro salt in ethyl alcohol.

Solution I

Brucine salt (0.4568 g.) in 25 cc. at 23° of anhydrous chloroform.
Polarimeter tube - two decimeters.

Time in hours	Reading	Zero reading	α	$[\alpha]_D^{23°}$
0:00	1.58	3.50	+1.92	+52.53
0:05	1.75	3.50	+1.75	+47.87
3:00	2.18	3.50	+1.32	+36.12
18:40	3.17	3.50	+0.33	+ 9.03
42:40	4.43	3.50	-0.93	-25.45
66:10	4.80	3.50	-1.30	-35.56

Solution II

Brucine salt (0.2058 g.) in 25 cc. of chloroform at 23°.
Polarimeter tube - 2 decimeters.

Time in Hours	Reading	Zero reading	α	$[\alpha]_D^{23}$
0:00	2.61	3.48	+0.87	+52.84
0:05	2.71	3.48	+0.77	+46.77
0:15	2.80	3.48	+0.68	+41.30
0:35	2.88	3.48	+0.60	+36.45
1:35	2.99	3.48	+0.49	+29.90
2:35	3.08	3.48	+0.40	+24.30
7:20	3.46	3.48	+0.02	+1.21
23:20	3.84	3.48	-0.36	-21.87
26:35	3.88	3.48	-0.40	-24.30
50:35	4.20	3.48	-0.72	-43.73
102:05	4.27	3.48	-0.79	-47.98

It seemed probable that both decomposition and racemization were occurring together in chloroform solution. The use of a basic solvent should inhibit decomposition.

A comparative study of the supposedly active brucine 9-_aci_-nitro-2-benzoylfluorene with the known mixture of diastereoisomers in pyridine made possible the separation of the two effects.

When both diastereoisomers were present, no change in rotation took place for a period of about thirty minutes. But when the single diastereoisomer, obtained by crystallization from alcohol in 50% yield, was studied, there was a constant change in rotation from the beginning.

Mutarotary Effect of Brucine 9-aci-nitro-2-benzoylfluorene in pyridine.

CURVE I

Brucine salt (0.3497g.) in 25 cc. of pyridine at 24°.
Polarimeter tube - two decimeters.

Time in hours	Reading	Zero reading	α	$[\alpha]_D^{24}$	K
0:00	1.53	3.48	+1.95	69.69	
0:10	1.55	3.48	+1.93	69.00	.000506
0:20	1.61	3.48	+1.87	66.83	.00105
0:45	1.74	3.48	+1.74	62.19	.00126
1:10	1.82	3.48	+1.66	59.33	.00115
1:42	1.89	3.48	+1.59	56.83	.00100
7:32	2.14	3.48	+1.34	47.89	.00024
23:52	2.33	3.48	+1.15	41.11	

Rotatory Effect of a Mixture of Potassium 9-aci-nitro-2-benzoylfluorene and Brucine Hydrochloride in Pyridine.

Solution I (Curve II)

Potassium 9-aci-nitro-2-benzoylfluorene (0.1640 g.) mixed with 0.2000 g. of brucine hydrochloride in 25 cc. of pyridine.

Rotation was studied in a two decimeter tube at 23°. Amount of brucine salt present was 0.3272g.

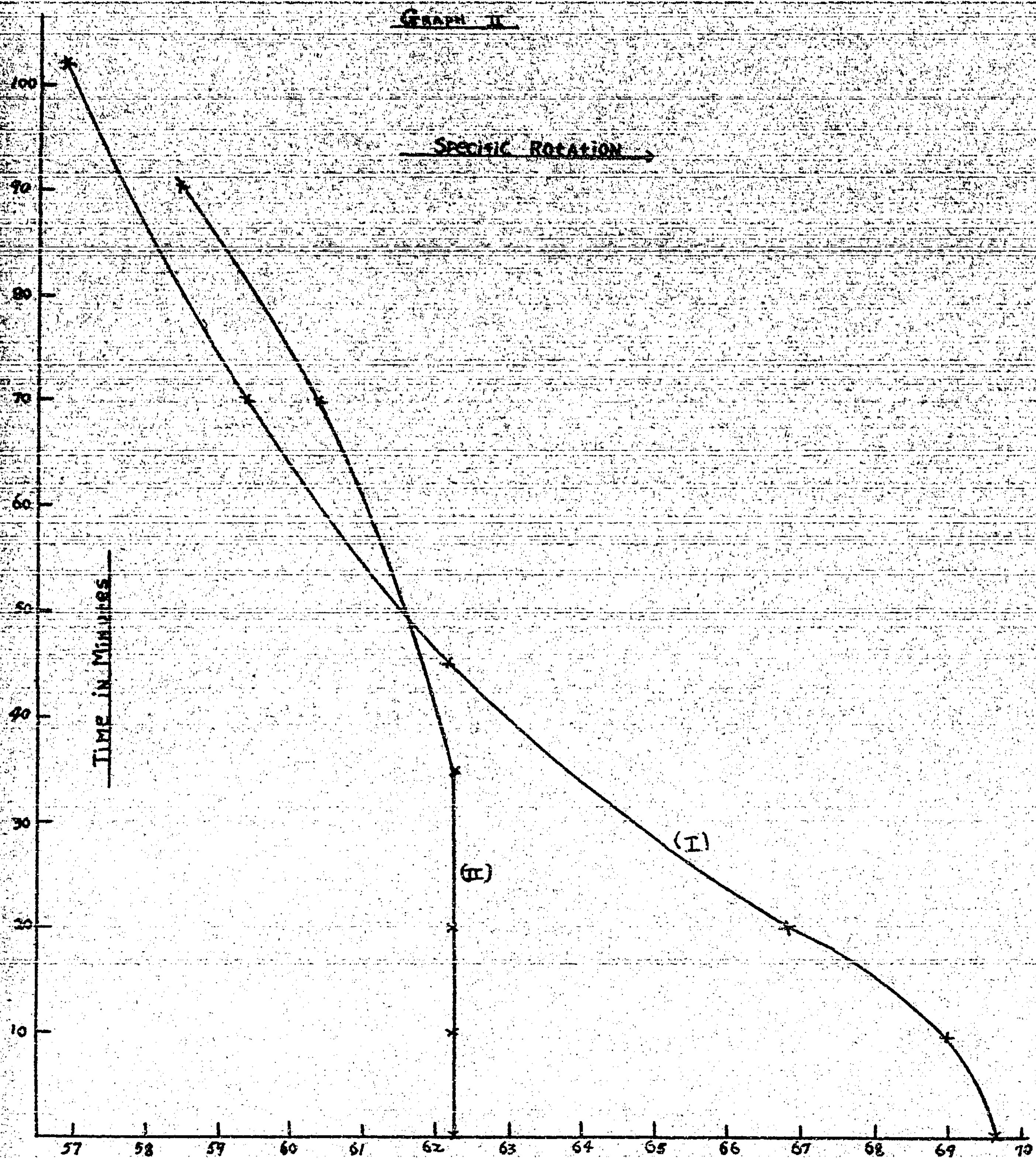
Time in hours	Reading	Zero reading	α	$[\alpha]_D^{23}$
0:00	1.85	3.48	+1.63	+62.27
0:10	1.85	3.48	+1.63	+62.27
0:20	1.85	3.48	+1.63	+62.27
0:35	1.85	3.48	+1.63	+62.27
1:10	1.90	3.48	1.58	+60.37
1:30	1.95	3.48	+1.53	+58.44
6:25	2.15	3.48	+1.33	+50.82
22:35	2.43	3.48	+1.05	+40.12
34:35	2.45	3.48	+1.03	+39.34
48:05	2.57	3.48	+0.91	+34.76
65:55	2.79	3.48	+0.69	+26.36
117:40	3.21	3.48	+0.27	+10.31

Solution II

Amounts and conditions same as in Solution I.

Time in hours	Reading	Zero reading	α	$[\alpha]_D^{23}$
0:00	1.94	3.48	+1.54	+58.83
0:30	1.94	3.48	+1.54	+58.83
1:10	2.02	3.48	+1.46	+55.78
1:35	2.14	3.48	+1.34	+51.19
2:55	2.25	3.48	+1.23	+46.99
18:30	2.45	3.48	+1.03	+39.34

Graph II


Specific Rotation →
Time in Minutes
100
90
80
70
60
50
40
30
20
10
57
58
59
60
61
62
63
64
65
66
67
68
69
70
(I)
(II)

A study of the curves shows, that the active brucine salt with alcohol of coordination(Curve, I,) shows a gradual change from +69.09, for about an hour at a constant rate(racemization). After this time, the slope of the curve changes indicating another type of reaction(decomposition).

The curve, representing the mixture of two diastereoismers(Curve II), shows no change in rotation for the first half hour. The specific rotation remains constant at 62.27°. At the end of this time, the rotation begins to change gradually due to decomposition of the salts.

These results indicate that when the brucine <u>aci</u>-nitro salt that has ethyl alcohol of coordination is dissolved in pyridine racemization takes place as the ethyl alcohol is lost. This occurs during the first hour. After this time decomposition of the salt takes place and the curve assumes a different slope.

That this is a racemization reaction can be shown by calculating the reaction constants or by plotting time against the log of the concentration. A racemization reaction is a monomolecular reversible reaction.

$$d \rightleftharpoons l$$

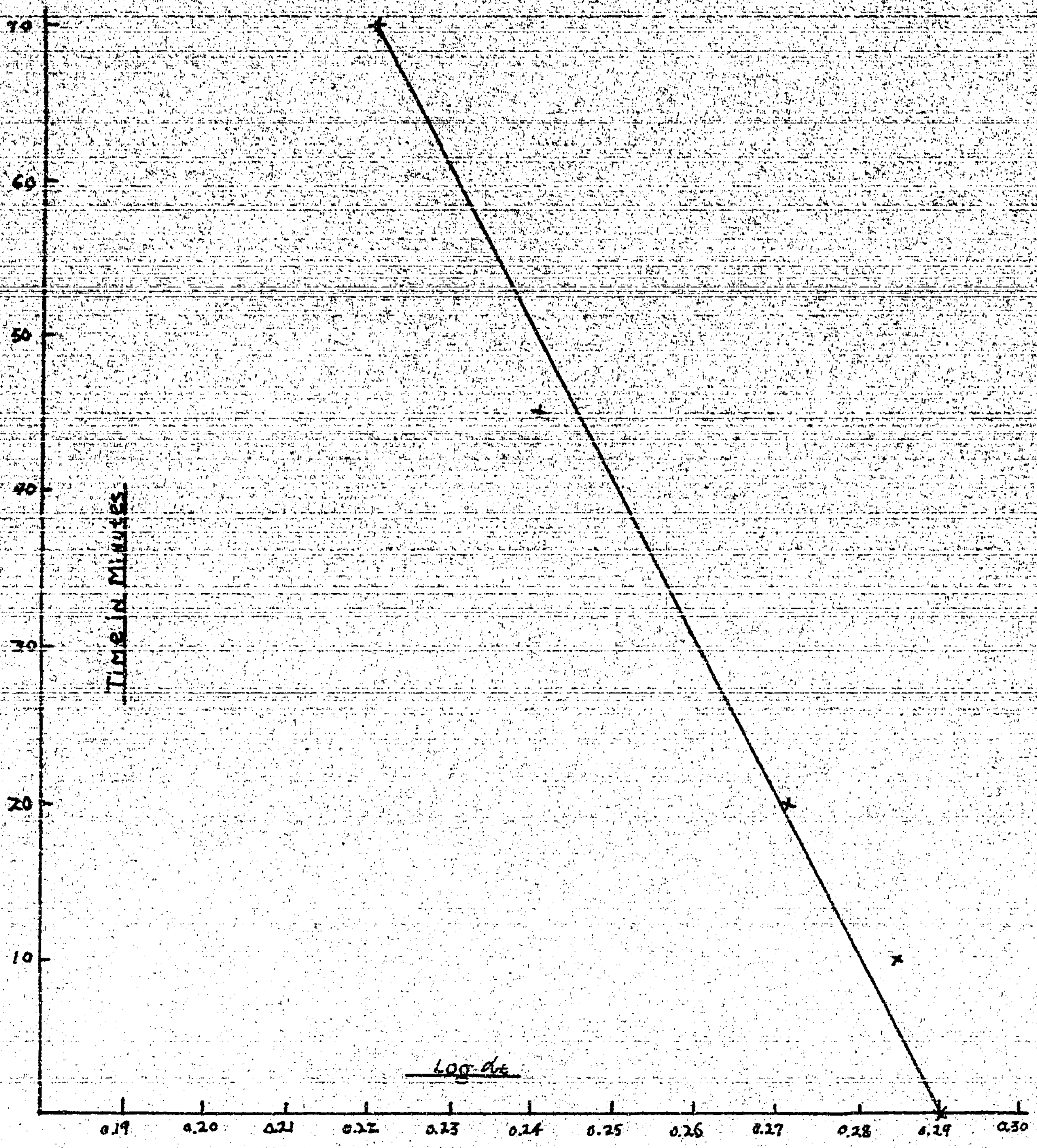
If(a) is the initial concentration of the d-form and (x) the amount of d-form that changes to l-form in time(t), then the change of concentration with time is given by the equation:

$$\frac{dx}{dt} = k(a-x)-kx$$

and

$$k = \frac{2.3}{2t} \log_{10} \frac{a}{a-2x}$$

GRAPH III

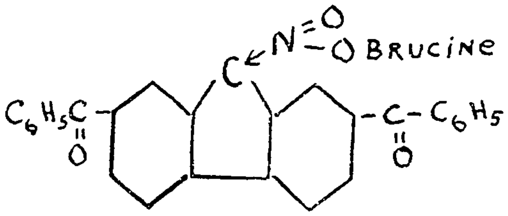

70
60
50
40
30
20
10
Time in Minutes
Log dt
0.19
0.20
0.21
0.22
0.23
0.24
0.25
0.26
0.27
0.28
0.29
0.30

then α_0 is proportional to (a) or the initial concentration and α_t is proportional to (a-2x) concentration after time (t). If (t) is plotted against log α_t a straight line is formed as is shown by graph III. The calculated reaction constants agree also fairly well except in the first case where an accurate reading at zero time is impossible. These constants are given in the table.

In the mixture of potassium 9-aci-nitro-2-benzoylfluorene and brucine hydrochloride(CurveII) in pyridine, there is no change for about the first half hour. This is so because here there is no possibility of racemization since both diastereoisomers are present. The change after this time is due to decomposition.

These results show that one diastereoisomer has been isolated.

If this conclusion is correct, a symmetrical aci-nitro compound should behave like the mixture of diastereoisomers. To test this reasoning, the brucine salt of the symmetrical 9-aci-nitro-2,7-dibenzoylfluorene was crystallized from alcohol and studied under identical conditions.



The salt had a high positive specific rotation in chloroform of +63.92, and in pyridine of +78°07°. It will be remembered that the **active** brucine 9-aci-nitro-2-benzoylfluorene had a lower specific rotation in pyridine than in chloroform. The effect in the (2,7) compound is, therefore, reversed.

When brucine 9-aci-nitro-2,7-dibenzoylfluorene was dissolved in pyridine, there was no change in rotation for about two hours. After this time, the rotation began to change gradually due to decomposition. The rotation of 0.3634 grams of the salt in 25cc. of pyridine at 25° in a two decimeter tube was +2.27, $[\alpha]_D^{25}$, +78.07. At the end of two hours there was no change; after six hours the rotation had changed to α, +1.38, $[\alpha]_D^{25}$, +72.56.

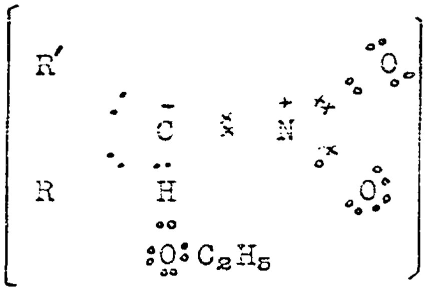
Since this brucine salt is symmetrical there is no possibility of optical activity in the aci-nitro compound. The rotation is due totally to salt formation. Hence, it should act similar to a mixture of the two diastereoisomers in pyridine. That it does, proves part of the rotation of the brucine 9-aci-nitro-2-benzoylfluorene with alcohol of coordination is due to the asymmetry of the molecule.

SUMMARY

Brucine hydrochloride reacts with potassium 9-*aci*-nitro-2-benzoylfluorene in alcoholic solution to give brucine 9-*aci*-nitro-2-benzoylfluorene with one molecule of alcohol of crystallization. One diastereoisomer of brucine 9-*aci*-nitro-2-benzoylfluorene was obtained.

The isolation of the one diastereoisomer indicates that asymmetry exists in the *aci*-nitro ion.

The alcohol of coordination plays an important part in preserving the asymmetry of the molecule. The alcohol may coordinate to the two electrons on the carbon thus:



Brucine.

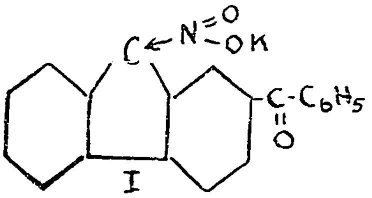
In doing this it prevents the electrons from resonating hence, stabilizing the ion and causing it to crystallize as an active brucine salt.

It was found also, in my previous thesis(86) that the *l*-methyl ester of 9-*aci*-nitro-2-benzoylfluorene was only stable in the presence of alcohol. Evaporation of the alcohol caused decomposition of the ester.

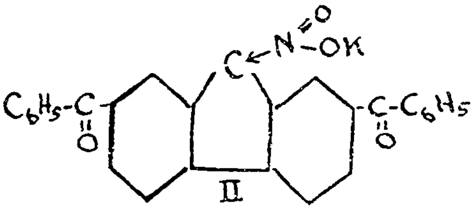
When the brucine salt is placed in a stabilizing or basic solvent such as pyridine, the alcohol first comes off and then the ion racemizes since pyridine does not hinder the racemization reaction. This takes place during the first hour and then decomposition begins to take place.

Therefore, since it has been demonstrated that the condensation of Wislicenus(28) can be extended to the preparation of complex nitro compounds, and that alkaloidal salts of the *aci*-nitro compounds can be prepared from an alcoholic solution from which they separate in crystalline form with one molecule of alcohol of coordination, there now only remains the problem of applying the methods discussed to a more stable aliphatic nitro compound. When such a compound is found and resolved, it may be possible to isolate it from the alkaloid in an active form thus giving a more definite answer to the question of the asymmetry of the carbon joined to the nitrogen in aliphatic nitro compounds.

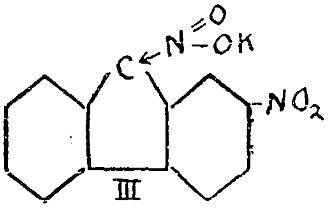
Besides potassium 9-*aci*-nitro-2-benzoylfluorene(I) the following new compounds have been prepared; potassium 9-*aci*-nitro-2,7-dibenzoylfluorene(II), potassium 9-*aci*-nitro-2-nitrofluorene(III) and potassium 9-*aci*-nitro-2-benzoyl-7-nitrofluorene(IV).



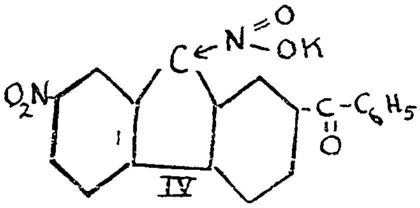
I



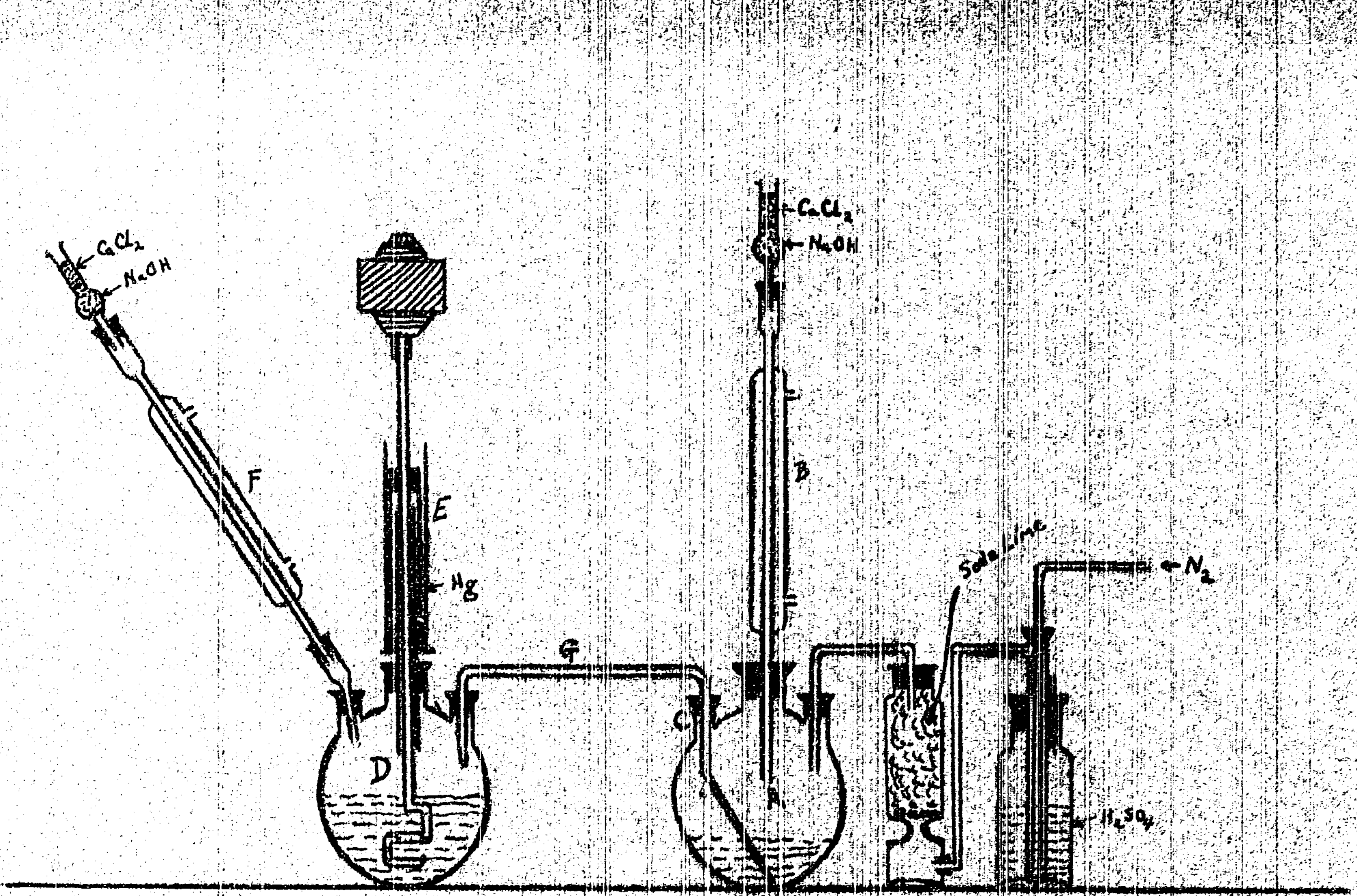
II



III



IV


$CaCl_2$
$NaOH$
F
E
Hg
D
G
C
A
$CaCl_2$
$NaOH$
B
Soda Lime
N_2
H_2SO_4

EXPERIMENTAL

A. Preparation of Brucine 9-*aci*-nitro-2-benzoylfluorene.

1. Preparation of potassium 9-*aci*-nitro-2-benzoylfluorene - An apparatus was assembled as shown in the diagram. After the apparatus was swept thorough with nitrogen gas 7.25 grams of clean potassium was added to flask(A), containing 50 cc's. of dry benzene. A dropping funnel containing 50cc's. of absolute ethyl alcohol was inserted at (C). Slowly the ethyl alcohol was added, drop by drop, until all the potassium was converted to potassium ethylate. This addition took from an hour to two hours. In 200 cc's. of hot dry benzene 50 grams of 2-benzoylfluorene was dissolved. This hot solution was added to flask(D) fitted with the mechanical mercury-sealed stirrer(E) and a condenser(F), containing a drying tube. The hot solution was stirred constantly so that a fine suspension of the 2-benzoylfluorene was formed when the solution had cooled. When the solution attained room temperature, 17.5 cc's. of ethylate nitrate was added with stirring. The dropping funnel at (C) was removed and tube (G) inserted. Nitrogen was allowed to pass into the flask. When condenser (B) was stoppered tightly the nitrogen forced the potassium ethylate from flask (A) into (D) at a constant rate. The potassium ethylate was added slowly. The solution at (D) turns orange on the first addition of potassium ethylate and then an orange-yellow

crystalline potassium salt began to precipitate. After all the potassium ethylate was added, the apparatus was corked tightly and the mixture was allowed to stand in an atmosphere of nitrogen for about twelve hours. After this time, the crystalline potassium 9-*aci*-nitro-2-benzoylfluorene was filtered with suction, washed with dry benzene and allowed to dry in the air. The yield was 54 grams or 82.5%.

9-Aci-nitro-2-benzoylfluorene - Two grams of potassium 9-*aci*-nitro-2-benzoylfluorene was dissolved in 100 cc. of boiling water, filtered and cooled. After cooling, dilute hydrochloric acid was added until a pale yellow precipitate was formed. The precipitate was filtered by suction, washed several times with water and dried in the air. The dry *aci*-form melted at 80-84°.

Five-tenths of a gram of the *aci*-form was dissolved in ether and to this was added excess(5cc.) concentrated hydrochloric acid. A yellowish oil at once appeared which on standing solidified. The solution showed no further change. On standing the ether evaporated causing the appearance of yellow crystals which melted at 113°. The crystals were not further investigated.

2. Brucine 9-*aci*-nitro-2-benzoylfluorene.

Preparation I.- Ten grams of potassium 9-aci-nitro-2-benzoylfluorene (one equivalent) was dissolved in 500 cc. of 95% ethyl alcohol at 70° and filtered. To this was added a hot solution of 12.20 grams of brucine hydrochloride (one equivalent) in 80 cc. of ethyl alcohol. The temperature of the final solution was 50°C. Immediately on addition a fine, crystalline precipitate of potassium chloride appeared. After about ten or fifteen minutes a yellow, crystalline brucine salt began to crystallize. The sides of container were scratched and more crystals appeared which settled to the bottom of the container. The crystals were filtered and triturated with water to remove the potassium chloride present and finally washed with water until the wash water gave no further test with silver nitrate. The yield was 11.1 grams or 50%. The brucine salt sintered at 160° and decomposed at 175°-185°.

A weighed sample of 0.3946 grams of the brucine salt in 25cc. of anhydrous chloroform when placed in a two decimeter polarimeter tube at 23°C gave α, +2.38, $[\alpha]_D^{23}$, +75.39°.

<u>Preparation II</u> - Twenty grams (one equivalent) of potassium 9-<u>aci</u>-nitro-2-benzoylfluorene in 1000 cc. of 95% ethyl alcohol dissolved at 70° and treated with 24.4 grams (one equivalent) of brucine hydrochloride in 200 cc. of ethyl alcohol gave a yield of 23 grams of the brucine salt on cooling or a yield of 51.8% of the theoretical.

A sample of 0.5020 grams in 25 cc. of anhydrous chloroform when placed in a two decimeter polarimeter tube at 23°C. gave α, +3.03°, $[\alpha]_D^{23}$, +75.75°.

Preparation III - The treatment of one equivalent of the potassium salt with two equivalents of brucine hydrochloride. In 1400 cc. of ethyl alcohol 17.2 grams of potassium 9-*aci*-nitro-2-benzoylfluorene was dissolved at 60°C. To this was added a solution of 40 grams of brucine hydrochloride in 200 cc. of 95% ethyl alcohol. The yield of the salt after cooling and filtering was 33.4 grams, a yield of 90% when based on one equivalent of the potassium salt to one equivalent of the brucine hydrochloride. The brucine salt sintered at 170° and decomposed at 175-180°.

A sample of 0.4568 grams in 25 cc. of anhydrous chloroform gave at 24°C α, +1.92, $[\alpha]_D^{24}$, +52.53°, in a two decimeter polarimeter tube.

This preparation shows the salting out effect of excess brucine hydrochloride.

Preparation IV - Treatment of one equivalent of the potassium salt with one equivalent of brucine and one equivalent of brucine hydrochloride. Ten grams of potassium 9-*aci*-nitro-2-benzoylfluorene was dissolved in 1500 cc. of 95% ethyl alcohol and mixed with 11.2 grams of brucine in 25 cc. of alcohol and 12.24 grams of brucine hydrochloride in 80 cc. of alcohol. On cooling, filtering, and washing the yield of the brucine salt was 18.5 grams or 60.7%. The salt sintered at 170° and decomposed at 180-184°.

A sample of 0.3985 grams in 25 cc. of anhydrous chloroform gave in a two decimeter tube at 23° α, +2.43°, $[\alpha]_D^{23}$ +76.22°.

Rotation of brucine in anhydrous chloroform. - Three-tenths of a gram of brucine in 25 cc. of chloroform gave an α, -2.79°, $[\alpha]_D^{23}$, -118.25° in a two decimeter tube at 23°C.

Rotation of brucine hydrochloride in anhydrous chloroform - A sample of .3008 grams in 25 cc. of chloroform gave an α, -0.43°, $[\alpha]_D^{23}$, -17.82° in a two decimeter tube at 23°C.

Preparation of Brucine salt from N-Butyl Alcohol - A sample of ten grams of potassium 9-*aci*-nitro-2-benzoylfluorene was dissolved in 900cc. of n-butyl alcohol at 100°. This solution after filtering was treated with 12.2 grams of brucine hydrochloride (one equivalent) in 100 cc. of n-butyl alcohol. The mixture yielded 6.2 grams of the brucine salt or 28%. The salt decomposed at 170-175°.

A sample of 0.2070 grams in 25 cc. of chloroform at 24° in a two decimeter tube gave α, +1.10, $[\alpha]_D^{24}$, +66.42.

1:1 Ratio of *Aci*-Nitro Compound to Brucine - A sample of 1.9721 grams of the brucine salt dissolved in 20cc. of chloroform was treated with 15 cc. of 6 N. sodium hydroxide at 24°C. The brucine salt decomposed and sodium 9-*aci*-nitro-2-benzoylfluorene precipitated. It was filtered into a weighed sintered crucible, washed, dried and weighed. A sample of 0.8145 grams of the sodium salt was obtained which was equivalent to 0.7590 grams of the *aci*-ion($C_{20}H_{12}O_3N$)

Calcd. for $C_{43}H_{39}O_7N_3 \cdot C_2H_5OH$: $C_{20}H_{12}O_3N$, 41.85

Found: $C_{20}H_{12}O_3N$, 38.49.

Analysis of Brucine in Brucine Salt - *Sample I.*

Brucine salt (1.0021 grams) treated with 15 cc. of 0.2N sodium hydroxide and extracted with four 50 cc. portions of benzene gave at 24° in a two decimeter tube α, -0.51°, after drying over calcium chloride. The 1.0021 grams of brucine salt was equivalent to 0.5243 of brucine in the extract. On the basis of this amount of brucine $[\alpha]_D^{24}$ was -97.27°.

Sample II. - Treatment of 0.5107 grams of the brucine salt, equivalent to 0.2720 grams of brucine, with 15 cc. of 0.2N sodium hydroxide gave an extract of 100 cc. with benzene. This solution in a two decimeter tube at 24° gave α, -0.47, $[\alpha]_D^{24}$, -86.40°.

A sample of 0.3 grams of brucine in 25 cc. of benzene gave α, -2.47, $[\alpha]_D^{24}$ -102.92 in a two decimeter tube at 24°.

These results show a 1:1 ratio of the *aci*-nitro and the brucine in the brucine 9-*aci*-nitro-2-benzoylfluorene, for if the ratio was one *aci*-nitro to two brucines the corresponding specific rotations for sample I and II, would be -71.14 and -63.08.

Analysis of Brucine-9-*aci*-nitro-2-benzoylfluorene.

	Weight of Brucine Salt	Wt. of CO_2 Found	Wt. of H_2O	% of C.	% H_2.
1)	0.2729	0.7229	0.1536	72.33	6.25
2)	0.2728	0.7193	0.1435	71.90	5.84
3)	0.2745	0.7274	0.1585	72.24	6.42
4)	0.2742	0.7200	0.1344	71.60	5.45
5)	0.3011	0.7903	0.1543	71.58	5.69
6)	0.3000	0.7852	0.1604	71.39	5.94
			Average =	71.84	5.93

Calc. for $C_{43}H_{39}O_7N_3$ = 72.77 5.50
Calc. for $C_{43}H_{39}O_7N_3 \cdot C_2H_5OH$ = 71.50 5.96

This analysis indicates that the brucine salt is in ratio of one *aci*-nitro ion to one brucine and that it has one molecule of ethyl alcohol of coordination.

Second Diastereoisomer of -Brucine 9-*aci*-nitro-2-benzoylfluorene.

Fractional Crystallization - Four grams of potassium 9-*aci*-nitro-2-benzoylfluorene were dissolved in 200 cc. of 95% ethyl alcohol at 70° and filtered. To the filtered solution 4.448 grams(one equivalent) of brucine hydrochloride in 50 cc. of alcohol at 70° was added. Final temperature of solution was 50°C. Four sets of crystals were obtained at the following temperatures.

Temperature range		Yield grams	%	Weight of Sample	α	$[\alpha]_D^{23}$
1.	50-35°	1.22	14.14	0.2982	+1.55	+66.48
2.	35-30°	2.33	27.58	0.3305	+1.85	+69.95
3.	30-25°	0.90	10.35	0.2839	+1.86	+64.82
4.	25-4°	0.52	6.16	0.2235	+1.06	+47.42

Total % yield = 58.53

The rotations were observed in a two decimeter tube at 23°C.

In 1, and 2, the samples were dissolved in 25cc. of pyridine. In 3, and 4 the samples were dissolved in 20 cc. of pyridine.

The total amount left in a solution of 232 cc. of ethyl alcohol was 3.47 grams, at 23° in a two decimeter tube, the solution gave α, +0.17, $[\alpha]_D^{23}$, +5.68. This shows that the second diastereoisomer has a low positive rotation.

Action of aequeous potassium hydroxide on active brucine 9-aci-nitro-2-benzoylfluorene. - A sample of 0.5420 of the brucine salt dissolved in 25 cc. of 0.2N aqueous potassium hydroxide gave α, -1.24, $[\alpha]_D^{24}$, -28.6 at 24° in a two decimeter polarimeter tube. The rotation of this salt calculated on the amount of brucine present, gave $[\alpha]_D^{24}$, -54.63. However, brucine would not dissolve in the 0.2N potassium hydroxide and so no rotation was taken of the free brucine.

Action of Alcoholic potassium hydroxide on the active brucine 9-aci-nitro-2-benzoylfluorene. - An alcoholic solution containing 5% potassium hydroxide dissolved brucine 9-*aci*-nitro-2-benzoylfluorene to give a solution which attained a constant rotation after about thirty hours.

A sample of 0.7898 grams of the brucine salt in 25cc. of alcoholic potassium hydroxide in a two decemimeter tube at 23° gave the following rotation.

Time in hours	Reading	Zero reading	α	$[\alpha]_D^{23}$
0:00	5.65	3.50	-2.15	-65.02
3:25	5.85	3.50	-2.35	-71.06
4:45	6.00	3.50	-2.50	-75.60
23:55	6.20	3.50	-2.70	-81.66
39:55	6.24	3.50	-2.74	-82.87

was calculated on the basis of the amount of free brucine present.

A sample of 0.4398 grams of brucine under the same conditions gave α, -2.94, $[\alpha]_D^{23}$, -83.34.

Action of potassium acetate on brucine 9-aci-nitro-2-benzoylfluorene - In 10 cc. of anhydrous chloroform 0.5595 grams of the brucine salt was dissolved. This solution was then treated with 15 cc. of a saturated solution of potassium acetate in anhydrous n-butyl alcohol. The solution gave the following readings in a two decimeter polarimeter tube at 23°.

Time in hours	Reading	Zero reading	α
0:00	5.20	3.50	-1.70
0:15	5.12	3.50	-1.62
1:15	5.06	3.50	-1.56
17:45	5.08	3.50	-1.58
22:15	5.11	3.50	-1.61
65:45	5.15	3.50	-1.65

At seventeen hours crystals began to form in the polarimeter tube. At the end of six-five hours the crystals were filtered off dissolved in pyridine but they gave no rotation. Attempts were made to crystallize the potassium salt immediately, but they only crystallized on prolonged standing even at -10°, which indicates that the active salt is more soluble than the inactive.

Analysis of the potassium salt - Samples of 0.4557 and 0.3447 gave a residue of 0.1067 and 0.0842 grams, respectively, of potassium sulphate when treated with sulphuric acid.

Calcd. for $C_{20}H_{12}O_3NK$: K, 11.05

Found: K, 11.05, 10.96

The Effect of a saturated solution of potassium acetate in n-butyl alcohol on brucine 9-aci-nitro-2-benzoylfluorene - A sample of 0.1121 of brucine 9-aci-nitro-2-benzoylfluorene, dissolved in 25 cc. of a saturated solution of potassium acetate in anhydrous n-butyl alcohol, gave α, -0.43° at 24° in a two decimeter tube. Calculated on the basis of the amount of brucine, this gave $[\alpha]_D$, -86.64. The sample of 0.1121 grams of brucine 9-aci-nitro-2-benzoylfluorene is equivalent to 0.0626 grams of brucine.

Addition of either chloroform or benzene to the solution precipitated only the potassium acetate.

The rotation of the active brucine 9-aci-nitro-2-benzoyl-fluorene in glacial acetic acid. - A sample of 0.4736 grams of brucine 9-aci-nitro-2-benzoylfluorene, equivalent to 0.2478 grams of brucine present, gave the following rotations at 24° in a two decimeter tube when dissolved in 25 cc. of glacial acetic acid.

Time in hours	Reading	Zero reading	α	$[\alpha]_D^{24°}$
0:00	3.42	3.53	+0.11	+5.54
0:35	3.61	3.53	-0.09	+4.04
21:45	3.61	3.53	-0.08	4.04

Sample of brucine 0.3550 grams in 25 cc. of glacial acetic acid under the same conditions gave α, -0.17, $[\alpha]_D^{24}$, - 6.00.

B. Preparation of Brucine 9-*aci*-nitro-2,7, dibenzoylfluorene.

1. Preparation of 2,7-dibenzoylfluorene - This compound was prepared from both 2-benzoylfluorene and fluorene by the use of Perrier's(87) modification of the Friedel-Craft reaction.

Preparation from 2-benzoylfluorene. - To a 1000 cc. beaker containing 28.4 cc.(2 equivalents) benzoyl chloride, 30 grams(two equivalents) of aluminum chloride was added, slowly(under the hood) with constant stirring. The mixture got warm and formed a dark brown solid mass. This solid mass was heated over a soft flame until a uniform melt was formed. Care was taken not to heat too strongly. This was then cooled to room temperature and 350 cc. of anhydrous carbon disulphide was added. The mixture was heated slowly over the steam bath, away from all flames, until all the solid dissolved. While the solution was heated over the steam bath, 30 grams(one equivalent) of purified 2-benzoylfluorene was slowly added. There was no evolution of heat but rapid addition of 2-benzoylfluorene caused boiling due to the rapid evolution of hydrogen chloride. The mixture was heated on the steam bath for about ten minutes and the carbon disulphide was evaporated, leaving a gummy brownish-red mass. The mass solidified on cooling to room temperature. To the solid mass was added 600 cc. of water mixed with 40 cc. of concentrated hydrochloric acid. This mixture was heated on the steam bath until the reaction was complete (half an hour). The precipitate was filtered after cooling to room temperature and recrystallized from 300 cc. of glacial acetic acid and 20 grams of boneblack. Creamy-white flakes crystallized out which melted at 194-195°, yield 58%.

The above mentioned reaction was tried with one equivalent of benzoyl chloride and one equivalent of aluminum chloride, but only the starting material was isolated at the end of the reaction.

Preparation from fluorene - In identically the same manner as discussed above, three equivalents of benzoyl chloride(117 cc.) was mixed with three equivalents of aluminum chloride(147 grams) in a 2000 cc. beaker. After the reaction was complete the mass was dissolved in 600 cc. of carbon disulphide and 55 grams of fluorene(one equivalent) was added. The carbon disulphide was evaporated and the product hydrolyzed in 1500 cc. of water mixed with 60 cc. of concentrated hydrochloric acid. The solid was filtered and recrystallized from 500 cc. of glacial acetic acid and 20 grams of bone black. The crystals melted at 194 to 195°. The yield was 36%.

To the mother liquor from which the crystals were obtained, water was added. A white product came out which was recrystalled from 200 cc. of alcohol. White crystals were obtained melting at 119-120° after three recrystallizations. This product is believed to be an isomeric benzoyl or dibenzoyl fluorene. Its presence accounts for the low yields obtained by the use of fluorene as a starting material.

2. Preparation of potassium 9-aci-nitro-2,7,-dibenzoylfluorene. - By using the apparatus described in section A, 1, (Preparation of potassium 9-aci-nitro-2-benzoylfluorene) 7.25 grams of potassium in 50 cc. of anhydrous ethyl alcohol was driven over by means of nitrogen into a mixture of 50 grams of 2,7-dibenzoylfluorene and 17.5 cc. of ethyl nitrate in 250 cc. of benzene. The first few drops of potassium ethylate causes the benzene mixture to turn yellow, and then upon further addition, a orange precipitate begins to precipitate. When all the potassium ethylate has been added, a reddish-brown mass was formed in the flask. This mixture was stirred constantly for about two hours and then it was allowed to stand over an atmosphere of nitrogen for about twenty-four hours. The reddish-brown mass was filtered, washed with benzene several times and dried in air. The final product was a crystalline powder. The yield was 65%.

Ten grams of the red salt was recrystallized from n-butyl alcohol. Flaky red crystals were obtained which contained n-butyl alcohol of crystallization.

Analysis. Calcd. for $C_{27}H_{16}O_4NK$: K, 8.56
Calcd. for $C_{27}H_{16}O_4NK\ C_4H_9OH$: K, 7.35
Found: K, 7.03, 7.06, 7.15, 6.94

Analysis of potassium 9-*aci*-nitro-2,7, dibenzoylfluorene which was not recrystallized from the butyl alcohol.

Calcd. for $C_{27}H_{16}O_4NK$: K, 8.56

Found: K, 8.73, 8.85

3. Brucine 9-aci-nitro-2,7-dibenzoylfluorene. - In 400 cc. of boiling ethyl alcohol 5 grams of potassium 9-*aci*-nitro-2,7-dibenzoylfluorene was dissolved and filtered. To this was added 4.74 grams of brucine hydrochloride in 100 cc. of alcohol. The final temperature was 80°. On cooling crystals began to come out at 50°, when the sides of the container were scratched. The solution before crystallization took place was deep red. It turned orange when the crystals began to precipitate. The crystals were filtered, triturated with water to remove the potassium chloride present, then washed with a little alcohol and dried in air. Yield was 5 grams or 51%.

A sample of 0.2204 grams of the brucine salt in 25 cc. of chloroform in a two decimeter tube at 24° gave α , +1.18, $[\alpha]_D^{24°}$, +66.92.

C. Preparation of Potassium 9-aci-nitro-2-nitrofluorene

By the use of the apparatus as described in section (A,1) nitrofluorene was condensed with ethyl nitrate in presence of potassium ethylate.

Potassium ethylate prepared from 2.78 grams of potassium and 20 cc. of anhydrous ethyl alcohol was added to a suspension of 15 grams of nitrofluorene in 100 cc. of dry benzene and 5.9 cc. of ethyl nitrate. The first few drops of potassium ethylate turned the solution reddish. When about half of the potassium ethylate had been added the solution turned bluish and the potassium salt began to crystallize out. After all the potassium ethylate had been added, the salt was allowed to stand in an atmosphere of nitrogen for about twenty-four hours, then it was filtered, washed with benzene and dried in air. A yield of 67% was obtained.

The salt was dark brown and slightly soluble in water. The water solution of the salt gave a pale yellow <u>aci</u>-form when treated with dilute hydrochloric acid. No analysis were obtained that gave consistent results because the compound was explosive.

Samples of 0.2280, 0.1815, 0.1430 yielded 0.1160, 0.0895 and 0.0655 grams of potassium sulphate when charred with sulphuric acid.

Calcd. for $C_{13}H_7N_2O_4K$: K, 13.29

Found: K, 22.84, 22.13, 20.56

Analysis seemed to indicate that a molecule of potassium ethylate was associated with the potassium salt.

Calcd. $C_{13}H_7N_2O_4K \cdot C_2H_5OK$: K, 20.67

D. Preparation of Potassium 9-*aci*-nitro-2-benzoyl-7-nitrofluorene.

Potassium 9-*aci*-nitro-2-benzoyl-7-nitrofluorene was prepared by the condensation of 2-benzoyl-7-nitrofluorene with ethyl nitrate in presence of potassium ethylate as described for the preparation of potassium 9-*aci*-nitro-2-nitrofluorene. It also was dark brown and explosive although not quite as unstable as potassium 9-*aci*-nitro-2-nitrofluorene.

Potassium ethylate, prepared from 3.28 grams of potassium and 25 cc. of anhydrous ethyl alcohol in benzene, was condensed with 25 grams of 2-benzoyl-7-nitrofluorene and 6.8 cc. of ethyl nitrate in 150 cc. of dry benzene. The salt was slightly soluble in water. The yield of the dark brown precipitate was 63%. The aqueous solution of the salt with dilute hydrochloric acid yielded a pale-yellow *aci*-form.

Samples of 0.3688 grams and 0.3559 grams gave, respectively 0.0897 and 0.0858 grams of potassium sulphate when charred with sulphuric acid.

Calcd. for $C_{20}H_{11}O_5N_2K$: K, 9.82

Found: K, 10.91, 10.79

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