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Preparation of organic hydrazides

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BOSTON UNIVERSITY
GRADUATE SCHOOL

Thesis

PREPARATION OF ORGANIC HYDRAZIDES

by

JEAN-PIERRE L. AMIEL
(Ingenieur E.P.C.I. 1956)

Submitted in partial fulfillment of the
requirements for the degree of
Master of Arts

1959

411
1957
222

Approved
by

First Reader.....*J. Philip Mason*.....
Professor of Chemistry

Second Reader.....*Norman H. Kiehl*.....
Assoc. Professor of Chemistry

ACKNOWLEDGEMENT

The author wishes to take this opportunity to express his indebtedness to Professor J. P. Mason who suggested the topic and whose constant guidance and encouragement have been most valuable and to Professor L. C. W. Baker who gave generously of his time and energy to make the completion of this degree program possible.

Topical Outline

A. Introduction	1
B. Discussion	6
C. Experimental Part	15
1. Preparation of N-methylamides and N-nitro-N-methylamides	15
a. Preparation of N-methylbenzamide	15
b. Preparation of N-Nitro-N-methylbenzamide	16
c. Preparation of p-nitro-N-methylbenzamide	18
d. Preparation of p-N-dinitro-N-methylbenzamide	19
e. Preparation of N-methylacetamide	21
f. Preparation of N-methylanisamide	23
g. Preparation of p-bromo-N-methylbenzamide	24
2. Reduction of N-nitroamides	26
D. Summary	28
E. Appendix	29
1. Addition products of Azodicarboxylic Esters	29
2. Preparation of diethyl hydrazodicarboxylate	39
3. Preparation of diethyl Azodicarboxylate	40
4. Attempted "Azo Reaction" with p-N-dinitro-N- methyl-benzamide	41
F. Bibliography	42
G. Abstract	45

INTRODUCTION

Numerous methods to prepare hydrazine derivatives have been described in the literature. An extremely attractive one, because of the ease of formation of the starting materials, is the reduction of azines, hydrazones and semicarbazones.

Several early attempts to reduce these substances failed. Mazourevich (28), using aluminum amalgam, obtained a mixture of primary and secondary amines. This was also the result of the attempt of Mailhe (27) when he tried the Sabatier-Senderens method of reduction by hydrogen over hot nickel. Thiele (42) succeeded in reducing electrolytically some aromatic azines but failed with aliphatic azines. Attempts to use Raney nickel yielded to production of primary and secondary amines (3, 46).

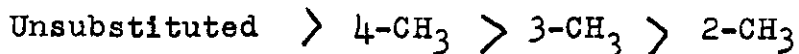
In 1921, independently, Lochte, Bailey, Noyes (25) and Taipale (36) succeeded in reducing dimethylketazine to diisopropylhydrazine using colloidal platinum according to the method of Skita (34). Neighbors and Bailey (30) reduced by the same way different semicarbazones and aliphatic hydrazones. Cohen (6) used platinum oxide to reduce the azines of isovalerophenone and p-phenylacetophenone.

In further investigation, Taipale (36,37,38,39,40,41), Ugryunov (43), and Egorova (18,19) studied the influence of

the azine structure on the rate of hydrogenations. If $RR'C=N-N=CRR'$ represents the structure of the aliphatic azines, they found that those with a straight chain were hydrogenated faster than those with an iso structure. For Azines of the same structure but of different molecular weight, the heavier the radical attached to nitrogen, the slower the hydrogenation. If methyl is given a 100 coefficient of "consumption of affinity" (40) the relative values for the other radicals are: H: 12; Et: 135; Pr: 200; IsoPr: 555; IsoBu: 700.

If there is a cyclic radical attached to nitrogen the rate is enhanced. The azine formed with hexahydrobenzaldehyde reacts two to three times faster than that formed with enanthaldehyde. There is a ratio of 5:1 between the rates of hydrogenation of the azines obtained with carvomenthone and with camphor.

Substitution on the ring decreases the rate. The azine of 2-methylhexahydrobenzaldehyde reacts more slowly than that of the unsubstituted aldehyde. This influence depends upon the position of the substituent: for the azines of cyclohexanone and of the 2-methyl, 3-methyl and 4-methyl substituted cyclohexanones the rate of hydrogenation is:

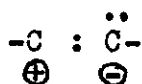


This sequence is probably due to steric factors rather than an inductive effect.

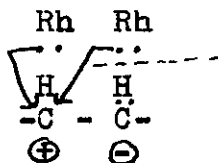
A recent detailed study by Hernandez and Nord (23) on the reduction of substituted p-nitrobenzenes and substituted ethylenic compounds arrives at the same conclusion. These authors use colloidal rhodium and not platinum as in the Skita method, but these two metals have the same electronic structure and have been shown to react in the same way which is not the case with palladium.

The authors found a linear relationship between the logarithm of the rate of the reaction of substituted nitrobenzenes and a value σ characteristic for each substituent and depending chiefly upon the electron shifting ability of the substituent (22).

In view of all these experimental results, they assume that hydrogenation with rhodium involves ionization of hydrogen. The rhodium atom has one electron in the outermost orbit, enabling hydrogen to form the unstable hydride $\text{Rh}:\text{H}$; this is confirmed by the fact that 100% of the hydrogen absorbed by rhodium is chemically bound (29). The $-\text{C}=\text{C}-$ bond tends to assume the following configuration:

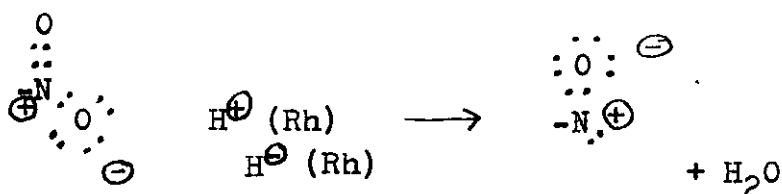


which attaches itself to the hydride because of the strong nucleophilic tendency of the $\overset{\ominus}{\text{C}}$. Thus the formation of an unstable intermediate complex can be conceived.

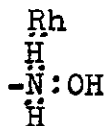


Another hydride molecule supplies the H^\ominus but the attack seems to be originated by the H^\oplus .

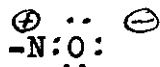
They propose the following mechanism for the reduction of the nitro group: $\text{NO}_2 \xrightarrow{1} \text{NO} \xrightarrow{2} \text{NHOH} \xrightarrow{3} \text{NH}_2$. Step 1 being an electrophilic attack on oxygen.



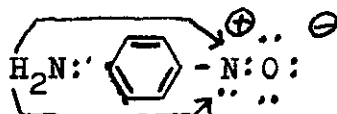
Step 3 may start with an electrophilic attack on nitrogen:



Step 2 is probably the one affected by the substituent. Since hydrogenation with rhodium requires the structure



a heavy electron density near the nitrogen atom should be prejudicial as in the case of p-aminonitrobenzene (or p-aminonitrosobenzene):

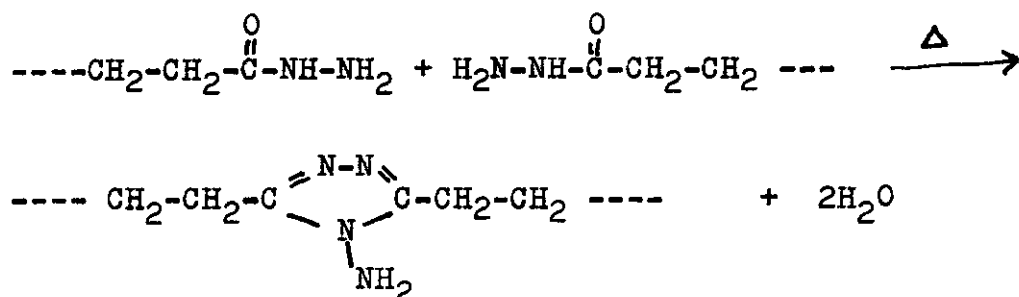


whereas a low density should increase the polarization of the NO group.

Another case of hydrogenation of the nitrogen-nitrogen bond is a recent study by Ainsworth (1) who investigated the action of Raney nickel on hydrazides of carboxylic acids. He found that when he used a large amount of Raney nickel, cleavage occurred with the production of an amide and ammonia, but with catalytic amount of catalyst no reaction occurred at the nitrogen-nitrogen bond. Adams' catalyst was found without effect on the nitrogen-nitrogen bond.

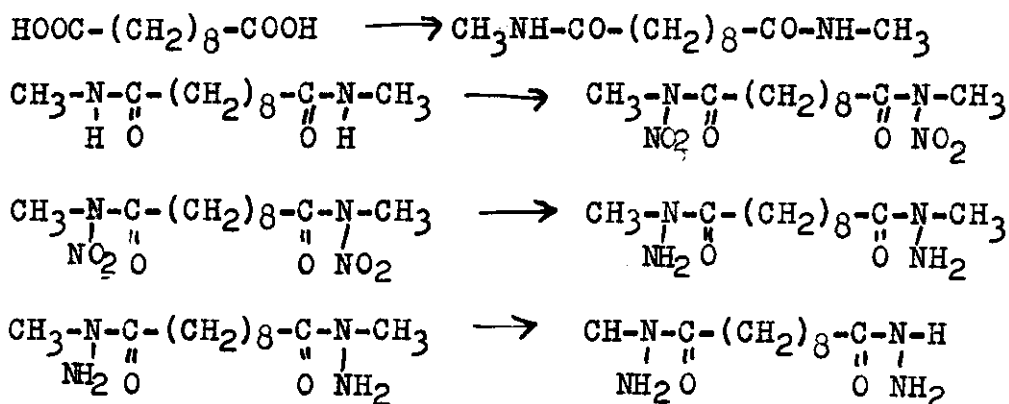
DISCUSSION

Among the monomers actually known to give linear polymers suitable for textile fibers, sebacyl dihydrazide has shown some very interesting properties. The polymerization proceeds as follows:



Unfortunately, hydrazine is too expensive a chemical to be used in an economical preparation of the hydrazide. Our purpose was to find another route to this hydrazide not using hydrazine.

We proposed the following steps:

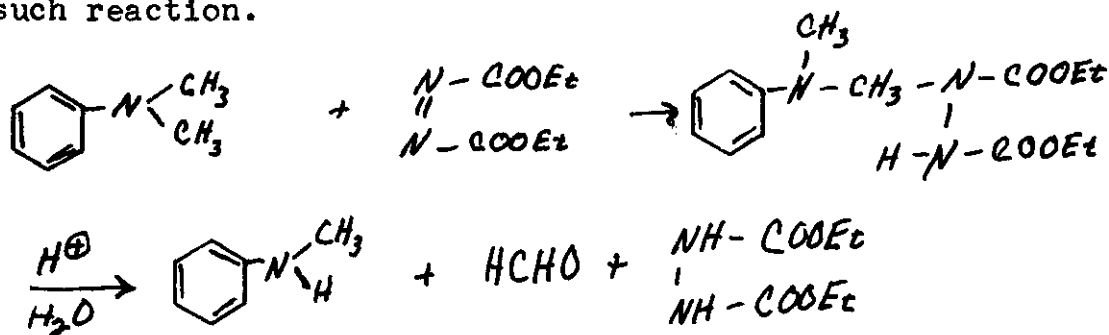


The preparation of N,N'-dimethylsebacamide is without problem. The introduction of a nitro group bound to a

nitrogen has been investigated by Curry and Mason (7) and gives a high yield of N-nitro compound.

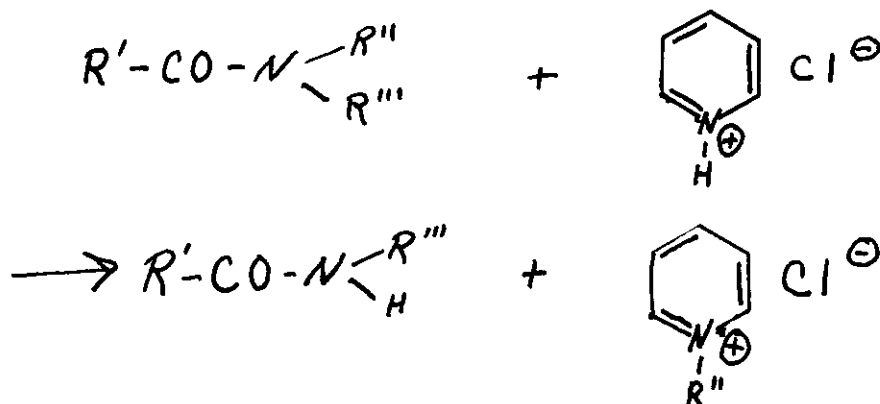
N-Nitro-N-substituted carbamates have been reduced to hydrazine derivatives in high yield by hydrogen using platinum black as a catalyst (5). The relative instability of the $>N-NO_2$ group requires the presence of an alkyl group attached to the nitrogen atom bearing the nitro group. It was hoped that the results obtained with carbamates could be easily extended to amides and that the reduction of N,N'-dinitro-N,N'-dimethylsebacamide would be possible under the same conditions.

The problem would then be to remove the methyl group. A very elegant way could be the use of diethyl azodicarboxylate. This reagent investigated by O. Diels gives additional products with compounds possessing an active hydrogen. Furthermore, treating the addition products formed with certain methylamines by acid produces a demethylation of the amine with evolution of formaldehyde, the following example being demonstrative of such reaction.



A survey of the reactions of azodicarboxylic esters with various compounds will be found on page 29.

Another possible method which could be adapted is the one described by E. Schaffer and D. Klamann (33) which consists of heating an amide or anilide with pyridine hydrochloride. There is a transfer of the alkyl group from the amide to the pyridine nucleus; e.g.,

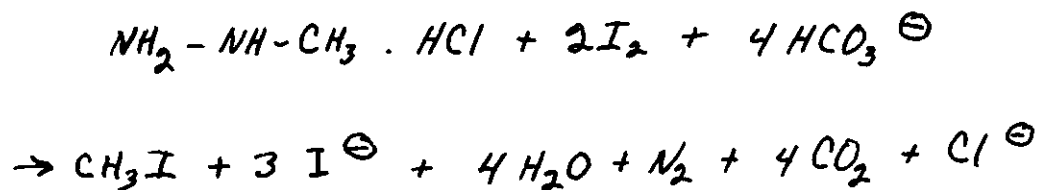


It was decided to attack the problem with a mono-functional acid giving a solid amide and a solid N-nitroamide (easier to purify and closer to those expected to be obtained with sebacic acid). Benzoic acid was tried but gave a very unstable viscous N-methyl-N-nitroamide. p-Nitrobenzoic acid was then used. Several attempts to reduce the N-nitro-N-methyl-p-nitrobenzamide yielded only cleavage of the nitrogen-nitrogen bond (with production of p-amino-N-methylbenzamide and ammonia). It was then decided to try to reduce N-nitro-N-methylbenzamide. Thus a new technique was investigated where the nitro compound was not isolated. The yields of hydrazine obtained by using this method were up to 24%. Thus, at this point of the work, three molecules of the type $R-CO-N(NO_2)-CH_3$ had been reduced. When R was an electron repelling group (OC_2H_5) a

high yield of hydrazine was obtained; with an electron withdrawing group (p-nitrophenyl) no hydrazine was produced and with the pure phenyl group the yield was 24%. These results seemed to indicate that the electron affinity of the R group is very important in the reduction of the compounds to hydrazine derivatives. It was then decided to reduce a series of compounds varying the electron affinity of R.

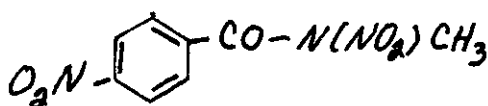
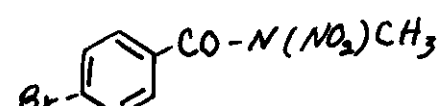
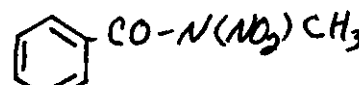
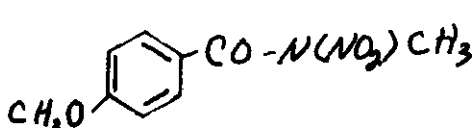
The procedure for these reductions is the following: A small amount of the N-methyl amide (about 0.3 mole) was nitrated by the theoretical amount of fuming nitric acid ($d = 1.49$) in the presence of acetic anhydride in the bottle to be used for the hydrogenation. The reaction mixture was stirred for half an hour by means of a magnetic stirrer and then 0.2g. of platinum black was added. The reaction bottle was placed in the hydrogenator, alternately evacuated and filled three times with hydrogen to remove all the air and then brought to the desired initial pressure. The mixture was stirred under a hydrogen pressure up to forty pounds per square inch. When the absorption of hydrogen had stopped, the platinum black was filtered off and the solvent was removed under reduced pressure. One hundred ml. of hydrochloric acid was added and the mixture was boiled for one hour. In cases where a non-volatile acid was produced at that stage, the solution was cooled and the acid was filtered off; this was the case for benzoic acid, p-nitrobenzoic acid, anisic

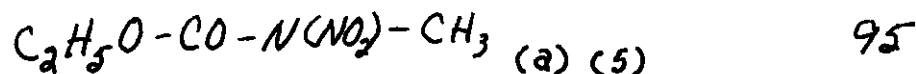
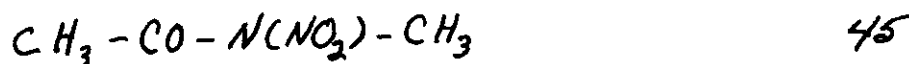
acid, p-bromobenzoic acid. After evaporation of the hydrochloric acid, the methylhydrazine hydrochloride was dissolved in 250 ml. of solution and an aliquot was titrated in sodium bicarbonate solution with standard iodine according to the method of Siggia.



The molecules reduced and the average yields obtained are shown in the following table:

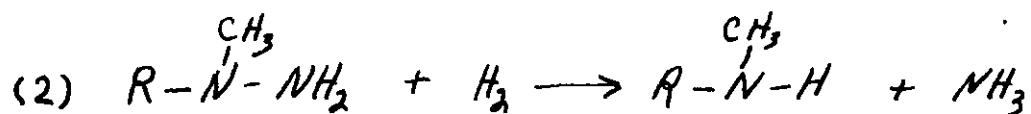
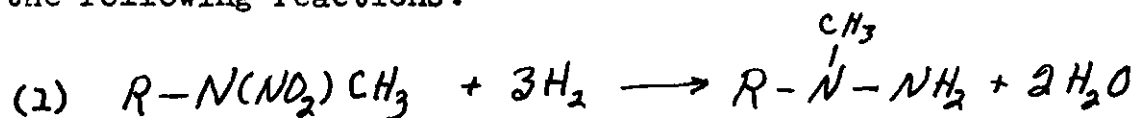
Reduction of N-Nitro-N-Methyl Amides

Amide	% Yield in Methylhydrazine
 (a)	0
	0
	24
	33



(a): Cases when the N-nitro product has been isolated and reduced.

The yields recorded this way are the over-all yields for the two reactions, nitration plus reduction. We assume that the nitration is quantitative or very close to it and that it does not depend upon the type of N-methyl amide used. To substantiate this assumption is the fact that in all reductions the amount of hydrogen absorbed is that expected for the following reactions:



Reaction (2) may or may not be complete. Nitric acid not being reduced under these conditions, the N-nitro group has to be present. Since the yields in hydrazine corresponding to the amount of hydrogen absorbed (ex. 7 moles for the reduction of p-N-dinitro-N-methylbenzamide to p-amino-N-

methylbenzamide and ammonia), attempts to stop the reaction when the theoretical amount of hydrogen to give 100% hydrazine had been absorbed were tried but did not give better yield.

The reduction reaction presents a certain number of noteworthy characteristics. The most important feature is the unpredictable character of this reaction. It has not been possible to reproduce at will the results. For reasons unknown at this moment some reductions using the same substrate give no or an extremely low yield of hydrazine whereas others, under the same conditions, give the expected results.

The purity of the reagents and of the solvents is certainly one factor. To eliminate impurities, all the solvents were refluxed over Raney Nickel and distilled less than a week before use. This gives a satisfactory desulfurization, sulfur being an extremely active poison of the catalyst. The reagents were always crystallized or distilled less than seventy-two hours before use. The stirring bars used were covered with Teflon and prepared and used solely for this reduction reaction. The contacts with atmospheric air were reduced to the minimum. Some of the nitrations were done under nitrogen atmosphere but no improvement was observed. The hydrogenation apparatus was equipped with a sulfur-free Neoprene stopper. The previous precautions deal with the poisoning of the catalyst: that is to say,

they are necessary in order to enable the reduction reaction to occur. But the fact that the reaction follows equation (2) rather than (1) may depend on other reasons.

Raney nickel had been previously tried by other workers (1), but in this case the reduction gives complete splitting of the nitrogen-nitrogen bond. It seems then that a powerful hydrogenation catalyst causes splitting. This may be interpreted from two different points of view. It may be looked at as a reaction going "too far"; i.e., first formation of the hydrazine derivative, then hydrogenolysis of this hydrazine, or it might be that an impurity acts as a promoter for a completely different path for the reaction, or it may be that the hydrogenolysis reaction occurs concurrently with the reduction.

If the first hypothesis is accepted, then the answer to the problem could be either using a less active catalyst or adding some inhibitor of the hydrogenolysis reaction. These inhibitors would of course depend upon the type of mechanism involved, e.g. free radical, attack by hydrogen ions, attack by hydride ions.

No study has been made to attempt to determine the mechanism, but another feature of the reaction may furnish some clues.

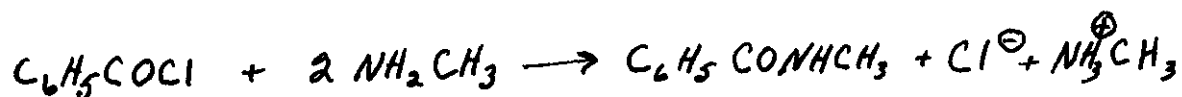
Whereas the solutions of N-nitroamides in the different solvents used are colorless, as soon as some hydrogen has

been absorbed, a bright green color appears which in turn disappears when the reduction stops or if the reaction mixture is brought in contact with air. This could indicate the presence of free radicals. But the influence of the electron affinity of the groups attached to the >N-NO_2 grouping seems to indicate a more polar mechanism.

EXPERIMENTAL PART

1. PREPARATION OF N-METHYL-AMIDES AND N-NITRO-N-METHYLAMIDES

a. Preparation of N-Methylbenzamide



N-Methylbenzamide was prepared by the reaction between benzoyl chloride and aqueous methylamine by the method of P. Van Romburgh. (44)

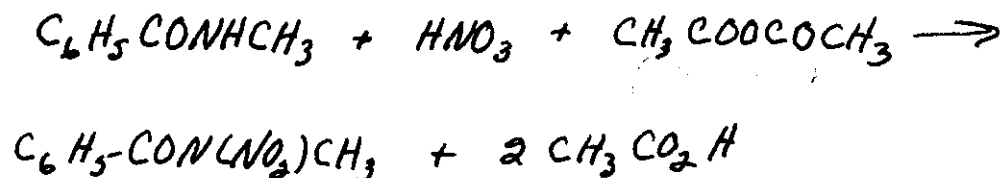
Ninety grams of 25% aqueous methylamine solution (0.75 mole) was placed in a 250 ml. three-necked flask equipped with a mechanical stirrer, a dropping funnel and a thermometer. The flask was cooled by means of an ice-salt bath and 42 grams (0.3 mole) of benzoyl chloride was added through the dropping funnel at such a rate that the temperature did not rise above 10°C. When the addition was over, the mixture was stirred another fifteen minutes. The white precipitate was filtered on a Buchner funnel and washed with two 50 ml. portions of iced water.

The dry raw material was dissolved in 220 ml. of ether, and precipitated by addition of 400 ml. of petroleum ether as proposed by Dunlap. (17). The crystals were separated on a Buchner funnel and washed twice with some petroleum ether. The solid was dried by allowing it to stand in an evaporating

dish overnight. The yield of purified product was 34g. (84%) and it had a melting point of 78°C. (literature: 78°C).

(44, 17)

b. Preparation of N-Nitro-N-Methylbenzamide



N-Methylbenzamide was nitrated by the method of Curry and Mason (7).

Twenty-eight grams of N-methylbenzamide (0.21 mole) was dissolved in 30 grams of acetic anhydride (0.3 mole) and 0.2 ml. of concentrated sulfuric acid in a 250 ml. three-necked flask equipped with a mechanical stirrer, a thermometer, and a dropping funnel. The flask was cooled by means of an ice bath. The theoretical amount of fuming nitric acid of specific gravity 1.49 (14.5 grams, 0.21 mole of pure nitric acid) was then added through the dropping funnel at such a rate that the temperature was kept between 20°C and 30°C. When the addition was completed, the ice bath was removed and stirring was continued for another thirty minutes. The mixture was then poured into 50 ml. of a 30% iced salt solution and extracted with ether. The ether solution was washed once with water, six times with 10% sodium bicarbonate, once more with water, then dried overnight over sodium sulfate.

The ether was distilled off on a water bath. The product at that time was an orange viscous liquid. The water bath had just been removed when the product decomposed violently.

Since the product was a liquid and seemed too unstable to be distilled, no further attempt was made to prepare and purify it.

c. Preparation of p-Nitro-N-Methylbenzamide

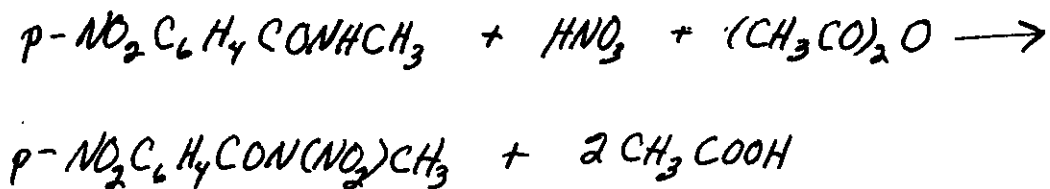


p-Nitro-N-methylbenzamide was prepared by the reaction of p-nitrobenzoyl chloride with aqueous methylamine. Two hundred grams of 25% aqueous methylamine (1.75 moles) was placed in a 500 ml. three-necked flask equipped with a thermometer and a mechanical stirrer. The flask was cooled by means of an ice bath. Ninety grams of powdered p-nitrobenzoyl chloride (0.48 mole) was added by portions small enough so the temperature was kept between 20°C and 30°C. When the addition was completed the stirring was continued for another hour. The mixture was then filtered on a Buchner funnel and washed with cold water.

The raw product was recrystallized from 50% ethanol.

The yield was 67g. (78%) and the melting point 217°C (45).

d. Preparation of p,N-Dinitro-N-Methylbenzamide



p-Nitro-N-methylbenzamide was nitrated by the method of Curry and Mason (7).

Twenty grams of p-nitro-N-methylbenzamide (0.11 mole) was dissolved in 17 grams of acetic anhydride (0.17 mole) and 0.2 ml. of concentrated sulfuric acid in a 250 ml. three-necked flask equipped with a mechanical stirrer, a thermometer and a dropping funnel. The flask was cooled by means of an ice bath. The theoretical amount of fuming nitric acid of specific gravity 1.49 (7.8g, 0.11 mole of pure nitric acid) was added through the dropping funnel at such a rate that the temperature was kept between 20°C and 30°C. When the addition was completed, the ice bath was removed and stirring was continued for another 30 minutes. The mixture was then poured into 100 ml. of a 15% iced salt solution and extracted by four portions of 40 ml. of ether.

The ether solution was washed three times with water, three times with 10% sodium bicarbonate, once more with water, then dried overnight over sodium sulfate.

The ether was distilled off and the product recrystallized twice from a mixture of ether and petroleum ether.

The yield was 15g. (60%) of light yellow crystals melting at 59-60°C.

Analysis performed by Carol K. Fitz.

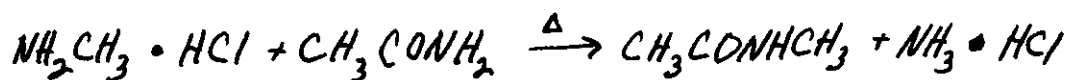
Calculated for $C_8H_7N_3O_5$: C, 42.67; H, 3.1; N, 18.7.

Found: C, 42.5; H, 3.1; N, 18.8.

e. Preparation of N-Methylacetamide

Two different methods have been used:

(1)

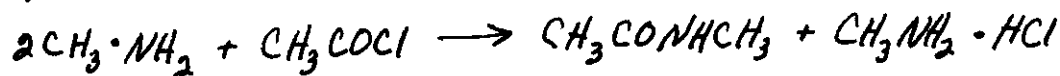


N-Methylacetamide was prepared by heating together methylamine hydrochloride and acetamide according to the method of A. Galat and B. Elion (20).

Methylamine hydrochloride (30g., 0.45 mole) was heated on the steam bath with 30 grams (0.5 mole) of acetamide in a 250 ml. flask equipped with a mechanical stirrer. The mass became liquid and after some minutes ammonium chloride began to precipitate. The heating was continued for thirty minutes and the mixture was then stirred for another thirty minutes. When it was cooled, 100 ml. of chloroform was added with stirring. The mixture was then filtered on a Buchner funnel, the ammonium chloride washed four times with 20 ml. of chloroform. The chloroform was distilled off, the raw N-methylacetamide was distilled and collected between 204 and 206°C.

The yield was 21 grams (65%).

(2)

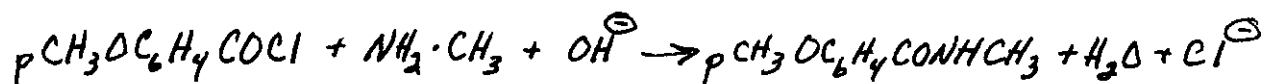
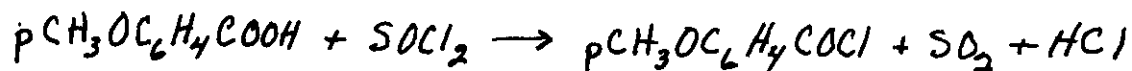


The action of dry methylamine on acetyl chloride was also used for the preparation of this compound.

Dry methylamine gas was prepared by dropping a 25% aqueous solution of methylamine on sodium hydroxide pellets, the gas formed being dried by passing through a tube filled with potassium hydroxide pellets. The dry methylamine was then bubbled through a solution of 40 grams (0.51 mole) of acetyl chloride in 200 ml. of anhydrous ether. The methylammonium chloride formed precipitated out. When no more precipitation occurred, the mixture was filtered on a Buchner funnel. The ether was distilled off and the raw product distilled. The product was collected between 204 and 206°C.

The yield was 28 grams (76%).

f. Preparation of N-Methylanisamide

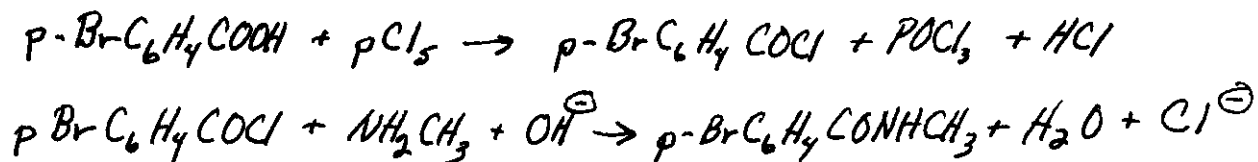


N-Methylanisamide was prepared according to the method of O. J. Brady and F. Dunn (4).

Ten grams (0.067 mole) of anisic acid was mixed with 50 grams of thionyl chloride in a 100 ml. flask equipped with a reflux condenser leading to a sodium hydroxide trap. The mixture was refluxed for an hour on the water bath, then the excess thionyl chloride was distilled off under reduced pressure. This product was then poured slowly into a cooled solution of 16 ml. of 25% methylamine solution (0.13 mole), 4 grams of sodium hydroxide (0.1 mole) and 80g. of water. This solution was stirred during the addition and for another thirty minutes. The granular precipitate was collected, washed with iced water, air dried and crystallized from benzene.

The yield was 9 grams (0.055 mole, 83%) of brilliant colorless needles M.P.: 116°C (literature: 116°C) (4).

g. Preparation of p-Bromo-N-Methylbenzamide



p-Bromobenzoyl chloride was prepared by the action of phosphorus pentachloride on p-bromobenzoic acid as reported by Sudborough (35).

Twenty grams (0.1 mole) of finely divided p-bromobenzoic acid was gently heated over the water bath with 21 grams (0.1 mole) of phosphorus pentachloride in a 250 ml. flask equipped with a sodium hydroxide trap. After one hour, the liquid was subjected to vacuum distillation.

Twenty grams of a colorless liquid, crystallizing at room temperature was collected at 132°C under a pressure of 18 mm. of mercury. Yield: 90%.

The preparation of the p-bromo-N-methylbenzamide was conducted as in the case of the N-methylanisamide (4). Seven grams (0.032 mole) of liquid p-bromobenzoyl chloride (at about 45°C) was slowly poured into a stirred, cooled solution of 8 ml. of a 25% methylamine solution (.06 mole), 2 grams of sodium hydroxide (.05 mole) and 40 grams of water. The stirring was continued for half an hour. The white precipitate was then filtered on a Buchner funnel, air dried and recrystallized from benzene.

The yield was 5.5 grams (.026 mole, 80%) of white needles. M.P.: 165-166°C.

Analysis performed by Carol K. Fitz.

Calculated for C_8H_8BrNO : C, 44.8; H, 3.7; N, 6.5.

Found: C, 45.0; H, 3.6; N, 6.5.

2. REDUCTION OF N-NITROAMIDES

a. The case of p-N-dinitro-N-methylbenzamide illustrates the procedure when the N-nitroamide was isolated. Five grams of the compound was dissolved in 50 ml. of 95% ethanol and 5 ml. of glacial acetic acid and 0.2 gram of platinum black was added. Hydrogenation was conducted under a maximum pressure of 35 pounds per square inch until no more hydrogen was absorbed. A strong odor of ammonia was noted when the bottle was opened. After filtering off the platinum, an aliquot was hydrolyzed and titrated for hydrazine with negative results. The solvent was distilled off and the orange solid residue recrystallized twice from chlorobenzene. This gave pink plates m.p. 170-172°C. Wenker (45) reported a melting point of 180°C. The elementary analysis agreed with that for p-amino-N-methylbenzamide.

Calculated for $C_8H_{10}N_2O$: C, 64.0; H, 6.7; N, 18.7.

Found: C, 64.1; H, 6.7; N, 18.6.

This proved the complete cleavage of the nitrogen-nitrogen bond. It was tried to prevent this by using a solvent from which the p-N-diamino-N-methylbenzamide would precipitate as soon as produced. Mixtures of ether and ethanol were tried but the reduction stopped immediately after appearance of the first solid material, certainly due to coating of the catalyst. In all these attempts, only traces of hydrazine were obtained.

b. The technique used when the N-nitroamide was not

isolated has been described in the discussion (page 9).

After nitration it was necessary to add more solvent to run the reduction. Several solvents were then used: more acetic anhydride, acetic acid or ethanol (in this case the final mixture being ethyl acetate, acetic acid and alcohol). The yields were not influenced by these variations of the solvent.

The temperature for the reaction has to be kept between 30 and 40°C. If it is lower than 30°C the reaction is very slow or even does not start at all. If it is higher, total cleavage of the nitrogen-nitrogen bond occurs invariably.

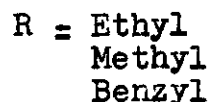
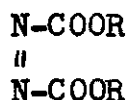
The catalyst may be used two or three times if it is not allowed to dry between experiments. It was kept under 95% alcohol and simply washed by decantation when alcohol was not used as a solvent.

The yields indicated on page 11 have been observed (within 5%) in at least three experiments giving positive results.

SUMMARY

It was hoped to prepare sebacyl dihydrazide by reduction of N,N'-dinitro-N,N'-dimethylsebacamide by hydrogen with platinum black catalyst. While studying this reduction step on monofunctional amide, the electron affinity of the R group in compounds of structure $R-CO-N(NO_2)-CH_3$ seemed to be a decisive factor in the production of hydrazine. It was found that if R is electron withdrawing, complete hydrogenolysis of the nitrogen-nitrogen bond occurs. The yield of hydrazine increases with the electron-releasing ability of R.

APPENDIX

I. ADDITION PRODUCTS OF AZODICARBOXYLIC ESTERS

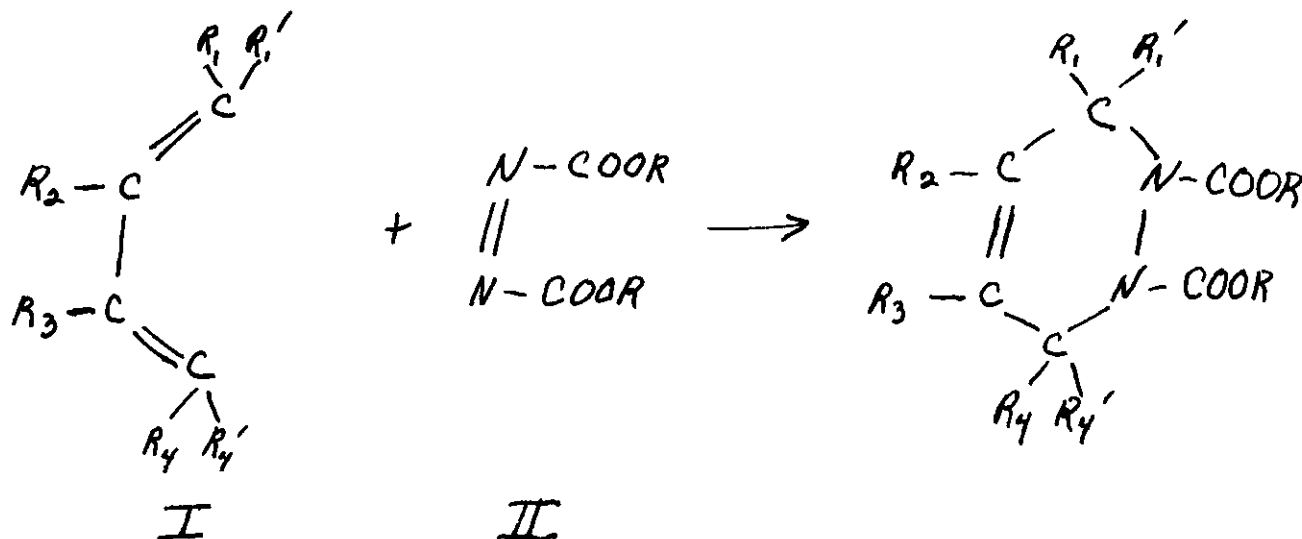
The preparation of azodicarboxylates was described for the first time by Curtius and Heidenreich (8) but no special attention had been given to this product until O. Diels investigated the different kind of addition reactions occurring between this compound and numerous other chemicals.

It is possible to separate these reactions into two groups:

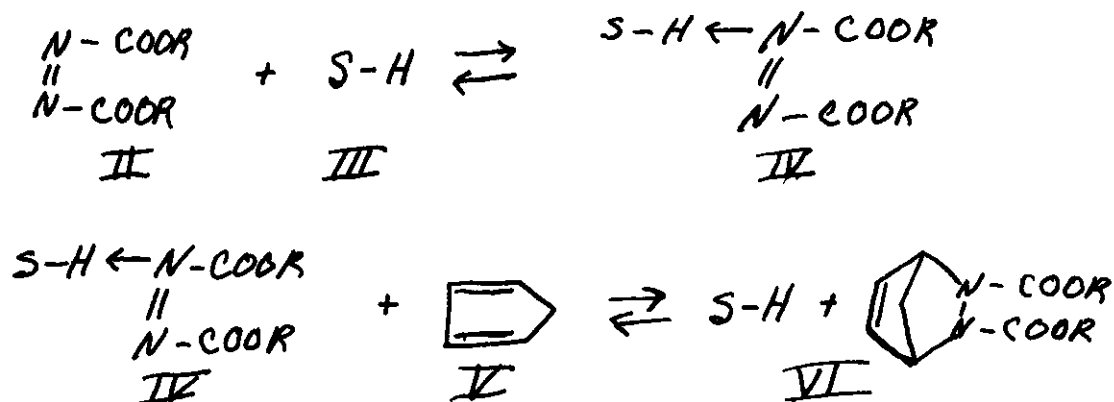
1. Reaction of the "Diels-Alder" type.
2. Reaction with molecules possessing an active hydrogen or "Azo Reaction".

"Diels-Alder" Type Reaction.

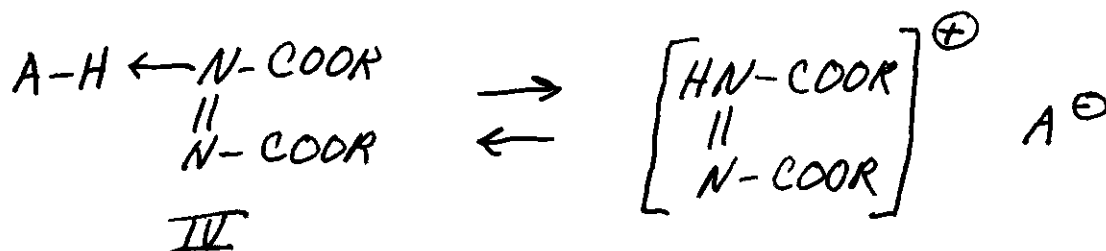
The general equation representing the reaction is:



Among the compounds giving this reaction are: butadiene and substituted butadienes (2), cyclopentadiene (11, 12, 26), styrene (12), 9.11-octadecadienoic acid (21). Kinetics studies (32) show that the reaction is second order (first order in I and in II) in inert solvents (benzene, dioxane, petroleum ether), but has a more complex kinetics in polar solvents of general formula S-H (MeOH, CHCl₃, CH₃CO₂H 96% and 100%, acetone). Complexes between the solvent and the azodicarboxylate have been proposed to interpret the results. Rodgman and Wright (32) have proposed the following mechanism:



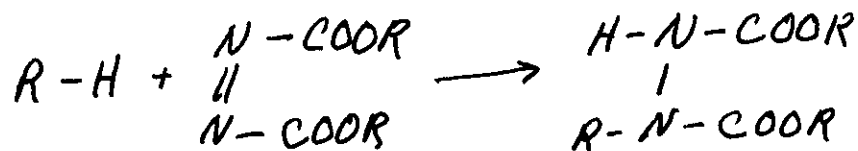
In the presence of a strong acid the rate is slower due to ionization of IV,



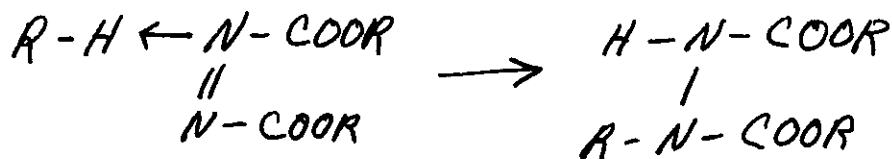
thus decreasing the concentration of the active species IV. Gast, Bell and Tecker (21), studying the reaction with 9,11-octadecadienoic acid, explained the differences in kinetics observed for the reaction by the fact that their long-chain diene is less active than cyclopentadiene used by Rodgman and Wright.

"Azo Reaction".

The general equation for the reaction, called the "Azo Reaction" by O. Diels, is:

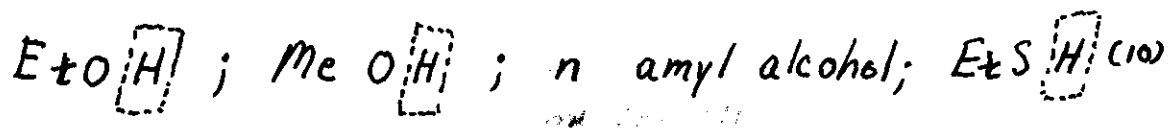


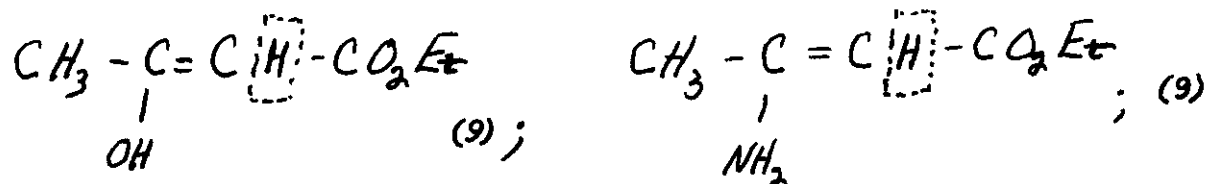
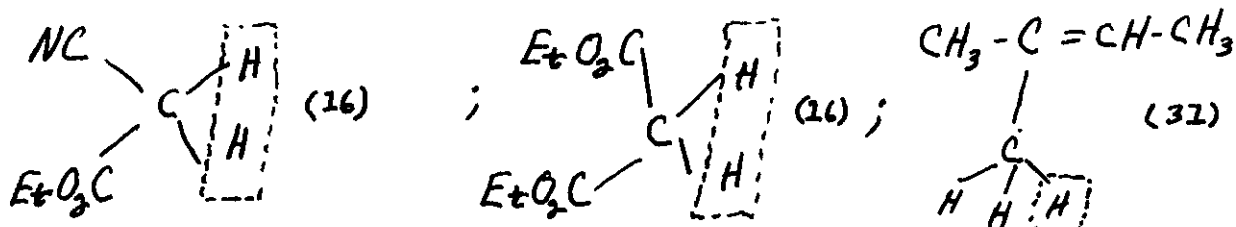
It is probable that an intermediate step is IV, previously seen,



this reaction being much slower than the addition to dienes.

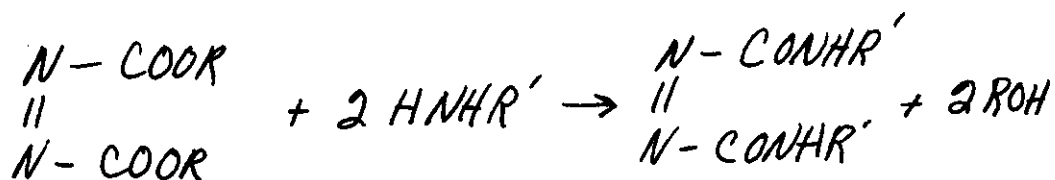
A great number of reagents give this reaction, for instance:



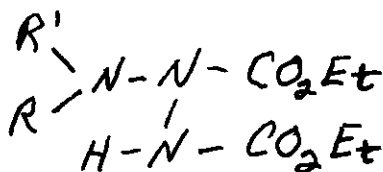


The addition occurs generally at room temperature by mere mixing of the reagents with or without solvents. Depending upon the reactivity of R-H, the addition product is formed in a few minutes or may take as long as several weeks.

Amines comprise a very interesting group of compounds involved in this reaction. Primary and secondary aliphatic amines generally give the amide,



However, dimethylamine and benzylmethylamine form unstable adducts formulated as,



Aromatic and certain tertiary aliphatic amines give well-crystallized addition products.

These amines fall into three classes which are, according to Diels' denomination: (15)

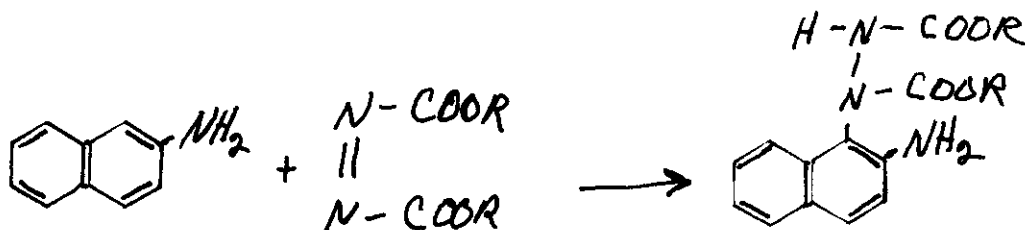
1. Naphthylamine type
2. Aniline type
3. N, N-Dimethylaniline type

1. Naphthylamine type.

The addition reaction occurs in two steps:

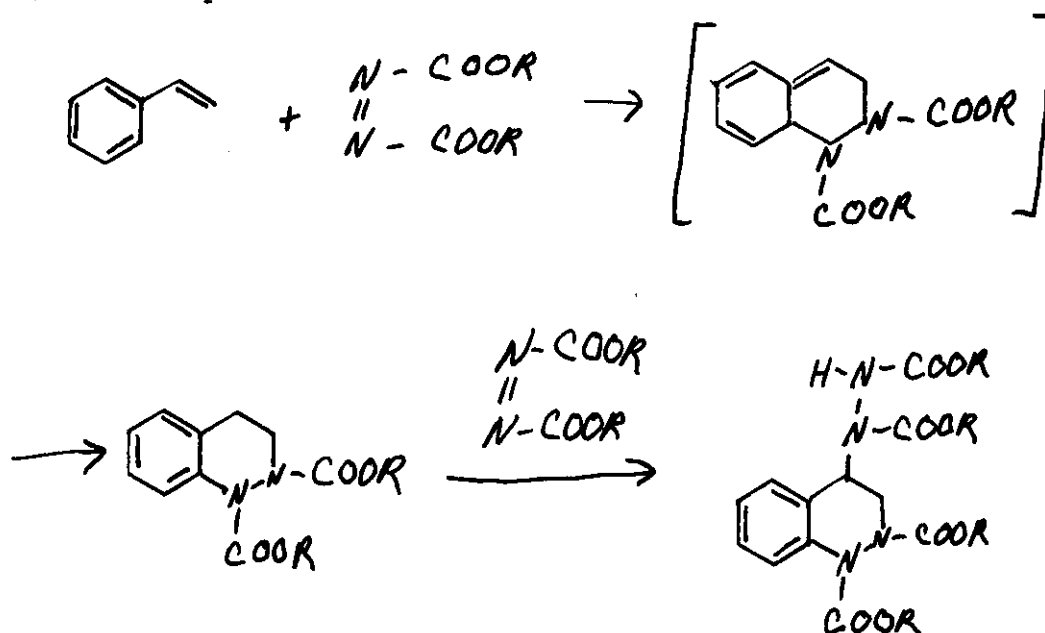
- a. The solution becomes brown-red or dark red.
- b. A colorless well-crystallized product separates.

The character of this group is that the addition products are very stable and may undergo further chemical reaction without decomposition. The azodicarboxylate is introduced in the ring:



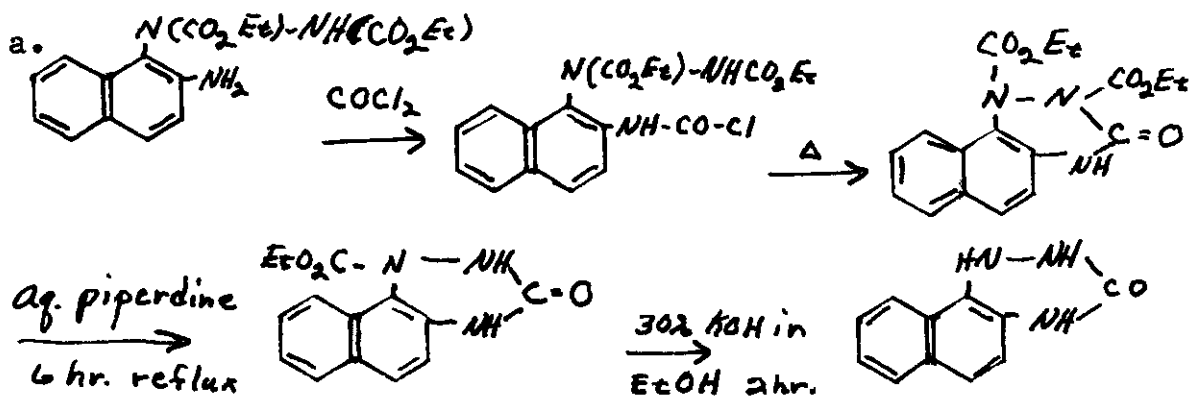
Reagents reacting in the same way are for instance:
 α -naphthylamine and N, N-dimethyl- α -naphthylamine
 (attachment in para position) p-aminosulfonic acid of
 naphthalene (β -position) meso aminoanthracene (para posi-
 tion).

With styrene, addition occurs to the Diels-Alder
 addition product:

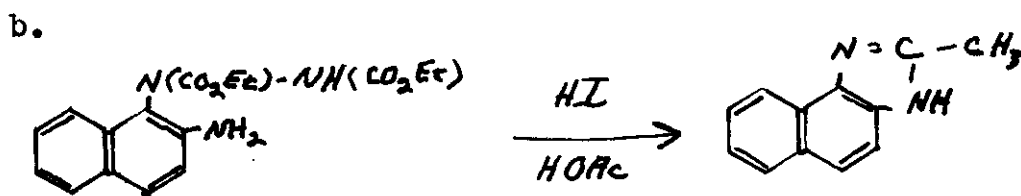


All of these structures have been proven by a large number
 of chemical evidences. The case of β -naphthylamine will be
 demonstrative. The following types of reactions were run
 with success with the addition product: acetylation, for-
 mylation, diazotization, formation of salt, thus proving the
 existence of a free amino group.

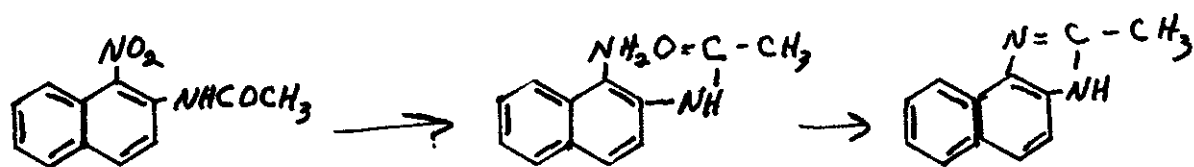
To prove that the addition occurs in the α position, two series of reactions were carried out:



This last product is a known compound prepared by other methods.



This product has already been obtained by reduction and condensation of 1-nitro-2-acetamidonaphthalene.



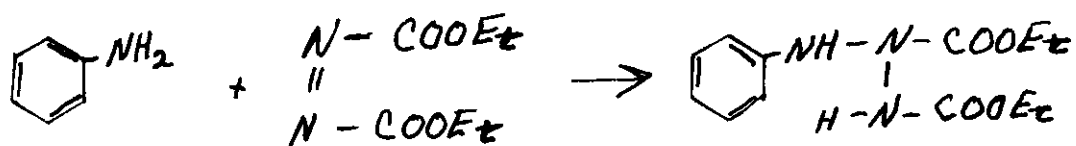
2. Aniline type.

Here also well-crystallized addition products are obtained but they are not stable enough to enter another chemical reaction without breaking down, giving back the

starting materials.

To this type belong aniline, o-and p-toluidines, m-xylidine (14).

Diels proposes the formation of a triazan:

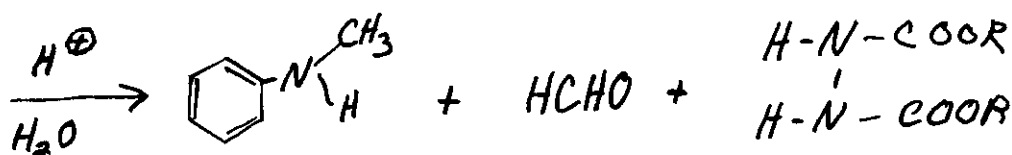
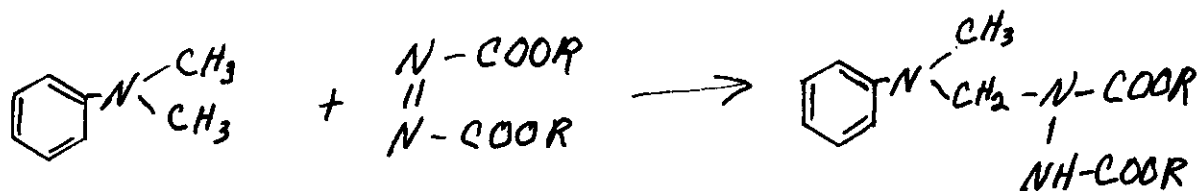


An interesting case is that of p-xylidine (9) which presents the characteristics of the two previous types.

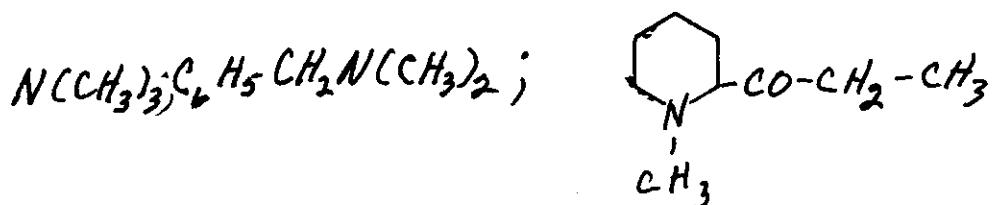
The following reactions are demonstrative:

3. N, N-Dimethylaniline type.

In this case, the addition product, when treated with acid, gives a demethylated amine with production of formaldehyde and hydrazodicarboxylate: (13)

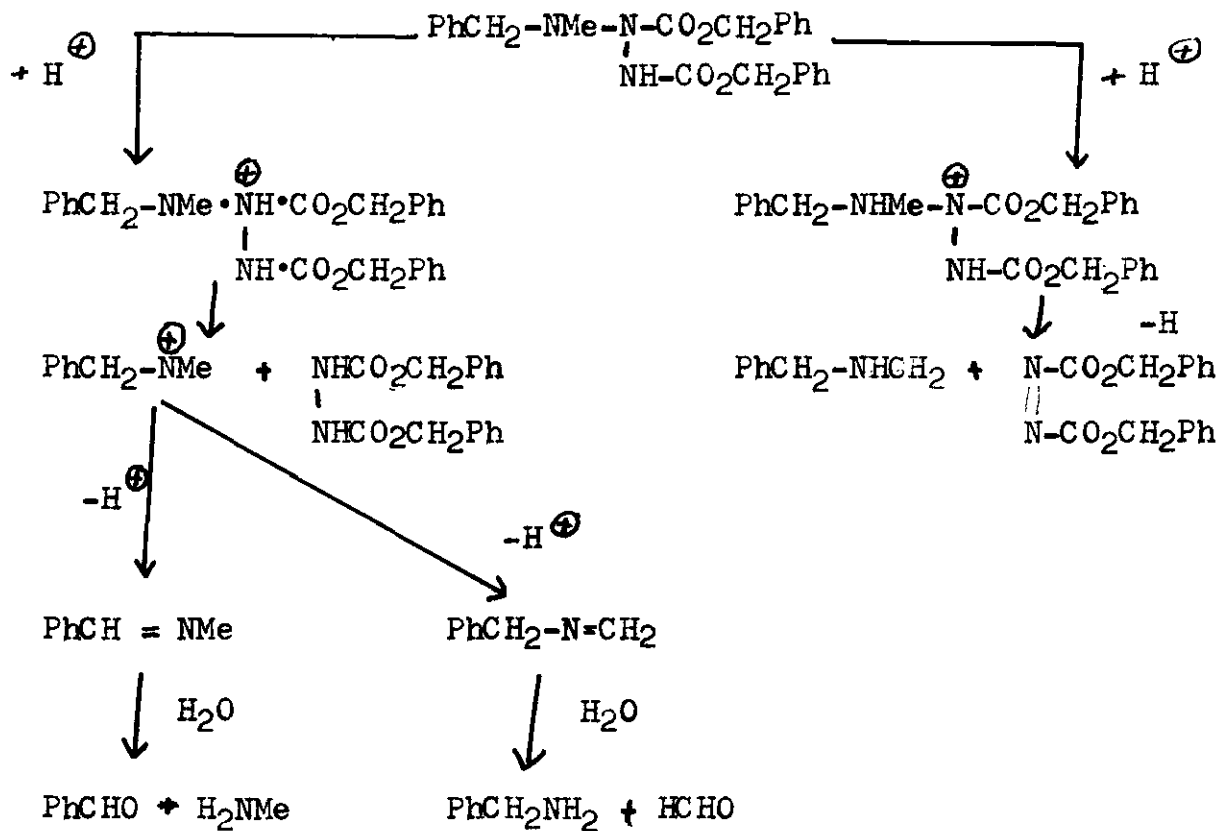


The following compounds give this type of reaction:



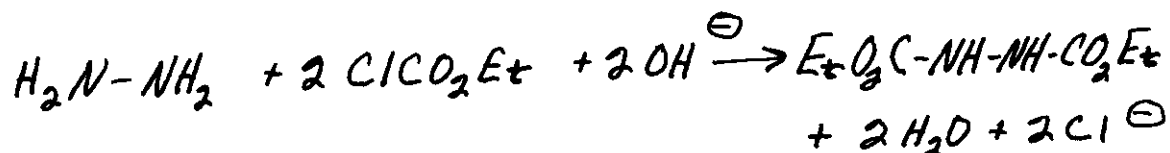
Using diethyl azodicarboxylate and dibenzyl azodicarboxylate with several amines, and measuring the amount of formaldehyde and benzaldehyde produced by acid treatment of the addition products, Kenner and Stedman (24) concluded that the triazan structure was the correct one in the case of secondary amines and proposed the following mechanism to

account for the acid-catalyzed decomposition of dibenzyl
1-benzyl-1-methyltriazan-2,3-dicarboxylate.



II. PREPARATION OF DIETHYL HYDRAZODICARBOXYLATE

Diethyl hydrazodicarboxylate was prepared by the reduction of ethyl chloroformate with hydrazine in the presence of sodium hydroxide.

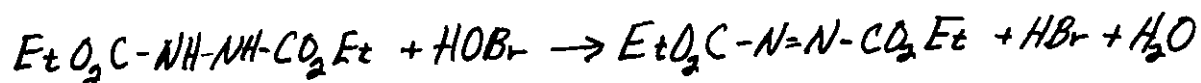


Sixteen grams of hydrazine (0.5 mole) was dissolved in 100 grams of water in a one liter three-necked flask equipped with a mechanical stirrer, a thermometer and a dropping funnel. The flask was cooled by means of an ice-salt bath. When the temperature of the solution was around 0°C, ethyl chloroformate (108.5g., 1 mole) and a solution of sodium hydroxide (40g., 1 mole in 100 grams of water) were added at such a rate that the temperature was kept under 10°C. After some minutes, a white solid separated. The addition lasted one and a half hours. When the addition was completed, the ice bath was removed, stirring was continued. The temperature in the flask rose to 45°C, then came back to room temperature.

The reaction mixture was filtered on a Buchner funnel, washed with two 50 ml. portions of iced water. The dry crude product weighed 73.5 g. (83.5%). It was recrystallized from boiling water and gave 60g. of white crystals (68.5%)
M.P. 130-132°C. (Lit: 130-132°C)

III. PREPARATION OF DIETHYL AZODICARBOXYLATE

Diethyl azodicarboxylate was prepared by hypobromite oxidation of the hydrazo compound as described by Kenner and Stedman (24).



A suspension of thirty-five grams (0.2 mole) of pulverized hydrazo compound in 250 ml. of water was placed in a 500 ml. three-necked flask equipped with a mechanical stirrer, a thermometer and a dropping funnel. To this ice-cooled suspension, 37 grams (0.23 mole) of bromine was added dropwise during fifteen minutes. After stirring another fifteen minutes, the product was extracted with the following volumes of ether: 200 ml., 100 ml., 100 ml. It was washed at 0°C with water, 10% sodium carbonate solution, very dilute thiosulphate and water once more. The ethereal solution was dried overnight over calcium chloride and the ether was distilled off. The residual oil was distilled under reduced pressure.

The product was an orange oil and weighed 24 grams (68.5%, boiling point: 108-110°C under 15 mm.).

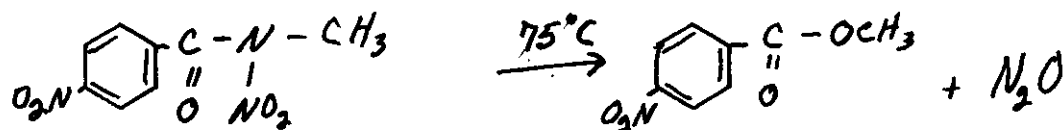
IV. ATTEMPT OF AN "AZO REACTION" BETWEEN DIETHYL AZODICARBOXYLATE
AND p-N-DINITRO-N-METHYLBENZAMIDE

Several attempts were made to obtain an addition product between the amide and the ester.

One hundredth of a mole of each constituent was mixed (2.25g. of amide, 1.74g. of ester) in 25 ml. of ether in the cold. After five weeks the starting materials were recovered unchanged. Traces of alkali or potassium acetate were added without result.

Attempts to run the reaction in boiling ether or mixtures of ether and petroleum ether, did not have any positive results.

When the mixture was heated to 75°C, a decomposition of the amide occurred according to the following reaction:



and the azodicarboxylate was recovered unreacted.

This decomposition of N-nitroamides is known to occur in presence of acid. The only way acid may be introduced in the reaction is bound to the azodicarboxylate. This is in accordance with the observation of MacKenzie (26) that it would exist as a labile complex between strong acids and azodicarboxylate. This complex would be decomposed on heating during the distillation but formed again during the condensation of the vapors.

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ABSTRACT

Due to the actual high price of hydrazine, this chemical cannot be used in an economical preparation of organic hydrazides. A synthesis of such hydrazides can be envisaged by the reduction of N-nitroamides. The problem is then to find a set of conditions under which no hydrogenolysis of the nitrogen-nitrogen bond occurs. This had been done with N-nitrocarbamates and it was hoped that the results could be extended to N-nitroamides: N-Nitro-N-methylamides were actually used in order to have a more stable N-nitro group. Demethylation of the hydrazide could be performed either by acid hydrolysis of the addition product obtained with diethyl azodicarboxylate or by heating with pyridinium chloride. After failure to reduce p-N-dinitro-N-methylbenzamide to hydrazine, a new technique was experienced by which the amide was nitrated and reduced directly without isolation of the N-nitroamide. Preliminary results suggested that the electron shifting ability of the R group in molecules of the type $R\text{CO-N}(\text{NO}_2)\text{CH}_3$ is very important in their reduction to hydrazide. Several molecules were then reduced with different R. It was found that the yield of hydrazine increases with the electron repelling ability of R.

A mechanism involving formation of an unstable platinum hydride is proposed for the reaction.

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A survey of the addition reactions of azodicarboxylic esters is given with the description of an attempt of "Azo reaction" between diethyl azodicarboxylate and p-N-dinitro-N-methylbenzamide.