

A STUDY OF THE REDUCTION OF
METHYL BENZOYLDIAZOACETATE

by

Donald N^Wth Thatcher

A THESIS

Presented to the Faculty of
The Graduate College in the University of Nebraska
In Partial Fulfillment of Requirements for the
Degree of Doctor of Philosophy
Department of Chemistry

Under the Supervision of Dr. James H. Looker

Lincoln, Nebraska

December 10, 1954

TITLE

A STUDY OF THE REDUCTION OF

METHYL BENZOYLDIAZOACETATE

BY

Donald Nixon Thatcher

APPROVED

DATE

James H. Looker

December 10, 1954

H. Armin Pagel

December 10, 1954

Cecil E. Vanderzee

December 10, 1954

Michael G. Boosalis

December 10, 1954

Charles M. Riley

December 10, 1954

SUPERVISORY COMMITTEE

The author would like to express his sincere appreciation to Dr. James H. Looker for the invaluable help and guidance on this study.

He is also indebted to E. I. du Pont de Nemours and Company for a teaching fellowship and to the Research Corporation of New York for a Frederick Gardner Cottrell grant in support of a portion of this work.

A special brand of thanks is given to his wife, Dona, whose encouragement and understanding aided materially in the completion of this investigation.

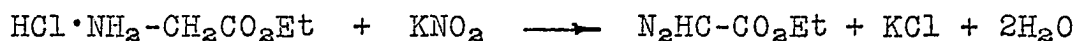
Table of Contents

Historical.	1
Graphical Summary	8
Discussion.	12
Experimental.	30
A. Preparation of Methyl Diazoacetate.	30
B. Preparation of Methyl Benzoyldiazoacetate	33
C. Reduction of Methyl Benzoyldiazoacetate	
Catalytically	33
1. Allophenylserine Methyl Ester Hydrochloride .	33
2. Allophenylserine.	35
3. Allophenylserine Methyl Ester	35
D. Reduction of Methyl Benzoyldiazoacetate by	
Aluminum Amalgam in Moist Ether	36
1. Isolation of Fractions.	36
2. Characterization of Compound A.	38
3. Characterization of Compound B.	40
E. Synthesis of Compounds Possibly Related to	
Compound A.	40
1. Ethyl β - β' -Dihydroxy- β , β' -Diphenyladipate	41
2. Ethyl Dibenzoylacetate.	42
3. Hydrogenation of Ethyl Dibenzoylacetate . . .	43
4. Bis-(α -Hydroxybenzyl)acetic Acid	44
5. Methyl bis-(α -Hydroxybenzyl)acetate.	44
6. Isolation of a Possible Second Form of	
bis(α -Hydroxybenzyl)acetic Acid.	45

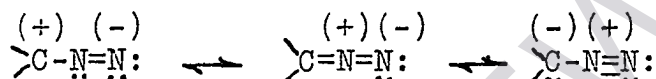
7.	Preparation of Dibenzoylacetic Acid by Alkaline Hydrolysis of Ethyl Dibenzoylacetate	46
8.	Preparation of Dibenzoylacetic Acid by Acid Hydrolysis of Ethyl Dibenzoylacetate.	47
F.	Reduction of Methyl Benzoyldiazoacetate by Ammoniacal Hydrogen Sulfide	47
1.	Methyl 5-Phenyl-1,2,3-thiadiazole-4- carboxylate	47
2.	5-Phenyl-1,2,3-Thiadiazole-4-carboxylic Acid.	48
3.	5-Phenyl-1,2,3-thiadiazole-4-carbonamide.	49
G.	Reaction of Methyl Diazoacetate with Aromatic Acid Chlorides.	49
1.	Reaction with 3,5-Dinitrobenzoyl Chloride	49
2.	Reaction with α -Naphthoyl Chloride	50
3.	Reaction with β -Naphthoyl Chloride	51
4.	Reaction with o-Iodobenzoyl Chloride.	51
H.	Reaction of 3,5-Dinitrobenzoic Acid with Methyl Diazoacetate	52
	Summary	53
	Bibliography.	54

HISTORICAL

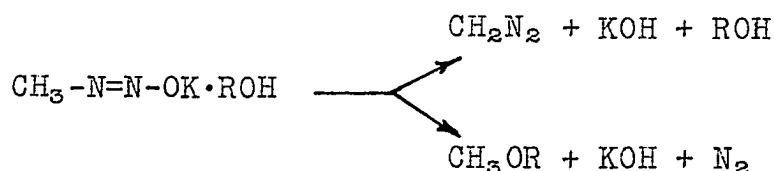
Curtius,¹ in 1883 prepared the first aliphatic diazo compound, ethyl diazoacetate, by the action of potassium nitrite on the hydrochloride of ethyl glycine.



This reaction initiated a great deal of work on aliphatic diazo compounds, with Von Pechmann² discovering the simplest member of this class of compounds, diazomethane, in 1894. The class is characterized by the presence of the group:



These aliphatic diazo compounds differ from aromatic diazonium compounds in constitution, and resemble them only in a very few reactions. They form no stable salts with acids and bases. However, a study of intermediates in the formation of diazomethane indicates that these intermediates may be analogous to the aromatic diazotates. Hantzsch and Lehmann³ were able to isolate at low temperatures a white potassium salt which gave diazomethane and potassium hydroxide upon warming. Analysis of the salt indicated a formula, $\text{CH}_3\text{-N=N-OK} \cdot \text{H}_2\text{O}$. If potassium ethylate in ethyl alcohol is used, the corresponding alcoholate is isolated. In the decomposition of the alcoholate, two modes of decomposition are evident:

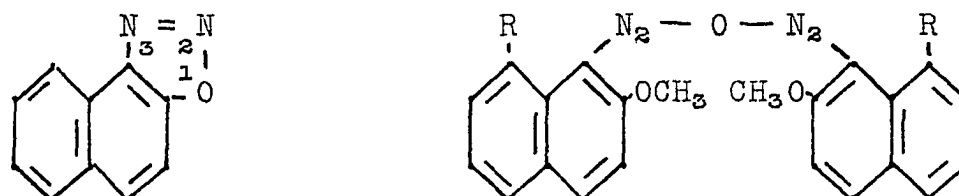


The mode of decomposition involving the loss of nitrogen is exactly paralleled by the decomposition of an aromatic diazotate in the presence of an alcohol, with the formation of an ether and nitrogen.

The nomenclature of compounds containing the aliphatic diazo group has not been standardized and care must be exercised in searching the literature. The simple diazoalkanes offer no difficulty, but more complex derivatives tend either to have a variety of names, or the same name will be applied to two or more different types of compounds. The term "diazoester or diazoacetic ester" is generally applied to such compounds as methyl diazoacetate and will be so used by this author. However the term "diazoester" has been applied to compounds having the structure, $R-CO_2-N=N-CH_2R'$. Those diazo compounds which have two carbonyl functions alpha to the diazo group may have a variety of names. In the older literature the term "diazo oxide", "diazoanhydride" or "furo-diazole" is often used because of the belief that these compounds contained a new ring system. Chemical Abstracts accepts the name 1,2,3-oxadiazole for this ring system. The term "diazoanhydride" has also been applied to compounds

56

having the following structures:



There are three rather general methods for the

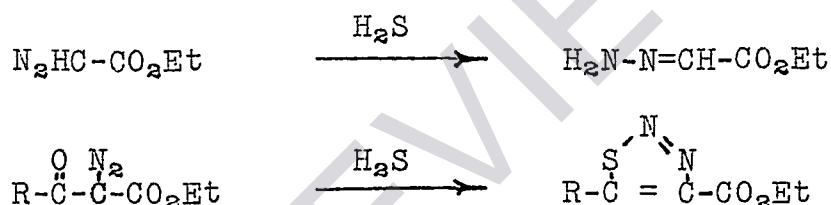
preparation of aliphatic diazo compounds. The first method may be considered as the decomposition of N-nitroso compounds with concentrated alkali. The precursor of the nitroso compound may be a substituted urethane,² a substituted urea,⁴ or an addition compound of the primary amine with mesityl oxide.^{5,6} The latter modification is capable of wide application. Diazo hydrocarbons up to C₈ have been made by this method, but the yield drops considerably as the length of the carbon chain increases. This general method is used commonly for the preparation of diazomethane.

The second general method is of more limited application. Whereas the majority of primary aliphatic amines react with nitrous acid to give nitrogen and an alcohol, a certain number of amines in which there is a "negative" or electron withdrawing group in the alpha position to the amino group give an aliphatic diazo compound. The most important examples are the α -amino acid esters, α -amino nitriles, and compounds such as α -aminoacetophenone. This method is applied commonly for the preparation of methyl and ethyl diazoacetate.

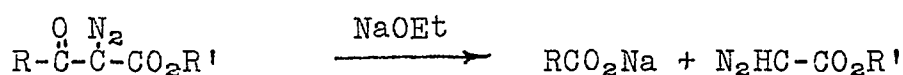
The third method involves the oxidation of the hydrazones of aldehydes and ketones with metallic oxides such as mercuric or silver oxide.³⁰ This method is valuable for diazo compounds containing aromatic hydrocarbon residues. For example, diphenyldiazomethane is prepared from benzophenone by this method.

In physical properties, and in stability toward acids and heat, the aliphatic diazo compounds vary widely. It may be said in general that those diazo compounds with a

hydrocarbon residue are brightly colored and comparatively unstable, those diazo compounds with one carbonyl in the alpha position are yellow and more stable, while those with two such groups are almost colorless and quite stable.⁸ This latter class is so stable that it has been thought to have a different constitution. Wolff proposed that these compounds should be called "diazoanhydrides", and that their structure can be represented by a 1,2,3-oxadiazole system instead of by an open chain formulation.²⁰ He based his theory upon the fact that simple diazo compounds are reduced to hydrazones or more highly reduced products with hydrogen sulfide, while "diazoanhydrides" gave thiadiazoles as reduction products.

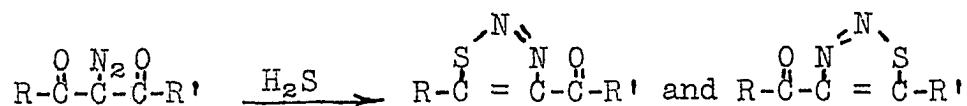


At present it seems that Wolff's conclusion is rather difficult to substantiate. Staudinger⁷ has shown, at least for some of Wolff's diazoanhydrides, that in the presence of sodium ethoxide these diazoanhydrides are decomposed in a manner similar to that shown by Dieckmann for all disubstituted β -ketonic esters.

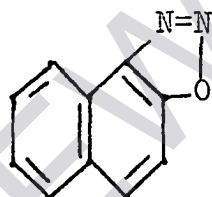
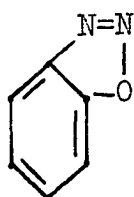


Also with an unsymmetrical diazo diketone, the action of hydrogen sulfide results in two isomeric thiadiazoles, because the ring may be closed with either carbonyl group.

The two corresponding isomeric oxadiazoles have never been isolated, and the one diazo diketone yields both thiadiazoles.



It might be expected that if the 1,2,3-oxadiazole system could exist, it would be stabilized in the form of the benz-1,2,3-oxadiazole, or the naphtho-2',1,2,3-oxadiazole, because of the known stability of phenols in the enolic rather than the ketonic form. These compounds have been extensively



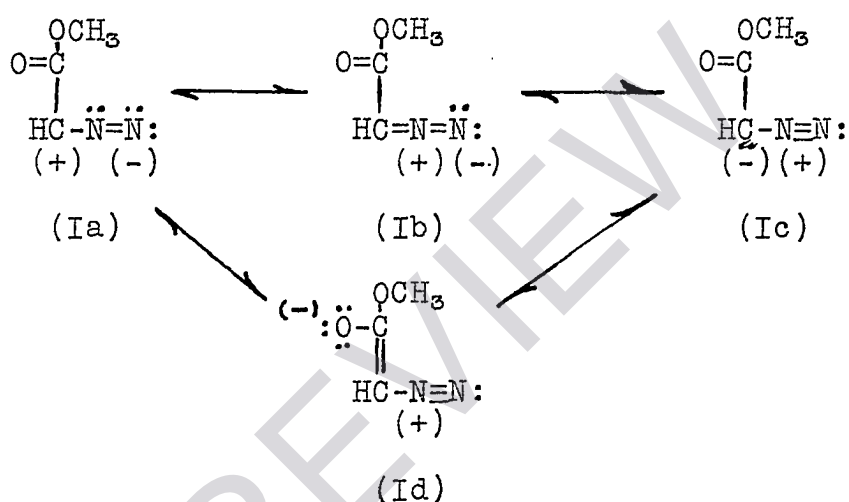
studied by various workers, but in no case has the 1,2,3-oxadiazole ring system been demonstrated unequivocally.

Rather, as Hodgson and Marsden ²² point out in their review article on the problem, all present evidence points to the conclusion that "diazoanhydrides" are resonance hybrids.

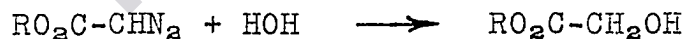
The diazoacetic esters, with which the present thesis is concerned, are very volatile, yellow colored liquids with a peculiar odor. They distill without decomposition with steam, or under reduced pressure. They are slightly soluble in water, but miscible with alcohol and ether. Dilute aqueous alkali will hydrolyze the ester with the formation of the salt of the diazo acid. Ethyl diazoacetate explodes violently when brought into contact with concentrated sulfuric acid. At temperatures near its boiling point, or at room temperature in the presence of copper sulfate, it decomposes to give

ethyl fumarate and nitrogen.²³ Concentrated ammonia converts the ester to diazoacetamide.

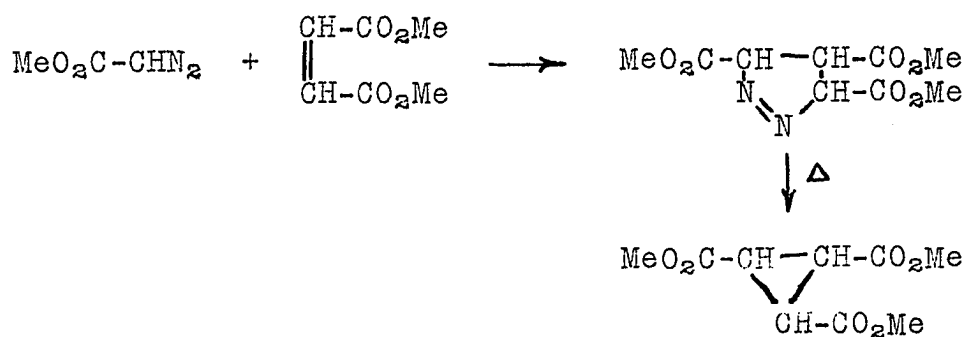
The diazoacetic esters react in a great variety of ways, with or without the loss of nitrogen. Since diazoacetic esters are resonance hybrids, in which four electronic structures make contributions, the reactions of the esters may be accounted for on the basis of one or more of the following electronic structures:



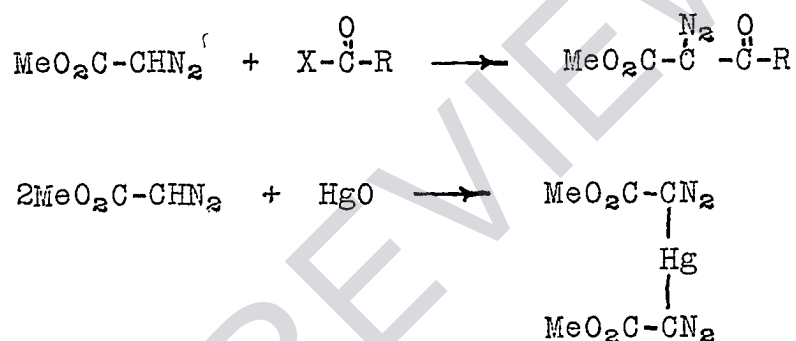
The reaction of water, acids, and halogens with the diazo esters results in loss of nitrogen.



The reaction of diazoacetic esters with aldehydes and ketones is complex, and the product isolated depends upon the carbonyl compound used. β -Ketoesters, ethylene oxide derivatives, and even ethers may be produced. Diazoacetic esters will add at an ethylene or acetylene link to give pyrazoline, pyrazole, or cyclopropane derivatives.



Lesser known are the reactions of diazoacetic ester in which the diazo group is left intact. Acylation, aroylation, and metallation of diazoacetic ester have been carried out.



These latter reactions are rather well known with diazomethane, but have not been extensively studied with diazoacetic esters.

Graphical Summary

Roman numerals accompanying the compounds correspond to those used in the discussion and experimental sections. The notation "N₂" will be used for the diazo grouping.

