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The Reaction to Ketoacylhydrazones with Lead Tetraacetate

Lavern M. Weisenberger

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THE REACTION OF KETOACYLHYDRAZONES
WITH LEAD TETRAACETATE

by

Lavern M. Weisenberger

A thesis presented to the Faculty of the
School of Graduate Studies in partial fulfillment
of the
Degree of Master of Arts

Western Michigan University
Kalamazoo, Michigan
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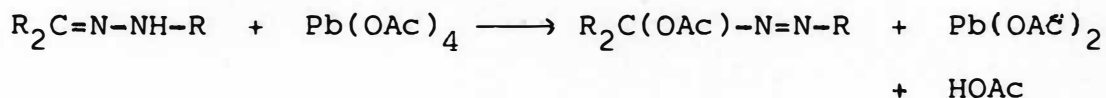
ACKNOWLEDGMENT

The author wishes to express his appreciation for the opportunity to work with, be guided by and to learn from Dr. Don C. Iffland. He is also grateful for any assistance, however small, he received from the members of the staff or fellow graduates.

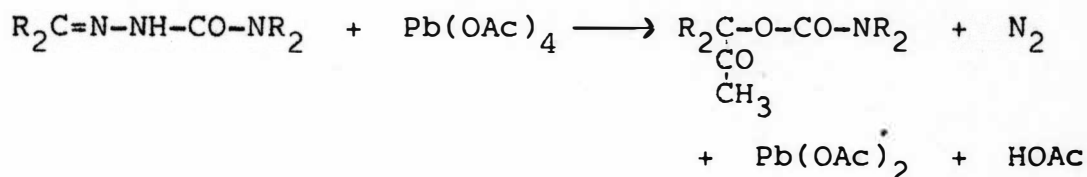
The author is also indebted to the National Institutes of Health for the support given for this research.

INTRODUCTION

It has been shown that ketohydrazones react with lead tetraacetate to give azoacetates in good yields (11) according to the following equation:



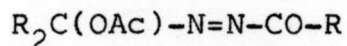
The reaction of the structurally related 4,4-di-substituted ketosemicarbazones with lead tetraacetate quite unexpectedly gave carbamates in good yields (10) presumably according to the following equation:



This anomalous behavior becomes understandable when it is assumed that the expected azoacetate is unstable and spontaneously decomposes to the carbamate. A mechanism involving a nucleophilic displacement at the amide carbonyl group and elimination of nitrogen has been proposed. The electron withdrawal effect and the elimination of nitrogen are thought to be the driving forces in this rearrangement.

Ketoacylhydrazones are structurally similar to ketosemicarbazones; however, the group attached to the

acyl carbonyl will be electron releasing and cause the carbonyl carbon to be less electrophilic. If this electron release is sufficient a rearrangement may not occur and, as in the case of ketohydrazones, an azoacetate might be isolated having the following structure:



Compounds of this nature may be of interest because of the potential biological activity of the azo function in the molecule. Aromatic azo compounds have shown anti-tumor activity (17) and activity against tubercle bacilli (16). Aromatic azo dyes have shown carcinogenic properties (1).

It is the intention of this study to investigate the reaction of several ketoacylhydrazones with lead tetraacetate in an attempt to obtain new azoacetates.

EXPERIMENTAL

In the following section all boiling and melting points are in degrees Centigrade and are uncorrected. The microanalytical data were obtained from the Galbraith Laboratories, Knoxville, Tennessee.

The infrared spectra were obtained with a Perkin--Elmer Model 21 recording spectrophotometer and the assignment of bands was made according to Bellamy (2).

The ultraviolet spectra were measured with a Beckman Model DB spectrophotometer with the compounds dissolved in 95% ethanol.

Gas-liquid chromatography was carried out with a F & M Dual Column Gas Chromatograph Model 720 with columns containing diethyleneglycolsuccinate on chromosorb.

A. Preparations of Ketoacylhydrazones

1. Acetone Acetylhydrazone.— Acetylhydrazine was prepared from 25 g. (0.5 mole) of hydrazine hydrate and 45 g. (0.5 mole) of ethyl acetate according to the procedure of Kost and Sagitullin (13). The crude acetylhydrazine was refluxed 30 min. with 100 ml. (1.36 mole) of acetone. Upon cooling 24 g. (86%) of acetone acetylhydrazone separated as white crystals, m.p. 138-140°. Lit: m.p. 137° (13).

2. Acetophenone Acetylhydrazone.- Crude acetylhydrazine was refluxed for 30 min. with 60 g. (0.5 mole) of acetophenone dissolved in 100 ml. ethanol. The material obtained upon cooling was recrystallized from diethyl ether. Forty-four grams (50%) of white crystalline acetophenone acetylhydrazone was obtained which melted at 130-131°.

Anal. Calc'd. for $C_{10}H_{12}N_2O$: C, 68.15; H, 6.87; N, 15.90. Found: C, 68.20; H, 6.90; N, 15.73.

3. 3-Pentanone Acetylhydrazone.- Crude acetylhydrazine was added to 64 g. (0.8 mole) of 3-pentanone dissolved in 100 ml. of ethanol. The solution was refluxed for one hour. Sixty grams of crude product was obtained after removing the solvent in vacuo. The residue was vacuum distilled. Forty-eight grams (48%) of 3-pentanone acetylhydrazone was collected at 104-108° and at 0.5 mm. and solidified as a white solid which melted at 62-65°.

Anal. Calc'd. for $C_7H_{14}N_2O$: C, 59.12; H, 9.92; N, 19.71. Found: C, 59.24; H, 9.96; N, 19.88.

4. Benzophenone Acetylhydrazone.- Forty grams (0.2 mole) of benzophenone hydrazone dissolved in 150 ml. of benzene was acetylated with 23 g. (0.23 mole) of acetic anhydride according to the procedure of Curtius and Rauterberg (3). A white crystalline product weighing

31.3 g. (68%) was obtained after recrystallization from methanol. M.p. 106-107°. Lit: m.p. 107° (3).

5. Acetone Benzoylhydrazone.- Benzoylhydrazine was prepared from 25 g. (0.5 mole) of hydrazine hydrate and 75 g. (0.5 mole) of ethyl benzoate in the same manner as acetylhydrazine. The crude benzoylhydrazine was refluxed 30 min. with 100 ml. (1.36 mole) of acetone. Upon cooling 28 g. (65%) of white crystalline acetone benzoylhydrazone was collected which melted at 140-142°. Lit: m.p. 142° (4).

6. Benzophenone Benzoylhydrazone.- Forty grams (0.2 mole) of benzophenone hydrazone dissolved in 150 ml. of benzene was mixed with 30 g. (0.21 mole) of benzoyl chloride and 30 g. of pyridine. After refluxing for one hour the cooled mixture was filtered and the precipitate was washed with benzene. The filtrate was concentrated and a yellow product collected. This material was thoroughly washed with pentane to yield 36.6 g. (60%) of white crystalline benzophenone benzoylhydrazone which melted at 115-116°. Lit: m.p. 116.5° (3).

B. Reaction of Ketoacylhydrazones with Lead Tetraacetate

1. Reaction of Acetone Acetylhydrazone.- A solution containing 13.7 g. (0.12 mole) of acetone acetylhydrazone

dissolved in 50 ml. methylene chloride was added slowly to a cooled solution containing 63.0 g. (0.14 mole) of lead tetraacetate dissolved in 150 ml. of methylene chloride. The solution was stirred with a magnetic stirrer and maintained at -5° to $+5^{\circ}$ in an ice-salt bath. The reaction mixture was stirred 30 min. after addition of the hydrazone solution. After mixing with 100 ml. of water the methylene chloride solution was filtered thru Celite, washed with water, aqueous sodium bicarbonate solution and again with water. The methylene chloride layer was dried over anhydrous sodium sulfate and concentrated by vacuum evaporation to leave a yellow liquid. Infrared spectrum of the yellow liquid indicated the presence of a carboxylic acid anhydride by a strong absorption band at 1820 cm^{-1} . After stirring with 10% aqueous sodium bicarbonate solution for 45 min. at 0° to $+5^{\circ}$ a crude product free of anhydride was obtained.* This yellow liquid was distilled at

* In this and all later reactions of acylhydrazones with lead tetraacetate as well as the earlier reactions of 4,4-disubstituted semicarbazones with lead tetraacetate (5) the crude reaction mixture contained carboxylic acid anhydrides as indicated by the strong absorption at 1820 cm^{-1} (the lower frequency anhydride

reduced pressure. The properties of the fractions collected are summarized in Table I.

TABLE I

Distillation of the Product from the Reaction of
Acetone Acetylhydrazone with Lead Tetraacetate

Fraction	B.p.	Pres.	Wt.	$n_D^{25^\circ}$
1	51-53 $^\circ$	1 mm.	1.22 g.	1.4198
2	53-53.5 $^\circ$	"	3.07 g.	1.4211
3	53.5-54 $^\circ$	"	3.14 g.	1.4212
4	54 $^\circ$	"	5.01 g.	1.4212
5	54-54.5 $^\circ$	"	2.28 g.	1.4214
6	54.5-56 $^\circ$	"	0.53 g.	1.4220

Fractions 2-6 represent a 68% yield of 2-acetoxy--
2-(acetylazo)propane: λ_{\max} , 314 $m\mu$ ($\epsilon = 200$); λ_{\max} ,
208 $m\mu$ ($\epsilon = 1300$).

Anal. Calc'd. for $C_7H_{12}N_2O_3$: C, 48.82; H, 7.03;
N, 16.27. Found: C, 48.74; H, 7.28; N, 16.45.

A small sample of 2-acetoxy-2-(acetylazo)propane was
treated in each of the following ways: 1. with aqueous
hydrochloric acid; 2. with aqueous acetic acid; 3. with

carbonyl band would be masked by other carbonyl absorp-
tions). This side reaction product was removed by
treatment with aqueous sodium bicarbonate.

aqueous alcoholic potassium hydroxide and 4. with anhydrous acetic acid-methylene chloride. In the first three cases the evolution of a gas, presumed to be nitrogen, was observed. No evolution was observed in the case of anhydrous acetic acid-methylene chloride.

The color of the yellow 2-acetoxy-2-(acetylazo)propane slowly faded on standing and became colorless in 20 days at room temperature and open to the air. No change in boiling range, index of refraction, infrared spectrum or ultraviolet spectrum below 360 μ were noted during or after this change. The only change observed was the disappearance of a weak absorption band at 403 μ (See Charts I and II.) as the change from yellow to colorless took place.

To test the effects of light, temperature, and air on this process, samples of 2-acetoxy-2-(acetylazo)propane were treated in the following manner and the change in color observed: 1. exposed to light at room temperature and open to the air; 2. exposed to light at room temperature in a closed container; 3. stored in the dark at room temperature in a closed container and 4. stored in the dark at 5°. The yellow sample open to air became colorless in twenty days. The yellow samples in closed containers exposed to light and stored in the dark faded at about the same rate, however, both changed more slowly than the sample exposed to air. The sample maintained at

Chart I

Absorption of "yellow" 2-Acetoxy-2-(acetylazo)propane

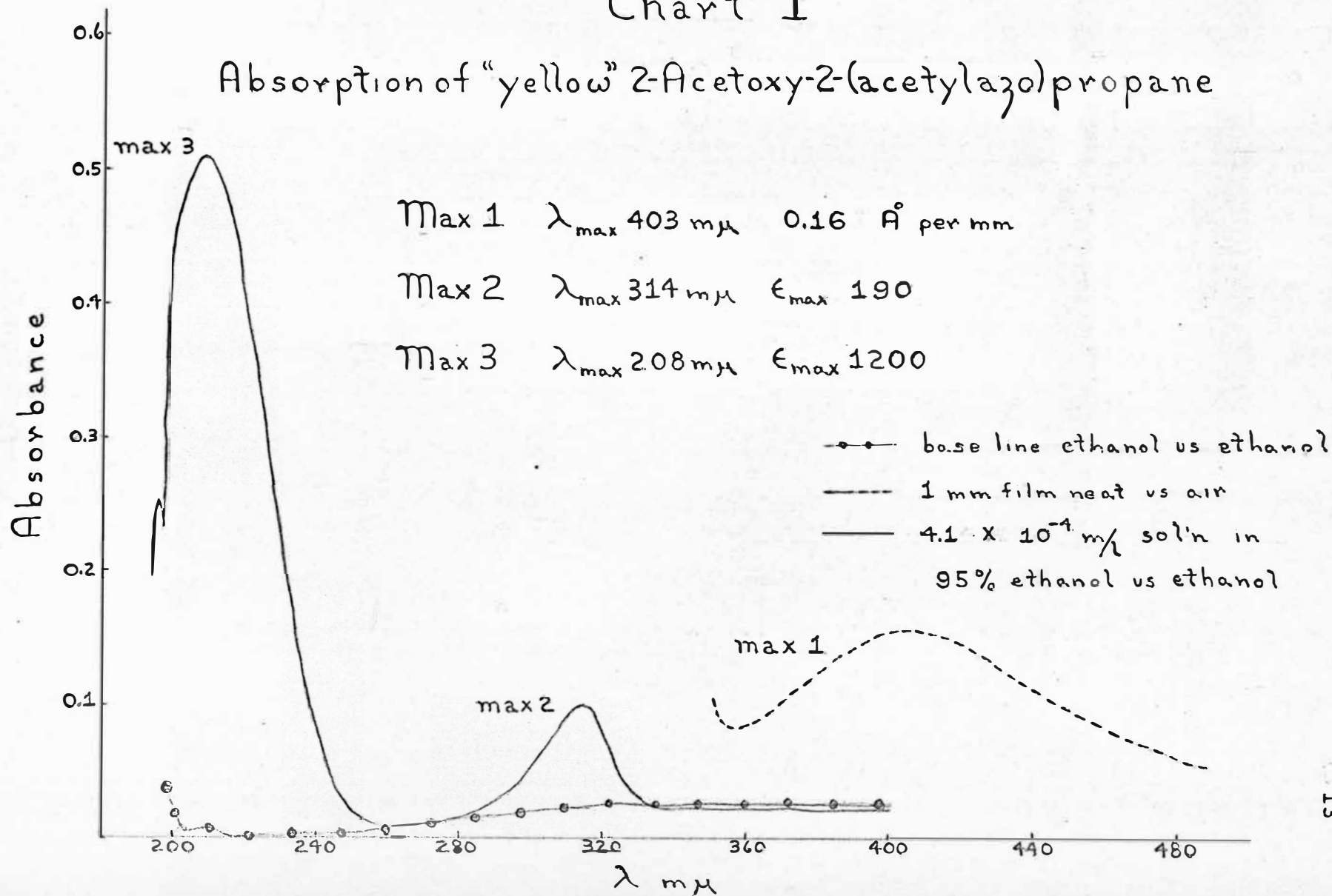


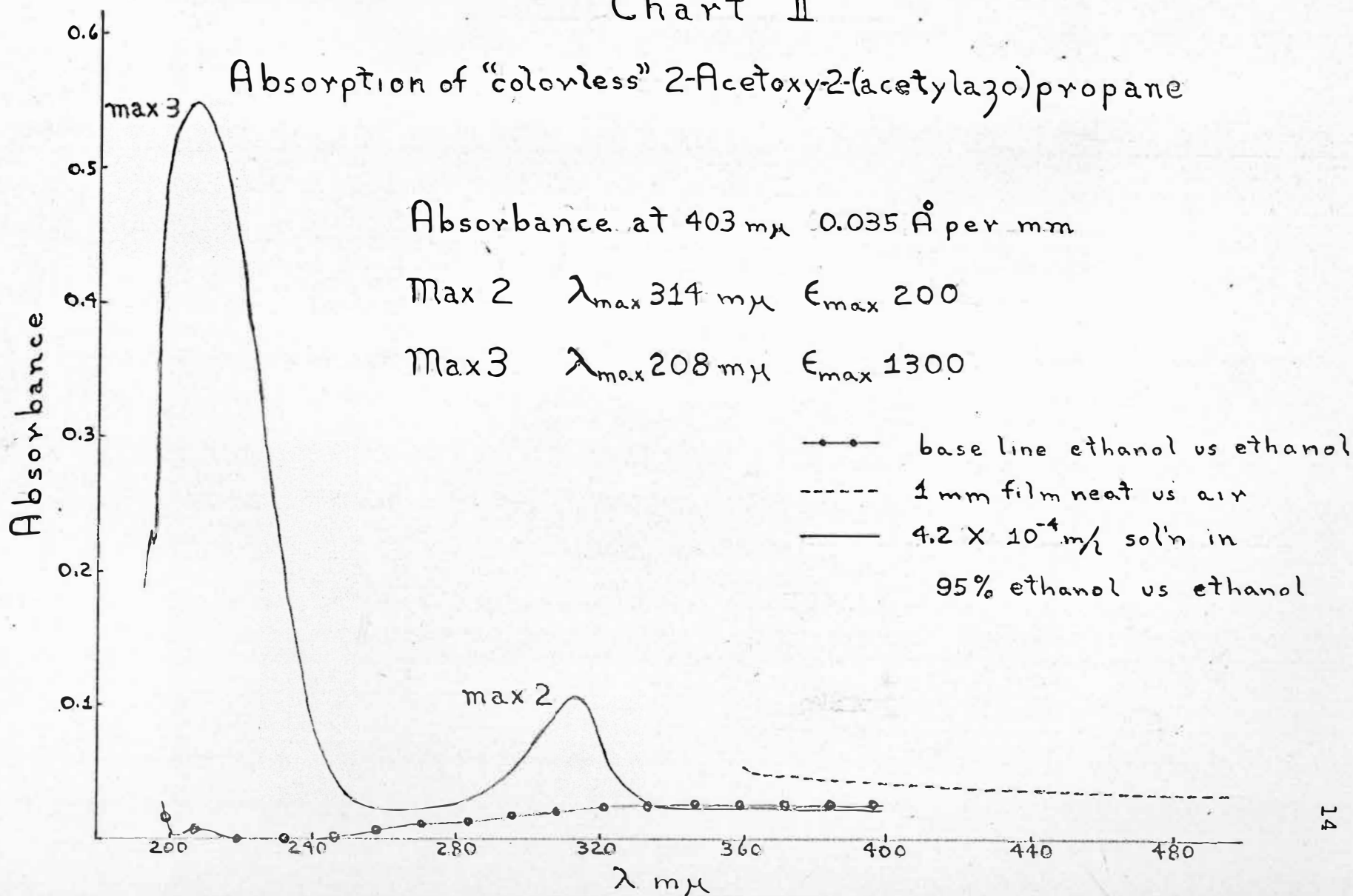
Chart II

Absorption of "colorless" 2-Acetoxy-2-(acetyloxy)propane

Absorbance at 403 m μ 0.035 A per mm

Max 2 λ_{\max} 314 m μ ϵ_{\max} 200

Max 3 λ_{\max} 208 m μ ϵ_{\max} 1300



5° in the absence of light faded still more slowly. One sample stored closed in a refrigerator at 5° failed to become colorless during a period of 5 months.

2. Reaction of 3-Pentanone Acetylhydrazone.— In the above manner, 15.3 g. (0.11 mole) of 3-pentanone acetylhydrazone was reacted with 55.0 g. (0.12 mole) of lead tetraacetate. After removal of anhydride by the aqueous sodium bicarbonate treatment, vacuum distillation of the yellow product provided material having the properties indicated in Table II.

TABLE II

Distillation of the Product from the Reaction of 3-Pentanone Acetylhydrazone with Lead Tetraacetate

Fraction	B.p.	Pres.	Wt.	$n_D^{25^\circ}$
1	68-77°	1 mm.	1.17 g.	1.4318
2	77-77.5°	"	2.25 g.	1.4333
3	77.5°	"	3.35 g.	1.4333
4	77.5°	"	3.93 g.	1.4333
5	77.5-78°	"	1.29 g.	1.4335
6	78-80°	"	0.89 g.	1.4342

Fractions 2-6 represent a 52% yield of 3-acetoxy--3-(acetylazo)pentane: λ_{\max} , 316 $m\mu$ (ϵ = 175); λ_{\max} , 212 $m\mu$ (ϵ = 1400).

Anal. Calc'd. for $C_9H_{16}N_2O_3$: C, 53.98; H, 8.06; N, 13.99. Found: C, 54.17; H, 8.16; N, 14.18.

The reaction of 3-pentanone acetylhydrazone with lead tetraacetate was repeated with the initial addition of 15 g. of magnesium oxide to the lead tetraacetate--methylene chloride solution in order to avoid an acid solution during the hydrazone addition. After allowing 30 min. for reaction, solids were removed by filtration before the treatment with water. In this case vacuum distillation of the yellow product gave 14.5 g. (66%) of 3-acetoxy-3-(acetylazo)pentane with properties identical to the azo compound obtained in the absence of magnesium oxide.

Samples of 3-acetoxy-3-(acetylazo)pentane were subjected to the same chemical tests as 2-acetoxy-2-(acetylazo)propane. In each test the results were identical.

In each sample of yellow 3-acetoxy-3-(acetylazo)pentane the color slowly faded upon standing at room temperature. No change was observed in boiling range, index of refraction or infrared spectrum during or after this change.

3. Reaction of Benzophenone Benzoylhydrazone.— Adapting the general procedure for the reaction of hydrazones with lead tetraacetate, 9.2 g. (0.031 mole) of benzophenone benzoylhydrazone was added to 15.0 g. (0.034 mole) of

lead tetraacetate containing 10 g. of magnesium oxide. After the usual reaction time the mixture was filtered to remove the solid and thoroughly washed with water. The oil residue decomposed with the evolution of a gas at room temperature. After three hours the evolution of gas appeared completed and the oil-solid mixture was dissolved in an ether-pentane (2-1) mixture. Upon cooling a pale yellow solid was obtained. Recrystallization from an ether-pentane mixture gave 3.4 g. (34%) of white solid which melted at 122-124°. This compound was shown to be α -phenylbenzoin acetate.

Anal. Calc'd. for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49.

Found: C, 79.81 and 79.85; H, 5.53 and 5.52.

Hydrolysis with 15% sulfuric acid gave α -phenylbenzoin, m.p. 86-87°. Lit: m.p. 84-86° (8).

4. Reaction of Benzophenone Acetylhydrazone.- In the usual manner 16.6 g. (0.070 mole) of benzophenone acetylhydrazone was reacted with 38.0 g. (0.086 mole) of lead tetraacetate. As the hydrazone was added the mixture developed a red color. The red oil remaining after vacuum evaporation of the solvent was shown to contain diphenyldiazomethane by a characteristic infrared band at 2040 cm^{-1} and spontaneous loss of the red coloration upon heating and upon addition of an acid. The quantity of diphenyldiazomethane formed in the reaction was not measured.

Identical results were obtained in the presence of magnesium oxide and by reversed order of addition of reactants, i.e., addition of lead tetraacetate solution to hydrazone solution. No attempt was made to identify or isolate other components from this red reaction product.

5. Reaction of Acetophenone Acetylhydrazone.— Using the general procedure 12.0 g. (0.068 mole) of acetophenone acetylhydrazone was reacted with 37.0 g. (0.083 mole) of lead tetraacetate containing 12 g. of magnesium oxide. After the 30 min. reaction time the mixture was filtered to remove solids and washed thoroughly with water. After removing the solvent by vacuum evaporation, the oily residue was cooled at -6° overnight. Twenty milliliters of pentane was added to the cooled residue and the mixture was filtered. The white crystalline product (0.8 g.) collected melted at $128-130^{\circ}$. This solid was identical to the starting hydrazone.

The pentane in the filtrate was removed in vacuo. The oil residue was heated to 50° to accelerate the decomposition. After four hours the evolution of the gas appeared complete. After removing the acid anhydrides with the aqueous sodium bicarbonate treatment, purification of the residue by vacuum distillation was attempted. The properties of the fractions collected are tabulated

in Table III.

TABLE III

Distillation of the Decomposition Mixture from
the Reaction of Acetophenone Acetylhydrazone
with Lead Tetraacetate

Fraction	B.p.	Pres.	Wt.	$n_D^{25^\circ}$
1	55-59 $^\circ$	1 mm.	0.37 g.	1.5242
2	59-69 $^\circ$	"	0.27 g.	1.5239
3	69-89 $^\circ$	"	0.49 g.	1.5051
4	89-94 $^\circ$	"	1.14 g.	1.4953
5	94-97 $^\circ$	"	1.42 g.	1.4959
6	97-101 $^\circ$	"	1.55 g.	1.4979
7	101-105 $^\circ$	"	1.38 g.	1.5002
8	105-109 $^\circ$	"	1.45 g.	1.5014
9	109-115 $^\circ$	"	0.58 g.	1.5050
10	residue			

Fractions of the above distillation were examined as follows: Infrared spectra of fractions 4, 5, and 8 showed acetate bands at 1740 cm^{-1} and 1240 cm^{-1} with a shoulder at 1715 cm^{-1} ; aromatic bands at 3040 cm^{-1} , 760 cm^{-1} and 690 cm^{-1} ; four aromatic bands from 1625-1450 cm^{-1} and methyl C-H bands at 2980 cm^{-1} , 2930 cm^{-1} and 1450 cm^{-1} . Fraction 4 gave a positive iodoform test. Qualitative elemental analysis of fractions 4 and 8 indicated the

absence of nitrogen.

Because of the apparent failure to obtain pure compounds by fractionation in the vacuum distillation, the material was not further examined.

6. Reaction of Acetone Benzoylhydrazone.- Following the usual procedure 14.0 g. (0.081 mole) of acetone benzoylhydrazone was reacted with 41.0 g. (0.092 mole) of lead tetraacetate containing 10 g. of magnesium oxide. After the 30 min. reaction time the mixture was filtered and then washed with water. After removal of the solvent in vacuo, the yellow oil residue decomposed with the evolution of a gas. After 24 hours at 30° the evolution appeared complete. The residue was dissolved in pentane and treated with aqueous sodium bicarbonate solution to remove acid anhydrides. After separation of the aqueous layer and removal of the pentane, purification by vacuum distillation was attempted. Properties of the fractions collected are indicated in Table IV.

Infrared spectrum of fraction 4 showed a broad carbonyl band at 1745-1730 cm^{-1} with a shoulder at 1720 cm^{-1} ; a second carbonyl band at 1685 cm^{-1} ; an acetate band at 1250 cm^{-1} ; aromatic bands at 3030 cm^{-1} and 700 cm^{-1} ; four aromatic bands between 1600-1450 cm^{-1} ; and methyl C-H bands at 2970 cm^{-1} , 2930 cm^{-1} and 1450 cm^{-1} . Fraction 3 gave a positive iodoform test. Fraction 3 gave a

TABLE IV

Distillation of the Decomposition Mixture from
the Reaction of Acetone Benzoylhydrazone
with Lead Tetraacetate

Fraction	B.p.	Pres.	Wt.	$n_D^{25^\circ}$
1	65-90 $^\circ$	1 mm.	0.33 g.	1.4952
2	90-107 $^\circ$	"	1.31 g.	1.5013
3	107-110 $^\circ$	"	2.08 g.	1.5027
4	110-114 $^\circ$	"	2.12 g.	1.5049
5	114-118 $^\circ$	"	1.06 g.	1.5072
6	118-125 $^\circ$	"	0.60 g.	1.5093
7	residue			

negative nitrogen test with qualitative elemental analysis.

Vacuum distillation of the reaction product obtained by a repetition of this reaction using the above indicated quantities gave the results shown in Table V.

Examination of fraction 3 with infrared spectra indicated aromatic bands at 3010 cm^{-1} , 755 cm^{-1} and 690 cm^{-1} ; methyl C-H bands at 2970 cm^{-1} , 2920 cm^{-1} and 1450 cm^{-1} ; and an acetate carbonyl band at 1735 cm^{-1} . Fraction 4 gave a positive iodoform test and a negative nitrogen test.

Fractions 2, 4, and 6 of each distillation were examined by gas-liquid chromatography. Three foot columns of diethyleneglycolsuccinate on chromosorb were

TABLE V

Distillation of the Decomposition Mixture from
the Reaction of Acetone Benzoylhydrazone
with Lead Tetraacetate

Fraction	B.p.	Pres.	Wt.	$n_D^{25^\circ}$
1	68-90 $^\circ$	1 mm.	0.55 g.	1.4973
2	90-97 $^\circ$	"	1.41 g.	1.4952
3	97-100 $^\circ$	"	1.99 g.	1.4952
4	100-103 $^\circ$	"	2.58 g.	1.4950
5	103-108 $^\circ$	"	0.85 g.	1.4950
6	108-122 $^\circ$	"	0.75 g.	1.5015
7	residue			

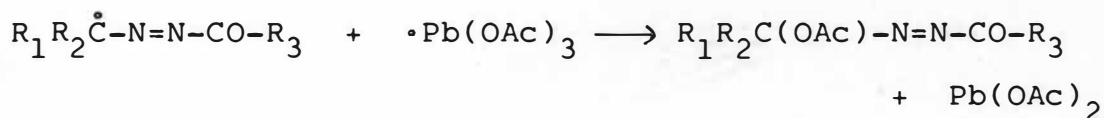
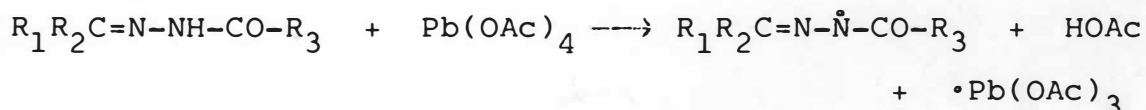
used with the following conditions: helium flow, 50 cc. per min.; programed from 70 $^\circ$ to 230 $^\circ$ at 20 $^\circ$ per min.; injector temperature, 200 $^\circ$; detector temperature, 250 $^\circ$; bridge current, 150 ma.; sample, 3.0 μ l. The two major components had retention times of 8.4 min. and 9.8 min. with a resolution satisfactory for isolation. The ratio of the first and second peak heights of fractions 2, 4, and 6 of the first run (Table IV) were, respectively: 0.81, 1.06 and 0.07. Similar ratios for fractions 2, 4, and 6 of the second run (Table V) were, respectively: 0.87, 0.64 and 0.93. The infrared spectrum of the substance indicated by the first peak showed benzoate absorption bands at 1730 cm^{-1} , 1275 cm^{-1} and 1225 cm^{-1} ; an

aliphatic keto band at 1705 cm^{-1} ; methyl C-H bands at 2960 cm^{-1} , 2915 cm^{-1} and 1450 cm^{-1} ; and aromatic bands at 3020 cm^{-1} , 750 cm^{-1} and 690 cm^{-1} . The infrared spectrum of the substance indicated by the second peak showed acetate bands at 1730 cm^{-1} and 1250 cm^{-1} ; an aryl keto band at 1685 cm^{-1} ; methyl C-H bands at 2960 cm^{-1} , 2905 cm^{-1} and 1450 cm^{-1} ; and aromatic bands at 3020 cm^{-1} , 700 cm^{-1} and 655 cm^{-1} . This infrared examination suggested the presence of the two possible rearrangement products: 3-hydroxy-3-methyl-2-butanone benzoate and hydroxydimethylacetophenone acetate. Because of the apparent similarity in the properties of the two rearrangement products and the failure to obtain adequate fractionation by vacuum distillation, no pure products were isolated.

DISCUSSION AND CONCLUSIONS

All the reactions in the previous section were conducted according to the procedure of Iffland, Salisbury, and Schafer (11). The products obtained from acetone acetylhydrazone and 3-pentanone acetylhydrazone were identified as 2-acetoxy-2-(acetylazo)propane and 3-acetoxy--3-(acetylazo)pentane.

In the reaction of ketohydrazones with lead tetraacetate, studied by Iffland, et al. (11), a free radical mechanism was proposed to account for the formation of the azoacetates. Since the ketoacylhydrazones are structurally related to the ketohydrazone and both react with lead tetraacetate under similar conditions, the same mechanism is likely involved in the formation of both azoacetates. If a free radical process is truly involved in this reaction of ketoacylhydrazones, a mechanism related to that described for ketohydrazones maybe as follows:



The structures of the azoacetates were established by elemental analysis, ultraviolet and infrared spectra, and chemical tests. The values for the percent of carbon, hydrogen and nitrogen were in agreement with theoretical values. The strong absorption at 208-212 μ and the weak absorption at 314-316 μ in the azoacetates obtained from ketoacylhydrazones correspond to the absorption bands in structurally similar α - β unsaturated ketones. For example, 3-buten-2-one exhibits a strong absorption band at 212.5 μ ($\log \epsilon = 3.85$) and a weak absorption at 320 μ ($\log \epsilon = 1.43$) (18). Infrared spectra of these azoacetates show strong acetate bands at 1740 cm^{-1} and 1225 cm^{-1} with a shoulder at 1715 cm^{-1} corresponding to the acyl carbonyl group. The azo group in azoacetates does not have absorption bands in the infrared useful for identification. The absence of the N-H band at 3160 cm^{-1} indicates the complete reaction of the hydrazone.

It has been observed that azoacetates undergo acid or alkaline catalyzed hydrolysis with the evolution of nitrogen gas (12). The new azoacetates were treated with aqueous hydrochloric acid, aqueous acetic acid, and aqueous alcoholic potassium hydroxide. In each of these tests the evolution of a gas, presumed to be nitrogen, was observed. These azoacetates failed to decompose in an anhydrous acetic acid-methylene chloride solution.

The reactions with lead tetraacetate were conducted in methylene chloride solution both in the absence and in the presence of suspended magnesium oxide. Initially it was believed that the decomposition of the azoacetate was accelerated by the presence of acetic acid formed in this reaction. This use of magnesium oxide as an insoluble base to neutralize acetic acid in this reaction was prompted by a procedure of Rabjohn (15) in which calcium oxide was added to a lead tetraacetate oxidation of benzophenone carboethoxyhydrazone in which an azoacetate is reported to be formed. The results of the above tests and the duplicate experiments indicate that acetic acid has little if any effect on the decomposition of the azoacetate developed and this use of magnesium oxide is unnecessary.

Unexpectedly the two freshly prepared yellow azoacetates slowly transformed to a colorless azoacetate indistinguishable from the yellow material in all properties except for the weak absorption at 403 m μ . This freshly prepared yellow azoacetate, upon standing in the presence of air, slowly faded and became colorless with no evidence of decomposition. The boiling range, index of refraction and infrared spectrum of this colorless material were identical with those of the original yellow azoacetate.

The ultraviolet spectra (See Charts I and II.) of the yellow and colorless materials showed maxima of the same intensity at 208 μ and 314 μ . This suggests the yellow and colorless materials are structurally equivalent. The yellow material displayed a maximum at 403 μ with an absorbance of 0.15 per mm. relative to air (ϵ_{max} approximately 2.5 based on a concentration of 6 m/l in the pure azoacetate, assuming a density of unity.), whereas, the colorless material had no maximum at 403 μ with an absorbance of 0.035 per mm. relative to air (ϵ approximately 0.6, calculated as above.).

The following processes have been considered in order to rationalize the color change observed in these azoacetates. First, the presence of an impurity similar in properties and composition to the azoacetate and indistinguishable from the azoacetate by the methods used for purification and identification. Such an impurity, if present, must be yellow in color and must decompose in the presence of air to a new colorless substance which is also indistinguishable from the azoacetate. These demands on the properties and structure of the colored impurity render this explanation unlikely. Second, the structure of the azo group in these molecules permit the possibility of cis and trans isomers. In freshly prepared azoacetate one configuration may be formed in preference to the other and on standing an

isomerization process may convert the initial configuration to the isomeric configuration. If in this case the more stable configuration (usually trans) is formed initially, as might be expected, the isomerization process would lead to the less stable or cis isomer. Such isomerization is frequently observed in the presence of high energy light. However, this yellow to colorless transformation was found independent of light and occurred at about the same rate in light or darkness. Thirdly, the alternate possibility that the cis isomer might be initially formed may present a reasonable explanation. In structurally related azomethane, the cis isomer has an absorption maxima at 353 m μ (ϵ = 240) and the trans isomer has an absorption maxima at 343 m μ (ϵ = 25) (9). In this model for comparison the cis isomer has an absorption at a slightly longer wavelength and greater intensity than the trans isomer. If this absorption relationship holds for the azoacetates the yellow material maybe assigned the cis configuration, although, it has absorption at considerably longer wavelength and at lower intensity than the azomethane. The process changing yellow to colorless may then be explained as a cis to trans isomerization and from the higher energy to the lower energy isomer and would be independent of the presence of light. If the trans azoacetate has a lower

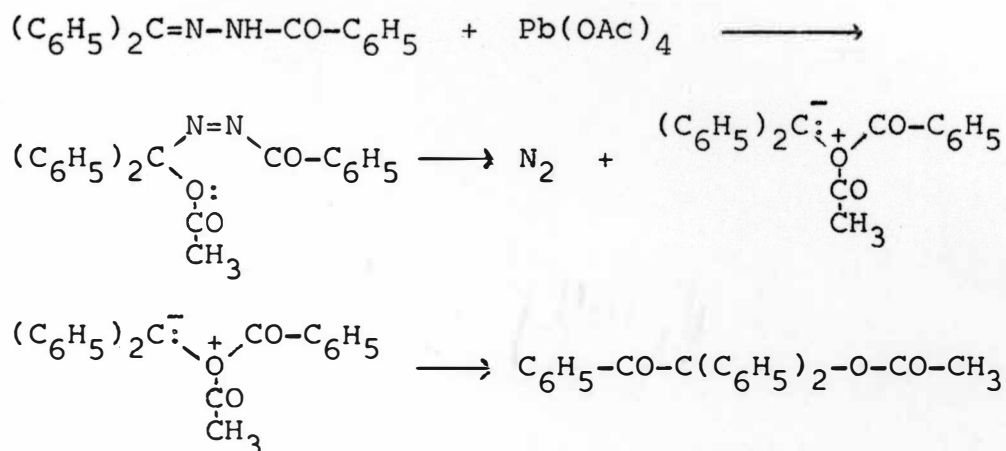
intensity absorption than the cis isomer, as this comparison would suggest, a very low value of ϵ or no maximum would be reasonable for the colorless material (Cf. Charts I and II).

In the reaction of benzophenone benzoylhydrazone the crude reaction product showed evidence of decomposition by the evolution of a gas, presumably nitrogen. This evolution proceeded rapidly at room temperature but could be nearly stopped by cooling to 5° . The crude product after decomposition yielded an oil-solid mixture. The oil was removed by washing with pentane and the solid was purified by recrystallization from an ether-pentane mixture to yield a white crystalline solid.

This solid product isolated from the reaction was shown to be α -phenylbenzoin acetate. Quantitative elemental analysis for carbon and hydrogen in the product agreed with theoretical values for α -phenylbenzoin acetate. Acid hydrolysis with sulfuric acid gave the expected α -phenylbenzoin. Infrared spectra of the α -phenylbenzoin showed a hydroxyl band at 3420 cm^{-1} and an aryl keto band at 1650 cm^{-1} along with the characteristic aromatic bands (3040 , 1600 , 1580 , 1500 , 1450 , and 685 cm^{-1}).

In the reaction of 4,4-disubstituted ketosemicarbazones with lead tetraacetate, a mechanism has been proposed (10) for the formation of an unstable azoacetate

followed by an intramolecular nucleophilic displacement at the amide carbonyl accompanied by the formation of nitrogen. By a 1,2-shift the zwitter ion is converted to the carbamate. In the present study of ketoacylhydrazones, the acyl carbonyl group is analogous to the amide carbonyl group on the semicarbazones, therefore, a similar mechanism may be postulated. Starting from benzophenone benzoylhydrazone these steps may be illustrated as follows:



In the above formulation, the zwitter ion may also undergo a 1,2-shift to the acetyl group rather than the benzoyl group. However, the electron withdrawal effect of the phenyl group will assist the 1,2-shift of the carbanion center to the benzoyl group. Since the methyl group is electron releasing the acetyl group is much less susceptible to such a 1,2-shift. The isolation of α -phenylbenzoin acetate is consistent with the above postulation.

In the reaction of benzophenone acetylhydrazone the mixture unexpectedly developed a red coloration. Infra-red spectrum of this crude reaction mixture showed a strong sharp absorption band at 2040 cm^{-1} . This band was not observed in the infrared spectra obtained from the reaction mixtures of the other acylhydrazones. When mixed with aqueous hydrochloric acid this crude reaction mixture readily evolved a gas with the loss of the red color. After this treatment with acid, the resulting yellow mixture no longer showed an absorption at 2040 cm^{-1} . Upon heating at 100° the red reaction mixture decomposed rapidly again with the evolution of a gas and loss of the red color. This red coloration is now believed caused by the presence of diphenyldiazomethane which absorbs at 2042 cm^{-1} (7) and has a red color. Furthermore, when treated with aqueous acid or upon heating diphenyldiazomethane decomposes with the loss of nitrogen and red color as noted above.

The formation of the red diphenyldiazomethane in this reaction of benzophenone acetylhydrazone with lead tetraacetate was unaffected by either the presence of magnesium oxide in the reaction mixture or by the reversed order of addition of reactants.

Davies also observed the formation of red reaction mixtures having an absorption at 2040 cm^{-1} when

benzophenone 4,4-diethylsemicarbazone was reacted with lead tetraacetate (6). No explanation for this red coloration was available.

Diphenyldiazomethane is conveniently prepared by the mercuric oxide oxidation of benzophenone hydrazone (14).

The crude reaction mixtures from the reactions of acetophenone acetylhydrazone and acetone benzoylhydrazone with lead tetraacetate decomposed slowly with the evolution of a gas at room temperature. These crude mixtures were heated to 50° to accelerate this decomposition. After removing the acid anhydrides from the decomposed mixtures, these mixtures were vacuum distilled in an attempt to obtain pure products.

Nine fractions were collected boiling from 55° to 115° at 1 mm. Hg (Table III) in the distillation of the decomposed reaction mixture from acetophenone acetylhydrazone. The major portion of the distillation consisted of five fractions boiling from 89° to 109° at 1 mm. Hg. Infrared spectra of these fractions indicated the presence of 3-hydroxy-3-phenyl-2-butanone acetate. Acetate bands were observed at 1740 cm^{-1} and 1250 cm^{-1} along with an aliphatic keto shoulder at 1715 cm^{-1} . A positive iodoform test and a negative nitrogen test in addition to the infrared spectra substantiate the

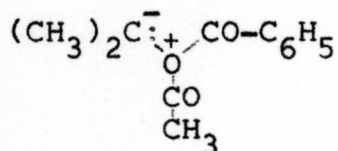
presence of 3-hydroxy-3-phenyl-2-butanone acetate. However, because of inadequate fractionation in the vacuum distillation, a pure fraction of this product was not isolated.

The mechanism postulated earlier for the product obtained from the reaction of benzophenone benzoylhydrazone with lead tetraacetate involving the formation of an unstable azoacetate which undergoes a nucleophilic displacement at the acyl carbonyl followed by a 1,2--shift of the zwitter ion would, in the case of acetophenone acetylhydrazone, lead to the formation of 3-hydroxy-3-phenyl-2-butanone acetate. The results observed above confirm the presence of the expected product.

The reaction of acetone benzoylhydrazone with lead tetraacetate was conducted twice. The vacuum distillation of the two decomposition mixtures lead to fractions having different properties (See Tables IV and V). Gas--liquid chromatographic examination of the fractions indicated two major components. The ratio of these peak heights indicates that the higher boiling component was richer in the product derived from the first run than that from the second run.

The zwitter ion formed on decomposition of this

reaction mixture may be represented as:



A 1,2-shift to the benzoyl carbonyl leads to the formation of hydroxydimethylacetophenone acetate. A 1,2-shift occurring to the acetyl carbonyl leads to the formation of 3-hydroxy-3-methyl-2-butanone benzoate.

Infrared spectrum of the compound shown by the first major peak is reasonable for 3-hydroxy-3-methyl-2-butanone benzoate based upon the benzoate absorption bands at 1750 cm^{-1} , 1275 cm^{-1} and 1225 cm^{-1} and an aliphatic keto band at 1705 cm^{-1} . The compound causing the second peak, as shown by infrared spectrum, was hydroxydimethylacetophenone acetate. This infrared spectrum showed acetate bands at 1730 cm^{-1} and 1250 cm^{-1} and an aryl keto band at 1685 cm^{-1} .

A negative nitrogen test and a positive iodoform test on the distillation product from each distillation are consistent with these observed results.

The information obtained on the decomposition products from the reaction of acetophenone acetylhydrazone and acetone benzoylhydrazone with lead tetraacetate is consistent with the results predicted from the mechanism postulated for the decomposition of an unstable azoacetate discussed earlier.

SUMMARY

New azoacetates were obtained in 50% - 70% yields by lead tetraacetate oxidation of two aliphatic ketoacylhydrazones.

From ketoacylhydrazones containing aromatic substituents, esters of disubstituted α -hydroxyketones were formed. This formation of these esters may be rationalized if an unstable azoacetate is formed which spontaneously undergoes decomposition and structural rearrangement.

The formation of diphenyldiazomethane has been demonstrated in the reaction of benzophenone acetylhydrazone with lead tetraacetate.

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VITA

The author was born in Owosso, Michigan on October 4, 1939. He attended St. Michael's High School, New Lothrop, Michigan. In September of 1957, he entered Aquinas College, Grand Rapids, Michigan where he obtained the B. S. degree in May, 1961.

In September of 1962, he received a teaching assistantship from Western Michigan University which extended for one year. He was awarded a research grant from the National Institutes of Health in September, 1962.