PART I: THE STRUCTURE OF THE SO-CALLED "6-PHENYL-1,4-
            DIHYDRO-as-TRIAZINE"
PART II: THE REACTIONS OF METHANOLIC SODIUM METHOXIDE
            WITH α-METHYL-α,β-DICHLOROPROPIONALDEHYDE

by

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## PART I: THE STRUCTURE OF THE SO-CALLED "6-PHENYL-1,4-DIHYDRO-as-TRIAZINE"

Historical

Biquards (1) report of the formation of 6-phenyl-1,4-dihydro-as-triazine (I) in 60 percent yield by the action of a large excess of either the ethyl or the methyl Grignard reagent on acetophenone semicarbazone at 80°C. followed by hydrolysis is of interest because of the apparently unique nature of both the synthesis and the product. This appears to be the only preparation of the dihydro-as-triazine ring which is not fused with another ring, and one of the few synthesis of the unfused as-triazine ring.

The evidence for the reported structure consists of a carbon, hydrogen and nitrogen analysis and the preparation and analysis of a chloroplatinate and of the mono- and di- acetyl derivatives. Unfortunately, the possibility of an isomeric structure was not seriously considered.

Statement of the Problem

The structure proposed by Biquard (1) for the condensation product is satisfactory for explaining the analysis data and reactions but it should be noted that these data would also apply to the isomeric structure. It would seem likely that ring closure by an aldol type condensation might produce the isomeric 3(5)-amino-5(3)-phenylpyrazole (II).

$$C_6H_5 \underset{\underset{H}{\overset{\|}{N-N-C-NH_2}}}{\overset{\|}{C-CH_3}} \xrightarrow{RMgX}$$ (I) or (II)
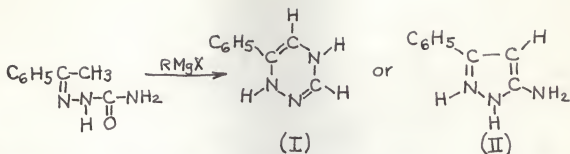
Compound (II) has been described twice previously, having been prepared in two other ways (2, 3) but the literature values of its melting point and the melting point of derivatives are not in agreement.

In order to obtain evidence on these points, the Biquard synthesis should be repeated and an unambigous method could be used for the synthesis of authentic 3(5)-amino-5(3)-phenylpyrazole for direct comparison with the Biquard condensation product. Derivatives of each should be prepared and infrared analysis used as an aid in comparison.

Experimental

Acetophenone Semicarbazone. Forty-eight grams (0.4 mole) of acetophenone was dissolved in 200 ml. of 95 percent ethanol. Then a mixture of 45 g. (0.4 mole) of semicarbazide hydrochloride, 67 g. (0.8 mole) of sodium acetate and 260 ml. of water was added with stirring. The mixture was heated on the steam bath for 30 minutes. Sixty-one grams (86 percent) of acetophenone semi-carbazone separated and was recrystallized as white plates, m. p. 198-200°C., from hot water.

The Biguard Condensation. The Grignard reagent was prepared
by adding a mixture of 400 g. (3.67 moles) of redistilled ethyl
bromide in 250 ml. of anhydrous ether, with stirring, to an ice
cooled mixture of 50 g. (2.0 gram-atoms) magnesium turnings under
150 ml. of anhydrous ether. Sixty-one grams (0.34 mole) of aceto-
phenone semicarbazone was added to this mixture in small portions
with continued stirring and cooling. After one hour of refluxing
600 ml. of anhydrous benzene was added and the ether then removed
by distillation. The benzene solution was refluxed for six hours
and became olive green in color. After the mixture cooled, 300 ml.
of saturated ammonium chloride solution was added dropwise. The
benzene was removed by suction filtration and the white residue
of magnesium salts was then air-dried and extracted with boiling
ethyl acetate. Addition of Skelly C to these extracts precipitated
the crude product which was contaminated with an orange impurity
apparently caused by air oxidation. The yield was 5 g. (10 percent)
of the purified condensation product which was obtained as white
plates, m. p. 125-126°C. by recrystallization from hot water,
reported, m. p. 126°C. (Biguard, 1).

The acetyl derivative was prepared by heating the conden-
sation product for 15 minutes with a ten-fold amount of acetic
anhydride. Upon cooling, the product separated and was recrystal-
lized as white needles, m. p. 156-157°C. from 95 percent ethanol.
Literature values are: monoacetyl derivative, 235°C.; diacetyl
derivatives, 156°C., 203°C. and 273°C. (Biguard, 1).

The picrate derivative was prepared in the usual manner and
recrystallized as yellow needles, m. p. 202-203°C. from 95

percent ethanol.

The hydrochloride salt was prepared by bubbling anhydrous hydrogen chloride into a solution of the free base dissolved in ether. A white hygroscopic solid was formed, m. p. 67-68°C. Literature value for the hydrochloride salt of 3(5)-amino-5(3)-phenylpyrazole: m. p. 78-80°C. (Moureu, 3).

β-Imino-β-phenylpropionitrile. A mixture of 97 g. (0.93 mole) of anhydrous benzonitrile and 41 g. (1.0 mole) of acetonitrile was added dropwise to a stirred mixture of 21 g. (0.9 gram-atom) of sodium sand and 400 ml. of anhydrous benzene, which was heated gently at first with an electric mantle. As soon as an exothermic reaction was noted, the heating was discontinued, and the reaction proceeded smoothly with much hydrogen evolution. The solution became bright orange in color as the mixture was refluxed overnight. After cooling 30 ml. of an aqueous solution of ammonium chloride was added to the mixture which became bright red and gave off ammonia gas. The mixture was then dried with anhydrous sodium sulfate, filtered and the benzene removed by vacuum distillation. A black residue was obtained which was purified by recrystallization to give 30 g. (21 percent) of white needles, m. p. 87-89°C. from ethyl acetate and Skelly C.

Authentic 3(5)-Amino-5(3)-phenylpyrazole. Seven and five tenths grams (0.15 mole) of 85 percent hydrazine hydrate was added to a mixture of 8.5 g. (0.05 mole) of β-imino-β-phenylpropionitrile in 100 ml. of 95 percent ethanol. After refluxing for six hours, the solvent was removed by vacuum distillation. The residue solidified on standing a few hours and was recrystal-

lized alternately from ethyl acetate-Skelly C and hot water to give
5 g. (62 percent) of white plates, m. p. 125-126°C. The litera-
ture values are: m. p. 119°C. (Meyer, 2) and m. p. 125-126°C.
Moureu, 3). The melting point was not effected by mixing with
the Biquard condensation product, and both gave the same infrared
spectrum in a Nujol mull with principle bands at 3.37, 6.27, 6.50,
9.18, 9.35, 10.12, 10.88 and 13.1 μ.

The acetyl derivative was prepared by heating the pyrazole
with a ten fold amount of acetic anhydride for 15 minutes and was
recrystallized as white needles, m. p. 156-157°C. from 95 percent
ethanol. Literature values are: monoacetyl derivative, m. p.
162°C., diacetyl derivative, m. p. 151°C., (Meyer, 2). The mix-
ture melting point of the diacetyl derivatives of the condensation
product and the authentic pyrazole was not depressed. The infrared
spectra (Nujol mull) of the two diacetyl derivatives were identical
and showed principal bands at 3.27, 5.74, 5.99, 6.60, 7.97, 8.70,
9.74, 10.75, 12.02, 12.60 and 12.92 μ.

The picrate derivative was prepared in the usual manner and
recrystallized as yellow needles, m. p. 202-203°C. from 95 per-
cent ethanol, reported, m. p. 202-203°C. (Moureu, 3). The mix-
ture melting point of the picrate derivatives of the condensation
product and the authentic pyrazole was not depressed.

Discussion

The Biquard synthesis was repeated, but the product was
obtained in much lower yield than previously reported in spite
of improvements in the isolation procedure. The product was

compared with authentic 3(5)-amino-5(3)-phenylpyrazole prepared by the condensation of hydrazine with β-imino-β-phenylpropionitrile. A detailed preparation of β-imino-β-phenylpropionitrile was not given in the literature but it was found that the condensation of benzonitrile with acetonitrile in the presence of sodium sand was a suitable method.

In comparing authentic 3(5)-amino-5(3)-phenylpyrazole with the Biquard condensation product it was found that they had identical melting points, mixture melting point, and infrared spectra. Similar melting point data were obtained on their picrate and diacetyl derivatives. The diacetyl compounds also had identical infrared spectra. This evidence demonstrates clearly that the Biquard product is actually 3(5)-amino-5(3)-phenylpyrazole.

<div align="center">Summary</div>

The reaction of acetophenone semicarbazone with Grignard reagents under "forcing" conditions has been shown to give 3(5)-amino-5(3)-phenylpyrazole, rather than 6-phenyl-1,4-dihydro-as-triazine, as previously reported by Biquard.

PART II: THE REACTIONS OF METHANOLIC SODIUM METHOXIDE
WITH α-METHYL-α,β-DICHLOROPROPIONALDEHYDE

Historical

The reactions of methanolic sodium methoxide with two
α,β-dichloroaldehyde compounds was studied by Krausz (10) who
assigned the 2,3-dimethoxyoxetane[1] structure to the dimethoxy
compounds formed.
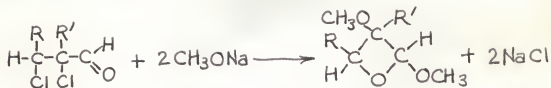
Since such compounds would be of interest in connection with
oxetane studies in progress at this laboratory, Ives (8) studied
these reactions in more detail using four different α,β-dichloro-
aldehydes (Ia).

Ives found that the oxetane structures written by Krausz (10)
were in error. An invalid assumption regarding the mode of re-
action of these compounds with water had caused Krausz (10) to
incorrectly interpret the reactions he had carried out. Ives (8)
showed that these dimethoxy compounds formed in methanol were
actually epoxide acetals--a structure different from anything
previously suggested.

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[1]It should be mentioned that the reaction of α,β-dichloro-
aldehydes with sodium methoxide had been studied earlier by
Lichtenberger and Naftali [Bull. soc. chim., 4, 325 (1937)] and
Kirmann and Lichtenberger [Comp. rend., 206, 1259 (1939)], who
showed that the products were cyclic acetals but could not
determine the size of the ring.

This conclusion was arrived at by following the reaction involving one molecule of sodium methoxide at a time. The first methoxide ion attacks at the carbonyl carbon, giving an α-methoxyoxirane (IIa), which reacts with a second methoxide ion to give the epoxyacetal (IIIa). The following mechanism is in accord with the results obtained by Stevens and his coworkers (15) on the reactions of sodium with α-chlorocarbonyl compounds and with α-methoxyoxiranes.

(Ia) → (IIa)

(IIIa)
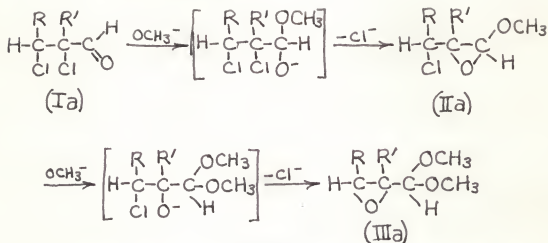
The other two dichloroaldehydes studied by Ives (8), α,β-diphenyl-α,β-dichloropropionaldehyde and α-methyl-α,β-dichloro-propionaldehyde gave different results but were studied in less detail. The reaction of the latter compound seemed of particular interest, because it was reported to give the dimethoxy compound which, upon hydrolysis, gave methylmalonaldehyde.
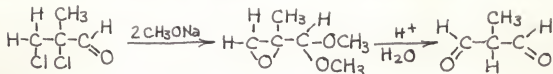
Unfortunately, there was not sufficient evidence to prove its formation. The 2,4-dinitrophenylhydrazone derivative of the hydrolysis product had a very high melting point which checked with the value reported by Pummerer (11) for the bis-2,4-dinitro-phenylhydrazone derivative of methylmalonaldehyde. However this derivative was not analyzed and no attempt was made to prepare any other derivative of the hydrolysis product.

Statement of the Problem

The series of compounds derived from α-methyl-α,β-dichloropropionaldehyde was not rigorously studied by Ives (8) and no attempt was made to isolate the intermediate chloromethoxy compound corresponding to (IIa). Therefore it was of interest to study in more detail the reactions of α-methyl-α,β-dichloropropionaldehyde with sodium methoxide and the acidic hydrolysis of the products formed.

Ives (8) found that the dimethoxy compound obtained in this series reacted differently from the other homologs studied. One difference was the apparent hydrolysis of this compound to methyl-malonaldehyde, which would be an extremely important reagent for organic synthesis, if there were a good synthesis. It has been reported only once before that it was obtained as a byproduct in minute yield and in an impure condition (Pummerer, 10).

The method planned for studying this problem was to carry out the reaction of α-methyl-α,β-dichloropropionaldehyde with one mole of sodium methoxide at a time and to determine the structure of the products at each stage. The tools available for studying the

products were acid hydrolysis, oxidative cleavage, reduction, elemental analysis, infrared analysis and the formation of aldehyde derivatives. A complete identification of methylmalonaldehyde was necessary because Ives (8) had not done so. Oxidation by nitric acid to methylmalonic acid, as used by Pummerer (11), for the oxidation of 2-methyl-1,3-dihydroxypropane, seemed a good method for proving this structure. It was planned to prepare other derivatives such as the condensation products of urea or guanidine with methylmalonaldehyde.

Experimental

α-Methyl-α,β-dichloropropionaldehyde (I). One hundred thirty grams (1.85 moles) of freshly distilled methacrolein was added to 800 ml. of anhydrous chloroform with rapid stirring. The mixture was cooled in an ice-salt bath while anhydrous chlorine was passed in at an adjusted rate so that the temperature did not rise above 15°C. When no more chlorine was absorbed, the light yellow solution was freed of excess chlorine by reducing the pressure. When the solution became colorless, the chloroform solvent was distilled through a foam breaking column. The residue was then distilled through the same column in vacuo. The yield was 237 g. (90.8 percent) of methacrolein dichloride, b. p. 60-62°C. at 30mm., n_D^{20} 1.4570. Literature values are: b. p. 122-123°C. at 740 mm., n_D^{20} 1.4569 (Brochet, 3).

α-Methyl-α-chloro-β-methoxypropionaldehyde (II). One hundred grams (0.71 mole) of methacrolein dichloride (I) was added dropwise with stirring to methanolic sodium methoxide [15.4 g. (0.67

gram-atom) of sodium dissolved in 500 ml. of anhydrous methanol which was cooled in an ice bath. The temperature of the mixture rose to that of the room overnight. The 37.8 g. (0.65 mole) of sodium chloride that separated, was removed by decantation and washed with methanol. These washings were combined with the body of the solution and then distilled over the steam bath under slightly reduced pressure to remove the methanol. The small amount of sodium chloride which separated was removed and washed with anhydrous ether; then these washings combined with the residue. After removal of the solvent the residue was distilled in vacuo through a six inch helix packed column, using a water bath. The yield was 67.8 g. (70 percent) of the chloromethoxy-aldehyde, b. p. 48°C. at 15 mm. or 62°C. at 30 mm., n_D^{20} 1.4389. The infrared spectrum of the product has characteristic absorption bands for the carbonyl group at 5.79χ and ether groups at 9.22μ. Other principal bands were found at 3.43, 3.53, 6.92, 7.22, 7.72, 8.25, 8.38, 8.95, 10.28, 11.03, 11.96 and 12.15χ. This compound gave a positive test for halogen and a positive Tollens test.

Analysis. Calculated for $C_5H_9O_2Cl$: Cl, 25.96; OCH_3, 22.73. Found: Cl, 25.95; OCH_3, 23.22.

The semicarbazone derivative of (II) was prepared in the usual manner and recrystallized as a white solid, m. p. 164-165°C. from water and ethanol. An attempt to prepare the 2,4-dinitrophenylhydrazone derivative of (II) resulted in the formation of this derivative of the hydrolysis product (V) only.

α-Methyl-α-chloro-β-hydroxypropionaldehyde (V). Thirty grams

(0.22 mole) of (V) was added to 150 ml. of one normal sulfuric acid with rapid stirring. The mixture was refluxed on the steam bath for 30 minutes. Then the mixture was cooled with ice and a saturated solution of sodium bicarbonate added dropwise until no more carbon dioxide was liberated. The solution was then extracted with six 50 ml. portions of ether and these extracts dried over anhydrous magnesium sulfate. The dried ether extracts were distilled in vacuo through a six inch helix packed column, using the water bath. The yield was 12.8 g. (47.5 percent) of the hydroxychloroaldehyde, b. p. 48°C. at 24 mm., n_D^{20} 1.4556. The infrared spectrum of the product had characteristic absorption bands for the carbonyl group at 5.28μ and hydrogen bonded hydroxyl group at 2.89μ. Other principal bands were found at 3.45, 3.53, 6.95, 7.29, 7.73, 7.86, 8.40, 8.84, 9.09, 10.34, 11.37 and 12.15μ. This compound gave a positive test for halogen and a positive Tollens test.

Analysis: Calculated for $C_4H_7O_2Cl$: Cl, 28.93. Found: 29.09.

An attempt was made to oxidize (V) with lead tetraacetate. In the procedure, 8.00 g. (.065 mole) of (V) in 75 ml. of benzene was refluxed with 29.0 g. (.065 mole) of lead tetraacetate for two hours with stirring. After removing the solid material by suction filtration the benzene solution was dried over anhydrous magnesium and then distilled to remove the benzene. The residue was then vacuum distilled in the usual way. Six and eighty-six one-hundredth grams (86 percent recovery) of starting material was obtained.

The 2,4-dinitrophenylhydrazone derivative of (V) was prepared
in the usual manner and recrystallized as orange needles, m. p.
124-125°C. from 95 percent ethanol and water. Attempts to make
the semicarbazone derivative of (V) were unsuccessful.

2-Methyl-1,3-dimethoxy-1,2-epoxypropane (III) from (I).
Sixty-three grams (0.45 mole) of methacrolein dichloride (I) was
added dropwise with stirring to methanolic sodium methoxide 19.55 g.
(0.85 gram-atom) of sodium in 400 ml. of anhydrous methanol which
was cooled in an ice bath. The temperature of the mixture rose to
that of the room over night. Forty and seven tenths grams (0.70
mole) of sodium chloride separated out and was removed by suction
filtration and washed with methanol. These washings were combined
with the body of the solution and the methanol then removed by
distillation under slightly reduced pressure. The sodium chloride
which separated was removed and washed with 200 ml. of ether and
this combined with the body of the solution. Forty milliliters of
a saturated sodium chloride solution was shaken with the residue
to remove the inorganic material. The aqueous layer which retained
the orange color was then extracted with four 25 ml. portions of
ether. After the combined ether extracts were dried over anhydrous
magnesium sulfate the residue was distilled in vacuo through a six
inch helix packed column, using a water bath. The yield was 32.1
g. (54.4 percent) of the dimethoxyepoxide, b. p. 53°C. at 20 mm.
or 48°C. at 15 mm., n_D^{20} 1.4134, reported, b. p. 65-68°C. at 27
mm., n_D^{20} 1.4200 (Ives, 8). The infrared spectrum of the product
had a characteristic absorption band for ether groups at 9.22λ
but no carbonyl bands. Other principal bands were found at 3.47,

3.53, 6.90, 7.30, 7.58, 8.24, 8.37, 8.94, 9.40, 9.75, 10.13, 10.27 and 11.07 γ. This compound gave a negative test for halogen and a negative Tollens test.

Analysis. Calculated for $C_6H_{12}O_3$: C, 54.52; H, 9.17; OCH_3, 46.98. Found: C, 54.36; H, 8.73; OCH_3, 46.79.

2-Methyl-1,3-dimethoxy-1,2-epoxypropane (III) from (II). Forty grams (0.29 mole) of (II) was added dropwise with stirring to methanolic sodium methoxide 6.4 g. (0.28 gram-atom) of sodium in 300 ml. of anhydrous methanol which was ice bath cooled. After the temperature of the mixture rose to that of the room over night, 15.5 g. (0.26 mole) of sodium chloride separated and was removed by decantation and washed with methanol. The combined solution and washings were distilled under slightly reduced pressure to remove the methanol. The light orange colored residue was shaken with 30 ml. of saturated sodium chloride solution and 200 ml. of ether, followed by extraction of the aqueous layer with four 25 ml. portions of ether. The combined ether extracts were then dried with anhydrous magnesium sulfate and distilled in vacuo as in the preparation of (III) from (I). The yield was 20.2 g. (52 percent) of the dimethoxyepoxide.

2-Methyl-2-hydroxy-1,1,3-trimethoxypropane (IV). Twenty grams (0.14 mole) of methacrolein dichloride (I) was added dropwise with stirring to methanolic sodium methoxide 9.5 g. (0.41 gram-atom) of sodium in 300 ml. of anhydrous methanol which was ice bath cooled. The temperature of the mixture rose to that of the room over night. Eleven and three tenths grams (0.19 mole) of sodium chloride separated and was removed by suction filtration,

followed by washing with methanol and drying. The filtrate and washings were distilled to remove the methanol, shaken with saturated sodium chloride solution which was then extracted with 100 ml. of ether, dried over anhydrous magnesium sulfate and then

distilled in the usual manner. The yield was 11.7 g. (50 percent) of the trimethoxyalcohol, b. p. $84^{\circ}C$. at 17 mm. or $90^{\circ}C$. at 25 mm., n_D^{20} 1.4248. The infrared spectrum of the product had a characteristic absorption band for the hydrogen bonded hydroxyl group at 2.91γ. Other principal bands were found at 3.43, 3.53, 6.90, 7.25, 7.36, 7.58, 8.37, 9.02, 9.20, 10.00, 10.31, 10.55 and 10.79γ.

Analysis. Calculated for $C_7H_{16}O_4$: C, 51.20; H, 9.84; OCH_3, 56.70. Found C, 50.69; H, 9.67; OCH_3, 56.71.

The allophenate derivative of (IV) was prepared by the method of Spielman and Barnes (14) which consisted of passing cyanic acid gas (generated by heating cyanuric acid) in large excess through approximately one half gram of the alcohol and then allowing the mixture to stand in the cold for two days. The product (containing regenerated cyanuric acid) was recrystallized as colorless cubes, m. p. $121-122^{\circ}C$. from 95 percent ethanol. Attempts to prepare the phenylurethane, $\checkmark$-napthylurethane, benzoate, p-nitrobenzoate or 3,5-dinitrobenzoate derivatives of (IV) were unsuccessful.

2-Methyl-2-hydroxy-1,3-dimethoxypropane (VII). Twenty grams (0.15 mole) of (III) was dissolved in 100 ml. of anhydrous ether and this solution added dropwise with stirring to a reduction mixture containing 2.9 g. (.076 mole) of lithium aluminum hydride

(100 percent excess) dissolved in 200 ml. of anhydrous ether.
The mixture was refluxed for six hours with constant stirring.
After cooling in an ice bath, 40 ml. of 20 percent sodium
carbonate solution was added dropwise with continued stirring.
The ether layer was decanted from the basic carbonate residue
which was then discarded. After drying with anhydrous magnesium
sulfate the ether solution was distilled in the usual manner.
The yield was 14.2 g. (70 percent) of the dimethoxyalcohol.
When anhydrous tetrahydrofuran was employed as the reacting
medium, (VII) was obtained in 75 percent yield and was free of
starting material. The dimethoxyalcohol distills at 59°C.
(20 mm.) or at 55°C. (16 mm.) and has a refractive index n_D^{20}
of 1.4148. The infrared spectrum of this compound has a charac-
teristic absorption band for the hydrogen bonded hydroxyl group
at 2.91μ. Other principal bands were found at 3.39, 3.53, 6.90,
7.25, 7.35, 7.57, 8.14, 9.04, 9.26, 9.87, 10.19, 10.39 and 10.87μ.
Hydrolysis of this compound by dilute sulfuric acid instantly
forms methacrolein which cannot be separated from the acidic
solution by distillation as reported by Hearne and DeJong (6).

Analysis. Calculated for $C_6H_{14}O_3$: C, 53.70; H, 10.54; OCH_3,
46.27. Found: C, 53.63; H, 10.93; OCH_3, 45.98.

The allophenate derivative of (VII) was prepared by the
method of Spielman and Barnes (14) and recrystallized as white
cubes, m. p. $127-128^\circ$C. from 95 percent ethanol. Attempts to
prepare the usual urethane, benzoate or nitro-substituted benzoate
derivatives of (VII) were unsuccessful.

Hydrolysis of (VII) in the presence of 2,4-dinitrophenyl-
hydrazine. The hydrolysis mixture was prepared by mixing 100 ml.
of concentrated sulfuric acid with 100 ml. of water. A 0.25 molar
2,4-dinitrophenylhydrazine solution was prepared by the method of
Johnson (9) using 85 percent phosphoric acid and ethanol as the
solvents. One hundred milliliters (.025 mole) of this solution
(68 percent in excess of the amount required to react with the
hydrolysis product when formed in theoretical yield) was added to
the hydrolysis mixture. Two grams (.015 mole) of (VII) was added
with stirring. An orange precipitate formed in approximately five
seconds at room temperature. After standing for 15 minutes, the
product was removed by suction filtration and then washed three
times with water. The yield of the dry 2,4-dinitrophenylhydrazone
derivative of methacrolein was 3.04 g. (81.5 percent). The per-
cent yield of methacrolein actually formed in the hydrolysis re-
action is approximately the same assuming the derivative formation
to be a nearly quantitative reaction. The derivative was recrys-
tallized as red-orange needles, m. p. 205-206°C. from xylene,
reported m. p. 205-206°C. (Shriner and Sharp, 13). The melting
point was not affected by mixing with the authentic 2,4-dinitro-
phenylhydrazone derivative of methacrolein.

Hydrolysis of (III) by One Normal Sulfuric Acid. Ten grams
of (III) was added to 50 ml. of N sulfuric acid with stirring.
After standing at room temperature for 30 minutes the hydrolysis
mixture was neutralized with sodium carbonate. This solution
was distilled almost to dryness at 100-104°C. under atmospheric
pressure. The distillate was shown to be an aqueous solution of

α-methyl-α,β-dihydroxypropionaldehyde (VIII) which reduced Tollens reagent and Fehlings solution even after standing for several weeks. Compound (VIII) could not be separated from the aqueous phase by fractionation or by combined salting out and continuous extraction with ether or chloroform. Therefore derivatives were prepared directly from the aqueous solution as in the procedure reported by Glattfeld and Mochel (5).

The di-p-nitrophenylhydrazone derivative (IX) of methacrolein glycol (VIII) was prepared by the method of Glattfeld and Mochel (5) which consisted of treating 5 ml. of the aqueous solution of (VIII) with 10 ml. of a 20 percent acetic acid solution of p-nitrophenylhydrazine and then warming the mixture on the steam bath for a few minutes. The fine red precipitate was recrystallized as fine dark red crystals, m. p. 262-263°C. from a minimum amount of 95 percent ethanol, reported, m. p. 264°C. (Glattfeld and Mochel, 5). The infrared spectrum of this derivative (IX) was obtained by the potassium bromide pelleting method and has a characteristic absorption band for the hydroxyl group at 3.09 μ. Other principal bands were found at 3.47, 6.28, 6.70, 6.82, 7.60, 7.68, 7.90, 8.48, 8.70, 8.85, 9.01, 9.72, 9.96 and 11.90 μ.

The 2,4-dinitrophenylhydrazone derivative of methacrolein glycol (VIII) was prepared by treating 10 ml. of the aqueous solution of (VIII) with 5 ml. of a 0.25 molar solution of 2,4-dinitrophenylhydrazine in 85 percent phosphoric acid as prepared by the method of Johnson (9). The derivative first separated as a yellow oil which, upon warming and scratching, soon solidified. The fine yellow precipitate was recrystallized as yellow leaves, m. p. 103-

104°C. from 95 percent ethanol. The infrared spectrum of this
derivative was obtained by the potassium bromide pelleting method
and has a characteristic absorption band for the hydroxyl group
at 3.09μ. Other principal bands were found at 3.47, 6.19, 6.35,
6.62, 6.65, 7.11, 7.44, 7.55, 7.91, 8.79, 9.06, 9.71, 10.22, 10.83μ.

Analysis. Calculated for $C_{10}H_{12}O_5N_4$: C, 44.78; H, 4.51; N,
20.89. Found: C, 43.29, 43.53; H, 4.76, 4.78; N, 21.20.

Modified Hydrolysis of (III) by Strong Sulfuric Acid. Twenty
grams (0.15 mole)(20 ml.) of (III) was dissolved in 60 ml. of
benzene and this mixture added dropwise with stirring to 80 ml.
of strong sulfuric acid (40 ml. of conc sulfuric acid in 40 ml.
of water) which was kept below 30°C. by external cooling. After
stirring for five minutes the benzene layer was decanted and
washed with 5 ml. of saturated sodium bicarbonate solution. The
aqueous layer was then extracted with two 50 ml. portions of
ether. Five grams of solid sodium bicarbonate and 50 ml. of water
was added for partial neutralization of the acid. The mixture was
immediately extracted with two 50 ml. portions of ether and these
extracts then washed with a saturated sodium bicarbonate solution
and combined with the benzene layer. These extracts were dried
over anhydrous magnesium sulfate and then distilled in vacuo
through a six inch helix packed column over the water bath. Five
grams (28 percent) of the product was obtained, which is believed
to be α-methyl-α-hydroxy-β-methoxypropionaldehyde (VI), and has a
boiling point of 63°C. at 30 mm., and a refractive index n_D^{20} or
1.4450. The infrared spectrum of this compound has characteristic
absorption bands for the hydrogen bonded hydroxyl group at 2.91μ,

carbonyl group at $5.76\,\mu$ and the ether group at $9.36\,\mu$. Other principal bands were found at 3.33, 6.70, 7.25, 7.54, 7.67, 7.96, 8.26, 8.46, 9.06, 10.13 and $11.88\,\mu$. This compound gave a positive Tollens test. No carbon, hydrogen or methoxyl analysis was obtained because this compound could not be isolated in later attempts to prepare it.

The 2,4-dinitrophenylhydrazone derivative of (VI) was prepared using a solution of 2,4-dinitrophenylhydrazine in posphoric acid as prepared by the method of Johnson (9). The derivative first separated as an orange oil which soon solidified upon warming and scratching. The precipitate was recrystallized as orange needles, m. p. 119-120°C. from 95 percent ethanol. The infrared spectrum of this derivative was obtained by the potassium bromide pelleting method and has a characteristic absorption band for the hydroxyl group at $3.09\,\mu$. Other principal bands were found at 3.45, 6.22, 6.31, 6.64, 7.05, 7.55, 7.66, 7.89, 8.19, 8.74, 9.01, 9.29, 10.20 and $11.86\,\mu$. An infrared spectrum of this compound in carbon tetrachloride solvent was also obtained and was found to have a characteristic absorption band for the carbonyl group at $5.82\,\mu$ but no hydroxyl group band appeared. The other principal bands were found in nearly the same locations as those in the pellet spectrum, however. Treatment of this compound with dilute sulfuric acid formed (X).

Analysis. Calculated for $C_{20}H_{22}O_{11}N_8$: C, 43.82; H, 4.02 N, 20.43. Found: C, 43.74; H, 3.70; N, 20.77.

Modified Hydrolysis of (III) in the presence of 2,4-Dinitrophenylhydrazine. The hydrolysis mixture was prepared by mixing

100 ml. of concentrated sulfuric acid with 100 ml. of water. One hundred milliliters of a 0.25 molar 2,4-dinitrophenylhydrazine solution, as prepared by the method of Johnson (9), (65 percent excess) was added to the hydrolysis mixture. Two grams (.015 mole) of (III) was added with stirring. A fine yellow precipitate formed slowly while the mixture was heated on the steam bath for six hours. When the mixture was diluted with 600 ml. of water, with stirring, a heavy yellow precipitate separated which was then removed by suction filtration, washed and dried. This crude product contained three compounds which were separated and purified in the following manner.

The dried residue was first extracted with five 100 ml. portions of boiling Skelly C. Upon slow cooling of the extracts, orange leaves crystallized which were believed to be impure 4-methyl-1-(2,4-dinitrophenyl)pyrazole (X). This material was further purified by refluxing with 10 ml. of concentrated hydrochloric acid for an hour. This solution was extracted with five 20 ml. portions of ethyl acetate which was then evaporated on the steam bath under an air stream. Three and seventy-five one-hundredths grams (48.5 percent) of (X) was obtained and recrystallized as straw colored needles, m. p. 154-155°C. from 95 percent ethanol. The infrared spectrum of this compound (X) was obtained by the potassium bromide pelleting method and did not have absorption bands for the hydroxyl group or the conjugated imino linkage. The principal bands were found at 6.27, 6.48, 6.55, 6.64, 7.14, 7.31, 7.43, 7.76, 9.74, 10.52, 10.90, 10.99, 11.37 and 11.93γ. This compound did not react with acidic 2,4-dinitrophenylhydrazine

and was found to be stable toward oxidation by potassium permanganate or concentrated nitric acid. Compound (X) was analyzed to determine nitro groups by the method of Vanderzee and Edgell (16).

Analysis. Calculated for $C_{10}H_8O_4N_4$: C, 48.38; H, 3.26; N, 22.57; NO_2, 37.07. Found: C, 48.27; H, 3.08; N, 22.59; NO_2 37.16.

The hydrochloride salt of the reduction product of (X), obtained in the nitro group determination, was prepared by passing anhydrous hydrogen chloride into a solution of the free base dissolved in ether. A white hygroscopic solid was formed, m. p. $133-134^{\circ}C$.

The residue remaining after extraction with boiling Skelly C was then extracted with five 100 ml. portions of ether to remove unreacted 2,4-dinitrophenylhydrazine. One and fifteen-hundredths grams (16.2 percent) of residue remained which was the impure di-2,4-dinitrophenylhydrazone derivative (XI) of (VIII). This derivative was purified by recrystallization from chlorobenzene and 95 percent ethanol as very fine dark orange platelets which decomposed to a black solid at $320^{\circ}C$. (darkening began at about $290^{\circ}C$.). An infrared spectrum of (XI) was taken by the potassium bromide pelleting method and has a characteristic absorption band for the hydroxyl group at 3.09μ. Other principal bands were found at 3.47, 6.23, 6.70, 7.07, 7.52, 7.63, 7.85, 8.19, 8.75, 9.16, 9.43, 9.72 and 11.96μ. Compound (XI) was analyzed to determine its equivalent weight through tin reduction by the Vanderzee and Edgell (16) method. Calculated equivalent weight: 16.52.

Found: 17.15.

Analysis. Calculated for $C_{16}H_{14}O_9N_8$: C, 41.56; H, 3.06.
Found: C, 41.57; H, 3.21.

Discussion

The reaction of one mole of methacrolein dichloride (I) with
0.95 mole of sodium methoxide in methanol gave a chloromethoxy
product in 70 percent yield. The chlorine analysis (by the
Carius method) and methoxyl analysis (by the Zeisel method) were
in agreement with the formula $C_4H_6OCl(OCH_3)$. At least four com-
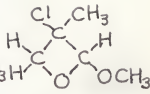pounds with this formula could be possible products of this
reaction:
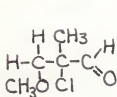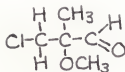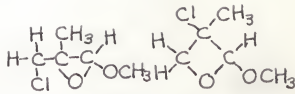
However this compound gave an immediate Tollens test and has
a strong infrared absorption band at 5.79μ, which is characteristic
of the carbonyl group. This evidence favors structures (II) and
(IIA) and also eliminates structures (IIB) and (IIC).

When this chloromethoxyaldehyde was hydrolized with one
normal sulfuric acid a 47.5 percent yield of the chlorohydroxy-
aldehyde was obtained. The possibility that β-hydroxyisobutyric
acid was formed as a side product was investigated but none was
found. Infrared analysis of the hydrolysis product indicated
the presence of the carbonyl and hydrogen bonded hydroxyl groups

but the absence of the ether group. This compound gave positive halogen and Tollens tests and a chlorine analysis was obtained which agreed with an empirical formula of $C_4H_7O_2Cl$. This evidence is compatible with two possible structures for the chlorohydroxyaldehydes (V) and (VA).


$$(V) \qquad\qquad (VA)$$
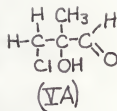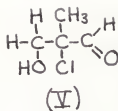
It can be seen that (VA) would undergo oxidative cleavage by lead tetraacetate whereas (V) would remain uneffected. Upon attempted oxidation of the hydrolysis product with lead tetraacetate by the method of Krausz (10) and Ives (8) there was an 86 percent recovery of starting material and no chloroacetone was found. This is reasonable indication that the chloromethoxy compound and its hydrolysis product are the α-chloroaldehydes (II) and (V) respectively.

Thus it has been shown that the oxirane (IIB) is not an intermediate in the formation of the dimethoxy compound from (I) as in the analogous reactions starting with 2,3-dichloro-2-ethylhexanal and α,β-diphenyl-γ,β-dichloropropionaldehyde reported by Ives (8). It may be concluded that the S_N2 attack of the methoxide ion at the primary chloride group of (I) is greatly favored over its attack at the aldehyde group and this may be explained by the absence of steric hinderance caused by the adjacent groups present in the examples reported by Ives (8).

The reaction in the ratio of one mole of methacrolein dichloride (I) with 1.9 moles of sodium methoxide in methanol yielded the dimethoxy compound which had a different refractive index but almost the same boiling point as the corresponding compound reported by Ives (8). Carbon, hydrogen and methoxyl analysis of this compound were obtained and indicated the formula $C_4H_6O(OCH_3)_2$. At least four compounds with this formula could be possible products of this reaction:

(II) $(IIIA)$ $(IIIB)$ $(IIIC)$
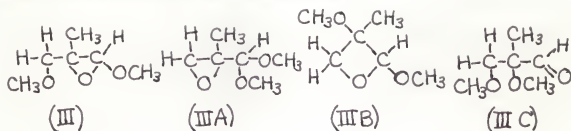
However infrared analysis of this compound indicated the absence of the carbonyl group and was not conclusive concerning the oxirane or oxetane linkages according to data on the corresponding bands given by Bellamy (1). Structure (IIIC) is therefore eliminated as a possibility here. Since it was shown that the action of a second mole of sodium methoxide on the chloromethoxy compound which has been definitely established as (II) gave the same dimethoxy compound as above, the structures (IIIA) and (IIIB) seem unlikely. However a separate means of proving the structure of the dimethoxy compound, in the form of a suitable derivative, is necessary.

The dimethoxy compound was reduced to the dimethoxyalcohol by lithium aluminum hydride in an ether or tetrahydrofuran solution. In the former case careful fractionation of the

product was necessary due to the 6° difference between the boiling points of the starting material and the alcohol. However, when tetrahydrofuran was employed as the reaction medium a larger yield was obtained which was free of starting material. Infrared analysis of the reduction product indicated the presence of the hydrogen bonded hydroxyl group, and a carbon, hydrogen and methoxyl analysis was obtained which indicated the formula $C_4H_8O(OCH_3)_2$. This evidence is in agreement with the structure of 2-methyl-2-hydroxy-1,3-dimethoxypropane (VII).

The reduction of (III) followed by hydrolysis would be expected to yield α-methylglycerol (VIIA) which would undergo a pinacol pinacolone rearrangement in the acidic medium, followed by dehydration, to form methacrolein, as reported by Hearne and deJong (6).

However it was found that acidic hydrolysis of the reduction product, followed by distillation, yielded a distillate containing only aqueous methanol. The hydrolysis reaction was then carried out in the presence of 2,4-dinitrophenylhydrazine with no inten-

tion of isolating free methacrolein. The product was compared
with the data reported by Shriner and Sharp (13) and with the
authentic 2,4-dinitrophenylhydrazone derivative of methacrolein.
The identical melting points and mixture melting points demon-
strate clearly that the hydrolysis product is methacrolein.

Additional evidence for the epoxide structure of (III) was
found in its reaction with another mole of sodium methoxide to
form the higher boiling trimethoxy compound, 2-methyl-2-hydroxy-
1,1,3-trimethoxypropane (IV), in 92 percent yield. The infrared
spectrum of this compound was very similar to that of the di-
methoxyalcohol (VII) and has a strong absorption band for the
hydrogen bonded hydroxyl group. Carbon, hydrogen and methoxyl
analysis were obtained and these indicated a formula of
$C_4H_7O(OCH_3)_3$, which is in agreement with the structure of (IV).

It may now be concluded that the dimethoxy compound, which
has been established as (III), was formed by the attack of the
methoxide ion on the carbonyl group of the intermediate (II).
The epoxide linkage of (III) is open to an S_N2 attack by a third
methoxide ion to form the trimethoxy alcohol (IV). The complete
reaction sequence is as follows:
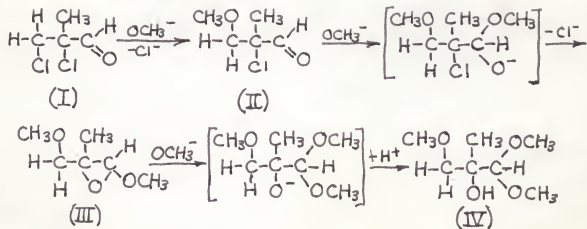
Compound (III) was then hydrolized with N sulfuric acid by the procedure of Ives (8) who reported the formation of methyl-malonaldehyde. However, upon extraction with ether no organic material was isolated. The technique of combined salting out and continuous extraction of the neutral or acidic solution with ether or chloroform was also unsuccessful as a means of separation. The possibility that the hydrolysis product was α-methyl-α,β-dihydroxypropionaldehyde was investigated at this point and in the course of literature search the work of Glattfeld and Mochel (5) was discovered.

These workers reported the preparation of α-methyl-α,β-dihydroxypropionaldehyde (VIII) by the following sequence:
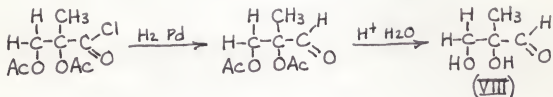

Although the diacetate compound was obtained in a pure state its hydrolysis product (VIII) could not be isolated by extraction with ether and therefore resembles the experience described in the preceding paragraph. Glattfeld and Mochel (5) found that when the aqueous solution of (VIII) was distilled, an aldehyde containing distillate was obtained which reduced Tollens reagent and Fehlings solution and it was possible to prepare phenylhydrazone and p-nitrophenylhydrazone derivatives from it.

Accordingly, distillation of the aqueous aldehyde solution was carried out here and was found to give an aqueous distillate

containing an aldehyde which reacted readily with p-nitrophenyl-hydrazine to give a red derivative having the same melting point as the di-p-nitrophenylhydrazone derivative (IX) of (VIII), reported by Glattfeld and Mochel (5). This evidence confirms the formation of (VIII) from (III) although an attempt to prepare the di-phenylhydrazone derivative of (VIII) was unsuccessful.

This derivative had been assigned the structure (IX) by Glattfeld and Mochel (5) on the basis of an elemental analysis which indicated an empirical formula of $C_{16}H_{16}O_5N_6$. Conversion of (VIII) to this compound is very unusual and cannot be accounted for by the accepted mechanism for osazone formation.
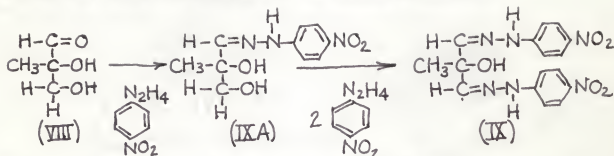
It seemed more reasonable that the compound they obtained was actually the bis-p-nitrophenylhydrazone derivative of methyl-malonaldehyde resulting from a pinacol pinacolone rearrangement of the dihydroxyaldehyde in the acidic medium. This structure would differ from (IX) by the absence of the hydroxyl group. Since Glattfeld and Mochel (5) presented no evidence for the structure of (IX) other than an analysis, an infrared spectrum of this derivative was taken to see if the hydroxyl group was present. The hydroxyl band showed up strongly thereby confirming the structure of (IX).

The aqueous distillate of the (III) hydrolsate also reacted

with the Johnson (9) reagent to form a 2,4-dinitrophenylhydrazone derivative. An infrared spectrum of this derivative indicated the presence of the hydroxyl group. A carbon, hydrogen and nitrogen analysis of this derivative was rather unexpected; it checks fairly well with the empirical formula, $C_{10}H_{12}O_5N_4$, suggesting one of the following structures:
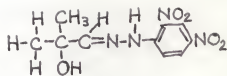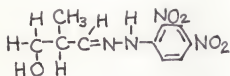

The attempted hydrolysis of (III) using N sulfuric acid was repeated several times but no methylmalonaldehyde was obtained. Then the hydrolysis method used by Gasson and his coworkers to convert epoxides to aldehydes (4) was attempted using strong (50 percent by volume) sulfuric acid as the hydrolysis medium but a very short reaction time (5 minutes). A small yield of an ether soluble oil was obtained which was found to reduce Tollens reagent. An infrared spectrum of this compound was obtained and has characteristic absorption bands for the hydrogen bonded hydroxyl, carbonyl and apparently ether groups (at 9.36μ) but no bands typical of the enolic double bond. Although extreme care was exercised in repeating in detail this modified hydrolysis reaction no more of this compound could be obtained for analysis and continued study. The special conditions necessary for the isolation of this substance, without further hydrolysis, are still unknown. In each case the only product that could be demonstrated

was the dihydroxyaldehyde (VIII).

This compound reacted with the Johnson (9) reagent to form the 2,4-dinitrophenylhydrazone derivative which is different from the derivative that was obtained directly from (VIII). The infrared spectrum of this derivative in carbon tetrachloride was found to be somewhat different from its potassium bromide pellet spectrum. The spectrum of the derivative in a carbon tetrachloride solution indicated the presence of the carbonyl group and the absence of the hydroxyl group, whereas the potassium bromide pellet spectrum indicated the presence of the hydroxyl group and what may be the ether linkage at 9.29μ, but no carbonyl group. An analysis was obtained which suggested an empirical formula of $C_{20}H_{22}O_{11}N_8$. The structure in closest agreement with this evidence is:
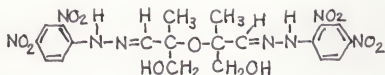
Although insufficient evidence is available, it is believed that the aldehyde resulting from the modified hydrolysis reaction is the intermediate, α-methyl-α-hydroxy-β-methoxypropionaldehyde (VI). It may be assumed that an incomplete hydrolysis reaction has taken place in which the terminal methoxyl group of (III) has not undergone cleavage. It is to be expected that acidic cleavage at the epoxide linkage of (III) is favored over cleavage at the terminal methoxyl group. The reaction involved in the for-

mation of the 2,4-dinitrophenylhydrazone derivative of the intermediate (VI) may be as follows:
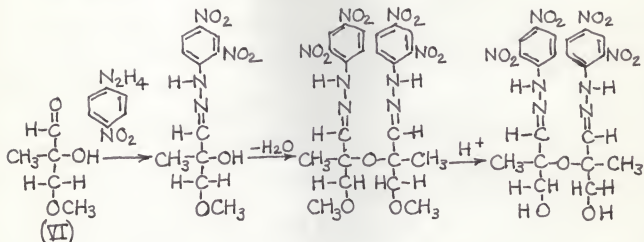
The modified hydrolysis reaction using strong sulfuric acid was then carried out in the presence of excess 2,4-dinitrophenylhydrazine. Three products were obtained: unreacted 2,4-dinitrophenylhydrazine; an orange compound with a very high decomposition point; and a straw colored compound as the major product. The orange compound was at first suspected of being the 2,4-dinitrophenylhydrazone derivative of methylmalonaldehyde, reported by Pummerer (11), because of its high decomposition point of about 320°C. However an infrared spectrum of this compound was obtained which indicated the presence of the hydroxyl group and was found to be similar to the spectrum of (IX). This derivative was analyzed to determine its equivalent weight through tin reduction by the Vanderzee and Edgell (16) method. This determination is based on the number of equivalents of tin consumed in the reduction of nitro groups and imino linkages of the 2,4-dinitrophenylhydrazone derivative. One nitro group requires three tin

atoms and one imino group requires one tin atom for reduction.

$$ArNO_2 + 3Sn + 6HCl \longrightarrow ArNH_2 + 3SnCl_2 + 2H_2O$$

$$ArNH-N=CHR + Sn + 2HCl \longrightarrow ArNHNHCH_2R + SnCl_2$$

A carbon, hydrogen analysis was also obtained and both analysis indicated an empirical formula of $C_{16}H_{14}O_9N_8$. This evidence is in perfect agreement with the structure of the bis-2,4-dinitrophenylhydrazone derivative (XI) of (VIII), the formation of which is similar to the formation of (IX) from (VIII).

The straw colored compound obtained as the major product was not believed to be a 2,4-dinitrophenylhydrazone derivative because of its color and infrared spectrum. The infrared spectrum of this compound indicated the absence of the hydroxyl group and conjugated imino linkage and strong bands were found at 6.55μ and 10.52μ. A carbon, hydrogen and nitrogen analysis indicated an empirical formula of $C_{10}H_8O_4N_4$. An analysis for the determination of nitro groups by the method of Vanderzee and Edgell (16) also was in agreement with this formula. It is assumed that only nitro groups are reduced here and that imino linkages common to 2,4-dinitrophenylhydrazone derivatives are absent.

The data to this point indicate that the straw colored compound is a pyrazole. With regard to the infrared spectra of pyrazoles, it has been shown by Rondestvedt and Chang (12) that bands at 6.80μ and 10.70μ are characteristic of the pyrazole ring. These values are in fair agreement with the preceding infrared

data of this compound.

Assuming that the straw colored compound is 4-methyl-1-(2, 4-dinitrophenyl)pyrazole (X) an attempt was made to oxidize the methyl group on the pyrazole ring with potassium permanganate by the method of Birkinshaw and his coworkers (2). Unexpectedly, no oxidation occurred and it was also found that this substance was not effected by concentrated nitric acid at room temperature. (X) also does not react with acidic 2,4-dinitrophenylhydrazine which would be expected if it has the pyrazole structure. It is of interest to note that (X) is formed when the 2,4-dinitro-phenylphenylhydrazone derivative of (VI) is treated with dilute sulfuric acid.

It may be reasoned that (VIII) reacts with 2,4-dinitro-phenylhydrazine to form the water soluble 2,4-dinitrophenyl-hydrazone (XIA) which may either react with excess 2,4-dinitro-phenylhydrazine to form (XI) or it may cyclize in the acidic medium to form (X). The reactions involved may be as follows:
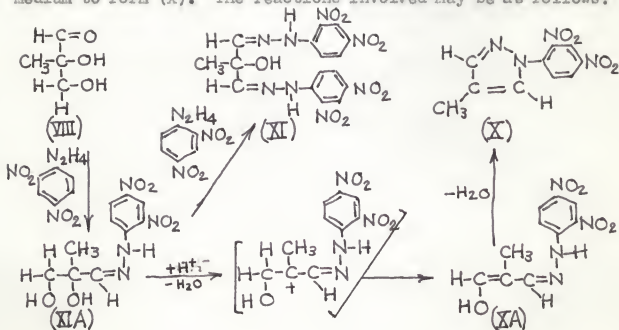
Thus it seems that the intermediate (XIA) may be able to undergo the pinacol pinacolone rearrangement in the acidic medium to form the half 2,4-dinitrophenylhydrazone derivative (XA) of methylmalonaldehyde which then immediately cyclized to (X) by splitting out water.

It seemed strange however that the intermediate (XIA) could undergo this type of rearrangement when previous efforts to do this seemed unsuccessful. Since (VIII) is closely related in structure to the simple sugars, it is difficult to see how it could be volatile and distill with water at a temperature of about 100°C., as Glattfeld and M₀chel (5) indicated. The iso-lation of the derivatives (IX) and (XI) of 2-methyl-2-hydroxy-malonaldehyde suggests that air oxidation of (VIII) to this com-pound may have occurred during standing and distillation, and therefore may actually be the substance accounted for in the distillate.

Recently a patent was issued to Hearne and Schwarzer (7) for a synthesis of (VIII) by the hydrolysis of (I) with sodium bicarbonate solution. They reported the isolation of (VIII) as a residue after removing the water under vacuum, thus indicating that it is not volatile. Upon treatment with acid, rearrangement to diacetyl apparently occurred, which is certainly an unusual rearrangement, but no methylmalonaldehyde was apparently obtained.

The results reported by Ives (8) thus seemed impossible to repeat. It is of interest in this connection that Mr. H. R. Guest of the Research and Development Department of the Carbide and Carbon Chemicals Co., Charleston, West Virginia, recently

Flow Sheet of Reactions

informed Dr. Scott Searles that he also had been unable to
hydrolize the dimethoxy compound to methylmalonaldehyde. It
was thought that compound (III) as prepared by Ives (8) might
have been contaminated with (IV) which could possibly rearrange
to methylmalonaldehyde.

However, when either one normal or strong (50 percent by
volume) sulfuric acid was used the only product obtained was
(VIII). The mechanism of the acidic hydrolysis of (III) and
(IV) are apparently similar and may both involve the formation
of the intermediate (VI) which is very difficult to separate
without further hydrolysis to (VIII).

Summary

The intermediate obtained in the formation of 2-methyl-
1,3-dimethoxy-1,2-epoxypropane (III) by the reaction of methanolic
sodium methoxide with α-methyl-α,β-dichloropropionaldehyde (I)
was found to be α-methyl-α-chloro-β-methoxypropionaldehyde (II)
rather than the corresponding chloromethoxyepoxide obtained in
analogous reactions reported by Ives. α-Methyl-α-chloro-β-
hydroxypropionaldehyde (V) is formed by the acidic hydrolysis of
(II). Attempted oxidation of (V) with lead tetraacetate confirmed
the structures of (II) and (V) as being α-chloroaldehydes.

Reduction of (III) by lithium aluminum hydride forms 2-methyl-
2-hydroxy-1,3-dimethoxypropane (VII), which upon acidic hydrolysis
forms methacrolein and thereby provides structure proof of (III)
and (VII). Compound (III) also reacts with a third mole of sodium
methoxide to form 2-methyl-2-hydroxy-1,1,3-trimethoxypropane (IV).

Compounds (III) and (IV) are completely hydrolized by one
normal sulfuric acid to α-methyl-α,β-dihydroxypropionaldehyde
(VIII) which could not be separated from aqueous solution but
was identified by the preparation of its di-p-nitrophenylhydrazone
derivative (IX). In one case, a modified acidic hydrolysis of
(III) yielded an intermediate (VI) which is believed to be α-
methyl-α-hydroxy-β-methoxypropionaldehyde. However, free methyl-
malonaldehyde as reported by Ives was never isolated in any of
the numerous hydrolysis attempts. When compound (III) was
hydrolized in the presence of 2,4-dinitrophenylhydrazine, two
products were obtained: the bis-2,4-dinitrophenylhydrazone
derivative (XI) of (VIII) and a substance believed to be
4-methyl-1-(2,4-dinitrophenyl)pyrazole (X).

ACKNOWLEDGMENT

LITERATURE CITED

Part I

1. Biquard, D.
   The action of mixed organomagnesium compounds on acetophenone semicarbazone. Bull. soc. chim. 3:656-65. 1936.

2. Meyer, E. van.
   Dimolecular nitriles. J. prakt. Chem. 90:1-52. 1914.

3. Moureu, C. and I. Lazennec.
   Condensation of hydrazines with acetylenic nitriles. general method of sythesising pyrazolonimines. (5-Imino-pyrazolines). Compt. rend. 143:1239-42. 1906.

Part II

1. Bellamy, L. J.
   The infra-red spectra of complex molecules. London: Methuen and Co. Ltd. p. 102-3. 1954.

2. Birkinshaw, J. H., A. E. Oxford and H. Raistrick.
   Penicillic acid, a metabolic product of penicillum puberulum bainier and penicillum cyclopium westiling. Biochem. J. 30:394-411. 1936.

3. Brochet, F.
   The action of chlorine on hot isobutyric alcohol. Bull. soc. chim. 15:20-2, 1896.

4. Gasson, E. J., A. R. Graham, A. F. Millidge, I. K. M. Robson, W. Webster, A. M. Wild and D. P. Young.
   Oxidation products of diisobutylene. Part II. The isomerisation of 1:2-epoxy-2:4:4-trimethylpentane, and some products derived from 2:4:4-trimethylpentanal. J. Chem. Soc. 2170-9. 1954.

5. Glattfeld, J. W. E. and W. E. Mochel.
   The preparation of dl-α,β-diacetoxyisobutyric aldehyde. J. Am. Chem. Soc. 60:1011-4. 1938.

6. Hearne, C. and H. W. deJong.
   Derivatives of allylic chlorides. Beta-methylglycerol and its derivatives. Ind and Eng. Chem. 33:940-3. 1941.

7. Hearne, G. W. and C. G. Schwarzer.
   Vicinal dials. U. S. Patent 2,600,766. July 17, 1952.

8. Ives, E. K.
    A Ph. D. dissertation. Kansas State College, Manhattan.
    1957.

9. Johnson, G. D.
    A new preparation of 2,4-dinitrophenylhydrazones.
    J. Am. Chem. Soc. 73:5888-9. 1951.

10. Krausz, F.
    α-and β-substituted aldehydes. Ann. chim. 4:811-31.
    1949.

11. Pummerer, R., H. Hahn, F. Johne and H. Kehlen.
    The photochemical synthesis of branched carbon chains from
    ether and formaldehyde. Ber. 75:867-81. 1942.

12. Rondestvedt, C. S. and P. K. Chang.
    Unsaturated sulfamic acids. V. Addition of diazomethane
    and phenyl azide to derivatives of ethylenesulfonic acid
    and its homologs. J. Am. Chem. Soc. 77:6532-40. 1955.

13. Shriner, R. L. and A. G. Sharp.
    Derivatives of methacrolein. J. Am. Chem. Soc. 62:2245.
    1940.

14. Spielman, M. A., J. D. Barnes and W. J. Close.
    Anticonvulsant drugs. III. Some allophenates. J. Am.
    Chem. Soc. 72:2520-22. 1950.

15. Stevens, C. L., W. Malik and R. Pratt.
    Isolation of an epoxyether from the reaction of an
    α-haloketone with base. J. Am. Chem. Soc. 72:4758-60.
    1950.

16. Vanderzee, C. E., and W. F. Edgell.
    Quantitative determination of aromatic nitro groups with
    tin. Anal. Chem. 22:572-4. 1950.

PART I: THE STRUCTURE OF THE SO-CALLED "6-PHENYL-1,4-
DIHYDRO-as-TRIAZINE"
PART II: THE REACTIONS OF METHANOLIC SODIUM METHOXIDE
WITH α-METHYL-α,β-DICHLOROPROPIONALDEHYDE

by

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PART I

A unique synthesis of 6-phenyl-1,4-dihydro-as-triazine has been reported which involves the reaction of acetophenone semicarbazone with Grignard reagents. However, the possibility of an isomeric structure was not seriously considered.

The isomeric compound was prepared by an unambigous method and then compared with the condensation product. Identical melting points, mixture melting point, and infrared spectra of each compound and its derivatives demonstrate clearly that the condensation product is actually 3(5)-amino-5(3)-phenylprazole.

PART II

It has been reported that certain α,β-dichloroaldehydes form oxirane compounds when treated with methanolic sodium methoxide. However the series of compounds formed from α-methyl-α,β-dichloropropionaldehyde was not rigorously studied. The object of this work is to study in more detail the reactions of α-methyl-α,β-dichloropropionaldehyde with sodium methoxide and the acidic hydrolysis of the products formed.

The intermediate obtained in the formation of 2-methyl-1,3-dimethoxy-1,2-epoxypropane from α-methyl-α,β-dichloropropionaldehyde was found to be α-methyl-α-chloro-β-methoxypropionaldehyde rather than the corresponding chloromethoxyepoxide which was obtained in analogous reactions, reported previously. Acidic hydrolysis of the intermediate formed α-methyl-α-chloro-β-hydroxypropionaldehyde which could not be oxidized by lead tetraacetate.

This evidence, together with elemental and infrared analysis con-
firmed the structures of the intermediate and its hydrolysis
product as being α-chloroaldehydes.

Reduction of 2-methyl-1,3-dimethoxy-1,2-epoxypropane by
lithium aluminum hydride formed 2-methyl-2-hydroxy-1,3-dimethoxy-
propane which undergoes acidic hydrolysis to methacrolein. Addi-
tional evidence for the epoxide structure of this compound is
found in its reaction with another mole of sodium methoxide to
form 2-methyl-2-hydroxy-1,1,3-trimethoxypropane.

Both the dimethoxyepoxide and the trimethoxyalcohol are com-
pletely hydrolized by one normal sulfuric acid to α-methyl-α,β-
dihydroxypropionaldehyde which could not be separated from its
aqueous solution but was identified through the preparation and
infrared analysis of its di-p-nitrophenylhydrazone derivative
which was reported in the previous literature. A modified
hydrolysis of the dimethyoxyepoxide was attempted several times
and yielded an intermediate which was believed to be α-methyl-
α-hydroxy-β-methoxypropionaldehyde. However, free methylmalon-
aldehyde was never isolated as previously reported.

When the dimethoxyepoxide was hydrolized in the presence of
2,4-dinitrophenylhydrazine, two products were obtained; the bis-
2,4-dinitrophenylhydrazone derivative of methacrolein glycol and
4-methyl-1-(2,4-dinitrophenyl)pyrazole. The assignment of the
latter structure was not conclusively proved because the compound
was inert to oxidation and cleavage and is based only on its
elemental and infrared analysis.