Ketene Acetals. VIII. The Reaction of Ketene Diethylacetal with α,β-Unsaturated Carbonyl Compounds

By S. M. McElvain and Harry Cohen

The characteristic polarization of an α,β-unsaturated carbonyl compound, $C=C-C=O$ to produce a positive or cationoid center of reactivity on the β-carbon atom suggested a study of the reaction of compounds of this type with ketene diethylacetal, which is known to have a strong anionoid center. It seemed of particular interest to determine whether a single molecule of ketene acetal would add to the unsaturated carbonyl structure or whether the reacting unit would consist of two molecules of the acetal in some such form as . . . $CH_2C(OEt)_2-CH_2C(OEt)_2$ . . . This latter type of behavior is reminiscent of an ordinary 1,4 addition. Indeed, it may be considered as a 1,4 intermolecular addition in which the establishment of the 2,3 double bond in the ordinary type is replaced by the formation of a single bond that joins the two units of the ketene acetal that are involved in the reaction. Two reactions of this latter type have been noted: (1) the addition of bromine to bromoketene acetal to form the ketal of a tribromoacetoacetic ester,[1] $Br_2CHC(OEt)_2CHBrCOOEt$, and the addition of a variety of acids across two molecules of ketene acetal to form ethyl O-ethylacetoacetate,[2] $CH_3C(OEt)=CHCOOEt$. The present paper reports the results of a study of the reaction of ketene diethylacetal with the following α,β-unsaturated carbonyl compounds: maleic anhydride, acetylenedicarboxylic ester, dimethylmaleic anhydride, quinone, dibenzalacetone, benzalacetone, benzalacetophenone and phorone.

In an ether solution ketene acetal reacts with maleic anhydride in a ratio of 4:1 to give, presumably, the cyclohexane derivative (I) which then passes, by the loss of alcohol, into 3,5-diethoxy-1,6-dihydrophthalic anhydride (II). This latter compound precipitates from the ether solution after a few hours as yellow crystals in a 70% yield. The alcohol that is lost by I converts an equivalent amount of ketene acetal into ethyl orthoacetate. When a mixture of ketene acetal and maleic anhydride in the ratio of 2:1 is allowed to stand in
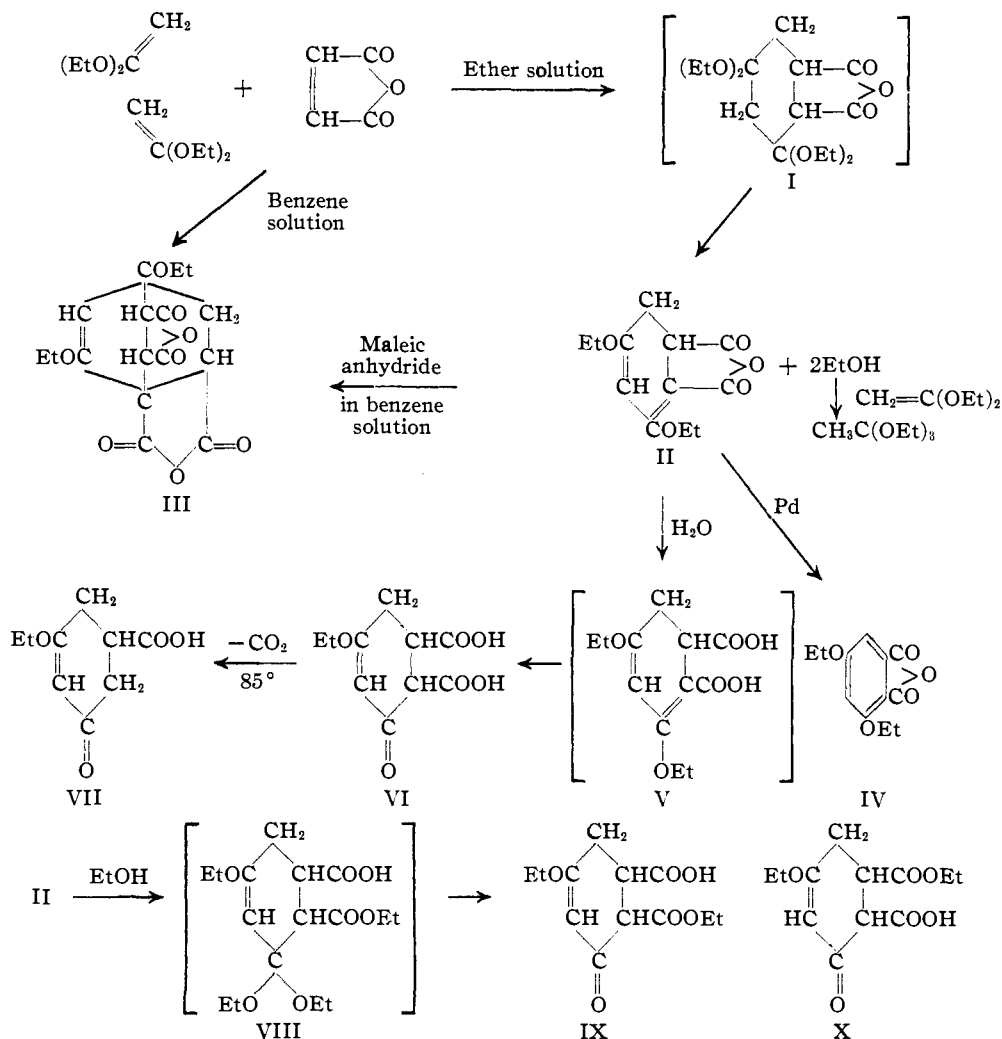
benzene solution for several days, none of the yellow anhydride (II) is noticed but in its stead a white solid, to which the bicyclooctene structure (III) is assigned, precipitates. This structure is the result of a 1,4 addition of maleic anhydride to the conjugate bonds of (II) and is substantiated by the fact that (III) is most readily prepared when (II) is heated with an equivalent of maleic anhydride in benzene solution. The reason that none of (III) is formed in the ether solution may be due to the fact that (II) is so insoluble in this solvent that it precipitates before it can react further with the maleic anhydride.

When the yellow anhydride (II) is moistened with water, it slowly turns to a white dibasic acid the analytical data for which indicate that it has the structure (VI). This dibasic acid loses carbon dioxide when heated to its melting point, 83–85°, and passes into the keto-acid (VII). The facile loss of an ethyl group in the hydrolysis of (II) is undoubtedly associated with the intermediate structure (V) which, it may be seen, is a vinylog of ethyl bicarbonate at the 2,3 positions in the ring. The β-keto-acid structure readily explains the decarboxylation of (VI) to form (VII).

The yellow anhydride (II) with absolute alcohol yields a half-ester to which the structure (IX) is assigned. The reasons for this structure are the ethoxyl content, neutral equivalent, and failure of the acid ester to decarboxylate on heating. This latter characteristic definitely excludes the isomeric compound (X) from consideration. The loss of the ethyl group from the 3-ethoxyl during the alcoholysis of the anhydride was unexpected and seems quite unusual. The only explanation that can be offered for this reaction presumes the intermediate formation of the ketal (VIII) by the addition of two equivalents of alcohol to (II), followed by the loss of ether from this ketal to produce (IX).

The main support for the structure of (II) is its dehydrogenation by palladium to the known 3,5-diethoxyphthalic anhydride (IV) and the hydrolysis of this anhydride to 3,5-diethoxyphthalic acid.[3] The corresponding N-phenylphthalimide

(1) Magnani and McElvain, This Journal, 60, 2210 (1938).

(2) McElvain and Kundiger, ibid., 64, 254 (1942).

(3) Fritsch, Ann., 296, 358 (1897).

CH₂
(EtO)₂C
CH₂
C(OEt)₂

+

CH—CO
           >O
CH—CO

Ether solution →

[
CH₂
(EtO)₂C   CH—CO
                    >O
H₂C   CH—CO
C(OEt)₂
]
I

Benzene solution ↓

COEt
HC   HCCO   CH₂
          |>O|
EtOC   HCCO   CH
C
O=C   C=O
      O
III

← Maleic anhydride in benzene solution

CH₂
EtOC   CH—CO
            >O + 2EtOH
CH   C——CO   CH₂=C(OEt)₂
COEt   CH₃C(OEt)₃
II

↓ H₂O   Pd ↘

CH₂
EtOC   CHCOOH   −CO₂   EtOC   CHCOOH   ←   [EtOC   CHCOOH]   EtO   CO
                 85°   >O
CH   CH₂   CH   CHCOOH   CH   CCOOH   CO
C   C   C   OEt
O   O   OEt
VII   VI   V   IV

II   EtOH →   [
CH₂
EtOC   CHCOOH
CH   CHCOOEt
C
EtO   OEt
]
VIII

→

CH₂
EtOC   CHCOOH
CH   CHCOOEt
C
O
IX

CH₂
EtOC   CHCOOEt
HC   CHCOOH
C
O
X

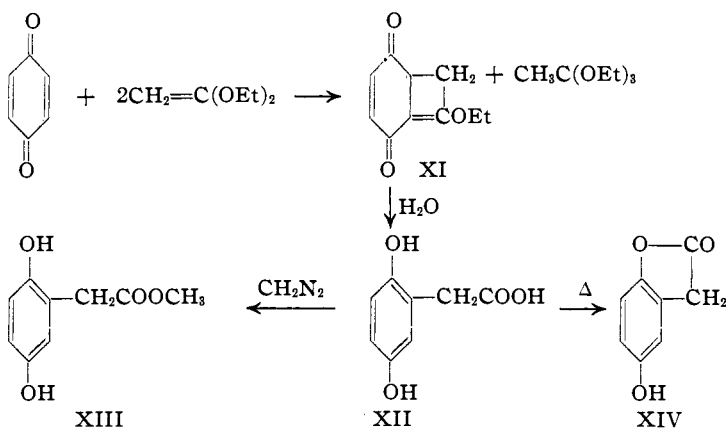could be prepared by heating either the anhydride (IV) or the acid with aniline.

It was also possible to obtain 3,5-diethoxyphthalic acid in small yield from the reaction of ketene acetal with acetylenedicarboxylic ester. This reaction, as might be expected, was very much more sluggish than that between the acetal and maleic anhydride; in fact, it was necessary to heat the reactants in a sealed tube at 195° for twenty-four hours in order to obtain any appreciable quantity of the phthalic acid from the reaction mixture. Under such conditions most of the ketene acetal was converted to polymers and pyrolysis products.

Since the condensation of maleic anhydride with ketene acetal produces a dihydrobenzene derivative, the formation of which requires the loss of one of the α-hydrogens of the anhydride, it seemed advisable to investigate the reaction be-

tween ketene acetal and dimethylmaleic anhydride which contains no such hydrogens. This anhydride showed no reaction with the acetal in refluxing benzene after twelve hours. At 175–180° in a sealed tube for fifteen hours a reaction occurred, since none of the starting materials was recovered. However, the reaction mixture on fractionation gave no definite fraction that could be characterized.

The reaction between benzoquinone and ketene acetal starts at about 80° and, without a solvent, becomes so violent that it cannot be controlled. In benzene solution, however, the reaction proceeds quite smoothly and two equivalents of the acetal are used up by each equivalent of the quinone. The main reaction product is a white crystalline material, m. p. 94–95°. The ethoxyl content of this compound indicates that it has the bicyclo-octadiene (XI) which is the result of

the addition of a single ketene acetal to one of the quinone carbon to carbon double bonds followed by the loss of ethyl alcohol. This alcohol converts the second equivalent of the acetal into ethyl orthoacetate, which was one of the lower boiling reaction products. The structure of the

$$ \text{(quinone)} + 2CH_2{=}C(OEt)_2 \longrightarrow \text{(XI)} + CH_3C(OEt)_3 $$

XI

$$ \xrightarrow{H_2O} $$

XIII $\xleftarrow{CH_2N_2}$ XII $\xrightarrow{\Delta}$ XIV

bicyclo-octadiene (XI) is shown by its hydrolysis to hydroquinone-acetic acid[4] (XII) and the conversion of this acid to its methyl ester (XIII) by diazomethane and to the corresponding lactone (XIV) by heating just above its melting point.[5]

The fact that XI is colorless is further evidence in favor of the structure assigned to it because the electronic conjugation of the ethoxyl group with the lower carbonyl group neutralizes the ketonic nature of this carbonyl. That is to say, the $O{=}\overset{|}{C}{-}\overset{|}{C}{=}\overset{|}{C}{-}OEt$ portion of XI is a vinylog of an ester and while quinone is vinylogous to the colored 1,2-diketones, XI is a vinylog of the colorless α-keto-esters.

It was not possible to cause a second molecule of ketene acetal to add to (XI). This failure to form a tricyclic structure parallels the results reported by Abuzov and Spekterman[6] who found that they could not force quinone to react with more than one equivalent of hexadiene.

Dibenzalacetone reacts with only one equivalent

of ketene acetal and gives 1,1 diethoxy-2-cinnamoyl-3-phenylcyclobutane (XV). In this case there is no elimination of alcohol and consequently no formation of ethyl orthoacetate. The product (XV) is converted by hydrolysis with dilute acid into β-phenyl-γ-cinnamoylbutyric acid (XVI) which proved to be identical with an authentic specimen prepared by the procedure of Borsche.[7] Bromination of (XV) produces ethyl β-phenyl-γ-bromo-γ-cinnamoyl-butyrate (XVII) by brominolysis of the cyclobutane ring followed by the loss of ethyl bromide. Further treatment with bromine produces a tribromo derivative (XVIII) by addition of bromine to the monobromo compound (XVII).

No definite product could be obtained from the reaction of ketene acetal and benzalacetone. When these reactants were allowed to reflux for ten hours, only ethyl acetate, ethyl ortho-acetate mixture formed. The main portion of this mixture was a non-distillable residue, the ethoxyl content (8.6%) of which indicated that it was a mixture of ketene acetal polymer and self-condensed benzalacetone.

$$ \begin{array}{l} C_6H_5CH{-}CHCCH{=}CHC_6H_5 \\ \quad | \qquad | \\ \quad CH_2{-}C(OEt)_2 \\ \qquad XV \end{array} \xrightarrow{H_2O} \begin{array}{l} C_6H_5CH{-}CH_2CCH{=}CHC_6H_5 \\ \quad | \\ \quad CH_2{-}COOH \\ \qquad XVI \end{array} $$

$$ EtBr + \begin{array}{l} C_6H_5CH{-}CHBrCOCH{=}CHC_6H_5 \\ \quad | \\ \quad CH_2{-}COOEt \\ \qquad XVII \end{array} \xrightarrow{Br_2} \begin{array}{l} C_6H_5CH{-}CHBrCOCHBrCHBrC_6H_5 \\ \quad | \\ \quad CH_2{-}COOEt \\ \qquad XVIII \end{array} + HBr $$

Benzalacetophenone, which does not have this tendency to undergo self-condensation, reacts with ketene acetal as does dibenzalacetone and forms 1,1-diethoxy-2-benzoyl-3-phenyl-cyclobutane (XIX). This product on hydrolysis yields β-phenyl-γ-benzoylbutyric acid[8] (XX) which was characterized as its semicarbazone.[9]

$$ \begin{array}{l} C_6H_5CH{-}CHCC_6H_5 \\ \quad | \qquad | \\ \quad CH_2{-}C(OEt)_2 \\ \qquad XIX \end{array} \qquad \begin{array}{l} C_6H_5CH{-}CH_2CC_6H_5 \\ \quad | \\ \quad CH_2{-}COOH \\ \qquad XX \end{array} $$

Phorone, $(CH_3)_2C{=}CHCOCH{=}C(CH_3)_2$, showed no signs of reaction with ketene acetal

(4) This acid is generally known as homogentisic acid which was first obtained from the urine of alcaptonurics (ref. 5). It has also been prepared by Hahn and Stenner, Z. physiol. Chem., 181, 88 (1929), by the ozonization of 2 allyl-hydroquinone dibenzoate and the hydrolysis of the resulting carboxylic acid.

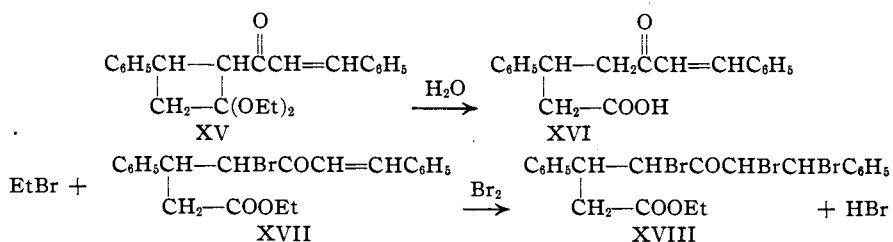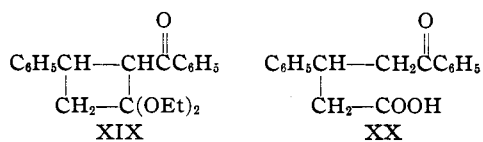(5) Cf. Wolkow and Baumann, Z. physiol. Chem., 15, 253 (1891).

(6) Abuzov and Spekterman, Chem. Abs., 35, 2498 (1941).

(7) Borsche, Ann., 375, 174 (1910).

(8) Vörlander and Knötzsch, ibid., 294, 332 (1897).

(9) Stobbe and Volland, Ber., 34, 655 (1901).

even after they were refluxed together for twelve hours. Practically all of the ketene acetal was recovered unchanged. Such behavior would seem to indicate that the methyl groups of phorone, by their inductive effect, sufficiently reduce the cationoid character of each of the carbons in the β-position to the carbonyl group to prevent the reaction of either of them with the anionoid center of ketene acetal.

Experimental

Reaction of Ketene Diethylacetal with Maleic Anhydride.—To a solution of 4.9 g. (0.05 mole) of maleic anhydride in 75 ml. of dry ether in a 125-ml. flask was added 11.6 g. (0.1 mole) of ketene acetal. The solution turned yellow and then red, and after one to two minutes the ether began to boil. The flask was cooled and after a few minutes the reaction subsided. The stoppered flask was then allowed to stand overnight. The yellow precipitate of 3,5-diethoxy-1,6-dihydrophthalic anhydride (II) was filtered off and washed with dry ether; it could be recrystallized from xylene but for practically all purposes the ether-washed material was satisfactory. The yield of product that melted at 110–111° amounted to 4.3 g. (71%).

Anal. Calcd. for $C_{12}H_{14}O_5$: C, 60.5; H, 5.9; C_2H_5O, 37.8. Found: C, 60.5; H, 6.1; C_2H_5O, 37.4.

Reactions of 3,5-Diethoxy-1,6-dihydrophthalic Anhydride: (a) With Maleic Anhydride.—A mixture of 1.2 g. of the anhydride and 1.0 g. of maleic anhydride was heated in 10 ml. of dry benzene for four hours. On cooling, 1.1 g. (60%) of the dianhydride of 1,5-diethoxy-3,4,7,8-tetracarboxy-bicyclo[2,2,2]octene-5 (III) settled out of the benzene solution. After recrystallization from a dioxane-cyclohexane mixture it melted at 253–255°.

Anal. Calcd. for $C_{16}H_{16}O_8$: C, 57.2; H, 4.76; C_2H_5O, 26.8. Found: C, 57.5; H, 5.0; C_2H_5O, 26.6.

(b) With Water.—To 1.2 g. of the dihydrophthalic anhydride (II) on a crystallizing dish was added a few drops of water. After several hours this mixture turned white and was washed with benzene. The dibasic acid, presumably (VI), so obtained melted at 83–85° and contained 19.3% ethoxyl (calcd., 19.7%). It showed a neutral equivalent of 128 (calcd., 114). When this acid was kept at its melting point for fifteen minutes it was decarboxylated to 3-keto-5-ethoxy-Δ^4-cyclohexenecarboxylic acid (VII). This acid weighed 0.9 g. and, after recrystallization from an ethyl acetate–petroleum ether (60–68°) mixture, melted at 124–125° and had a neutral equivalent of 188 (calcd., 184).

Anal. Calcd. for $C_9H_{12}O_4$: C, 58.7; H, 6.5; C_2H_5O, 24.5. Found: C, 58.8; H, 6.6; C_2H_5O, 24.9.

(c) With Alcohol.—A mixture of 4.9 g. of the dihydrophthalic anhydride (II) and 20 ml. of absolute alcohol was refluxed for four hours. The main portion of the alcohol was then removed under diminished pressure from the red solution, and the separated solid, 2-carbethoxy-3-keto-5-ethoxy-Δ^4-cyclohexenecarboxylic acid (IX), filtered and washed with dry ether. Additional quantities of this keto-acid could be obtained by further concentration of the mother liquor. After recrystallization from ethyl acetate

the yield of material that melted at 148–149° amounted to 2.3 g. (43%). It had a neutral equivalent of 252 (calcd., 256).

Anal. Calcd. for $C_{12}H_{16}O_6$: C, 56.3; H, 6.3; C_2H_5O, 35.1. Found: C, 56.2; H, 6.2; C_2H_5O, 35.1.

(d) Dehydrogenation with Palladium.—In a 500-ml. flask fitted with a stirrer and condenser were placed 5 g. of palladium, 25 g. of 3,5-diethoxy-1,6-dihydrophthalic anhydride and 280 ml. of dry xylene. The mixture was refluxed and stirred for twenty-four hours. After this time the catalyst was removed by centrifuging the warm solution and then on cooling 7.4 g. of 3,5-diethoxyphthalic anhydride separated from the solution. Concentration of the mother liquors yielded an additional 2 g. of the anhydride. After recrystallization from a dioxane-cyclohexane mixture the anhydride melted[3] at 137–138° and contained 37.8% (calcd., 38.1) ethoxyl. Hydrolysis converted this anhydride into the 3,5-diethoxyphthalic acid[3] which, after recrystallization from an alcohol-water mixture, melted at 178–180°.

3,5-Diethoxy-N-phenylphthalimide.—A mixture of 1.5 g. of the 3,5-diethoxyphthalic anhydride and 1.5 ml. of aniline was heated in an oil-bath at 170° for twenty minutes. On cooling the semi-solid reaction mixture was treated with 10 ml. of water and 2 ml. of a saturated sodium bicarbonate solution and filtered. The remaining solid was washed with 10 ml. of 10% hydrochloric acid solution and twice with 10 ml. portions of water. The remaining phthalimide was warmed with 5 ml. of alcohol containing a few drops of acetone and filtered. This treatment removed most of the yellow color from the imide and left 1.8 g. (92%) of it as a white solid that melted at 164–166°. Recrystallization from dioxane or ethyl acetate gave a product that melted at 167–168°.

Anal. Calcd. for $C_{18}H_{17}O_4N$: C, 69.5; H, 5.5; C_2H_5O, 28.9. Found: C, 69.5; H, 5.5; C_2H_5O, 28.9.

Reaction of Ketene Acetal and Acetylenedicarboxylic Ester.—A mixture of 9.8 g. of acetylenedicarboxylic ester[10] and 30 g. of ketene acetal was heated in a sealed tube at 195° for twenty-four hours. After the removal of material that distilled up to 180° (1 mm.), a small residue was left. Fractionation of the distillate so obtained gave no definite fraction. To the residue was added 10 ml. of a 30% solution of potassium hydroxide and the mixture allowed to stand for four days. After extraction with ether the aqueous alkaline solution was then acidified and filtered. The 3,5-diethoxyphthalic acid so obtained weighed 0.5 g. and melted at 171–172°. When converted to the anhydride and the phthalimide derivative, products were obtained that produced no lowering in melting point when mixed with the corresponding derivatives of the 3,5-diethoxyphthalic acid obtained from the palladium dehydrogenation of (II).

Reaction of Ketene Acetal and Dimethylmaleic Anhydride.—A mixture of 5 g. of dimethylmaleic anhydride and 20 g. of ketene acetal showed no sign of reaction when heated at 80° or in solution in refluxing benzene. If, however, the mixture was heated at 175–180° for fifteen hours in a sealed tube the following indefinite fractions could be

(10) "Organic Syntheses," **18**, 3 (1938); Ruhemann and Beddow, *J. Chem. Soc.*, **87**, 1121 (1900).

distilled after the removal of the ethyl acetate and ethyl orthoacetate: (a) 2.2 g., b. p. 55–119° (1 mm.); (b) 1.3 g., b. p., 119–139° (1 mm.); (c) 2.1 g., b. p., 139–201° (1 mm.); (d) 2.1 g., b. p., 201–206° (1 mm.).

The Reaction of Ketene Acetal and Benzoquinone.—A mixture of 27 g. of benzoquinone and 60 g. of ketene acetal in 110 ml. of dry benzene was allowed to reflux for twelve hours. The benzene was removed by distillation and the remaining material heated at 100° (12 mm.) to remove the ethyl orthoacetate. The residue was then distilled at 2 mm. and the fraction (39 g.) boiling at 110–170° collected. On redistillation the fraction that boiled mainly at 136–144° (1 mm.) amounted to 29 g. and solidified on cooling. Recrystallization from a benzene–petroleum mixture gave 7-ethoxy-2,5-diketo-bicyclo[4,2,0]octadiene-3,6 (XI), m. p., 94–95°.

Anal. Calcd. for $C_{10}H_{10}O_3$: C, 67.4; H, 5.6; C_2H_5O. 25.3. Found: C, 67.0; H, 5.9; C_2H_5O, 25.0.

Hydrolysis of (XI) to Hydroquinone-acetic Acid (XII).— A mixture of 5 g. of (XI) and a solution of 2.5 ml. of concentrated hydrochloric acid and 25 ml. of water was refluxed for twelve hours. After cooling the solution was extracted with six 20-ml. portions of ether. The ether solution after evaporation left 4.2 g. of crude hydroquinone acetic acid which, after recrystallization from an ethyl acetate–petroleum ether (b. p. 60–68°) mixture, melted at 144–146°.[4]

Methyl Hydroquinone-acetate.—To 0.3 g. of hydroquinone-acetic acid was added an ether solution of diazomethane until the characteristic yellow color of the diazo compound persisted. The solution then was filtered, the ether evaporated, and the remaining methyl hydroquinoneacetate recrystallized from an ethyl acetate–petroleum ether mixture. It melted at 116–117°.

Anal. Calcd. for $C_9H_{10}O_4$: C, 59.4; H, 5.5; CH_3O, 17.0. Found: C, 59.8; H, 5.5; CH_3O, 17.0.

Reaction of Ketene Acetal with Dibenzalacetone.—A mixture of 5.5 g. of ketene acetal and 7.7 g. of dibenzalacetone was heated at the refluxing temperature of the acetal for twelve hours after which time the excess acetal was removed under diminished pressure. The remaining light colored oil was dissolved in 30 ml. of warm alcohol. On cooling and scratching the sides of the container 10.1 g. of 1,1-diethoxy-2-cinnamoyl-3-phenyl-cyclobutane (XV) crystallized. After filtering, washing with alcohol and drying it melted at 87–88°.

Anal. Calcd. for $C_{23}H_{26}O_3$: C, 78.8; H, 7.4; C_2H_5O, 25.7. Found: C, 78.7; H, 7.7; C_2H_5O, 26.0.

A mixture of 1 g. of 1,1-diethoxy-2-cinnamoyl-3-phenyl-cyclobutane, 2 ml. of concentrated hydrochloric acid, 6 ml. of water and 10 ml. of dioxane was refluxed for twelve hours, and then the main portion of the solvent removed under diminished pressure. From the remaining residue 0.8 g. of β-phenyl-γ-cinnamoyl-butyric acid (XVI) separated. After recrystallization from an alcohol–water mixture it melted at 157–158° and gave no depression with an authentic specimen of this acid prepared by the procedure of Borsche.[7]

One equivalent of bromine in carbon tetrachloride reacted rapidly with 1,1-diethoxy-2-cinnamoyl-3-phenyl-cyclobutane (XV) in the same solvent. From 0.87 g. of

(XV), after evaporation of the solvent and recrystallization of the solid residue from petroleum ether, 0.6 g. of ethyl β-phenyl-γ-bromo-γ-cinnamoylbutyrate (XVII), m. p. 111–112°, was obtained.

Anal. Calcd. for $C_{21}H_{21}O_3Br$: Br, 20.0; C_2H_5O, 11.2. Found: Br, 19.9; C_5H_2O, 11.3.

When 1.75 g. of (XV) was treated with 2 equivalents of bromine in carbon tetrachloride as described above, 1.6 g. of ethyl β,γ-diphenyl-γ. ε,ζ-tribromo-ϑ-keto-caproate (XVIII), m. p. 171–172°, was obtained. This product was recrystallized from ethyl acetate.

Anal. Calcd. for $C_{21}H_{21}O_3Br_3$: Br, 42.8; C_2H_5O, 8.0. Found: Br, 43.0; C_2H_5O, 8.2.

Reaction of Ketene Acetal with Benzalacetophenone.—A mixture of 22 g. of ketene acetal and 15.6 g. of benzalacetophenone was refluxed for twelve hours. After this time the excess of ketene acetal was removed under diminished pressure and the remaining reaction product fractionated. The following fractions were collected: (a) 1 g., b. p. 162–164° (0.5 mm.); (b) 6.9 g., b. p. 164–168° (0.5 mm.); (c) 15.3 g., b. p. 168–170° (0.5 mm.); (d) 0.8 g., b. p. above 170° (0.5 mm.). Fraction (c) was pure 1,1-diethoxy-2-benzoyl-3-phenyl-cyclobutane (XIX).

Anal. Calcd. for $C_{21}H_{24}O_3$: C, 77.7; H, 7.4; C_2H_5O, 27.8. Found: C, 77.3; H, 7.7; C_2H_5O, 27.7.

Fraction (b) was practically pure (XIX) since it gave as high a yield of β-phenyl-γ-benzoylbutyric acid[8] (XX) as did fraction (c) when it was hydrolyzed by the procedure described above for the hydrolysis of 1,1-diethoxy-2-cinnamoyl-3-phenylcyclobutane (XV). This acid melted at 155–156° and yielded a semicarbazone[9] that melted at 211–212°.

Summary

The reactions between ketene diethylacetal and a variety of α,β-unsaturated carbonyl compounds have been studied and the structures of the reaction products determined.

With maleic anhydride two equivalents of the acetal add in the form, —$CH_2C(OEt)_2$—CH_2C-$(OEt)_2$—, to the carbon to carbon double bond of the anhydride to form, presumably, a cyclohexane derivative that loses two equivalents of alcohol and passes into 3,5-diethoxy-1,6-dihydrophthalic anhydride. This latter compound was dehydrogenated over palladium to 3,5-diethoxyphthalic anhydride. The acid corresponding to this anhydride also was prepared in small yields by the saponification of the non-distillable residue from the reaction of ketene acetal and acetylenedicarboxylic ester. Other reactions of 3,5-diethoxy-1,6-dihydrophthalic anhydride are discussed.

When benzoquinone and ketene acetal react a single molecule of the acetal adds to one of the carbon to carbon double bonds of the quinone. This addition product loses alcohol and passes

into a bicyclo-octadiene (XI), which is converted by hydrolysis into hydroquinone-acetic acid (homogentisic acid).

Both dibenzalacetone and benzalacetophenone react with one equivalent of ketene acetal to produce 1,1-diethoxy-2-cinnamoyl(or benzoyl)-3-phenyl-cyclobutane. Each of these products may be hydrolyzed to the known β-phenyl-γ-cinnamoyl(or benzoyl)butyric acid.

Neither dimethylmaleic anhydride nor phorone reacts with ketene acetal under conditions that caused satisfactory reactions with the other α,β-unsaturated carbonyl compounds.

MADISON, WISCONSIN   RECEIVED OCTOBER 27, 1941

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Transformation of Tetramethylglucoseen-1,2 into 5-(Methoxymethyl)-2-furaldehyde

BY M. L. WOLFROM, E. G. WALLACE AND E. A. METCALF

Raymond[1] has made the very reasonable and stimulating suggestion that 2,3,4,6-tetramethyl-d-glucoseen-1,2 (I) may be the intermediate in the interconversion of tetramethylglucose and tetramethylmannose in dilute alkali. This interconversion has been investigated by Lewis and his students.[2] Tetramethylglucoseen was then synthesized in crystalline condition in this Laboratory.[3] It was found that this substance was not oxidized by Fehling solution and was thus not alkali-sensitive. Lewis and co-workers[2] noted that the equilibrated alkaline solution of tetramethylglucose exhibited an abnormally high hypoiodite consumption which was brought to a normal value by acid treatment. Tetramethylglucoseen was found[3] to consume four atoms of iodine per mole, or a value of 200% "apparent tetramethylaldohexose."

The behavior of tetramethylglucoseen in acid media was then of interest. It was soon found that it did not form a mixture of tetramethylmannose and tetramethylglucose and was thus not an intermediate in the interconversion of these two sugars. Its behavior in acid media was nevertheless of interest and a report of this study is the subject of the present communication.

The final product of the acid treatment of tetramethylglucoseen has been found to be 5-(methoxymethyl)-2-furaldehyde (III). This was identified by freezing point ($-8°$), analysis, and by its behavior with Fehling solution and with acid resorcinol. Further confirmation of identity

was afforded by the preparation of three crystalline derivatives and comparison of two of these with authentic specimens prepared by other methods. These derivatives were the oxime (m. p. 97–98°), semicarbazone (m. p. 163.5–164.5°) and acid (5-(methoxymethyl)-2-furoic acid of m. p. 67.5–68.6°). This aldehyde (III) is also the product obtained on the acid treatment of tetramethylfructofuranose[4] and it is of interest to note that the methylated pentoses produce furaldehyde on treatment with mineral acids.[5]

The conversion of tetramethylglucoseen into 5-(methoxymethyl)-2-furaldehyde by mineral acidity is, however, a complex reaction and some information was obtained regarding its course.
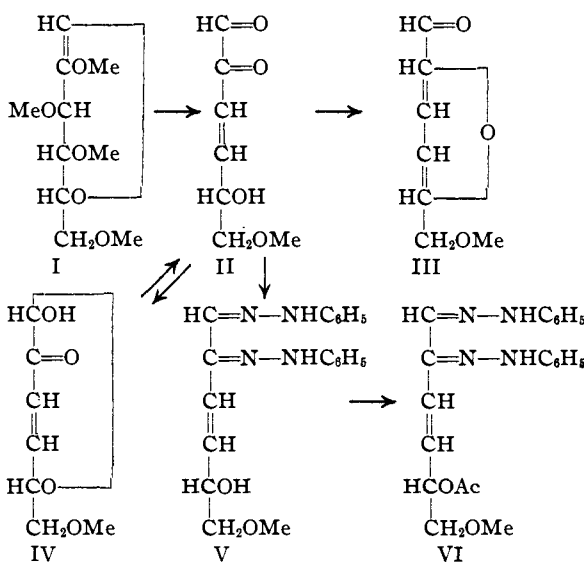
(1) A. L. Raymond in Gilman, "Organic Chemistry," John Wiley and Sons, New York. N. Y., 1938, Vol. II, p. 1512.

(2) M. L. Wolfrom with W. Lee Lewis, THIS JOURNAL, 50, 837 (1928); R. D. Greene with W. Lee Lewis, ibid., 50, 2813 (1928); cf. J. H. Simons and H. C. Struck, ibid., 56, 1947 (1934).

(3) M. L. Wolfrom and D. R. Husted, ibid., 59, 2559 (1937).

(4) W. N. Haworth, E. L. Hirst and V. S. Nicholson, J. Chem. Soc., 1513 (1927).

(5) C. E. Gross with W. Lee Lewis, THIS JOURNAL, 53, 2772 (1931); H. T. Neher with W. Lee Lewis, ibid., 53, 4411 (1931); H. G. Bott and E. L. Hirst, J. Chem. Soc., 2621 (1932).