

precipitate being obtained. The precipitate was dissolved in acetone, filtered and the pentamethylphenol allowed to crystallize, m. p. 128°.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.82; mol. wt., 164.24. Found: C, 79.62; H, 10.10; mol. wt. (cryoscopic in benzene), 161.9.

Summary

A new method for methylating aromatic compounds is reported, using methyl ether-boron

fluoride as a methylating agent. The method has some advantages over methylation by means of the Friedel-Crafts reaction.

The complete methylation of phenol has been accomplished.

Further work is being done in this Laboratory on the use of methyl ether-boron fluoride as a methylating agent.

NOTRE DAME, INDIANA

RECEIVED MARCH 29, 1939

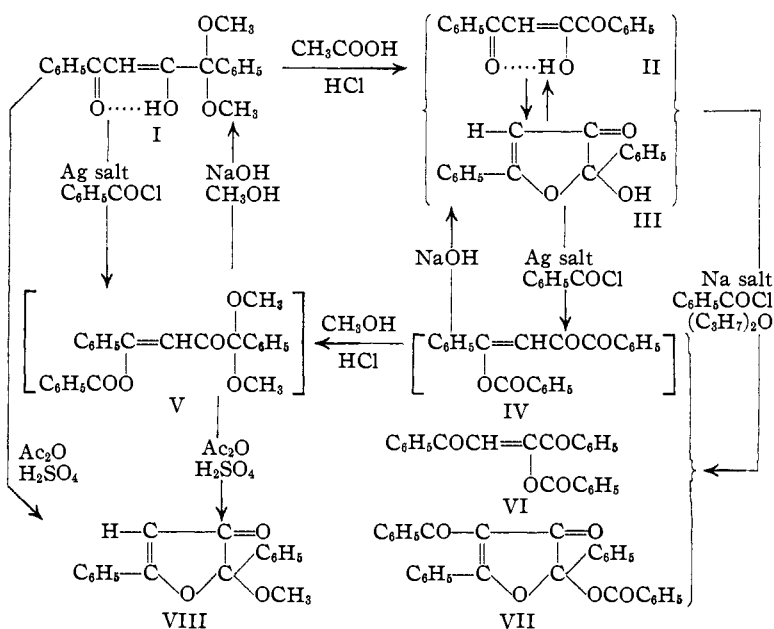
[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

4,4-Dimethoxy-1,4-diphenyl-1,3-butanedione Enol

BY ROBERT E. LUTZ AND JAMES M. SMITH, JR.

1,4-Diphenyl-4,4-dimethoxy-1,3-butanedione enol (I), derived from 1,4-diphenyl-1,2,4-butanetrione enol (II) through methylation of the 1-keto group, was obtained purely by accident and has been investigated because of its close relationship both to β -diketones and to the 1,2,4-triketone enols which have been the subject of recent studies in this Laboratory.¹ It was obtained in 10-15% yields as a by-product in the benzoylation of diphenylbutanetrione sodium enolate (II). In this reaction the products usually isolated were the previously described¹ oxygen and carbon benzoyl derivatives VI and VII.² The ketal enol (I) was obtained regularly in addition to these products when the solvent, isopropyl ether, was partly evaporated and methanolic sodium hydroxide was then added slowly to the reaction mixture (the original object of this procedure was to hydrolyze the oxygen-benzoyl products directly and facilitate the isolation of the carbon-benzoyl product). The formation of the ketal grouping evidently resulted from rapid acid-catalytic methylation of the terminal carbonyl group of an intermediate oxygen-benzoyl product, probably IV, the necessary acid being produced through liberation of hydrogen chloride by

methanolysis of the excess benzoyl chloride before sufficient alkali had been added to complete the neutralization and hydrolysis. The ketal enol evidently is formed first as its benzoate (V) and is not actually liberated in the free enolic state (I) until after the digestion with excess alkali at the end of the procedure. The probable sequence of reactions is outlined in the first diagram and the proof of structure of the ketal enol and evidence supporting the proposed mechanism of its formation are treated in the following discussion.

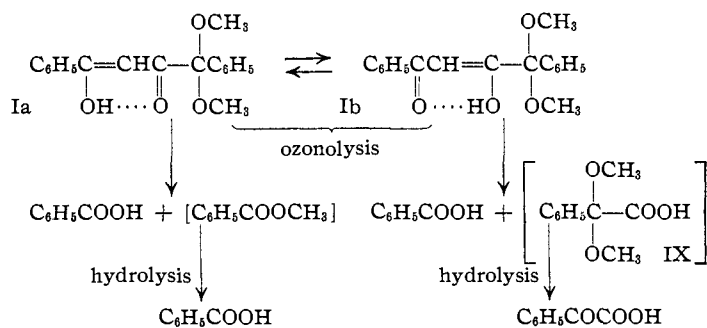


(1) Lutz and Stuart, *THIS JOURNAL*, (a) **58**, 1885 (1936); **59**, (b) 2316, (c) 2322 (1937); Lutz and Wood, *ibid.*, **60**, (d) 229, (e) 705 (1938).

(2) Further details and discussion on these two products will be presented in later papers.

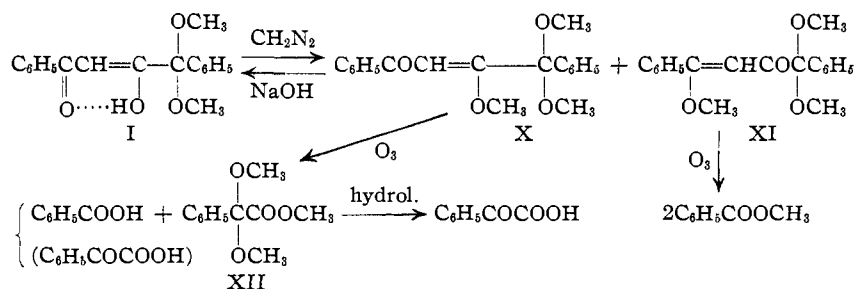
The ketal enol contains two methoxyl groups. It reacts with sodium carbonate or sodium hydroxide, and gives sodium and silver salts, both

of which are obtainable as solids. It gives a red coloration with ferric chloride, and is completely enolized as shown by the K. Meyer titration. It does not react with *o*-phenylenediamine. It is extraordinarily resistant toward alkaline hydrolysis and withstands the action of boiling 50% aqueous sodium hydroxide. When heated with hydrochloric-acetic acid mixtures it is hydrolyzed to diphenyl-1,2,4-butane-trione enol, II. The fact that it is enolic indicates that it is a β -diketone and that the terminal carbonyl is the one which has been affected and converted into the ketal group. The location of one methoxyl was proved definitely by conversion of the compound by means of acetic anhydride and sulfuric acid into 2,5-diphenyl-2-methoxyfuranone-3, VIII, the structure of which is known.¹ Ozonization proceeds in a manner consistent with the structure assigned, giving results which indicate that the tautomeric form Ia is the more reactive phase under these circumstances. The products were benzoic acid, methyl benzoate (hydrolyzed and isolated as benzoic acid), and a small amount of phenylglyoxylic acid which was evidently in the form of its ketal IX since it did not react to form the semicarbazone until hydrolyzed with boiling dilute hydrochloric acid. The following diagram best expresses these results.



Only the ketal enol formulation I accounts for all of the above facts. The alternative cyclic structure, $\begin{array}{c} \text{H}-\text{C}=\text{C}-\text{OH} \\ | \quad | \\ \text{C}_6\text{H}_5 \quad \text{C}_6\text{H}_5 \\ \diagdown \quad \diagup \\ \text{CH}_2\text{O} \quad \text{O} \quad \text{C} \quad \text{C} \\ \diagup \quad \diagdown \\ \text{O} \quad \text{OCH}_3 \end{array}$, while it is consistent with many of the reactions, is excluded because it does not account for the stability of the compound as an enol or for the results of ozonization of both the enol and its methyl ether.

Methylation of the ketal enol with diazomethane gives largely the enol ether X in yields of 50%. A considerable amount of the non-crystalline structurally isomeric enol ether XI was obtained also; this was vacuum distilled and characterized. Both ethers were shown to contain three methoxyl groups, and both were hydrolyzed back to the ketal enol (I).



The structure of the enol ether X was demonstrated rigorously by ozonization which gave benzoic acid, only a trace of phenylglyoxylic acid, and a non-acidic product. The latter was isolated and characterized, and shown to be phenylglyoxylic acid methyl ester dimethyl ketal, XII, as follows: it contains three methoxyl groups, does not react with semicarbazide under conditions wherein phenylglyoxylic acid and its methyl ester both give crystalline semicarbazones easily, and is converted in good yield by hydrolysis with alkali into phenylglyoxylic acid which was isolated as the semicarbazone. The structure of the isomeric enol ether XI was also shown by ozonization which produced methyl benzoate in a yield of more than one molecule, thus demonstrating conclusively the location of a methoxyl group at each end of the chain. These results complete the proof of structure of the ketal enol I.

Benzoylation of the silver salt of the ketal enol gives a product which appears to consist largely of the oxygen benzoate, V (not isolated as a solid or characterized), as was shown by the following reactions carried out directly on the crude product: (a) mild alkaline hydrolysis gave benzoic acid and the ketal enol; (b) treatment with acetic anhydride and sulfuric acid brought about conversion into 2,5-diphenyl-2-methoxyfuranone-3, VIII (checking independently the position of one of the two methoxyl groups), and (c) ozonolysis gave chiefly benzoic acid and methyl benzoate

and only a very small amount of phenylglyoxylic acid (if a cyclic structure or an open chain structure analogous to VI were involved, large amounts of phenylglyoxylic acid would have been formed).

Incidental to these experiments an attempt was made to prepare the corresponding oxygen-benzoate of diphenylbutanetrione enol itself, namely, IV. In the various benzoylations of the sodium salt of the enol II, which have been previously described, this oxygen-benzoate undoubtedly was formed but only in small amounts. When the *silver* salt of II was treated in isopropyl ether with benzoyl chloride, however, the oxygen-benzoate IV evidently was produced in very considerable quantity. Neither the known 2-oxygen-benzoate VI nor the carbon-benzoyl derivative VII was formed in the reaction in significant amounts (these compounds crystallize easily and would have been isolated if present). We were unable to obtain the compound IV in a crystalline form or to demonstrate its existence rigorously, but the following reactions carried out directly on the crude material clearly indicated that it was present as the major constituent of the crude benzoylation product. Treatment with methanolic hydrogen chloride followed by methanolic sodium hydroxide gave the ketal enol I in 42% yield (incidentally this became the best method of preparation of the latter). Hydrolysis gave benzoic acid and diphenylbutanetrione enol II. Ozonolysis produced large amounts of benzoic acid and smaller amounts of phenylglyoxylic acid (in contrast with the oxygen-benzoate VI which gave the latter in good yield). The amount of phenylglyoxylic acid produced in the ozonization, however, was too large to be accounted for on the assumption that only the oxygen-benzoate IV was produced; the results seem to indicate that about 60–70% of IV was present together with as much as 20–30% of a 2-oxygen-benzoate presumably stereoisomeric with VI.

The evidence supporting the suggested mechanism of the accidental formation of the ketal enol I in the benzoylation of diphenyl-1,2,4-butanetrione enol (outlined in the first diagram) may now be considered advantageously. In this connection the following points should be mentioned. Dibenzoylbenzoyloxyethylene, VI, and diphenylbutanetrione enol itself, II, when treated with benzoyl chloride and then with methanolic alkali under the conditions of this experiment, give none of the ketal enol, and therefore are not involved

in the formation of the latter. The intermediates in the reaction are non-enolic and the ketal enol is not produced until after the treatment with excess of alkali. The primary intermediate is therefore very evidently the above described oxygen-benzoate IV which can be produced in much better yield by benzoylation of the silver salt of the enol II; this hypothesis is supported by the fact that reactions upon materials from both of the aforementioned sources led to similar results and to the ultimate production of the ketal enol. The secondary intermediate is presumed to be the enol benzoate, V, and to result from rapid catalytic methylation of the primary product IV. This secondary compound is formed directly in much better yield by acid-catalytic methylation of the product of benzoylation of diphenylbutanetrione silver enolate, as described above, or by benzoylation of the silver salt of the ketal enol itself. The presence of V in the products from these two sources was shown by the following three experiments carried out upon each sample independently, namely: alkaline hydrolysis to benzoic acid and the ketal enol, conversion by means of acetic anhydride and sulfuric acid into diphenylmethoxyfuranone, VIII, and ozonolysis to benzoic acid and methyl benzoate.

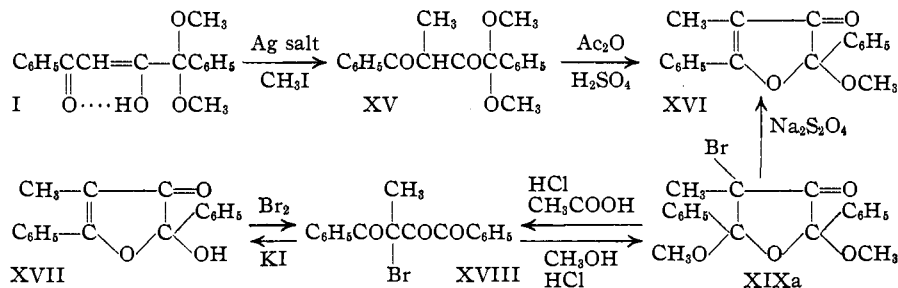
In view of the foregoing facts, then, there can be little doubt as to the course of the reaction as pictured in the first diagram, and as to the actual existence of the enol benzoates, IV, and V. It is surprising that the enhanced reactivity of the terminal carbonyl group rendering it capable of ketal formation appears only in the oxygen benzoate IV, and not in the isomeric 2-oxygen-benzoate, VI, or in other derivatives of diphenylbutanetrione enol, including even the supposed 4-methoxy compound,^{1a} $C_6H_5C(OCH_3)=CHCO-COC_6H_5$, which have been tested out in typical experiments.

A summary of the benzoylation results in this field is of interest and may now conveniently be given. Benzoylation of the *sodium salt* of diphenylbutanetrione enol (I) in isopropyl ether produces all of the three possible products which may be listed as follows: (a) the carbon-benzoyl product, isolable as 4-benzoyl-2,5-diphenyl-2-hydroxyfuranone-3 or as its 2-benzoate, VII, in yields of 10–15%; (b) the 2-oxygen-benzoate, dibenzoylbenzoyloxyethylene, VI, isolable as such or hydrolyzed and recovered as the enol, II, in yields of 10–15%; and (c) the structurally iso-

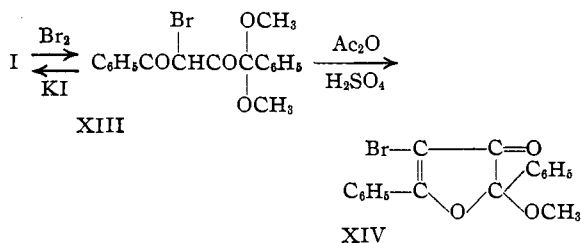
meric oxygen-benzoate, IV, not isolated but giving rise to the ketal enol, I, in 10–15% yields. Benzoylation of the *silver salt*, however, appears to involve no carbon-benzoylation and gives chiefly one of the two possible oxygen-benzoylation products. In the case of the ketal enol attempts to benzoylate the sodium salt failed but the silver salt reacts readily (and in the same sense as does diphenylbutanetrione silver enolate) to give largely the oxygen-benzoate, V.

Bromination of the ketal enol in alcohol or chloroform gives the monobromo diketone XVIII in nearly quantitative yield. This product does not enolize, gives no reaction with ferric chloride, and does not react further with bromine under ordinary conditions. It is easily reduced by potassium iodide or sodium hydrosulfite to regenerate the ketal enol. Attempts to enolize it with

Methylation of the silver salt of the ketal enol gave the carbon-alkylation product XV in good yield. No other products were isolated. The new methyl compound contains only two methoxyls and is not easily hydrolyzed by alkali; it is not, therefore, an enol ether, and the two methoxyls must correspond to those of the original ketal group. The structure was demonstrated by conversion by means of acetic anhydride and sulfuric acid into 2,5-diphenyl-2-methoxy-4-methylfuranone-3, XVI, which is known.^{1b} The keto form appears to be the stable one and attempts to obtain an enolic modification failed. This is to be contrasted with the case of the corresponding carbon-methyl derivative of diphenylbutanetrione enol itself, where cyclization is possible and where the stable hydroxyfuranone, XVII, is the only form isolable.



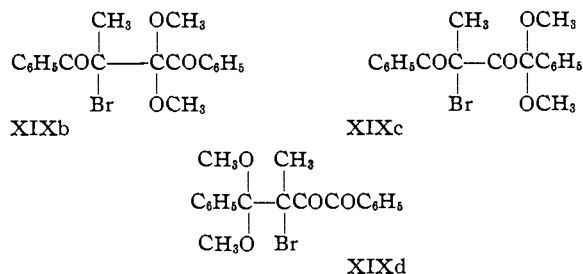
sodium alcoholate brought about reduction instead, the ketal enol I being the only product isolated. With acetic anhydride and sulfuric acid, it was converted into the known bromomethoxyfuranone XIV.



In the case of the monobromo derivative of diphenylbutanetrione enol itself, cyclization of the enol to the stable hydroxyfuranone renders it impossible to tell whether the open chain enol or keto form would be inherently the more stable; however, in the dimethyl series⁸ where cyclization apparently is excluded for steric reasons, the enol form of the monobromo derivative appears to be the more stable.

(3) Lutz and Terry, unpublished results.

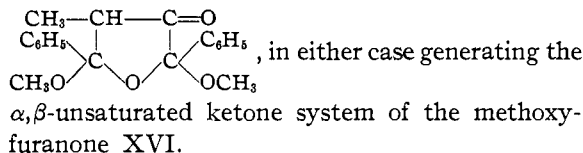
In an earlier communication^{1b} a ketal of XVIII, the bromo derivative of the carbon-methylation product of diphenylbutanetrione enol, was described and regarded as probably having the open chain structure, XIXb. The 1-carbonyl group of XVIII might have been involved instead, however, and XIXc is therefore a possible alternative formula. In either case the ketal formation would be the result of enhanced activity of a carbonyl group in an α -diketone system. Formula XIXd was not considered because the isolated terminal carbonyl group of the triketone should not be reactive.



In a reinvestigation of this substance we have

been able to demonstrate rigorously the location of one of the methoxyls at one end of the chain. Reduction in ethanol solution with sodium hydro-sulfite or with catalytic hydrogen gives 2,5-diphenyl-2-methoxy-4-methylfuranone-3, XVI. In this reaction the bromine has been eliminated together with one of the two methoxyl groups; the other methoxyl remains and is obviously in its original position since rearrangement is most unlikely under the conditions involved. The formulas XIXb and d are therefore excluded. The only other possible open-chain formula, XIXc, however, appears to be open to question because the compound is not reduced back to the ketal XV under conditions which effect immediate reduction of halogen from the various 3-halogeno-1,2,4-triketones, including XVIII, and from the bromo derivative of the ketal enol itself (XIII). The cyclic formulation XIXa was then considered. Although it has in it halogen alpha to a carbonyl group which should be easily reducible, it is a different structural type and might well be reduced somewhat less readily. Its relation to 2,5-diphenyl-2-hydroxy-4-methyl-furanone-3, XVII, and to the carbon-methyl derivative of the ketal enol, XV, is outlined in the diagram.

Positive evidence for the cyclic structure, XIXa, is found in the striking fact noted above that one of the methoxyl groups is invariably lost during reduction under conditions which would not be expected to cause disturbance or partial hydrolysis of the ketal group. The stability of the ketal linkage is demonstrated by the following facts: (a) the bromo ketal XIII is reduced under similar conditions but without loss of a methoxyl group, and (b) the ketal linkage in XV, the product which would be expected in the reduction of XIX if the open chain formula XIXc were correct, is not affected by conditions closely approximating those involved in the ethanol-sodium hydrosulfite reduction. The simultaneous elimination of the bromine and methoxyl during reduction, therefore, cannot reasonably be accounted for in terms of the open-chain ketal formula XIXc, but is consistent with the cyclic structure XIXa. The reaction may reasonably be interpreted in either of two ways, namely: (a) as a 1,4-reaction at the bromine and at the oxygen of the adjacent methoxyl, or (b) as a reductive elimination of bromine followed by spontaneous loss of methanol from the hypothetical intermediate saturated 2,5-dimethoxy - 2,5 - diphenyltetrahydrofuranone - 3,



Experimental Part

1,4-Diphenyl-4,4-dimethoxy-3-butanedione Enol, I.—Twenty-five grams of 1,4-diphenyl-1,2,4-butanetrione silver enolate, prepared according to the directions of Lutz and Stuart,^{1a} and dried in a vacuum desiccator over calcium chloride, was suspended in 100 cc. of absolute isopropyl ether; 9.9 g. of benzoyl chloride was added dropwise to the mechanically stirred mixture which was then refluxed for thirty minutes on a steam-bath. The precipitate of silver chloride was filtered off and the bulk of the solvent removed by evaporation under diminished pressure on a water-bath maintained at 50°. Five cc. of benzoyl chloride and then 10 cc. of methanol were added to the residual oil; then, with cooling in an ice-bath, 200 cc. of 10% sodium hydroxide in 80% methanol was added slowly, the mixture finally being warmed to 60° to complete the hydrolysis of the benzoates. Sodium benzoate crystallized from the solution. The mixture was then diluted with 2 liters of water and acidified with dilute hydrochloric acid. The precipitate was filtered off, dissolved in ether and extracted five times with 25-cc. portions of saturated sodium bicarbonate solution to remove the benzoic acid. The ether solution was then evaporated and the resulting oil crystallized on standing and cooling to give 7 g. of nearly pure product melting at 112–113°. Runs on a larger scale gave poorer yields. It was purified by repeated crystallizations from isopropyl alcohol, and obtained as colorless needles melting at 114° (corr.). It is quite soluble in most organic solvents and dissolves directly in 5% aqueous sodium hydroxide solution. It dissolves slowly in aqueous sodium carbonate solution when warmed.

Anal. Calcd. for $\text{C}_{18}\text{H}_{18}\text{O}_4$: C, 72.45; H, 6.1; OCH_3 , 20.8. Found: C, 72.66; H, 6.1; OCH_3 , 20.5.

The enol gave a deep red coloration in alcohol with ferric chloride. It did not react with *o*-phenylenediamine when heated in alcoholic solution with an excess of the reagent for five minutes.

The Preparation of the Ketal Enol I through Benzoylation of the Sodium Salt of Diphenylbutanetrione Enol (II).—As pointed out in the introduction the ketal enol was formed when the reaction mixture from this benzoylation was worked up. While the method is inferior as a means of preparation of I, details of the procedure are given because of the interest in the mechanism of the reaction and in the other products formed.

Twenty grams of the sodium salt of diphenylbutanetrione enol^{1a} was suspended in 100 cc. of dry isopropyl ether and 30 cc. of benzoyl chloride was added dropwise with mechanical stirring, the mixture being heated for three hours and filtered from sodium chloride and some 4-benzoyl-2-benzoyloxy-2,5-diphenylfuranone-3, VII, which separated at this point. The filtrate was evaporated under reduced pressure at room temperature to a thick oil to which was then added slowly with cooling in an ice-bath

200 cc. of 10% sodium hydroxide in 80% methanol. The sodium benzoate partially crystallized. After the mixture stood for three hours it was warmed to 60° to complete the hydrolysis. The mixture was then diluted with water to 2 liters, acidified with hydrochloric acid, and the resulting precipitate was filtered and dissolved in ether. Twenty-five extractions with saturated sodium bicarbonate solution were required to remove all of the 4-benzoyl-2,5-diphenyl-2-hydroxyfuranone-3. From these extracts on acidification, benzoic acid and the furanone crystallized and were separated by leaching the combined product on the filter funnel with hot water which removed the benzoic acid. The yield of the furanone was 5 g. The ether solution was then evaporated, giving an oil which on standing overnight deposited 3 g. of the ketal enol I. The addition of a little isopropyl alcohol usually facilitated the crystallization. From the filtrates small amounts of diphenylbutanetrione enol II were recovered.

A series of experiments was carried out on a number of compounds under conditions closely approximating those above in order to obtain information concerning the possibility that these compounds might be involved as intermediates in the formation of the ketal enol. The free diphenylbutanetrione enol reacted only partly to give small yields of dibenzoylbenzoyloxyethylene, VI, and in only one instance a trace of the ketal enol. Dibenzoylbenzoyloxyethylene, VI, reacted further only very slowly under these reaction conditions. Various attempts at catalytic methylation of the triketone enol (II) and the 2-enol benzoate (VI) in isopropyl ether, pure methanol, and in benzene, with benzoyl chloride added to furnish the acid through methanolysis, or with sulfuric acid instead, either were without effect or produced 2,5-diphenyl-2-methoxyfuranone, but in no case led to the formation of the ketal enol. The crystalline methyl ether of diphenylbutanetrione enol, $C_6H_5COCH=C(OCH_3)COC_6H_5$, and the 4-methyl ether, prepared by the action of diazomethane on the enol,^{1a} gave no ketal enol when subjected to the above procedure.

Reactions of 1,4-Diphenyl-4,4-dimethoxy-1,3-butanedione Enol. Conversion into Diphenylmethoxyfuranone (VIII).—A sample of the ketal enol was allowed to stand overnight in absolute methanol saturated with hydrogen chloride. The cyclic ether VIII was produced in excellent yield.

One gram of the ketal enol was suspended in 20 cc. of acetic anhydride containing one drop of concentrated sulfuric acid. The mixture was allowed to stand a half hour at 25°, and decomposed in the usual manner in ice water. A yield of 0.75 g. (85%) of the methoxyfuranone, VIII, was obtained, and was purified by crystallization from isopropyl alcohol and identified by mixture melting point.

Hydrolysis.—A solution of 0.5 g. of the ketal enol I in 10 cc. of concd. acetic acid and 0.5 cc. of concd. hydrochloric acid was refluxed for thirty minutes. Dilution with water gave 0.36 g. of nearly pure diphenylbutanetrione enol (a yield of 90%) which was purified by crystallization from ethyl acetate-petroleum ether mixtures and identified by mixture melting point with an authentic sample.

A sample of the ketal enol was recovered unchanged as

the sodium salt after treatment for two hours under refluxing with (a) 1.5 equivalents of sodium methylate in methanol, (b) 10% sodium hydroxide in 80% methanol, and (c) 50% aqueous sodium hydroxide solution.

Ozonolysis.—Ozone was passed through a solution of 1.6 g. of I in dry chloroform at 0° for six hours and the solvent then evaporated in a stream of dry air. The residue was digested with 10 cc. of water and then leached out with 30 cc. of saturated sodium bicarbonate solution. Extraction with ether and subsequent evaporation gave the non-acidic product which was hydrolyzed with methanolic potassium hydroxide, giving 0.14 g. of benzoic acid. The bicarbonate solution on acidification gave 0.7 g. of benzoic acid, but treatment of the remaining solution with semicarbazide hydrochloride gave no precipitate of phenylglyoxylic acid semicarbazone (even traces of phenylglyoxylic acid would have given a precipitate under these conditions). When these residual solutions were boiled with dilute hydrochloric acid, however, and semicarbazide again added, 0.07 g. of phenylglyoxylic acid semicarbazone was isolated and identified by mixture melting point with an authentic sample.

1,4-Diphenyl-3,4,4-trimethoxy-2-butenone-1, X.—A solution of 16 g. of the ketal enol I in absolute ether was treated with two equivalents of diazomethane in the same solvent, the mixture being allowed to stand overnight and then evaporated under reduced pressure to remove the solvent. The resinous residue was dissolved in ethyl alcohol, the enol ether crystallizing as colorless prisms in a yield of 8.7 g. (52%). It was purified by repeated crystallization from isopropyl alcohol or from 70% ethanol and melted at 115° (corr.).

Anal. Calcd. for $C_{18}H_{20}O_4$: C, 73.0; H, 6.41; OCH_3 , 29.8. Found: C, 72.65; H, 6.6; OCH_3 , 30.3.

Action of Alcoholic Hydrogen Chloride.—A sample of the above product (0.05 g.) was suspended in methanol which had been saturated at 0° with dry hydrogen chloride. The mixture was allowed to stand overnight and on evaporation under reduced pressure gave 0.035 g. of nearly pure 2,5-diphenyl-2-methoxyfuranone-3 which was purified and identified by mixture melting point.

Hydrolysis.—The ether was recovered unchanged (a) after standing for two hours at 25° with 1.5 equivalents of sodium methylate in methanol, and (b) after being subjected for fifteen minutes to the action of refluxing 5% methanolic sodium hydroxide.

When 0.1 g. of the ether was treated for half an hour with 10 cc. of refluxing 25% methanolic sodium hydroxide and the mixture poured into 20 cc. of water, 0.04 g. of the ketal enol sodium salt (I) separated and was recovered. On acidification the filtrate deposited 0.02 g. of the free enol. The total yield of the salt and the free enol was 61%.

One-tenth gram of the ether was subjected for half an hour to the action of 5 cc. of refluxing concd. acetic acid containing 5 drops of concd. hydrochloric acid. On dilution with water 0.04 g. of nearly pure diphenylbutanetrione enol, II, precipitated and was purified and identified by mixture melting point.

Ozonization.—Three grams of the methyl ether in 40 cc. of dry chloroform was ozonized for four hours at 0°, the solvent subsequently being evaporated in a stream of dry air. Water was then added and the mixture heated for a

short time to ensure complete hydrolysis of the ozonides. Sodium bicarbonate was then added, and after digestion the solution was extracted with ether to remove the non-acid material. From the latter, on subsequent evaporation, hydrolysis of the resulting oil with potassium hydroxide, and then treatment with semicarbazide hydrochloride, a yield of 45% of phenylglyoxylic acid semicarbazone was obtained and identified by mixture melting point with an authentic sample. From the sodium bicarbonate solution on acidification a 43% yield of benzoic acid was obtained. Addition of semicarbazide hydrochloride to the filtrate gave a trace of phenylglyoxylic acid semicarbazone.

In another experiment on 1.97 g. of the methyl ether, the ethereal solution of the non-acidic oil obtained as described above was divided into three equal parts. One portion was evaporated, and the resulting oil treated with 10 cc. of methanol containing three equivalents of potassium hydroxide; after boiling this solution for five minutes, 10 cc. of water was added and the solution again boiled for fifteen minutes; on acidification and treatment with semicarbazide, 0.15 g. of the semicarbazone of phenylglyoxylic acid was obtained. The second portion of the ether solution was evaporated, and 10 cc. of methanol, 0.5 g. of semicarbazide hydrochloride, and 0.5 g. of anhydrous sodium acetate were added, followed by enough water to bring about solution of the solid materials. The solution was then made slightly alkaline with sodium carbonate. No precipitate was formed after standing overnight at room temperature (if phenylglyoxylic methyl ester had been present under these conditions it would have precipitated as the very difficultly soluble semicarbazone). The solution was then diluted with water and the phenylglyoxylic ester ketal was extracted with ether. The solvent was evaporated and the oily residue was treated with 10 cc. of methanol, 1 cc. of water and 5 drops of concd. hydrochloric acid and the mixture then boiled for fifteen minutes. On dilution with water, neutralization, and treatment with semicarbazide hydrochloride no semicarbazone could be obtained even after standing for several days with further dilution with water. The ketal and ester groupings finally were hydrolyzed by extracting the oil with ether, evaporating off the solvent and taking the oil up in methanolic potassium hydroxide and then boiling. On subsequent neutralization and treatment with semicarbazide hydrochloride, 0.05 g. of phenylglyoxylic acid semicarbazone precipitated quickly. Careful extraction of the remaining solution failed to reveal the presence of any benzoic acid.

Phenylglyoxylic acid methyl ester semicarbazone, $C_6H_5C(=NNHCONH_2)COOCH_3$, was prepared by the following three methods. (a) A sample of phenylglyoxylic acid semicarbazone was added to an ether solution of an excess of diazomethane, and the ester obtained as fluffy colorless needles on evaporation of the solvent and crystallization from ethyl acetate-petroleum ether mixtures or from isopropyl ether. (b) A solution of 1 g. of phenylglyoxylic acid semicarbazone in 10 cc. of methanol saturated with dry hydrogen chloride at 0° was allowed to stand overnight. Partial reaction had occurred and 0.3 g. of the ester was separated from unchanged acid and identified by mixture melting point with the above sample. (c) A sample of phenylglyoxylic acid methyl ester was prepared

and treated under conditions approximating those involved in the ozonization of the ketal enol methyl ether described above.

A solution of 1 g. of dibenzoylmethoxyethylene, $C_6H_5COCH=C(OCH_3)COC_6H_5$, in 40 cc. of dry chloroform was ozonized at 0° for six hours and the solvent evaporated and the oily residue hydrolyzed with water in the usual way. Treatment with sodium bicarbonate and extraction with ether separated the acids from phenylglyoxylic methyl ester. The latter, obtained as an oil from evaporation of the ether solution, was taken up in 10 cc. of methanol and treated with 0.5 g. of semicarbazide hydrochloride. On partial dilution with water and standing overnight, 0.2 g. of crude crystalline material was deposited and after purification was identified as phenylglyoxylic methyl ester semicarbazone by mixture melting point with the sample prepared as described above (a). The semicarbazone melted when pure at 123.5° (corr.).

Anal. Calcd. for $C_{10}H_{11}O_3N_3$: N, 19.0. Found: N, 19.1.

Hydrolysis.—A solution of 0.05 g. of the ester in 10 cc. of methanol with 0.015 g. of potassium hydroxide and one drop of water was allowed to stand for six hours at room temperature. A precipitate appeared which dissolved on dilution with water. Upon acidification and standing a mass of fine colorless needles, melting at 263° with decomposition, deposited and gave no mixture melting point depression with authentic samples of phenylglyoxylic acid semicarbazone. The melting point, however, was considerably higher than that reported in the literature for this compound, consequently the sample was further purified by repeated crystallization from ethanol. It was obtained as colorless feathery needles melting at 259° (corr. with decomposition) and was analyzed.

Phenylglyoxylic Acid Methyl Ester Dimethyl Ketal, XII.—A partially successful attempt was made to isolate this product from the ozonization of 8 g. of the ketal enol ether X. The ether extract containing the non-acidic products was dried for twelve hours over calcium chloride and the solvent was then evaporated. The residue was fractionally distilled in the high vacuum oven at 60–110° on to a cold finger condenser, and 2 g. of a clear faintly yellow mobile oil obtained. This was redistilled. However, successive drops showed some variation in refraction index and the compound was very evidently not pure. The best sample showed $n_D^{25} 1.5038$.

Anal. Calcd. for $C_{11}H_{14}O_4$: C, 62.8; H, 6.7; OCH_3 , 44.3. Found: C, 63.2; H, 5.9; OCH_3 , 38.1.

While these analyses were not satisfactory, they leave little doubt that the compound is the dimethyl ketal XII with some persistent impurity present. Unfortunately lack of material prevented further and more elaborate purification.

Hydrolysis of 0.75 g. of XII by means of 0.6 g. of potassium hydroxide in 7 cc. of 70% methanol, refluxing for fifteen minutes and working up in the usual way, gave 0.71 g. of phenylglyoxylic acid semicarbazone melting at 199° (a yield of 97%) which was identified by mixture melting point.

From the foregoing facts it is evident that the impurity present in the best samples of the ketal ester XII is free phenylglyoxylic methyl ester resulting from partial

hydrolysis of the ketal grouping. This would account for the low methoxyl, high carbon and low hydrogen analyses, and for the high yield of phenylglyoxylic acid on hydrolysis.

1,4-Diphenyl-1,4,4-trimethoxy-1-butanone-3, XI.—The alcohol filtrate from the crude isomeric enol ether X, obtained as described above by the action of diazomethane on 16 g. of the ketal enol (I), was evaporated in a current of dry air on a water-bath, and about 6 g. of a yellow oil was obtained. Half of this was fractionally distilled in the high vacuum oven at 135–140°, the product being collected dropwise on a cold finger condenser. The refractive index on successive drops of the pale yellow, viscous distillate became constant at n_D^{25} 1.5838.

Anal. Calcd. for $C_{18}H_{20}O_{11}$: OCH₃, 29.9. Found: OCH₃, 29.5.

Hydrolysis.—A sample of the above (0.11 g.) in 10 cc. of 20% methanolic potassium hydroxide was refluxed for fifteen hours and the solution then diluted to 100 cc. with water. On acidification and extraction with ether, 0.1 g. of the ketal enol (I) was isolated and identified by mixture melting point.

Ozonization of the oil in the usual way in dry chloroform at 0° for ten hours gave, on hydrolysis and treatment with sodium bicarbonate, a non-acidic oil which distilled at 194° and which was further identified as methyl benzoate by hydrolysis in good yield to benzoic acid. Unfortunately, a part of the methyl benzoate was lost through accident; nevertheless the yield (pure) was 52%, showing conclusively that more than one molecule had been produced by the ozonization. The sodium bicarbonate solution of the acidic products gave on acidification a trace of benzoic acid, and also a trace of phenylglyoxylic, which was isolated as its semicarbazone and identified.

The ketal enol sodium salt was prepared by treating the ketal enol in methanol directly with the calculated amount of sodium methylate solution. The sodium salt crystallized from solution as colorless needles and was filtered off and washed with methanol. Further purification (unnecessary for ordinary use) was effected by crystallization from ethanol. The salt is difficultly soluble in cold water and alcohol.

Anal. Calcd. for $C_{18}H_{17}O_4Na$: Na, 7.2. Found: Na, 7.5.

The ketal enol silver salt was prepared by adding the calculated amount of 2% silver nitrate solution to a cold aqueous solution of the sodium salt of the ketal enol. It was obtained as a white powder which was not stable and in time turned dark, particularly when exposed to light, or when an excess of silver nitrate was used in the preparation. It was usually handled by filtering as quickly as possible, purified by thorough washing with water, and stored in a vacuum desiccator.

Anal. Calcd. for $C_{18}H_{12}O_4Ag$. Ag, 26.6. Found: Ag, 27.0.

Benzoylation of the Ketal Enol.—Pyridine-benzoic anhydride mixtures at refluxing temperature or upon long standing at room temperature were without effect. The sodium salt in aqueous alkaline solution, when treated with an excess of benzoyl chloride, gave only unchanged ketal enol when the mixture was worked up in the usual way.

Benzoylation of the Ketal Enol Silver Salt.—A sample of the salt (0.66 g.) which had been dried for several days in a vacuum desiccator, was suspended in 85 cc. of absolute isopropyl ether and 0.5 cc. of benzoyl chloride was added, the mixture being stirred mechanically. Precautions were taken against admission of moisture, including pre-drying of all apparatus. After refluxing for two hours and filtering to remove silver halide, the solution was extracted repeatedly with saturated aqueous sodium bicarbonate solution to hydrolyze the benzoyl chloride and to remove benzoic acid. The isopropyl ether solution on evaporation left a colorless oil which we were unable to crystallize. The oil was dissolved in 15 cc. of methanol. One-third of this solution was added to 10 cc. of methanol saturated at 0° with dry hydrogen chloride. After standing overnight and working up the product, 0.1 g. (69%) of 2,5-diphenyl-2-methoxyfuranone-3 was obtained and identified. A second 5-cc. portion of the methanol solution (one-third of the total) was treated with 5 cc. of 50% methanolic potassium hydroxide solution, the mixture being allowed to stand for two hours, then heated to 60°, diluted with water, and acidified. The solution was then extracted with ether, from which the benzoic acid was removed by repeated extraction with saturated sodium bicarbonate solution. From the latter solution on acidification, 0.06 g. of benzoic acid was recovered, a yield of 72%. From the ether solution, on evaporation, 0.15 g. of the ketal enol was recovered and identified (yield, 86%). The third 5-cc. portion of the methanol solution of the ketal enol benzoate was evaporated to dryness under reduced pressure and the oil treated with 10 cc. of acetic anhydride and three drops of concd. sulfuric acid. On hydrolysis and working up the product in the usual way, 0.05 g. of 2,5-diphenyl-2-methoxyfuranone-3 was isolated and identified.

Ozonization.—Four grams of crude oily ketal enol benzoate, V, freshly prepared as described above, was ozonized for four hours in 40 cc. of dry chloroform at 0°, the solvent then being evaporated and the ozonides hydrolyzed with water in the usual way. The product was treated with sodium bicarbonate solution and, after digestion, the mixture was extracted with ether. From the sodium bicarbonate solution upon acidification benzoic acid appeared and was filtered off. Treatment of the solution with semicarbazide hydrochloride gave 0.2 g. of phenylglyoxylic acid semicarbazone (a yield of 9.5%), and from the filtrate, on extraction with ether, more benzoic acid was recovered, the total yield being 0.7 g. (30% of the calculated two equivalents). The non-acidic oil was obtained from the ether solution on evaporation. This was hydrolyzed with potassium hydroxide and gave approximately one equivalent of benzoic acid, but no phenylglyoxylic acid was detected in the filtrate.

Ozonization of a sample of the crude ketal enol benzoate, prepared by the action of methanolic hydrogen chloride on the enol benzoate, IV, obtained from diphenylbutanetrione silver enolate, was carried out as follows: a sample of the silver salt of II was suspended in absolute isopropyl ether and treated with benzoyl chloride, the mixture being refluxed for thirty minutes and filtered to remove silver chloride. The solvent was removed by evaporation at room temperature under reduced pressure and the oily product treated with benzoyl chloride and then with

methanol. The mixture after standing for ten minutes was diluted with 10% sodium hydroxide in 80% methanol and further diluted with water. The solution was then extracted with ether. A small portion was evaporated to an oily residue and treated with acetic anhydride and sulfuric acid, yielding 2,5-diphenyl-2-methoxyfuranone-3 which was identified. The bulk of the ether solution was then evaporated and the oily residue dissolved in chloroform and ozonized, yielding benzoic acid and a non-acidic oil which was shown to be methyl benzoate by hydrolysis which gave only benzoic acid and no phenylglyoxylic acid (even small amounts of the latter respond to the semicarbazide test and would have been found if present).

Benzoylation of Diphenylbutanetrione Enol Silver Salt.—A suspension of 13.5 g. of silver salt in 150 cc. of isopropyl ether (dried over sodium) and 5.4 g. of benzoyl chloride was refluxed for thirty minutes with mechanical stirring. The precipitate of silver chloride was filtered off and the solvent removed by evaporation under reduced pressure at room temperature. The nearly colorless oily residue, which we were unable to induce to crystallize, was dissolved in 100 cc. of absolute ether and portions were tested as follows.

(a) The oil obtained from 5 cc. of the ether solution was dissolved in 10 cc. of methanol saturated at 0° with dry hydrogen chloride. On standing overnight and evaporating at room temperature under reduced pressure, a crystalline residue was obtained which was digested and washed with cold methanol and identified by mixture melting point as 2,5-diphenyl-2-methoxyfuranone-3. The yield was 0.3 g.

(b) The oily product from evaporation of 10 cc. of the ether solution was taken up in 10 cc. of 10% potassium hydroxide in 80% methanol and the solution heated to 60° and allowed to stand for thirty minutes. The mixture was then diluted with water, acidified, and extracted with ether. The ether layer was extracted several times with saturated sodium bicarbonate solution and evaporated, leaving a residue of 0.6 g. of diphenylbutanetrione enol which was identified by mixture melting point.

Ozonization of a sample of the crude enol benzoate, IV, was carried out as follows: 3.8 g. of diphenylbutanetrione silver enolate was suspended in 80 cc. of absolute isopropyl ether and 1.3 cc. of benzoyl chloride was added. The mixture was then stirred mechanically for two hours with refluxing. The silver halide was filtered off and washed, the filtrate chilled in the ice-bath, and washed, once with ice cold 1% sodium hydroxide solution to remove unchanged enol, and then three times with ice water. The oily product obtained by evaporation of the ether solution under reduced pressure, which now gave no ferric chloride test for free enol, was taken up in 40 cc. of dry chloroform and a stream of ozonized oxygen passed through for nine hours at 0°. The solvent was removed by evaporation and the ozonides were decomposed with water in the usual way. The product was digested with saturated sodium bicarbonate solution for twelve hours. The non-acidic material was extracted by means of ether and hydrolyzed with methanolic potassium hydroxide, giving on acidification 0.4 g. of benzoic acid and 0.65 g. of crude water insoluble material which gave 0.15 g. of ketal enol when purified by crystallization from ethanol (hydrolysis of un-

changed material, (IV) had been incomplete and acid catalytic methylation resulted). From the sodium bicarbonate solution on acidifying 1.7 g. of benzoic acid (86% of the calculated three equivalents) was obtained, and the aqueous filtrates when treated with semicarbazide gave 0.5 g. of phenylglyoxylic acid semicarbazone (44% of one equivalent).

The K. Meyer titration of the ketal enol was carried out by dissolving the sample in ethanol and cooling to -19° in an ice- and salt-bath. An excess of freshly prepared bromine solution in ethanol, precooled to -19°, was added with mechanical stirring. This operation was followed within one second by the addition of β -naphthol to destroy the excess of bromine. Upon addition of potassium iodide and warming to 40°, iodine was liberated, and on titration in the usual way showed almost complete enolization (92-94%). On dilution of the resulting mixture with water, making alkaline with sodium carbonate and boiling off part of the alcohol, then acidifying, the ketal enol precipitated and was recovered and identified.

2 - Bromo - 4,4 - dimethoxy - 1,4 - diphenyl - 1,3 - butanedione, XIII.—To a solution of 0.2 g. of the ketal enol in ethanol at -18° was added with mechanical stirring a solution of one equivalent of bromine in the same solvent, also precooled to -18°. The bromine was used up and a slight excess was added, imparting a persistent coloration to the solution. Upon neutralization and dilution with aqueous sodium carbonate and extraction with ether, a nearly quantitative yield of the bromo diketone XIII was obtained (0.24 g.). It was purified by repeated crystallizations from ethanol and obtained as colorless prisms melting at 122° (corr.). It did not give a color test with alcoholic ferric chloride.

Anal. Calcd. for $C_{18}H_{17}O_4Br$: C, 57.3; H, 4.5. Found: C, 57.2; H, 4.3.

Bromination of the sodium salt of I in aqueous medium, adding the bromine in a small volume of ethanol, gave results almost identical with the above.

Conversion of the bromo diketone to 4-bromo-2,5-diphenyl-2-methoxyfuranone-3, XIV, was brought about in two ways as follows. (a) A suspension of 0.05 g. of XIII in 5 cc. of acetic anhydride and one drop of concd. sulfuric acid was allowed to stand for fifteen minutes and was then hydrolyzed and worked up in the usual way, giving a crude product which after one crystallization from methanol weighed 0.03 g. (62%) and was identified by mixture melting point; and (b) a solution of XIII in saturated methanolic hydrogen chloride, upon standing overnight at room temperature, produced a similar result.

Attempts to convert the bromo diketone XIV into an enolic form or a sodium enolate failed. When sodium methylate was used reduction occurred and only the ketal enol I was isolated.

Reduction with sodium hydrosulfite was carried out in 80% ethanol upon refluxing for thirty minutes and the ketal enol was produced in good yield.

1,4 - Diphenyl - 4,4 - dimethoxy - 2 - methyl - 1,3 - butanedione, XV.—A suspension of 0.67 g. of the ketal enol silver salt in 25 cc. of absolute isopropyl ether and 0.5 cc. of methyl iodide was stirred mechanically and refluxed for five hours and then filtered to remove silver halide. On evaporation of the solvent 0.35 g. of crystalline product

was obtained, a yield of 60%. It was purified by repeated crystallization from isopropyl alcohol or 70% ethanol and was obtained as colorless prisms melting at 87° (corr.). It did not give a color reaction with alcoholic ferric chloride and was insoluble in alkali.

Anal. Calcd. for $C_{19}H_{19}O_4$: C, 73.0; H, 6.41; OCH_3 , 19.9. Found: C, 73.0; H, 6.0; OCH_3 , 19.95.

All attempts to obtain a sodium enolate through the action of sodium hydroxide or sodium methylate were unsuccessful. No evidence of appreciable enolization was obtained.

Conversion to 2,5-diphenyl-2-methoxy-4-methylfuranone-3, XVI, was brought about in two ways: (a) a solution of 0.05 g. of XV in 10 cc. of saturated methanolic hydrogen chloride, allowed to stand overnight at room temperature, and worked up in the usual way, gave 0.03 g. (67%); and (b) 0.05 g. of XV in 10 cc. of acetic anhydride and one drop of concd. sulfuric acid, after standing for thirty minutes at room temperature, and hydrolyzed in water and worked up in the usual way, gave 0.035 g. of product (70%) which was identified by mixture melting point with an authentic sample.

A sample of XV was recovered unchanged after subjecting it to the action of sodium hydrosulfite in boiling 80% ethanol for thirty minutes.

4 - Bromo - 2,5 - dimethoxy - 2,5 - diphenyl - 4 - methyl-tetrahydrofuranone-3, XIXa (previously described as 3-bromo - 2,2 - dimethoxy - 1,4 - diphenyl - 3 - methylbutanedione-1,4,^{1b} XIXb) was prepared according to the directions of Lutz and Stuart.^{1b} Attempts to reduce the compound under the following conditions were without effect: (a) 0.1 g. was dissolved in 10 cc. of methanol containing 2 drops of concd. hydrochloric acid and an excess of potassium iodide, and the mixture was then refluxed for thirty minutes; and (b) 0.05 g. was dissolved in 5 cc. of concd. acetic acid, 0.5 g. of potassium iodide was added, and the mixture was boiled for five minutes. In both cases unchanged material was recovered and identified.

Reduction of 0.1 g. was effected in 10 cc. of 80% ethanol with 0.5 g. of sodium hydrosulfite upon refluxing the mix-

ture for thirty minutes with stirring. On dilution with water and extraction with ether 0.06 g. (84%) of 2,5-diphenyl-2-methoxy-4-methylfuranone-3 was isolated and identified by mixture melting point.

Catalytic hydrogenation of 0.05 g. with 0.05 g. of palladium on calcium carbonate as catalyst in 3 cc. of ethanol, using a semi-micro hydrogenation system, showed absorption of approximately the calculated amount of hydrogen. On filtering, evaporation of the solvent, and then crystallization from 70% ethanol, 0.03 g. of 2,5-diphenyl-2-methoxy-4-methylfuranone-3 melting at 64-65° was obtained and identified by mixture melting point with an authentic sample.

Summary

The preparation, mechanism of formation, and proof of structure of 4,4-dimethoxy-1,4-diphenyl-1,3-butanedione enol are discussed.

The benzylation of 1,4-diphenyl-1,2,4-butanetrione sodium enolate has now been shown to give the carbon-benzoyl and both of the two possible oxygen-benzoyl derivatives, but the silver salt gives largely oxygen-benzoyl derivatives.

The reactions of 4,4-dimethoxy-1,4-diphenyl-1,3-butanetrione enol are reported and include the following: benzylation of the silver salt gives largely one of the two possible oxygen-benzoates; diazomethane converts the compound into the two expected structurally isomeric methyl ethers; bromination gives the bromo diketone; and methylation of the silver salt gives the carbon-methyl derivative.

The ketal obtained from 3-bromo-1,4-diphenyl-3-methyl-1,2,4-butanetrione is shown to have a cyclic structure.

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Halogen Substituted Benzopyrylium Salts

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The general structure of the benzopyrylium salts has been established but the exact arrangement of the double bonds and assignment of a definite position to the positive charge have not been settled. Benzopyrylium salts differ from simple oxonium salts of ethers and γ -pyrones. The latter are produced by a pure addition reaction whereas the formation of benzopyrylium salts involves an actual reaction with an acid and elimination of water. In this respect they resemble the carbonium salts derived from triarylcarbinols

and hence it has been suggested that the benzopyrylium salts are carbonium or carbenium salts¹ in which the positive charge may be on either carbon atom 2 or 4 which has been designated as the "heteropolar atom." If this is the case it is possible that the carbonium ion may exist in several tautomeric (or resonance) forms.

(1) Dilthey, *J. prakt. Chem.*, **94**, 53 (1916); *ibid.*, **95**, 107 (1917); *Ber.*, **58**, 261 (1920); *J. prakt. Chem.*, **131**, 1 (1931); *ibid.*, **138**, 42 (1933); *Ber.*, **64**, 2082 (1931). See Hill, *Chem. Rev.*, **19**, 27 (1936); for a summary of the evidence bearing on the structure of benzopyrylium salts.