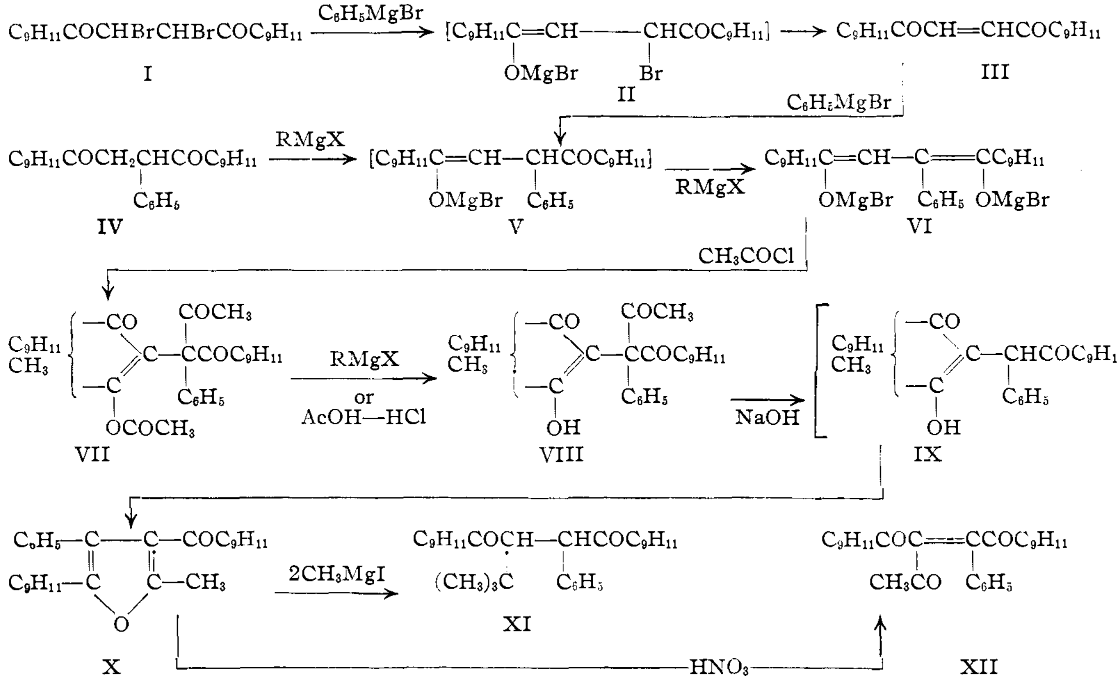
[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

The Acylation of the Di-enolate of 1,4-Dimesityl-2-phenylbutanedione-1,4

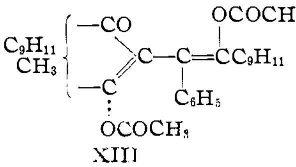
BY ROBERT E. LUTZ AND WILLIAM G. REVELEY[1]

This investigation came as the result of an attempt to obtain dimesitylbutanedione di-enolate, $C_9H_{11}C(OMgBr){=}CH{-}CH{=}C(OMgBr)C_9H_{11}$, possibly a stereoisomer of the one described in the preceding paper,[2] by reductive enolization of dibromodimesitylbutanedione (I). When the product of this reaction was treated with acetyl chloride, there resulted a compound which analysis showed to be a triacetyl derivative and to contain an additional phenyl group. In this reaction, especially when an insufficient quantity of phenylmagnesium bromide was used, there always could be isolated dimesitylbutenedione (III) which evidently was an intermediate and could be used in place of the dibromide (I) to give the same end result. The course of the changes involved may best be pictured as reductive enolization at one α-bromocarbonyl group, 1,4-loss of magnesium halide to give dimesitylbutenedione (III), 1,4-addition of phenylmagnesium bromide to give V, enolization to the dienolate VI, and finally acylation to the triacetyl derivative VII.

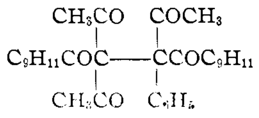


The dienolate VI, of course, is best prepared directly from dimesitylphenylbutanedione (IV) or dimesitylbutenedione (III) by the action of phenylmagnesium bromide.

The triacetyl compound obtained as described above is regarded as an enol acetate of a di-(carbon-acetyl) derivative of VI on the basis of the following evidence. Hydrolysis of the compound by means of concentrated hydrochloric and acetic acids at room temperature or by means of Grignard reagent eliminated only one acetyl group. This and only this acetyl is therefore presumed to have been attached to oxygen as in formula VII. The facile cleavage of only one acetyl group appears to exclude the alternative di-enol diacetate formula (XIII), but it does not exclude the tri-carbon-acetyl formula (XIV) because a compound of this type might undergo facile cleavage of one acetyl group.



XIII



$$\underset{CH_3CO}{\overset{CH_3CO}{C_9H_{11}CO\overset{|}{\underset{|}{C}}}}{-}\underset{C_6H_5}{\overset{COCH_3}{\overset{|}{\underset{|}{C}}COC_9H_{11}}}$$

XIV

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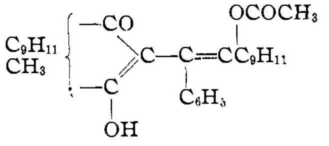
[1] Philip Francis duPont Fellow, 1939-1940. Present location, National Aniline and Chemical Company, Buffalo.

[2] Lutz, Reveley and Mattox, THIS JOURNAL, 63, 3171 (1941).

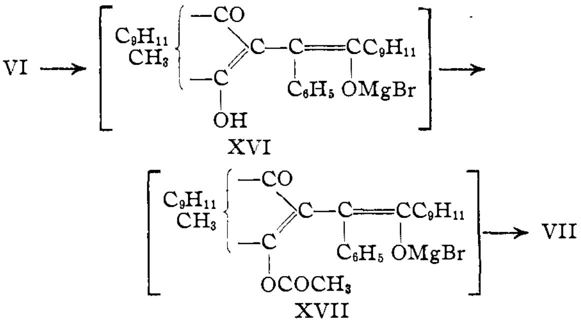
The product of hydrolysis of the triacyl compound, namely, VIII, was enolic and gave a typical ferric chloride color reaction which indicated beyond doubt the β-diketone enol system and consequently the 3-carbon-acetyl group. Furthermore, the enol reacted immediately and quantitatively with methylmagnesium iodide with evolution of one molecule of methane. The location of this carbon-acetyl group at the 3-position was demonstrated independently by the action of sodium hydroxide which caused elimination of the third acetyl group and at the same time furanization to X. The structure of the furan and the location of its methyl group were subsequently determined by conversion with methylmagnesium iodide into dimesityl-*t*-butylbutanedione[3] (XI) and by the characteristic oxidative ring fission to the corresponding unsaturated triketone[4] XII.

The third acetyl group of VII must be attached at the 2-carbon, rather than through oxygen at the only alternative 1-position (*cf.* XIII and XV), because this group resists acid hydrolysis and cleavage by Grignard reagent to a degree greater than would have been expected of a 1-oxygen-acyl group even though the latter grouping would be sterically hindered to some extent. The slow evolution of a second molecule of methane at 100° by the action of methylmagnesium iodide on VIII indicated enolization of this 2-carbon-acetyl group, a result which distinguishes between the formula VIII and the alternative one, XV, since the latter would have shown only one active hydrogen and two additions.



XV

The course of the acylation of the di-enolate VI probably involves three steps as follows: first, carbon-acylation at the 4-enolate group to give XVI, followed by oxygen-acylation of the resulting β-diketone enol group to give XVII, and then carbon-acylation at the 1-enolate group to give VII. The basis for this particular order of reactions is the fact that the compound VIII, containing the free β-diketone enol group and with the second carbon-acetyl group already located at the 1-enolate position, could not then be acylated to the triacetyl compound VII in repeated independent experiments under comparable conditions. Perhaps the presence of the 2-acetyl group of VIII contributes enough steric hindrance to block acylation at the β-diketone enol group, or possibly an intermediate, XVI or XVII, involves a more favorable configuration or more reactive state than in the case of direct reaction with the enol VIII.



XVI

XVII

The foregoing results show that carbon rather than oxygen-acylation of both di-enolate groups of dimesitylphenylbutanedione is the dominant type of reaction. This is perhaps not surprising in view of the fact that the free enolic or di-enolic forms ketonize with relative ease.[5]

Experimental Part

The Di-bromomagnesium Di-enolate of 1,4-Dimesityl-2-phenylbutanedione-1,4 (VI).—This was obtained, as described in the introduction, from dibromodimesitylbutanedione (I) by the action of phenylmagnesium bromide. Since this method is an inferior one, details will be omitted. The best preparation started with dimesitylphenylbutanedione (IV), which was allowed to react with methylmagnesium iodide under the conditions of the Zerewitinoff determination of active hydrogen. In a quantitative test, 1.8 equivalents of methane was evolved in less than two minutes at room temperature. Secondary reactions evidently interfere since on hydrolysis only poor yields of the saturated diketone could be obtained. Attempts to prepare a monoenolate by allowing the reaction to go at a low temperature (0°) were unsuccessful, and attempts to make a bromo derivative failed. Attempts to obtain a monoenolate and a monoacetate through addition of phenylmagnesium bromide to dimesitylbutenedione (III) at low temperature in a bath of ethanol and solid carbon dioxide, also failed to produce significant results.

2,3-Diacetyl-1,4-dimesityl-2-phenylbutanedione-1,4 Enol Acetate (VII).—A suspension of the di-enolate VI was prepared by adding 44 g. of dry powdered dimesitylbutenedione (III) in small portions with vigorous stirring

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[3] Lutz and Reveley, This Journal, 63, 3180 (1941).

[4] Lutz and Boyer, *ibid.*, 63, 3189 (1941).

[5] This comment is based on the observation by Kohler and Baltzly that in a great many instances [Kohler and Baltzly, *ibid.*, 54, 1594 (1932); Fuson, Fisher, Ullyot and Fugate, *J. Org. Chem.*, 4, 111 (1939)] highly hindered and more than usually persistent enols show a lowered tendency toward carbon-acylation and an enhanced tendency toward oxygen-acylation.

over the course of one hour to a solution of phenylmagnesium bromide made from ten grams of magnesium in ethyl ether and maintained at 25°. The mixture was then refluxed for twelve hours under an atmosphere of nitrogen. cooled thoroughly in an ice and salt mixture, and poured slowly with vigorous stirring into 600 cc. of dry ether containing 90 cc. of acetyl chloride. at −10°. The operation was carried out under dry nitrogen and the temperature was not allowed to exceed 0°. The di-enolate dissolved immediately and the solution turned red. then yellow. and a white precipitate separated. After stirring for half an hour with the temperature at 0°, the mixture was hydrolyzed by means of a large excess of crushed ice. The ether solution was separated, washed with water, with dilute sodium bicarbonate solution, and then repeatedly with water. The ether solution was evaporated on a steambath and gave a partially crystallized residue which was dried at 100° under reduced pressure. The crystals were separated: and from the oil upon treatment with ligroin a second crop of crystals was obtained, giving a total yield of 27.1 g. Repeated crystallization from a ligroin–ethyl acetate mixture raised the melting point to 182° (rectilinear plates).

Anal. Calcd. for $C_{34}H_{36}O_5$: C, 77.8; H, 6.9. Found: C, 77.8; H, 6.74.

The preparation from *meso*-dibromodimesitylbutanedione (I) was carried out by adding 10 g. of (I) to a solution of phenylmagnesium bromide made from 3 g. of magnesium in 100 cc. of isopropyl ether, with refluxing for half an hour, and treatment as above with acetyl chloride. The yield of VII was 4.5 g. The use of smaller amounts of Grignard reagent led to resinous products from which small amounts of dimesitylbutenedione (III) were isolated.

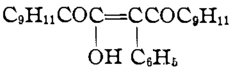
Similar results, but smaller yields, were obtained when dimesitylbutanedione (IV) was enolized by means of phenylmagnesium bromide and then treated similarly with acetyl chloride.

Attempts to ozonize this compound produced only intractable resinous products. The compound reacted vigorously at room temperature with methylmagnesium iodide and on hydrolysis the enol VIII was produced in good yield. Upon heating with methylmagnesium iodide at 100°, one equivalent of methane was evolved slowly but, upon hydrolysis, no crystalline product was obtained.

Alkali Hydrolysis.—A solution of five grams of VII in 50 cc. of 25% aqueous sodium hydroxide was refluxed for twelve hours. An oily layer separated. On cooling and extracting with several portions of ligroin and concentrating this solution, 2.5 g. of the furan, X, crystallized. Ether extraction of the aqueous solutions from the above separation gave a small amount of crystalline material (0.75 g.) which crystallized from ligroin as feathery needles melting at 162.5°. It gave a blue-green color reaction with alcoholic ferric chloride.

Anal. Calcd. for $C_{28}H_{28}O_3$: C, 81.5; H, 6.8. Found: C, 81.4; H, 6.8.

From this analysis, it seems likely that the new compound is an oxidation and hydrolysis product, possibly



$$\underset{\displaystyle OH}{C_9H_{11}CO\overset{}{C}}{=}\underset{\displaystyle C_6H_5}{C}COC_9H_{11}$$

XVIII

XVIII. The compound formed a crystalline salt when treated with alcoholic sodium hydroxide, which on treatment with acid regenerated the enol.

2,3-Diacetyl-1,4-dimesityl-2-phenylbutanedione Enol (VIII).—Three-tenths gram of VII was dissolved in warm concd. acetic acid. This solution was cooled and treated with 2 cc. of concd. hydrochloric acid. After standing for one hour at room temperature, the solution was diluted with cold water, and a white crystalline precipitate melting at 175–176° was obtained. Purification by crystallization from ethyl acetate–ligroin mixture raised the melting point to 181.5° (diamond-shaped prisms). A mixture melting point with the starting material showed a 20° depression. It gave a red-violet color reaction with alcoholic ferric chloride.

Anal. Calcd. for $C_{32}H_{34}O_4$: C. 79.6: H, 7.1. Found: C, 79.76; H, 7.25.

Methylmagnesium iodide reacted quickly within one minute with evolution of one equivalent of methane. The starting material was recovered on hydrolysis. When heated at 100° with excess methylmagnesium iodide, a second molecule of methane was evolved slowly over the course of three hours. A brilliant red solution resulted and no starting material could be recovered on hydrolysis.

The Action of Acetic Anhydride and Sulfuric Acid.—Two-tenths gram of VIII in 10 cc. of acetic anhydride was treated with 10 drops of concd. sulfuric acid and after standing for five minutes at room temperature the solution was hydrolyzed with ice water. Extraction with ether gave an oil which was taken up in ethanol and gave 0.1 g. of colorless crystals. Upon repeated crystallization from this solvent, it melted at 214.5° and gave a qualitative test for sulfur. It was soluble in alkali and gave no ferric chloride color test.

Anal. Calcd. for $C_{32}H_{32}O_6S$: C. 70.55; H, 5.9. Found: C, 70.84; H, 5.9.

Acylation Attempts.—All experiments designed to convert the enol VIII back to the acetate VII failed; no reaction occurred. These experiments include conditions as nearly identical as possible with those under which the original preparation of VII was carried out. involving the bromomagnesium enolate. and also the action directly on the enol, of acetyl chloride alone. and acetyl chloride and pyridine, heated to boiling.

3-Mesitoyl-5-mesityl-2-methyl-4-phenylfuran (**X**).—A solution of 5 g. of VII and 2 g. of sodium hydroxide in 50 cc. of 95% ethanol was refluxed for five minutes. Upon cooling and diluting with water a viscous oil was obtained and extracted by means of several portions of ligroin. The ligroin solution was washed with water and evaporated under diminished pressure to a small volume. Crystallization occurred giving 3.8 g. of colorless truncated prisms. No trace of the compound believed to be XVIII could be found. Repeated crystallization brought the melting point to 113°.

Anal. Calcd. for $C_{30}H_{30}O_2$: C, 85.3; H, 7.2. Found: C, 85.57; H, 7.2.

Similar results were obtained when the enol VIII was used in the above experiment instead of VII. No trace of the compound believed to be XVIII could be obtained in this reaction or when aqueous alkali was used instead.

With methylmagnesium iodide the furan showed no active hydrogen. No reaction occurred at room temperature within three hours, and the material could be recovered. At refluxing temperature of ether, however, or upon long standing at room temperature, addition occurred.[6]

Summary

Acylation of 1,4-dimesityl-2-phenylbutanedione-1,4 di-enolate gives a di-carbon-acyl derivative in the form of an enol acetate; this is easily hydrolyzed to the enol, 2,3-diacetyl-1,4-dimesityl-2-phenylbutanedione-1,4 enol; and further hydrolysis by alkali eliminates the 2-acetyl group and gives 3-mesitoyl-5-mesityl-2-methyl-4-phenylfuran the structure of which was proved by reactions.

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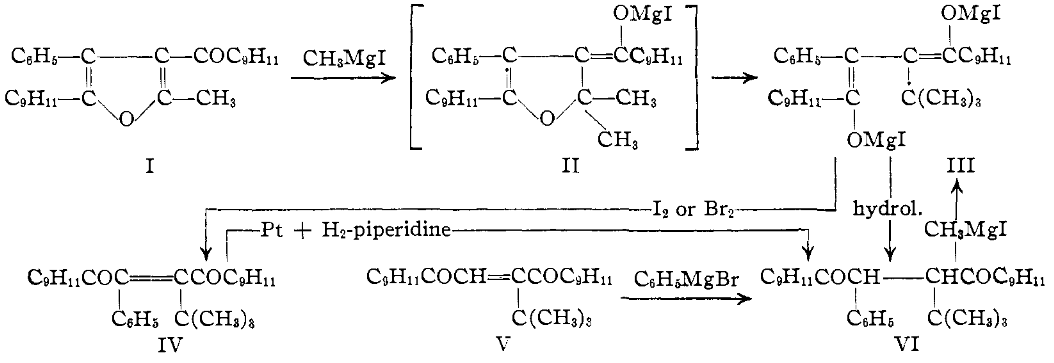
[6] See the following paper, Lutz and Reveley, This Journal, **63**, 3178 (1941).

[Contribution from the Cobb Chemical Laboratory of the University of Virginia]

1,4-Addition of Methylmagnesium Iodide to an α,β-Unsaturated Ketone System Involving the Double Bond of a β-Aroylfuran Nucleus, and Ring Cleavage of the Resulting Vinyl Allyl Ether System[1]

By Robert E. Lutz and William G. Reveley[2]

An interesting reaction between methylmagnesium iodide and 3-mesitoyl-5-mesityl-2-methyl-4-phenylfuran (I) was discovered during the determination of the structure of this compound.[3] Two molecules of methylmagnesium iodide were consumed and the *t*-butyl saturated diketone (VI) was produced. The structure of this as well as the confirmation of the structure of the furan itself came as the result of consideration of the few reactions conceivable under the circumstances and the subsequent synthesis of the end-product in another way. The reaction steps are best pictured as



On the basis of the furan structure (I), addition of methylmagnesium iodide at the mesitoyl carbonyl group would be inconceivable because of steric hindrance. However, the furan double bond and the carbonyl group form a conjugated system in which the terminal positions are unhindered and available for 1,4-addition. The primary addition product therefore must be the magnesium enolate (II). Analogy for this reaction is the 1,4-addition of phenylmagnesium bromide to α,β-diphenylbenzalacetophenone, involving a double bond of a phenyl group conjugated with the carbonyl.[4] The reaction with the furan (I) differs from this in two respects: it proceeds with a higher order of speed, evidently because of the far different and greater reactivity of the furan nucleus as compared with that of the analogously substituted phenyl group; and it gives an intermediate (II) which is incapable of rearrangement back into the aromatic structure.

It was to be expected that the vinyl allyl ether system present in II, namely, $C{=}C{-}O{-}C{-}C{=}C$, would be reactive and easily cleaved by the Grignard reagent. Analogies for this reaction are the several known fissions by Grignard

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[1] Presented at the Atlantic City meeting of the American Chemical Society, September, 1941.

[2] Philip Francis du Pont Fellow, 1939–1940; present location, National Aniline and Chemical Co., Buffalo, New York.

[3] *Cf.* Lutz and Reveley, This Journal, **63**, 3175 (1941).

[4] Kohler and Nygaard, *ibid.*, **52**, 4128 (1930); *cf.* also Gilman, Kirby and Kinney, *ibid.*, **51**, 2252 (1929).