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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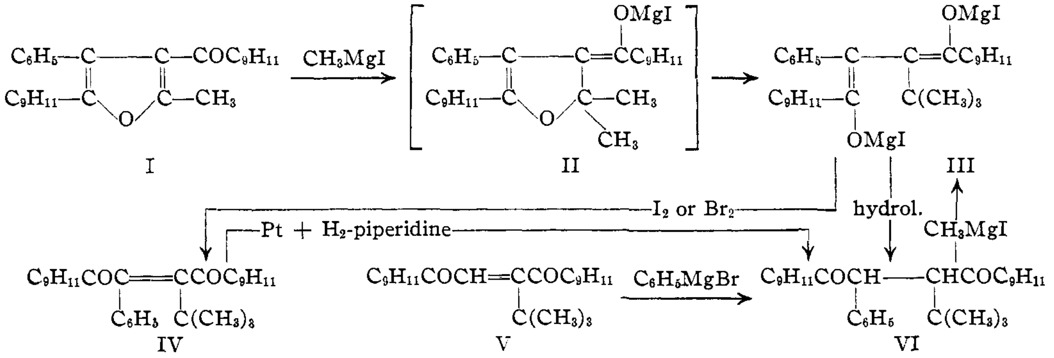
[6] See the following paper, Lutz and Reveley, THIS JOURNAL, 63, 3178 (1941).

[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).

reagent of phenyl allyl ethers in which the phenyl group corresponds in a sense to the dihydrofuran double bond of II. The compounds in the morphine alkaloid series, namely, thebaine, desoxycodeine-C, pseudocodeinone, and dihydropseudocodeinone enol acetate, in which the 6,7-double bond is conjugated with the oxygen bridge, add Grignard reagent readily with fission of the oxygen bridge linkage[5]; however, it is not yet known whether these reactions are 1,2 or 1,4 because the locations of the in-going alkyl and aryl groups have not yet been determined. In the case of the simple allyl aryl ethers which react similarly[6] it would be impossible from the cleavage products to tell whether reaction had occurred 1,2 or 1,4; and in the case of cinnamyl phenyl ether where the two modes of reaction would lead to different products no attempt was made to isolate or determine the structure of the alkylated hydrocarbon, which would be necessary to decide this point. The reaction between methylmagnesium and the vinyl allyl ether system of the intermediate (II)—if it were 1,2, as proved to be the case—would lead to the formation of a *t*-butyl group as indicated in formula III. This structure and that of the end-product (VI) were proved by synthesis of the latter through 1,4-addition of phenylmagnesium bromide to 2-*t*-butyl-1,4-dimesityl-2-butenedione-1,4 (V).[7]

The di-enolate obtained in the reaction between the furan (I) and methylmagnesium iodide (namely, III) underwent the characteristic oxidation to the unsaturated diketone (IV) when treated with iodine or bromine. The saturated diketone (VI) was enolizable to a di-enolate (III or a stereoisomer) which was also oxidizable to the corresponding unsaturated diketone (IV). Reduction of the unsaturated diketone (IV) by means of catalytic hydrogen in the presence of piperidine as a ketonization catalyst gave the saturated diketone (VI). These transformations substantiate the conclusions drawn above.

The results of this investigation indicate that the double bond of a furan nucleus in conjugation with a carbonyl group can play a role not far different from that of a double bond in an ordinary α,β-unsaturated ketone and actually does so without significant difficulty in the reaction with Grignard reagent when the carbonyl group is so hindered sterically as to be unreactive itself. This type of 1,4-reaction with Grignard reagent will undoubtedly prove to be general, not only for α- and β-aroyl furan types but also for other analogously substituted heterocyclic compounds with rings which are reactive in the same sense as the furan nucleus.

It is also evident from these results that the facile vinyl allyl ether cleavage by the Grignard reagent is a general type of reaction. This cleavage should occur with the analogous conjugated systems with nitrogen in place of oxygen.

Experimental Part

The action of methylmagnesium iodide on the furan (I) appears to go in two successive steps. When the reaction was run in ethyl ether for seventy minutes a product was obtained which decomposed at 125° and melted *in vacuo* at 176°. This interesting compound is now under investigation and will be considered in a later report.

2-*t*-Butyl-1,4-dimesityl-3-phenylbutanedione-1,4 (VI).—Nine and seven-tenths grams of the furan (I) was added portionwise to a vigorously stirred solution of five equivalents of methylmagnesium iodide in 100 cc. of ethyl ether over a period of twenty minutes, the mixture being maintained at room temperature. Isopropyl ether (100 cc.) was added and the ethyl ether distilled off through a fractionating column. The mixture now under isopropyl ether was refluxed under an atmosphere of dry nitrogen for 2.3 hr.; it was then cooled and poured into ice and hydrochloric acid. The isopropyl ether layer was separated, washed in succession with water, dilute sodium bicarbonate, and water. Upon evaporation on a water-bath, a residual oil was obtained which was dissolved in ligroin. The product crystallized as flat needles melting at 164.5°; yield, 5.85 g. It was purified by repeated crystallization from ligroin.

Anal. Calcd. for $C_{32}H_{38}O_2$: C, 84.54; H, 8.4. Found: C, 84.7; H, 8.1.

A second preparation is as follows: 0.32 g. of *t*-butyldimesitylbutenedione (V)[7] was added to 10 cc. of ethyl ether containing four equivalents of phenylmagnesium bromide at room temperature. After standing for ten minutes the mixture was hydrolyzed with ice and hydrochloric acid and the ether layer was separated, washed, and evaporated. The yellow oil remaining could not be induced to crystallize. Assuming that it may have contained the product in a mono or di-enolic form, it was treated for a half hour with boiling 2% potassium hydroxide in 95% ethanol. Upon cooling, diluting with water, extracting with ether, washing with water, and evaporating, an oil was again obtained which was dissolved in ligroin. Upon cooling 0.12 g. of VI crystallized and was identified by mixture melting point.

An attempt to prepare this compound (VI) from 1,4-dimesityl-2-phenylbutenedione-1,4, $C_9H_{11}COCH{=}C(C_6H_5)$-$COC_9H_{11}$, by the 1,4-addition of *t*-butylmagnesium chloride, failed. The conditions were approximately as above.

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[5] Small and Yuen, This Journal, **58**, 192 (1936); Small, Fitch and Smith, *ibid.*, **58**, 1457 (1936); Lutz and Small, *ibid.*, **57**, 2651 (1935); Small, Turnbull and Fitch, *J. Org. Chem.*, **3**, 204 (1938); Small and Fry, *ibid.*, **4**, 509 (1939).

[6] Lüttringhaus, v. Soaf and Hauschild, *Ber.*, **171B**, 1673 (1938).

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

The only crystalline product isolated was dimesitylphenylbutanedione, $C_9H_{11}COCH_2CH(C_6H_5)COC_9H_{11}$, which was the result of reduction. This product was identified by mixture melting point.

When the compound VI was treated with methylmagnesium iodide in the Zerewitinoff apparatus, one molecule of methane was evolved rapidly at room temperature, and when heated to 100° a second molecule was slowly evolved over thirty minutes; the final volume of methane was 1.9 moles. When the reaction mixture was hydrolyzed with ice and hydrochloric acid the starting material was recovered in 91% yield.

When a stream of dry hydrogen chloride was bubbled through a solution of the compound in boiling concd. acetic acid for thirty-two hours, an amorphous product was obtained which fused over a wide range and defied attempts to crystallize it. Distillation in the vacuum oven gave a glassy liquid. This may have been the furan, but it was not investigated further.

2-*t*-Butyl-1,4-dimesityl-3-phenyl-2-butenedione-1,4 (IV).—A sample (1.15 g.) of *t*-butyldimesitylbutenedione (V) was added to 8 cc. of ether containing four molecules of phenylmagnesium bromide at 0°. After standing for fifteen minutes the mixture was poured slowly with stirring into 75 cc. of ethanol containing 0.5 cc. of bromine, at −10°. Aqueous sodium bisulfite was then added and the product extracted with ether. Upon evaporation, the oily residue was crystallized from ethanol; yield 0.96 g. Repeated crystallization from ligroin gave rhombic prisms melting at 183°.

Anal. Calcd. for $C_{32}H_{36}O_2$: C, 84.9; H, 8.0. Found: C, 84.7; H, 8.2.

This compound (IV) was obtained also by enolization of the saturated diketone (VI) by means of methylmagnesium iodide and pouring the resulting mixture into alcoholic iodine or bromine maintained at −10 to 0°. In both cases yields of about 40% of the unsaturated diketone (IV) were isolated and identified by mixture melting points.

Reduction of IV by means of zinc dust and 80% acetic acid, refluxing for thirty minutes, gave an amorphous product very similar in character to that obtained in the attempted furanization of the saturated diketone. It was not investigated further.

Catalytic reduction of 0.2 g. of IV in 10 cc. of ethanol and 2 cc. of piperidine, using 0.02 g. of platinum oxide, showed absorption of one molecule of hydrogen in two hours. Upon filtering and diluting slowly with water, 0.2 g. of crystals separated and on recrystallization from ligroin was identified by mixture melting point as the saturated diketone (VI).

Summary

Methylmagnesium iodide adds 1,4 to the α,β-unsaturated ketone system of a β-mesitoyl furan, involving the double bond of the furan nucleus. The resulting dihydrofuran enolate undergoes a vinyl allyl ether cleavage by addition of a second molecule of methylmagnesium iodide. The structure of the final product and the presence of *t*-butyl group were demonstrated by reactions and synthesis.

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

The Stereochemistry of the Enols and Di-enols of 2-*t*-Butyl-1,4-dimesitylbutanedione-1,4. A Proof of 1,4-Reduction of an α-Bromoketone

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

The study of enols and their stereochemistry is difficult because those enols which are so substituted as to be persistent are affected by steric hindrance and usually fail to show many of the characteristic reactions. Nevertheless, at present a number of monoenols,[2] enediols,[2a,3] and di-enols[2c,4] have been investigated and some have been isolated in persistent or permanent crystalline forms. A preliminary investigation of the enols and dienols in the trimesitylbutanedione series has already been reported,[2c] and this paper deals with a similar survey of the 2-*t*-butyl-1,4-dimesitylbutanedione series and a study of the effect of the *t*-butyl group.

The Synthesis of the Dimesityl-*t*-butyl Series.—The first approach to this series came through the investigation of the reaction between methylmagnesium iodide and 3-mesitoyl-5-mesityl-2-methylfuran (I). This reaction had been carried out originally as a test for active hydrogen before the structure of the furan was known. The course of the reaction was deduced from the analysis of the product (IV) and from consideration of the limited possibilities involving addition of two molecules of methylmagnesium iodide.[2c] A second synthesis subsequently carried out through 1,4-addition of *t*-butylmagnesium chloride to dimesitoylethylene (V), confirmed this conclusion

[1] Philip Francis du Pont Fellow, 1939–1941; present location, National Aniline and Chemical Company, Buffalo, New York.

[2] (a) Kohler and Thompson, THIS JOURNAL, **59**, 888 (1937); (b) Kohler, Tishler and Potter, *ibid.*, **57**, 2517 (1935); (c) Lutz and Kibler, *ibid.*, **62**, 360 (1940); (d) Fuson, Corse and McKeever, *ibid.*, **62**, 3250 (1940).

[3] (a) Lutz and Wood, *ibid.*, **60**, 705 (1938); (b) Fuson and Corse, *ibid.*, **61**, 975 (1939); (c) Thompson, *ibid.*, **61**, 1281 (1939).

[4] Lutz and Reveley, *ibid.*, **61**, 1854 (1939).