

particularly reduction, of the dimolecular oxidation product of the  $\beta$ -hydroxyfuran, namely,

2,2'-bis-(2,5-diphenylfuranone-3).

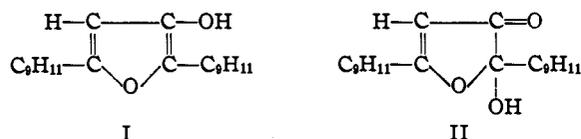
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[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

### 3-Hydroxy-2,5-dimesitylfuran and Related Compounds

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This report deals with an attempt to prepare 2,5-dimesityl-3-hydroxyfuran (I) and 2-hydroxyfuranone-3 (II). It was anticipated that the magnesium derivative of the hydroxyfuran could be made by the action of the Grignard reagent on the acetoxyfuran (IV); however, because of steric hindrance,<sup>2</sup> it seemed unlikely that the hydroxyfuranone could be obtained by the usual methods, although it might well be stable when once formed. Evidence for the existence of the hydroxyfuran now has been obtained but the hydroxyfuranone remains as yet unknown.

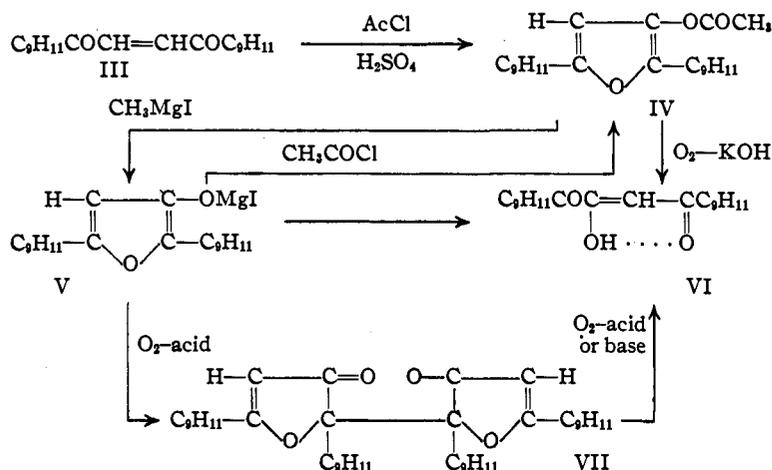


In the preparation of quantities of the acetoxyfuran (IV) by the action of acetyl chloride and

of a compound which was shown to be dimolecular ( $C_{44}H_{46}O_4$ ) and formed by hydrolysis of the acetoxyfuran and oxidation. This dimolecular compound, which is presumed to be the bis-furanone (VII), had previously been obtained by the action of concd. hydrochloric and acetic acids on the 4-hydroxy-1,4-dimesityl-1,3-butanedione 1-enol ether (IX),<sup>3</sup> but its structure was not known at that time.

The acetoxyfuran (IV) reacted with methylmagnesium iodide to give the iodomagnesium enolate (V) which could be converted back into the acetoxy compound by means of acetyl chloride. The iodomagnesium derivative reacted with benzoyl chloride to give the analogous benzoyloxy compound which in turn could be converted back into the acetate (IV) by treatment successively with the Grignard reagent and with acetyl chloride.

Unsuccessful attempts were made to isolate the



free hydroxyfuran (I). This compound was undoubtedly present in the non-crystalline product of hydrolysis of the iodomagnesium enolate (V) because, when this product was allowed to stand, oxygen was absorbed slowly and in time increasingly large amounts of the crystalline dimolecular oxidation product (VII) could be isolated. When the acetoxyfuran was hydrolyzed by means of alcoholic alkali, slow absorption of approximately one equivalent of oxygen was observed; but in this case the product isolated was the

sulfuric acid on dimesitylolethylene (III)<sup>3</sup> consistently high yields were obtained when special care was taken during hydrolysis of the excess of reagent to avoid hydrolysis of the acetoxyfuran itself. Otherwise there was produced large amounts

triketone enol (VI), formed probably through hydrolysis to the hydroxyfuran (I), oxidation to the hydroxyfuranone (II) and finally rearrangement. The dimolecular oxidation product (VII) when suspended in an alkaline medium under the same conditions did not undergo any change and probably, therefore, was not involved in this particular

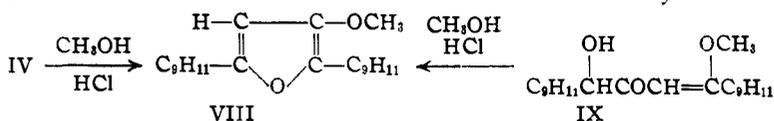
(1) Present location National Aniline Division, Allied Chemical and Dye Corp., Buffalo.

(2) Cf. Lutz and Wood, *THIS JOURNAL*, 80 (a) 229, (b) 705 (1938); (c) Lutz and Terry, *J. Org. Chem.*, 7, 274 (1942).

(3) Lutz and Terry, *ibid.*, 7, 320 (1942).

transformation, although upon prolonged treatment with acid or base it was in the end converted by oxidative cleavage into the triketone enol (VI).

The acetoxyfuran (IV) was converted by means of methanolic hydrogen chloride into a compound which according to analysis has one methoxyl group in place of the acetoxy. This compound appears to be the methoxyfuran (VIII). It is identical with the compound obtained previously by the action of methanolic hydrogen chloride under more extreme conditions on one of the 1-methyl ethers of 4-hydroxy-1,4-dimesityl-1,3-butanedione enol, namely, (IX). This enol ether is at the same state of oxidation as the methoxyfuran.



It will be noticed that the methoxyl groups in the 1-enol ether (IX) and the methoxyfuran (VIII) are attached to different carbon atoms.

A shift of methyl by addition and elimination might reasonably be supposed during the reaction, and is supported by the fact that methanol was necessary to this transformation whereas ethanol under similar conditions produced a different compound.

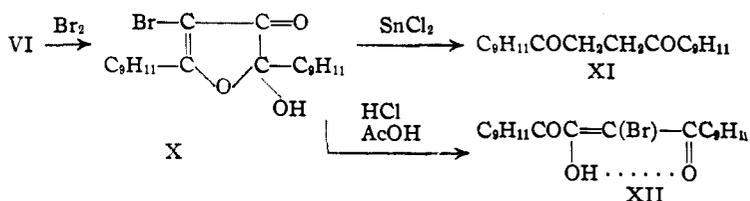
The structure of the supposed methoxyfuran (VIII) has not as yet been established rigorously. The compound, as would be expected from the structure proposed, failed to react with most reagents, including zinc and acetic acid, sodium methoxide, the Grignard reagent, the acetyl chloride-sulfuric acid reagent, and ketone reagents. It was converted by means of nitric acid into the triketone enol (VI).

The autoxidation product obtained from the hydroxyfuran (I),<sup>4</sup> insofar so its reactions have been studied, appears to be analogous to the bisfuranones of the di- and triphenyl series, and consequently it has been assigned the structure (VII). As already mentioned, this compound was cleaved by acid or base, albeit with some difficulty, to give the triketone enol (VI). Cleavage occurred also, and more readily than in the case of the di- and triphenyl analogs, when the compound was treated with the Grignard reagent; the net result was reduction with regeneration of

the iodomagnesium derivative of the hydroxyfuran (V) which was subsequently isolated as the acetoxyfuran (IV).

It might appear from the above-described facile cleavages that the dimolecular compound is held together by an oxygen or a peroxide linkage. Although this hypothesis is not excluded, it seems unlikely in view of the very slow reaction with potassium iodide.

The action of bromine on the dimolecular compound (VII), in contrast with the results in the di- and triphenyl series, apparently involved oxidative cleavage as well as bromination at the available furan  $\beta$ -positions. The product has tentatively been formulated as the 4-bromohydroxyfuranone (X) because of the facile reduction to dimesitylbutanedione (XI) and the conversion by acid hydrolysis into bromodimesitylbutanetrione enol (XII). The latter transformation demonstrated the location of the halogen atom.



This bromo compound (X) is of interest because, assuming that it is correctly formulated, it is the first to be prepared of the type II in which there exists a high degree of steric hindrance at the 2-position. Direct preparation through cyclization of the open-chain triketone enol (XII) has not been accomplished and is evidently prevented by steric hindrance. The conversion in the opposite direction from the hydroxyfuranone (X) to the open-chain enol (XII) occurs less easily than the analogous transformation in the diphenyl series, as would be expected.

The reaction between the Grignard reagent and the bromohydroxyfuranone (X) is of obvious interest but it has led to new compounds the study of which has had to be postponed.

The action of acetic anhydride and sulfuric acid on the dimolecular product (VII) was investigated because at the time the experiment was performed we supposed the compound to be the hydroxyfuranone (II) and we were hoping to convert it into dimesitylacetoxyfuranone. However, the product of this reaction proved instead to be a

(4) Lutz, McGinn and Bailey, *THIS JOURNAL*, **65**, 843 (1943).



**3-Benzoyloxy-2,5-dimesitylfuran.**—A solution of the bromomagnesium derivative made from 3 g. of the acetoxyfuran (IV) was added to a solution of 6 g. of benzoyl chloride in 20 cc. of ether. After standing for five minutes the mixture was cooled and hydrolyzed with 10% hydrochloric acid. The ether layer was washed several times with 5% hydrochloric acid and 5% sodium carbonate and was then evaporated. The residue crystallized from ethanol; yield 2.5 g. of stout colorless needles which melted after repeated recrystallization at 116–116.5°.

*Anal.* Calcd. for  $C_{23}H_{25}O_3$ : C, 82.0; H, 6.65. Found: C, 81.7; H, 7.2.

The action of ethylmagnesium bromide on the benzoyloxy compound, followed by reaction with acetyl chloride gave the acetoxyfuran in good yield.

**2,5-Dimesityl-3-methoxyfuran (VIII).**<sup>2</sup>—A suspension of 4 g. of acetoxydimesitylfuran (IV) in 30 cc. of methanol saturated with dry hydrogen chloride was allowed to stand for twenty-four hours in a glass-stoppered flask. Solution occurred. Evaporation gave a yellow solid which was recrystallized from methanol; yield 3.2 g. Recrystallizations from methanol raised the melting point to 90–91°.

*Anal.* Calcd. for  $C_{22}H_{26}O_2$ : C, 82.36; H, 7.54;  $OCH_3$ , 9.3. Found: C, 81.94, 82.46, 82.72, 82.41, 82.33; H, 7.56, 7.44, 7.58, 7.50, 7.45;  $OCH_3$ , 9.24, 9.3.

This compound was prepared in equally good yield by passing dry hydrogen chloride through a refluxing solution of *cis*-1-hydroxy-4-methoxy-1,4-dimesityl-3-butene-2-one (IX).<sup>3</sup>

The action of a mixture of 13 cc. of concd. acetic acid and 1 cc. of concd. nitric acid on 1 g. of the methoxyfuran (VIII) at 100° for one hour produced largely non-crystalline material from which 0.2 g. of yellow crystals was isolated and identified by mixture melting point as the triketone enol (VI).

The action of phosphorus pentachloride in chloroform at 40° produced non-crystalline materials.

The following reagents were without effect: (a) the Grignard reagent, (b) acid hydrolysis at refluxing temperature ( $AcOH-HCl$ ), (c) methanolic potassium hydroxide and sodium methoxide (refluxing), (d) acetyl chloride and concd. sulfuric acid, (e) hydroxylamine and semicarbazide under a variety of conditions, and (f) zinc dust and concd. acetic acid.

**The Dimolecular Oxidation Product (VII) 2,2'-bis-(2,5-dimesitylfuranone-3).**—This compound had been obtained twice in prior investigations<sup>2,3</sup> but its nature was not then recognized. The formation of this compound from the hydroxyfuran had already been mentioned. The best method of preparation is as follows.

An ethereal solution of the bromomagnesium derivative made from 3 g. of the acetoxyfuran (IV) was hydrolyzed with 10% hydrochloric acid and the ether layer was washed several times in succession with 5% hydrochloric acid and water. Evaporation of the ether left an orange colored oil; this was taken up in methanol and the solution was allowed to stand open to the air for thirty hours. Long, thin, needle crystals separated in a yield of 1.9 g. Recrystallization from ethyl acetate brought the melting point to 184–185°.

*Anal.* Calcd. for  $C_{44}H_{46}O_4$ : C, 82.72; H, 7.26; mol.

wt., 639. Found: C, 82.46, 82.42; H, 7.28, 7.34; mol. wt.<sup>6</sup> (freezing point, benzene), 627. Active hydrogen (Kohler-Richtmyer apparatus at 100°), 0.49, 0.51; additions, 0.92, 1.02 (calculations based on formula VII).<sup>7</sup>

Conversion to the triketone enol (VI) was effected easily by refluxing for two hours a suspension of the compound (VII) in a 10:1:1 mixture by volume of concd. acetic acid and hydrochloric acids and water. The suspended solid dissolved within five minutes after beginning the refluxing. Under these conditions, approximately 50% unchanged material was recovered, and a 20% yield of the triketone enol was isolated. When refluxing was continued for longer periods of time, more of the triketone enol was obtained and also some mesitoic acid.

The action of ethylmagnesium bromide followed by treatment with acetyl chloride or benzoyl chloride under conditions as employed in the case of the acetoxy-furan and described above, gave the acetoxy (IV) and benzoyloxyfurans.

The action of stannous chloride in a 5:1. concd. acetic-hydrochloric acid mixture produced an oil which on long standing in ethanol solution regenerated the dimolecular compound (VII).

The dimolecular compound was recovered unchanged when treated (a) with methanolic potassium hydroxide at room temperature for twenty-four hours, and (b) hydroxylamine in alkaline media, and in piperidine (with refluxing).

**4-Bromo-2-hydroxy-2,5-dimesitylfuranone-3 (X).**—A solution of 1.2 g. of bromine in 12 cc. of carbon tetrachloride was added dropwise to a solution of 2 g. of the dimolecular compound (VII) in 30 cc. of the same solvent. The solution was heated at 40° until the bromine color was discharged, and was then evaporated. The residual oil was crystallized from methanol; yield 1.7 g. After repeated crystallization from methanol it melted at 143–144°.

*Anal.* Calcd. for  $C_{22}H_{22}BrO_3$ : C, 63.6; H, 5.6. Found: C, 63.6; H, 5.7.

The action of acid (a mixture of 15 cc. of concd. acetic acid, 1 cc. of water and 10 drops of concd. hydrochloric acid) under refluxing for two hours gave the 3-bromo-1,4-dimesityl-1,2,4-butanetrione enol (XII) in good yield.

The action of 2 *N* sodium methoxide in methanol under refluxing for twelve hours was without effect.

The action of methylmagnesium iodide (2 cc. of 1.9 *N* solution) in isoamyl ether on 0.2 g. of X under an atmosphere of nitrogen at 100° involved the evolution of no methane. The product was a colorless solid (yield 0.15 g.). After repeated recrystallization the new compound melted at 159.5–160°. It contained halogen and gave the analyses: Calcd. for  $C_{22}H_{22}BrO_3$ : C, 64.0; H, 6.3. Found: C, 64.1, 63.95; H, 6.5, 6.8. Acid hydrolysis gave another new halogen-containing compound of m. p. 139–139.5°; yield about 50%. These two compounds will be investigated at a later time.

Reduction of 1 g. of the bromo compound (X) by 4 g. of stannous chloride in 50 cc. of a 5:1. mixture by volume of concd. acetic acid and hydrochloric acids under refluxing for five minutes gave an oil which crystallized from methanol (yield 0.4 g.). This product was fractionally

(6) Determination by Newton H. Shearer.

(7) Measurements by Dr. Vernon Mattox.

