Summary

A convenient method for preparing aryl substituted 1,4-dithienes by the acid hydrolysis of β-keto alkyl sodium thiosulfates has been established. The effect of substitution of different groups and their position on the yields obtained by this method has been investigated.

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[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Hydroxy Furans. I. Beta Hydroxy Triphenylfuran

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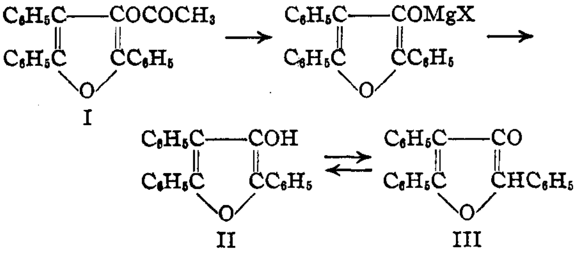
Hydroxy furans, though of considerable interest in connection with the recurrent idea that furan is aromatic in character, appear to be completely unknown. Dihydrofuran derivatives which might pass into α-hydroxy furans by enolization and acyl derivatives from which β-hydroxy furans might be formed by hydrolysis have been in hand for many years but the former are not known to enolize and the latter have not been hydrolyzed successfully. Thiele[1] treated the acetate of β-hydroxy triphenylfuran with alcoholic potassium hydroxide but reported only that the product was a substance which was soluble in alkalies and which appeared to be a transformation product of the hydroxy furan.

On repeating Thiele's experiment we found that when the acetate is treated in the usual manner with acids or bases hydrolysis is accompanied by oxidation and the products bear no simple relation to the parent compound. By hydrolyzing with acids in an atmosphere of nitrogen, however, it was possible to secure a solution which manifestly contained the hydroxy furan because it decolorized bromine instantaneously and absorbed oxygen from the air. When this solution was saturated with oxygen it deposited a sparingly soluble, crystalline peroxide—a reaction which was employed to detect the presence of the hydroxy furan.

By appropriate manipulation of the solutions obtained by hydrolyzing the acetate with acids it is possible to isolate a crystalline solid which has the composition of the hydroxy furan. This solid is, doubtless, the furanone formed from the hydroxyl compound by ketonization, because the solutions from which it has been separated as completely as possible still form peroxide rapidly and in quantities far in excess of any that can be obtained from saturated solutions of the solid. Moreover, solutions of the solid form peroxide much more slowly than those obtained from the acetate.

These relations indicate that the change from the acetate to the solid product occurs in two steps—hydrolysis and ketonization. These steps can be separated by treating the acetate with a Grignard reagent and cautiously acidifying the product with a mineral acid. The Grignard reagent converts the acetate quantitatively into a magnesium halide derivative of the hydroxy furan and the concentrated solution that is obtained by acidification in the presence of ether cannot contain more than minimal quantities of the keto form because it does not respond to inoculation until it has been left for several hours in the presence of acids. The successive steps in the process must, therefore, be represented as follows



I II III

The relations between the keto and hydroxyl forms is the same as that of open chained keto-enol tautomers but, for various reasons, it is difficult to determine the relative quantities of the two substances in equilibrium. Direct titration with bromine is not feasible because solutions of the resulting bromo compound are deep yellow in color and the results of indirect titrations are vitiated by the unavoidable formation of peroxide.

The peroxide appears to be constituted like the crystalline compounds which are formed by the autoxidation of the enolic modifications of mono ketones. Like these other peroxides it is easily

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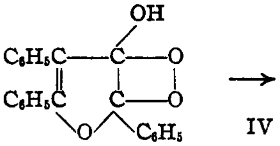
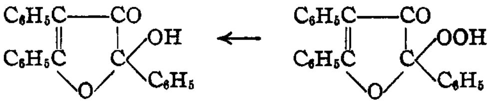
[1] Thiele, *Ber.*, **31**, 1249 (1898).

reduced and like them, also, it loses only one atom of oxygen when it is reduced catalytically in a neutral solvent. The reduction product, however, is not the usual oxanol but a hydroxy furanone which is constituted like the hydroxy ketones that are formed by the rearrangement of the oxanols. These reactions can be interpreted almost equally well by means of the cyclic formula IV and the open chained formula IVa but inasmuch as the peroxide is certainly formed from the hydroxy furan and is insoluble in alkalies the latter seems improbable.

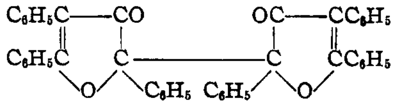


IV



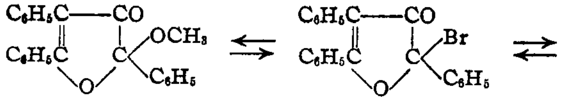
V IVa

The hydroxy furanone V is also the principal product that is formed from the peroxide by other reducing agents but in these cases it is accompanied by variable quantities of the dimolecular product VI.

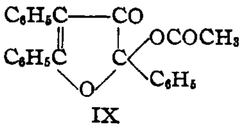


VI

The bromo compound that is formed by the action of bromine on the hydroxy furan is likewise an interesting type of furan derivative. In solution copper bronze converts it into the dimolecular product and when it is heated above its melting point it forms the dimolecular product with liberation of free bromine. This bromo compound and the hydroxy furanone are interconvertible, the bromo compound being hydrolyzed by boiling water and the hydroxyl compound being converted into the bromo compound by hydrogen bromide. By suitable reactions both the hydroxy ketone and the bromo compound can also be converted into the same methoxyl compound and the same acetate.

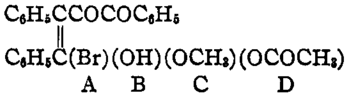


VIII VII



IX

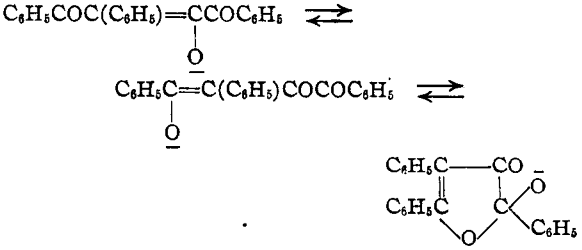
These four compounds—V, VII, VIII and IX—are evidently constituted alike. As an alternative to the cyclic formulas by which we have represented them it was necessary to consider also the corresponding series of open chained formulas, namely



$$\begin{array}{l} C_6H_5CCOCOC_6H_5 \\ \quad\| \\ C_6H_5C(Br)(OH)(OCH_3)(OCOCH_3) \\ \qquad\ \ A \qquad B \qquad C \qquad D \end{array}$$

These formulas can be discarded on the following grounds. (1) The furan ring in the hydroxy furan would not be expected to open under the action of cold bromine and the bromo compound A would not regenerate the hydroxy furan when reduced catalytically in a neutral medium. (2) The enol B would be sufficiently acidic for methylation with diazomethane; the hydroxy furanone is not affected by this reagent. (3) The methoxyl compound would be hydroyzed by bases; our compound is not—like other acetals it is hydrolyzed easily with acids.

In absolute ether metallic sodium converts the hydroxy furanone into a brilliant yellow sodium compound which is unusually versatile. It reverts to the hydroxy ketone when it is acidified and it forms the cyclic methoxyl compound when it is methylated with methyl iodide or dimethyl sulfate. Acetyl chloride converts it into the cyclic acetate and bromine transforms it into an open chained bromo compound, $C_6H_5COC(C_6H_5)BrCOCOC_6H_5$, which reverts to the hydroxy ketone when reduced. And when it is boiled with water it is cleaved to desoxybenzoin and phenyl glyoxylic acid. The solutions of the sodium compound, therefore, behave as if they contained three different anions in a very mobile equilibrium.



As will be seen from the foregoing account, hydroxy triphenylfuran has some quite unexpected properties. To what extent it is typical of the class of hydroxy furans cannot be estimated until the experiments under way with less highly phenylated members are completed. The behavior of the completely phenylated compound brings no evidence to the support of those who are inclined to attribute aromatic or even "superaromatic" character to furan.

Experimental Part

There are two methods of hydrolyzing the acetate of hydroxy triphenylfuran which are equally easy to carry out in an atmosphere of nitrogen and which yield products of equal purity, namely, treatment with an organic magnesium compound followed by acidification, and digestion with sulfuric acid in aqueous acetic acid. The choice between these methods depends upon the object of the operation; the first method is more convenient for the preparation of a peroxide, while the second method is best for the preparation of a concentrated solution of the hydroxy furan and the isolation of the ketonic form. The procedure is illustrated by the following experiments.

Hydrolysis and Preparation of Peroxide.—To a solution of methylmagnesium iodide prepared in an atmosphere of nitrogen from 1.45 g. of magnesium was added, in small portions, 9.5 g. of the solid acetate. The acetate dissolved in the cold and a solid magnesium compound began to separate. The mixture was boiled for several hours, then decomposed with iced sulfuric acid in an atmosphere of nitrogen. The ethereal layer was washed thoroughly with ice water and dried over calcium chloride. An attempt to inoculate the solution with the sparingly soluble ketonic form was unsuccessful but when oxygen was passed into it the crystallization of peroxide began immediately and 7.3 g. was deposited within half an hour. (The filtrate from the peroxide later deposited 0.8 g. of the hydroxy ketone and 0.5 g. of the dimolecular product.)

Hydrolysis and Preparation of the Keto Furan.—A suspension of 15 g. of the acetate in a solution composed of 75 cc. of acetic acid, 10 cc. of water and 2 cc. of concentrated sulfuric acid was boiled under nitrogen for an hour. The resulting slightly yellow solution was diluted with water and extracted with ether. The ethereal layer was washed three times with water and twice with sodium bicarbonate. The keto form began to crystallize during the washing; its precipitation was completed by evaporating the ether in a current of nitrogen and gradually displacing it with low-boiling petroleum ether. The yield was 9.5 g. From the filtrate oxygen precipitated 4.1 g. of peroxide. The relative quantities of ketone and peroxide were not affected by the length of time during which the acetic acid solution was boiled.

2,4,5-Triphenyl Furanone-3, III.—The solid product which was obtained in the foregoing experiment was dried at 60° over phosphorus pentoxide in a Fischer pistol, and then recrystallized. By dissolving it rapidly in boiling ether and immediately chilling the solution it is possible to recrystallize it in the air and, as it is sparingly soluble in cold ether, the quantity of peroxide that is formed in the filtrate is small. It crystallizes in transparent prisms and it melts at 112°.

Anal. Calcd. for $C_{22}H_{16}O_2$: C, 84.6; H, 5.1. Found: C, 84.5; H, 5.1.

The solid ketone is comparatively stable in the air but eventually even the purest samples begin to deteriorate. It is insoluble in alkalies but when it is added to methylmagnesium iodide it consumes one mole of reagent and liberates one mole of gas as it is converted into the magnesium halide derivative of the hydroxy furan. Its solution in ether absorbs oxygen slowly and decolorizes bromine, the products being identical with those obtained from solutions of hydroxy furan.

3-Hydroxy-2,4,5-triphenylfuran Peroxide, IV.—The peroxide that is obtained in the manner described under the first method of hydrolysis is analytically pure. It is very sparingly soluble in the common organic solvents but it can be recrystallized by solution in dioxane and reprecipitation with petroleum ether. It crystallizes in small prisms. In a capillary tube it decomposes vigorously at about 120° and when it is heated on a spatula it decomposes with a flash but without detonation.

Anal. Calcd. for $C_{22}H_{16}O_4$: C, 76.7; H, 4.6. Found: C, 76.5; H, 4.0.

The peroxide is insoluble in dilute alkalies but when it is shaken with 5% aqueous sodium hydroxide it is gradually cleaved into the hydroxy furanone and hydrogen peroxide. Dilute alcoholic solutions likewise convert it into the hydroxy ketone and alcoholic solutions of acids transform it into the mixture of hydroxy ketone and dimolecular compound that is obtained when the acetate is hydrolyzed in the presence of air.

2-Hydroxy-2,4,5-triphenyl Furanone-3, V.—When a solution of the peroxide in ethyl acetate was shaken with hydrogen in the presence of platinum it absorbed one mole of hydrogen with great rapidity and the product was almost pure hydroxy ketone. The hydroxy ketone was also the principal product that was formed when the peroxide was reduced with potassium iodide in glacial acetic acid or zinc and acetic acid. It is most easily recrystallized from benzene from which it separates in very pale yellow needles melting at 191°. Its solutions in all solvents are yellow in color.

Anal. Calcd. for $C_{22}H_{16}O_3$: C, 80.5; H, 4.9. Found: C, 80.4; H, 5.1.

The Dimolecular Reduction Product, VI.—The dimolecular product is sparingly soluble in all common solvents but as it separates from solutions very slowly it is usually found in the mother liquors of solutions from which the more soluble products have been removed. It was purified by recrystallization from benzene and acetone. It separated in minute plates and it melted at 272–274°.

Anal. Calcd. for $C_{44}H_{30}O_4$: C, 85.0; H, 4.8. Found: C, 84.9; H, 5.0.

Synthesis.—The structure of the dimolecular product is based on the following synthesis. A solution of 1.5 g. of the bromo ketone VII in 35 cc. of benzene was shaken with 2.0 g. of copper bronze for five hours at the ordinary temperature. The yield was 1.2 g.

2-Bromo-2,4,5-triphenyl Furanone-3, VII.—The bromo compound can be obtained by adding bromine to any solution that contains the hydroxy furan but it is most readily prepared in quantity by brominating the acetate itself. For this purpose a suspension of the acetate in carbon tetrachloride is treated with an equivalent quantity of bromine and the mixture is boiled until all the bromine has disappeared. The yield is quantitative. The bromo compound was recrystallized from benzene and petroleum ether from which it separated in yellow plates melting at 154°, with decomposition into the dimolecular compound.

Anal. Calcd. for $C_{22}H_{15}O_2Br$: C, 67.5; H, 3.9. Found: C, 67.5; H, 4.0.

2-Chloro-2,4,5-triphenyl Furanone.—A solution of 1 g. of the hydroxy furanone in 6 g. of thionyl chloride was boiled for thirty minutes and then evaporated in a vacuum. The solid residue was crystallized from benzene–petroleum ether, from which it separated as pale yellow transparent prisms melting at 149–150°.

Anal. Calcd. for $C_{22}H_{15}O_2Cl$: C, 76.2; H, 4.3. Found: C, 76.1; H, 4.2.

2-Methoxy-2,4,5-triphenyl Furanone-3, VIII.—The methoxyl compound is formed when a few drops of sulfuric acid are added to a methyl alcohol solution of the hydroxy ketone. It is most readily prepared in quantity by dissolving the very active bromo compound described in the preceding paragraph in boiling methyl alcohol and cooling the solution. It crystallizes from methyl alcohol in stout prisms and it melts at 138°.

Anal. Calcd. for $C_{23}H_{18}O_3$: C, 80.7; H, 5.3; OCH_3, 9.1. Found: C, 80.4; H, 5.5; OCH_3, 9.2.

The methoxyl compound was cleaved by digestion with alcoholic sodium hydroxide but it was hydrolyzed to the hydroxy ketone by sulfuric acid in dilute acetic acid.

2-Ethoxy-2,4,5-triphenyl Furanone-3.—The ethoxyl compound, formed by boiling solutions of the bromo compound in ethyl alcohol, crystallizes in prisms and melts at 111°.

Anal. Calcd. for $C_{24}H_{20}O_3$: C, 80.9; H, 5.7. Found: C, 80.7; H, 6.1.

2-Acetoxy-2,4,5-triphenyl Furanone-3, IX.—The acetate, formed by adding a few drops of sulfuric acid to a warm solution of the hydroxy ketone in acetic anhydride, crystallizes in minute prisms and melts at 138–139°. Methyl alcohol containing a small quantity of sulfuric acid changes it to the methoxyl compound and in dilute acetic acid containing sulfuric acid it is hydrolyzed to the hydroxy ketone.

Anal. Calcd. for $C_{24}H_{18}O_3$: C, 77.8; H, 4.9. Found: C, 77.6; H, 5.3.

Action of Sodium on the Hydroxy Furanone.—When strips of sodium are introduced into a suspension of the finely powdered hydroxy ketone under absolute ether, hydrogen is evolved, the solution assumes a yellow color and the hydroxy ketone is gradually replaced by a yellow sodium compound which crystallizes in stout needles. By removing the excess of sodium mechanically, collecting the solid rapidly on a glass funnel and washing it thoroughly with low-boiling petroleum ether it is possible to prepare the sodium compound in a form in which it is stable in dry air.

In dry ether acids, including carbon dioxide, regenerate the hydroxy furanone from the sodium compound, acetyl chloride converts it into the acetate of the hydroxy ketone and both methyl iodide and dimethyl sulfate convert it into the methoxyl compound.

α-Bromo-α-benzoylbenzyl Phenyl Diketone, XI.—The sodium compound obtained from the hydroxy ketone reacts instantaneously with bromine forming a bromo compound that crystallizes from ether–petroleum ether in small yellow prisms and melts at 111°. Unlike the cyclic bromo compound VII the open chained compound is not affected either by boiling water or by boiling methyl alcohol. It, however, liberates iodine from potassium iodide and the bromine can also be replaced catalytically with hydrogen. The reduction product in each case is the hydroxy ketone.

Anal. Calcd. for $C_{22}H_{15}O_3Br$: C, 64.8; H, 3.7. Found: C, 64.9; H, 3.8.

Summary

This paper describes the preparation and properties of a β-hydroxy furan. The substance closely resembles open chained enols. Its solutions have the properties of keto-enol systems. Like a few of the most active enols it combines rapidly with free oxygen to form a crystalline peroxide. It does not in any respect resemble the hydroxyl derivatives of aromatic hydrocarbons.

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