into phytol itself, so that these reactions may constitute the basis for a new synthesis of this alcohol.

6. With "phytol ketone" available, the tocopherol synthesis of Smith and Miller[6] becomes practicable, since it is no longer dependent upon a source of phytol.

Minneapolis, Minnesota Received December 1, 1942

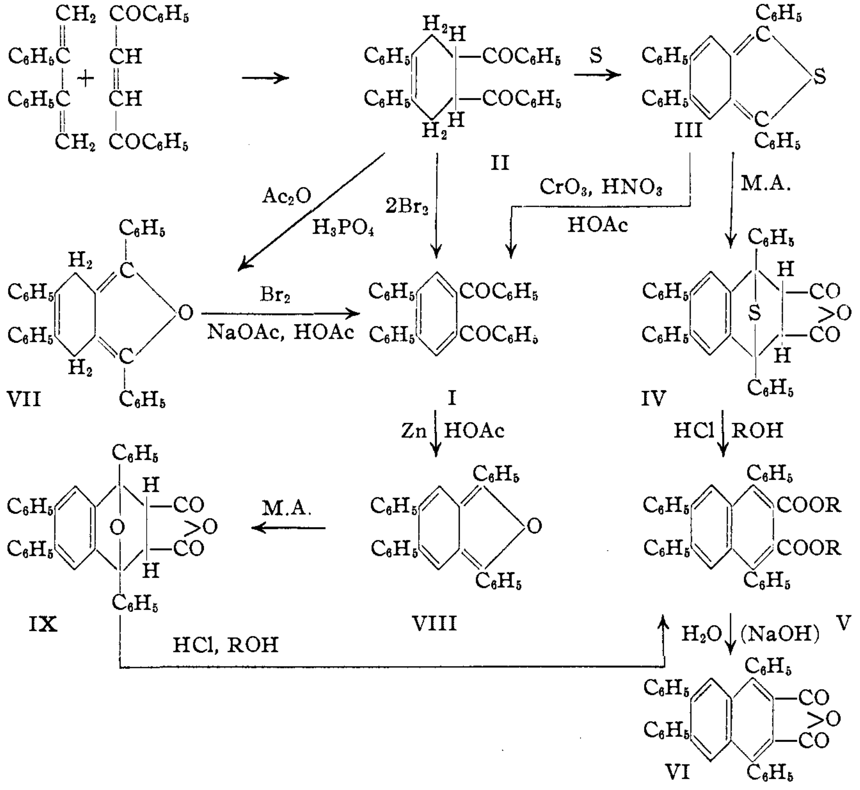
[Communication No. 917 from the Kodak Research Laboratories]

An Instance of the Diene Synthesis with an Isobenzothiophene

By C. F. H. Allen and J. W. Gates, Jr.

4,5-Diphenyl-1,2-dibenzoylbenzene I was needed for use as a reference compound in some other work. The obvious way to secure this substance was by means of the diene synthesis, adding dibenzoylethylene to 2,3-diphenylbutadiene, and dehydrogenating; it is known that dibenzoylethylene can be added to dienes.[1,2] The desired addition compound II was readily obtained, but when it was heated with sulfur for dehydrogenation, the product was bright yellow, with a strong greenish fluorescence. It was subsequently found to contain an atom of sulfur, which fact at once suggested that it was an isobenzothiophene III, by analogy with similar properties of isobenzofurans.[3,4,5]

Like other thiophenes it fails to add methyl iodide nor is it oxidized to a sulfone, but it does add maleic anhydride. The new addition product IV is the first instance of the isolation of a substance containing a sulfur atom as a bridge across a six-membered ring. Other attempts to employ thiophenes in the diene synthesis have been unsuccessful[6] or the sulfur has been eliminated as hydrogen sulfide[7] during the reaction.



The sulfur-bridged substance dissociates into its components at its melting point (245°). It is very sparingly soluble in most solvents. When an alcoholic suspension is saturated with hydrogen chloride and heated for four hours, hydrogen sulfide is evolved and the anhydride is converted to an ester; without isolation, the ester V was hydrolyzed by sodium hydroxide, and, upon acidification, the anhydride VI of 1,4,6,7-tetraphenylnaphthalene-2,3-dicarboxylic acid resulted. The sulfur bridge was not removed by lead salts, nor did it add methyl iodide or methyl *p*-toluenesulfonate under any conditions.

In contrast to the 4,5-dialkylated addition products, the diphenyl analog does not add bro-

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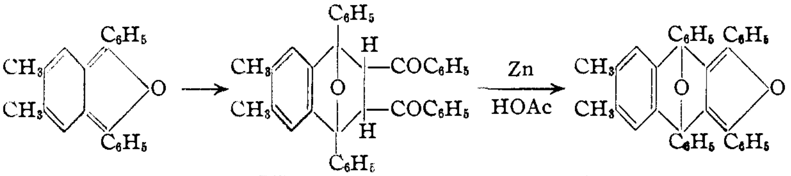
(1) Adams and Geissman, This Journal, 61, 2083 (1939).
(2) Adams and Gold, *ibid.*, 62, 56 (1940).
(3) Dufraisse and Priore, *Bull. soc. chim.*, [5] 5, 502 (1938).
(4) Barnett, *J. Chem. Soc.*, 1326 (1935).
(5) Norton, *Chem. Rev.*, 31, 474 (1942).
(6) Dufraisse and Daniel, *Bull. soc. chim.*, [5] 4, 2063 (1937).
(7) Clapp, This Journal, 61, 2733 (1939).

mine, but it is readily dehydrogenated to the desired dibenzoylbenzene I. The addition product II is easily dehydrated to a dihydroisobenzofuran VII, which, upon treatment with bromine in an acetic acid solution containing sodium acetate, also gives the dibenzoylbenzene I. The same diketone is also produced by the action of nitric or chromic acids in acetic acid upon the isobenzothiophene III.

On reduction with zinc and acetic acid, the diketone I gave the isobenzofuran VIII, which readily formed an addition product IX with maleic anhydride. This was converted into the same tetraphenylnaphthalenedicarboxylic anhydride VI mentioned above by a similar procedure involving esterification and hydrolysis. The analogy between the furan and thiophene series is thus complete.

The addition product formed by the use of 2,3-dimethylbutadiene[2] gave only ill-smelling oily products on treatment with sulfur. The dimethylated isobenzofuran X readily added to dibenzoylethylene; a molecular weight determination indicated that the new addition product XI was dissociated in solution. With zinc and acetic acid, this diketone gives a yellow, fluorescent substance, presumably the isobenzofuran XII since it adds maleic anhydride and quinone.



X XI XII

Experimental

The first addition product II was secured by refluxing equimolar amounts of the components, 2,3-diphenylbutadiene[8] and *trans*-dibenzoylethylene,[9] in alcohol or xylene. The astonishing effect that the solvent has on yield and purity merits attention. In alcohol the yield was 90% in four hours, whereas after twenty-four hours in xylene it was but 60%; furthermore, in the higher-boiling solvent, some of the yellow isobenzofuran VII was formed as a contaminant. Similar behavior has been mentioned before.[2,5] The properties of all the new substances are collected in Table I.

1,3,5,6-Tetraphenylisobenzothiophene III was prepared by heating 4.4 g. of the addition product with 0.7 g. of sulfur for one-half hour at 200–220°. The yield was 60–70%. It does not add methyl iodide at 150°. Upon oxidation with chromium trioxide or nitric acid in acetic acid, it gave 4,5-diphenyl-1,2-dibenzoylbenzene I, described below.

TABLE I

PROPERTIES OF NEW SUBSTANCES

No.	Crystal form	M. p., °C.	Empirical formula	Analyses, % Calcd. C	H	Found C	H
II	Prisms	154–155	$C_{32}H_{26}O_2$	86.9	5.9	86.7	5.7
III	Needles[a]	227–228	$C_{32}H_{22}S$[c]	87.7	5.0	87.6	4.9
IV	Prisms	245 dec.	$C_{36}H_{24}O_3S$[d]	80.9	4.4	80.5	4.0
I	Prisms	196–197	$C_{32}H_{22}O_2$	87.7	5.0	87.7	5.0
VI	Needles	310 dec.	$C_{36}H_{22}O_3$	86.0	4.4	85.8	4.2
VII	Needles[b]	276–277	$C_{32}H_{24}O$	90.6	5.7	90.1	5.2
VIII	Needles[a]	286–287	$C_{32}H_{22}O$	91.0	5.2	90.7	4.9
IX	Prisms	246–247	$C_{36}H_{24}O_4$	83.1	4.6	82.8	4.8
VIa	Needles	310 dec.	$C_{36}H_{24}O_4$	83.1	4.6	83.1	4.5
XI	Rods[e]	169	$C_{38}H_{30}O_3$	85.4	5.6	85.1	5.5
XII	Needles[f,g]	194–195	$C_{38}H_{30}O_2$	88.4	5.4	87.9	5.7
XIII	Prisms	271–272	$C_{42}H_{32}O_6$	79.5	5.3	78.9	4.9
XIV	Rods	145–146	$C_{44}H_{32}O_4$	84.6	5.1	84.1	5.7
XVI	Prisms	105–106	$C_{25}H_{16}O_5$	75.8	4.0	76.0	4.2

[a] Lemon yellow, green fluorescence, especially in solution. [b] Pale yellow, brilliant green fluorescence, solid and solution. [c] Calcd. S, 7.3: found, S, 6.8. [d] Calcd. S, 6.0; found, S, 5.9. [e] Slight green fluorescence, owing to dissociation. [f] Orange-yellow, green fluorescence, especially in solution. [g] Inactive in the Grignard machine.

1,4,6,7-Tetraphenyl-1,4-thio-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic acid anhydride IV was obtained by refluxing 2 g. of the isobenzothiophene in 4 g. of maleic anhydride for one-half hour, and crystallizing from xylene; the yield was 1.7 g. The new addition product dissociated at its melting point; maleic anhydride distilled away and the isobenzothiophene remained. It did not add methyl *p*-toluenesulfonate at 200° or methyl iodide in nitromethane solution or when heated with it in a sealed tube at 150°.

1,3,5,6-Tetraphenyl-4,7-dihydroisobenzofuran VII was formed on heating 5 g. of the addition product II in 75 cc. of acetic anhydride with a few drops of 85% phosphoric acid at 110–120° for ten minutes. The product (4.4 g.) was crystallized from xylene.

4,5-Diphenyl-1,2-dibenzoylbenzene I resulted when the above dihydro compound (4.2 g.) VII was suspended in 55 cc. of acetic acid containing 5 g. of anhydrous sodium acetate, and, at the boiling point, adding 3.2 g. of bromine in 15 cc. of acetic acid. After five minutes the solution was diluted slowly with 10 cc. of water. The yield was 3.5 g.

It was also obtained by bromine dehydrogenation of the addition product II, and by oxidation of the isobenzothiophene III.

1,3,5,6-Tetraphenylisobenzofuran VIII was secured by refluxing for three minutes, a solution of 2 g. of the diketone I in 100 cc. of acetic acid, after the addition of 5 g. of zinc dust. The yellow furan crystallized on cooling of the filtered solution. A white substance, m. p. 248–250°, separated (as rods) from the filtrate, on standing; it was not investigated. The same two substances were also obtained by the use of alcoholic sodium hydroxide and zinc dust.

1,4,6,7-Tetraphenyl-1,4-oxido-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic acid anhydride IX was isolated after cooling a hot benzene (30 cc.) solution of 1.5 g. of the furan VIII and 0.5 g. of maleic anhydride; the

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(8) Allen, Eliot and Bell, *Can. J. Research*, **17**, 75 (1939).

(9) "Organic Syntheses," **20**, 29 (1940).

yield was 1.5 g. It forms a yellow melt, indicating dissociation.

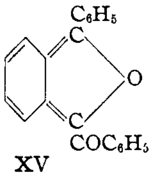
1,4,6,7-Tetraphenylnaphthalene-2,3-dicarboxylic Acid VIa.—A suspension of 1.5 g. of the previous anhydride (IX) in 150 cc. of dry methanol was saturated with hydrogen chloride, and then refluxed for four hours, while the current of hydrogen chloride was continued. The solvent was removed, and the pasty residue taken up in 200 cc. of ethanol. After the addition of 6 g. of sodium hydroxide in 50 cc. of water, and six hours of refluxing, it was acidified and extracted with chloroform. One gram of the acid crystallized. It melts at 310° with decomposition.

The anhydride VI was secured by a similar procedure from the thio analog IV, but using xylene as a solvent. It likewise melts at 310° with decomposition; there is no depression on admixture. While the acid is white, the anhydride has a slight yellow tint.

1,4-Diphenyl-6,7-dimethyl-2,3-dibenzoyl-1,4-oxido-1,2,3,4-tetrahydronaphthalene XI was produced on refluxing a mixture of 10 g. of 2,7-diphenyl-4,5-dimethylisobenzofuran,[2] 8 g. of *trans*-dibenzoylethylene and 500 cc. of ethanol for four hours; the yield was 17 g. after recrystallization from benzene. It was highly dissociated in boiling benzene: mol. wt., calcd., 534: found, 304, 316.

The Furan XII.—A solution of 5 g. of the above diketone XI in 100 cc. of boiling acetic acid was boiled for one minute after the addition of 10 g. of zinc dust. Upon cooling, 3.5 g. of deep orange-yellow crystals separated. In color and fluorescence this substance resembles the other isobenzofurans. It formed addition products with maleic anhydride and with *p*-benzoquinone XIV; the former is hydrolyzed to the acid XIII during the manipulation. The acid is soluble in aqueous sodium carbonate. Since XII is not formed by acetic acid or zinc acetate alone, some reduction must be involved; it is possible that an oxygen bond is attacked, but the structure is admittedly not proved.

In an earlier paper[10] an isobenzofuran ketone XV was described. We have since found that it resembles other isobenzofurans[5] in giving an addition product XVI with maleic anhydride. Thus, the benzoyl group does not have any unfavorable effect on this reaction.



XV

Summary

A sulfur-bridged substance has been obtained for the first time, making use of a new isobenzothiophene in the diene synthesis. The sulfur atom seems to be inactive and unable to participate in addition. The bridge is removed by alcoholic hydrogen chloride as hydrogen sulfide.

Some new isobenzofurans are described. They are strongly fluorescent.

Both series of products have been converted into derivatives of 1,4,6,7-tetraphenylnaphthalene.

[10] Allen and Gates, THIS JOURNAL, **65**, 1230 (1943).

ROCHESTER, N. Y. RECEIVED MARCH 30, 1943

[CONTRIBUTION FROM THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH, DIVISION OF ORGANIC CHEMISTRY]

Steroids with Double Bonds between Quaternary Carbon Atoms. I. The Oxidation of α-Ergostenyl Acetate

BY HOMER E. STAVELY AND G. NORRIS BOLLENBACK

A number of natural and derived steroids are known which contain nuclear double bonds terminating at one of the bridgehead carbon atoms 8, 9 or 14, or lying between two of them. Thus four singly unsaturated cholesterol isomers, α-, β-, γ- and δ-cholestenol[1] and their C_{28} homologs α-, β- and γ-ergostenol[2] have been prepared. The double bond positions denoted by the Greek letters are α, $\Delta^{8,14}$; β, $\Delta^{14,15}$; γ, $\Delta^{7,8}$; δ, $\Delta^{8,9}$. Double bonds in the α, γ and δ positions cannot be hydrogenated catalytically, but in the presence of platinum or palladium catalyst and hydrogen, the 7,8 (γ) and 8,9 (δ) double bonds are shifted to the 8,14 (α) position.[1,2,3] Unequivocal proof for the position of the double bond has been obtained only in the case of β-ergostenol[4] and γ-cholestenol[1(a),5] but the structures of the α and δ compounds have been inferred from their chemical behavior with a high degree of probability. Nevertheless some confusion and contradiction exists in this field and better proof for the double bond position in some of these compounds is to be desired. Since the double bond present in a γ($\Delta^{7,8}$)- or δ($\Delta^{8,9}$)-stenol can be isomerized with hydrogen and palladium or platinum catalyst and the product (α-stenol) can in turn be isomerized by hydrochloric acid to a β-stenol of known structure ($\Delta^{14,15}$), it is logical to assign the 8,14 position to

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[1] (a) Schenck, Buchholz and Wiese, *Ber.*, **69**, 2696 (1936); (b) Windaus, Linsert and Eckhardt, *Ann.*, **534**, 22 (1938).

[2] Reindel, Walter and Rauch, *Ann.*, **452**, 74 (1927); Windaus and Langer, **506**, 105 (1933).

[3] Although a few investigators have attempted to carry out the double-bond isomerization by shaking with a hydrogenating catalyst in a nitrogen atmosphere, it is the opinion of the authors that hydrogen is essential for isomerization. This will be discussed in a later publication.

[4] (a) Achtermann, *Z. physiol. Chem.*, **225**, 141 (1934); (b) Laucht, *ibid.*, **237**, 236 (1935).

[5] Wintersteiner and Moore, THIS JOURNAL, in press.