reflux six hours and decomposed with 10 cc. of 5% acetic acid, and the ether solution was washed with aqueous sodium bicarbonate, dried and evaporated in nitrogen. The dark residue was taken up in 5 cc. of boiling benzene, cooled and filtered to give 0.35 g. of crude 1,4,9-trihydroxy-9-phenyl-2,3-benzofluorene as a brown solid, m.p. 222–226° (dec.) (other specimens melted as low as 185°), soluble in alkali. The substance was converted to 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone in ten minutes by acetic acid at 100°.

9-Hydroxy-9-phenyl-2,3-benzofluorene-1,4-quinone, obtained by oxidation of the hydroquinone in ether with silver oxide, formed bright orange-yellow prisms from ether, m.p. 193–194°. The compound gave a pink solution in alcoholic alkali, a greenish-yellow vat and a dark olive solution in sulfuric acid. The ultraviolet and visible absorption maxima in ethanol solution lay at 258 mμ (log ε 4.34), 308 (3.86) and 417 (3.41).

Anal. Calcd. for $C_{23}H_{14}O_3$: C, 81.64; H, 4.17. Found: C, 81.37; H, 4.45.

A solution of 0.03 g. of the quinone in 3 cc. of acetic acid mixed with a solution of 0.1 g. of stannous chloride dihydrate and 0.1 cc. of 6 *N* hydrochloric acid in 1 cc. of water and heated ten minutes at 100° deposited when cold 0.02 g. of dark red needles of 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone, m.p. 223–227°.

1,4-Diacetoxy-9-hydroxy-9-phenyl-2,3-benzofluorene, obtained from the trihydroxy compound, acetic anhydride and sodium acetate or the quinone by reductive acetylation, formed white prisms from dilute acetic acid or ether–petroleum ether, m.p. 187.5–189°. The substance tended to separate as a gel from non-aqueous solvents. The ultraviolet absorption maxima in chloroform lay at 256 mμ (log ε 4.66), 265 (4.56) (inflection), 276 (4.50), 290 (4.18), 303 (4.28), 316 (4.34), 330 (3.09) (inflection) and 348 (2.68).

Anal. Calcd. for $C_{27}H_{20}O_5$: C, 76.40; H, 4.75. Found: C, 76.46; H, 5.44.

A mixture of 0.1 g. of 4-hydroxy-9-phenyl-2,3-benzo-1-isofluorenone, 3 cc. of acetic anhydride and a drop of sulfuric acid was warmed five minutes at 60°, cooled and treated with 0.3 g. of sodium acetate, 1 cc. of acetic acid and 4 cc. of water, shaken vigorously to hydrolyze the anhydride and chilled. The product, 0.14 g. of yellow solid, m.p. 182–199° (dec.), afforded on recrystallization from ethyl acetate–ligroin pure **1,4,9-triacetoxy-9-phenyl-2,3-benzofluorene** as white prisms, m.p. 223–226° (dec., bath preheated to 210°). The decomposition point is sensitive to impurity: certain samples melted near 230°, whereas material precipitated from acetic acid by water sometimes melted below 160°. The ultraviolet absorption maxima in chloroform lay at 256 mμ (log ε 4.60), 265 (4.57), 275 (4.55), 291 (4.19), 303 (4.26) and 316 (4.32).

Anal. Calcd. for $C_{29}H_{22}O_6$: C, 74.67; H, 4.75. Found: C, 74.57; H, 5.05.

A solution of 0.4 g. of 1-acetoxy-4-methoxy-2,3-benzofluorenone in 10 cc. of benzene was added to a cold solution of phenyllithium from 0.8 cc. of bromobenzene and 0.1 g. of lithium in 5 cc. of ether, boiled half an hour under reflux and poured into 20 cc. of cold 10% sulfuric acid. The organic phase, washed, evaporated, taken up in 3 cc. of benzene and 3 cc. of petroleum ether and chilled, deposited 0.15 g. of **1,9-dihydroxy-4-methoxy-9-phenyl-2,3-benzofluorene**, which formed pale yellow prisms from benzene–ligroin, soluble without color in aqueous alcoholic alkali. The substance heated slowly turned orange at 140° and melted at 175–179° (dec.); the "instantaneous" decomposition point appeared to be near 193°.

Anal. Calcd. for $C_{24}H_{18}O_3$: C, 81.34; H, 5.12. Found: C, 81.17; H, 5.11.

4-Methoxy-9-phenyl-2,3-benzo-1-isofluorenone could be obtained from 1,9-dihydroxy-4-methoxy-9-phenyl-2,3-benzofluorene by fusion at 190° or by solution in acetic acid at 100° or sulfuric acid at room temperature. In addition, when 20 mg. of the phenol and 0.15 g. of potassium hydroxide were dissolved in 1 cc. of methanol and 3 cc. of water and boiled under reflux 20 minutes, the dark mixture on dilution with 10 cc. of water and filtration afforded 15 mg. of bright orange methoxyisofluorenone, m.p. 152–153.5°.

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[Contribution from the Western Regional Research Laboratory[1] and the Rice Institute]

Reaction between 2,6-Di-*t*-butyl-*p*-cresol and Bromine

By Galvin M. Coppinger[2] and Tod W. Campbell[3]

Received October 6, 1952

Bromine reacts with 2,6-di-*t*-butyl-*p*-cresol in methyl alcohol, *t*-butyl alcohol or acetic acid to form, respectively, 2,6-di-*t*-butyl-4-methyl-4-methoxy-2,5-cyclohexadienone, 3,5-di-*t*-butyl-4-hydroxybenzaldehyde and 3,5-di-*t*-butyl-4-hydroxybenzyl acetate. The reaction proceeds through formation of 2,6-di-*t*-butyl-4-bromo-4-methyl-2,5-cyclohexadienone. An explanation of subsequent reactions leading to the reported products is suggested.

In a recent publication[4] 3,5-di-*t*-butyl-4-hydroxybenzaldehyde (I) was reported as the principal product of the reaction between bromine and 2,5-di-*t*-butyl-4-methyl-4-*t*-butylperoxy-2,5-cyclohexadienone in acetic acid. Efforts to synthesize this aromatic aldehyde by the usual methods proved unsuccessful. However, a small yield was obtained by treatment of 2,6-di-*t*-butyl-*p*-cresol with bromine in acetic acid in the presence of sodium acetate. Some aspects of this unusual reaction are considered in this paper.

It was observed that when the reaction between bromine and 2,6-di-*t*-butyl-*p*-cresol (IIIc) was carried out in commercial *t*-butyl alcohol or in a mixture of *t*-butyl alcohol and water, the yield of the aldehyde was increased and the time of reaction greatly shortened. Bromination in acetic acid containing a little water permitted the isolation of the aldehyde in high yield also, the reaction being considerably slower than in *t*-butyl alcohol. If on the other hand the reaction was allowed to proceed in methyl alcohol or in a mixture of methyl alcohol and water, the only product obtained was a compound which possessed an ultraviolet spectrum characteristic of a substituted 2,5-cyclohexadienone,[4,5] exhibiting a maximum at 234 mμ, with an ε of 10,000 in 95% ethyl alcohol, 232 mμ in iso-

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[1] Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

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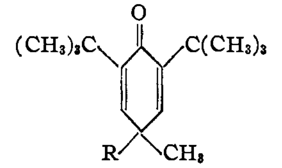
[4] T. W. Campbell and G. M. Coppinger, This Journal, **74**, 1469 (1952).

[5] H. Dannenberg, *Abhand. preuss. Akad. Wiss.*, **21**, 3 (1939); L. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd Ed., Reinhold Publishing Co., New York, N. Y., 1941, p. 193.

octane. It did not possess a band characterizing the hydroxyl group of a hindered phenol in the infrared.[6]

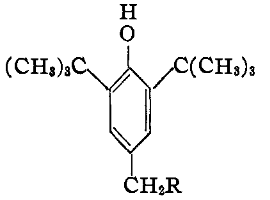
Analysis indicated the formula $C_{16}H_{26}O_2$ which would correspond to the compound IIa



IIa, R = OCH_3
b, R = $OCH_2CH_2CH_3$
c, R = Br

The corresponding propyl ether IIb was isolated when propyl alcohol was employed as solvent.

When the bromination was carried out in glacial acetic acid the product of the reaction was 3,5-di-*t*-butyl-4-hydroxybenzyl acetate (IIIa).



IIIa, R = $OCOCH_3$
b, R = OH
c, R = H

However, if the bromination was done in a mixture of acetic acid and water at room temperature it was possible with care to isolate a compound whose structure may be represented by IIc. This compound has a maximum in the ultraviolet at 248 mμ in isoöctane with an ε of 14,000. The infrared spectrum has no band in the hydroxyl stretching region and exhibits a doublet at 6.05, 6.11 μ, which may be ascribed to a ketone conjugated with a double bond.[4]

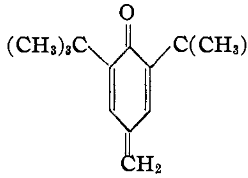
The formation of the aldehyde I required two moles of bromine for each mole of starting material, while the formation of compounds IIa, b, c, and IIIa required 1 mole.

When the bromocyclohexadienone IIc was dissolved in methyl alcohol, the product obtained was the methyl ether IIa; a solution of IIc in glacial acetic acid produced the benzyl acetate IIIa. Finally, when IIc was dissolved in a mixture of *t*-butyl alcohol and water or acetone and water, the compound isolated was the benzyl alcohol IIIb.

Treatment of the benzyl alcohol IIIb with one mole of bromine in *t*-butyl alcohol or in methyl alcohol permitted the isolation of the aldehyde I as the exclusive product. The benzyl acetate was unaffected by bromine under the same conditions.

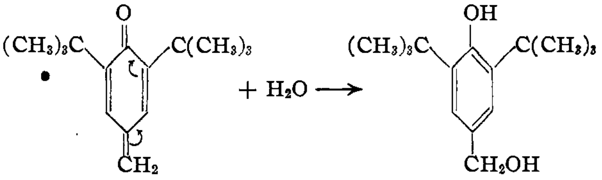
These observations would indicate that the reaction between 2,6-di-*t*-butyl-*p*-cresol and bromine consists initially of the transfer of a bromonium ion, (Br^+), to the 4-position of the phenol with the elimination of the phenolic proton to form the bromocyclohexadienone IIc. Fries and Brandes[7] have reported a similar result from the bromination of mesitol. Other phenols substituted in the 2-, 4- and 6-positions afford the appropriately substituted cyclohexadienones on bromination.[8,9] The bromocyclohexadienone IIc in methyl or propyl alcohol undergoes replacement of bromine to form the ethers, IIa or IIb.

Elimination of HBr from the bromocyclohexadienone IIc would lead to the formation of the quinone methide, IV



IV

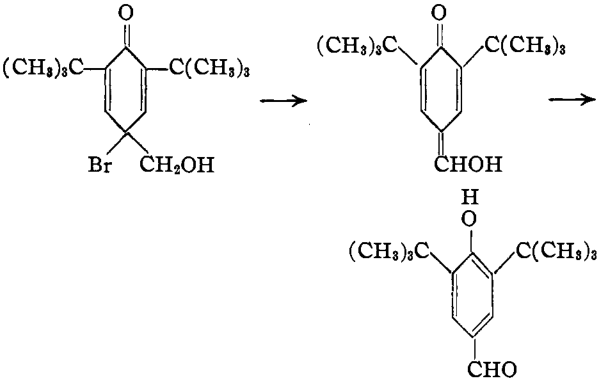
Attack by water could accomplish the formation of the benzyl alcohol, IIIb, in a manner similar to



IIb

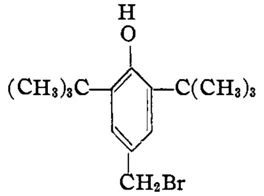
When the attacking species is acetic acid this sequence would account for the formation of the substituted benzyl acetate IIIa.

If the resulting benzyl alcohol IIIb is again brominated, in a manner analogous to the bromination of the original phenol, elimination of HBr would lead to the formation of a compound tautomeric with 3,5-di-*t*-butyl-4-hydroxybenzaldehyde (I).



I

There is no direct evidence for the formation of an intermediate quinone methide. The precursor of the benzyl alcohol IIIb may be



Fries and Brandes[7] have reported that 2,4,6-trimethyl-3,4,5-tribromo-3,5-cyclohexadienone rearranges to 2,6-dimethyl-3,5-dibromo-4-bromomethylphenol on heating or on long standing. However no compounds which might be expected to be derived from this sequence, for example 3,5-di-*t*-butyl-4-hydroxybenzyl-*t*-butyl ether, were observed.

[6] W. C. Sears and L. J. Kitchen, THIS JOURNAL, **71**, 4110 (1949).

[7] K. Fries and E. Brandes, *Ann.*, **542**, 48 (1939).

[8] J. Thiele and H. Eichwende, *Ber.*, **33**, 673 (1900).

[9] C. Elston, A. T. Peters and F. M. Rowe, *J. Chem. Soc.*, 367 (1948).

Experimental

2,6-Di-*t*-butyl-4-methyl-4-methoxy-2,5-cyclohexadienone.—One gram of 2,6-di-*t*-butyl-*p*-cresol was dissolved in 50 cc. of methyl alcohol, and 0.23 cc. of bromine was added at room temperature; the temperature of the solution rose immediately. After filtering, the product was washed with thiosulfate solution and water, and recrystallized from methyl alcohol. The yield of short blunt needles was quantitative, m.p. 94°.

Anal. Calcd. for $C_{16}H_{26}O_2$: C, 76.7; H, 10.5. Found: C, 76.5; H, 10.4.

The same reaction was carried out in a solvent mixture of 50 cc. of methyl alcohol and 5 cc. of water, with identical results.

The 2,6-Di-*t*-butyl-4-methyl-4-*n*-propoxy-2,5-cyclohexadienone.—The conditions outlined above were repeated in *n*-propyl alcohol as solvent. The product was obtained in nearly quantitative yield, m.p. 53°.

Anal. Calcd. for $C_{18}H_{30}O_2$: C, 77.6; H, 10.9. Found: C, 77.0; H, 10.9.

3,5-Di-*t*-butyl-4-hydroxybenzaldehyde.—One gram of 2,6-di-*t*-butyl-*p*-cresol was dissolved in 50 cc. of *t*-butyl alcohol, and 0.46 cc. of bromine was added at room temperature. At the end of 2 hours the aldehyde crystallized in large lustrous pink plates. The product was filtered, washed with thiosulfate solution and with water, and recrystallized from methyl alcohol to give 0.9 g., 85% yield, of lustrous pearly plates, m.p. 189°.

When the reaction between 2,6-di-*t*-butyl-*p*-cresol (1 g.) and bromine (0.46 cc.) was carried out in a mixture of 20 cc. of acetic acid and 5 cc. of water at a temperature of 40° for 2 hours, there was recovered upon cooling 0.91 g. of the aldehyde.

When glacial acetic acid was used as the solvent and the reaction repeated as above, it was possible to isolate at the end of two hours in 80% yield, only the compound 3,5-di-*t*-butyl-4-hydroxybenzyl acetate. If the reaction was allowed to proceed at room temperature for 3 days there resulted upon removal of the solvent, in addition to the benzyl acetate, a highly colored crystalline material which was not further investigated. No aldehyde was obtained.

2,6-Di-*t*-butyl-4-bromo-4-methyl-2,5-cyclohexadienone.—One gram of 2,6-di-*t*-butyl-*p*-cresol in a solution of 12 cc. of acetic acid and 3 cc. of water was treated with 0.23 cc. of bromine at room temperature. Very shortly, yellow needles separated out of the solution. After filtering, the solution was diluted with water and the resulting oil was taken up in ether. The ether solution was washed with cold water and a cold solution of sodium bicarbonate. The ether was removed and the solid material remaining recrystallized from methanol–water mixture.

The yellow needles obtained initially were recrystallized from petroleum ether. The yield of 2,6-di-*t*-butyl-4-bromo-4-methyl-2,5-cyclohexadienone was 0.65 g., 45% yield, m.p. 91–91.3°.

Anal. Calcd. for $C_{15}H_{23}BrO$: C, 60.3; H, 7.75. Found: C, 60.5; H, 7.83.

The material recovered from ether yielded 0.50 g. (40%) of 3,5-di-*t*-butyl-4-hydroxybenzyl acetate. The compound melted at 98.1–98.3° and did not depress the melting point of a sample of the compound prepared by another method described below.

3,5-Di-*t*-butyl-4-hydroxybenzyl Alcohol.—This compound was prepared by the reduction of 3,5-di-*t*-butyl-4-hydroxybenzaldehyde with lithium aluminum hydride.[10] The reaction permitted the isolation in 90% yield of the desired product, melting at 137.7–138.1°.

Anal. Calcd. for $C_{15}H_{24}O_2$: C, 76.1; H, 10.2. Found: C, 75.5; H, 10.0.

The acetate of the benzyl alcohol was obtained by treatment with acetyl chloride, m.p. 98.3–98.5°. The phenolic OH is not acetylated.

Reaction of 2,6-Di-*t*-butyl-4-bromo-4-methyl-2,5-cyclohexadienone (IIc). In Methyl Alcohol.—When 200 mg. of IIc was dissolved in 1 cc. of methyl alcohol, the yellow color of the solution was rapidly discharged and upon dilution with water and cooling there was obtained in quantitative yield 2,5-di-*t*-butyl-4-methyl-4-methoxy-2,5-cyclohexadienone, m.p. and mixed m.p. 94°.

In Acetic Acid.—In a solvent of glacial acetic acid (5 cc.), 200 mg. of IIc yielded 150 mg. of 3,5-di-*t*-butyl-4-hydroxybenzyl acetate. The compound was recovered and purified as outlined above, m.p. and mixed m.p. 98°.

In Acetone and Water.—Two hundred milligrams of IIc was dissolved in a mixture of 55 cc. of acetone and 0.5 cc. of water and allowed to stand at room temperature for 30 minutes. After cooling there was obtained in quantitative yield 3,5-di-*t*-butyl-4-hydroxybenzyl alcohol, m.p. and mixed m.p. 137.9°.

In *t*-Butyl Alcohol.—A solution of 200 mg. of IIc in 5 cc. of *t*-butyl alcohol and 1 drop of water was allowed to stand for 30 minutes at room temperature. There was isolated upon dilution with water 80 mg. of 3,5-di-*t*-butyl-4-hydroxybenzyl alcohol, m.p. and mixed m.p. 138°. In addition a small amount of the parent phenol, 2,6-di-*t*-butyl-*p*-cresol was also obtained.

Reactions of 3,5-Di-*t*-butyl-4-hydroxybenzyl Alcohol (IIIb). In *t*-Butyl Alcohol.—If a solution of 200 mg. of IIIb in 5 cc. of *t*-butyl alcohol was treated with 0.05 cc. of bromine, it was possible to isolate in nearly quantitative yield in a manner outlined above, 3,5-di-*t*-butyl-4-hydroxybenzaldehyde, m.p. and mixed m.p. 189°.

In Methanol.—When the reaction above was repeated using methyl alcohol as solvent (5 cc.), the only product isolated was the substituted benzaldehyde, in essentially quantitative yield.

Acknowledgments.—We wish to acknowledge the kindness of Dr. E. S. Lewis for permitting the completion of a portion of this work at The Rice Institute and for his helpful suggestions. We wish to thank Mr. G. F. Bailey for a part of the spectral measurements and Mr. L. M. White and Miss G. E. Secor for ultimate analysis.

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[10] R. F. Nystrom and W. Brown, THIS JOURNAL, **69**, 1197 (1947).