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# OXIDATIVE CONDENSATION OF CATECHOLS AND RESORCINOLS

A. C. Waiss, Jr., J. A. Kuhnle, J. J. Windle, and A. K. Wiersema
Western Regional Research Laboratory, Agricultural Research Service
U. S. Department of Agriculture, Albany, California 94710

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In connection with our investigation of polyphenol oxidation reactions we found that an equimolar solution of 3-isopropylcatechol and orcinol (0.01 M) mixed with 1 N sodium hydroxide in the presence of air rapidly forms a dark green color and gives a relatively stable (half-life greater than 24 hr.) free radical signal as shown in Fig. 1a. Since the EPR spectrum could not be accounted for by either of the starting materials or their self-condensation products we have undertaken to identify the product responsible for this spectrum.

Vapor phase chromatography of the trimethylsilyl ether of the product mixture, prepared by treatment of the total extracted phenolic mixture with hexamethyldisilazane (1), indicated that the condensation reaction yielded mainly one product and only negligible amounts of side products. Upon hydrolysis the major product trimethylsilyl ether peak gave an EPR signal identical to the original mixture.

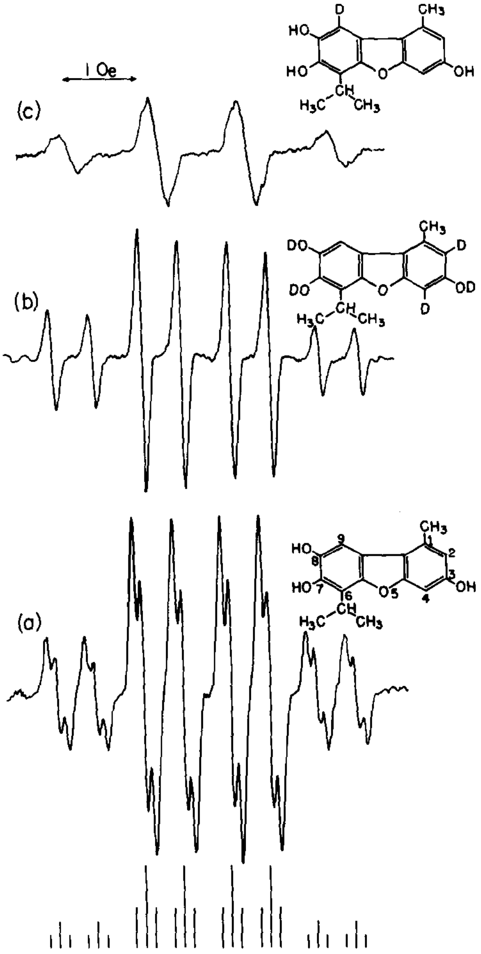
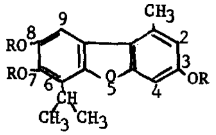
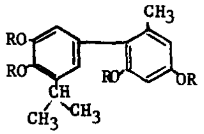


FIG. 1. EPR spectra from radical anions of (a) 1-methyl-3,7,8-trihydroxy-6-isopropyldibenzofuran and its reconstructed spectrum based on assigned hyperfine coupling constants, (b) 1-methyl-3,7,8-trihydroxy-6-isopropyldibenzofuran-2,4-$d_2$,$d_3$ and (c) 1-methyl-3,7,8-trihydroxy-6-isopropyl-dibenzofuran-9-d.

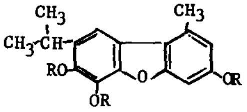
The structure of the 3-isopropylcatechol-orcinol condensation product was established to be 1-methyl-3,7,8-trihydroxy-6-isopropyldibenzofuran (Ia) from the following supporting evidence: The trimethylsilyl ether IB, analyzed for $C_{25}H_{40}O_4Si_3$ (2), displayed UV maxima at 313, 303, 295, and 259 mμ (cyclohexane). The nuclear magnetic resonance spectrum of Ib indicated the presence of an isopropyl group (6H doublet at 8.63 τ, 1H heptet at 6.47 τ, J = 7.0 c.p.s.), two <u>meta</u> proton signals (3.53 and 3.24 τ, J = 2.0 c.p.s.) broadened by coupling to an Ar-$CH_3$ group (3H singlet at 7.39 τ), and an uncoupled proton peak (singlet at 2.88 τ). When heated with acetic anhydride and potassium acetate trimethylsilyl ether Ib was converted to its corresponding acetate Ic, m.p. 179-180°, analyzed for $C_{22}H_{22}O_7$. The structure of the acetate was confirmed by UV and NMR spectroscopy. The hydrolysate of acetate Ic, as with trimethylsilyl ether Ib, gave an EPR spectrum identical to that produced by the original isopropylcatechol-orcinol mixture.



Ia R = H
Ib = $SiMe_3$
Ic = Ac



IIa R = H
IIb = $SiMe_3$
IIc = Ac



III

In order to establish the sequence of the C-C and C-O bond formation and position of the isopropyl group in dibenzofuran Ia the condensation reaction was allowed to proceed only partially in a limited supply of air for 10 sec. and was then quenched with acid. Vapor phase chromatography of the trimethylsilyl ethers of this reaction mixture gave two major product peaks corresponding to dibenzofuran Ib and biphenyl IIb. The position of the C-C linkage in biphenyl IIa was conclusively demonstrated by the NMR spectra of its trimethylsilyl ether IIb and acetate IIc; each displayed two pairs of meta proton doublets (3.93, 3.59 and 3.73, 3.42 $\tau$ for IIb and 3.25, 3.08, and 3.15, 3.02 $\tau$ for IIc, J = 2.0 c.p.s. for all protons). The isolation of biphenyl IIa as the intermediate limits the structure of dibenzofuran to two possibilities, that of Ia and III. Structure III is excluded from consideration since the dibenzofuran gave a negative Gibbs test (3).

The EPR spectrum of the radical anion dibenzofuran Ia (Fig. 1a), consists of a quartet with intensity ratios 1:3:3:1 due to a hyperfine coupling to three equivalent protons with a coupling constant of 1.22 Oe. Each of these lines is split into a doublet by a single proton with a coupling constant of 0.56 Oe and each of these is again split into three lines with intensity ratios 1:2:1 and coupling constant of 0.13 Oe, indicating coupling to two equivalent protons. The result is a twenty-four line spectrum with relative intensity of 1:2:1:1:2:1:3:6:3:3:6:3:3:6:3:3:6:3:1:2:1:1:2:1) (Fig. 1a). The hyperfine coupling constants of dibenzofuran Ia were assigned with the aid of its deuterium analogs. Since the rate of hydrogen-deuterium exchange in the benzene nucleus of resorcinols at pH 14 is instantaneous while no appreciable exchange in catechols is observed in several hours (4), it was possible to condense 3-isopropylcatechol and orcinol-2,4,6$d_3$,$d_2$ in deuterium oxide with sodium hydroxide-d and to obtain the EPR spectrum of the radical anion of 2,4-dideuterio analog of Ia (Fig. 1b). Similarly the condensation of orcinol with 3-isopropylcatechol-4,5,6-$d_3$,$d_2$ in aqueous sodium hydroxide gave dibenzofuran with deuterium at position 9 (Fig. 1c). With the above results and the fact that the ratio of the hyperfine splitting of the proton to the deuteron ($A_H/A_D$) equals 6.51, it was then possible to assign the quartet as due to the methyl group ($A_{CH_3}$ = 1.22 Oe), the doublet to $H_9$ ($A_{H_9}$ = 0.56 Oe), and the triplet to $H_2$ and $H_4$ ($A_{H_2} = A_{H_4} = 0.13$ Oe). No hyperfine coupling from the isopropyl group was observed.

The formation of dibenzofuran through mixed condensation reaction of catechols and resorcinols was found to be quite general. It is interesting to note that although self-condensation of catechols and resorcinols have been reported to proceed rapidly (5) we observe very little, if any, product of this type from our reaction. Details on the mechanism of this oxidative condensation are being examined and the technique of employing the difference in hydrogen-deuterium-exchange rate for facilitating the interpretation of polyphenol EPR spectra is further explored.

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