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DIMERS OF ISOEUGENOL BY DYE-SENSITIZED PHOTOOXIDATION

K. Eskins, C. Glass, W. Rohwedder, R. Kleiman, and J. Sloneker

Northern Regional Research Laboratory,* Peoria, Illinois 61604

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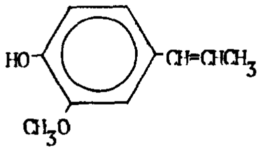
The oxidation of isoeugenol to a variety of compounds is well documented in the literature (1-5). We have extended this research by examining the effect of dye-sensitized photooxidation on isoeugenol (I), a monomer that has been implicated in the biosynthesis of lignin (6).



I

Isolation of "lignol-like" dimers from the photomixture gives reason to consider the possibility that photooxidation may contribute to lignin synthesis.

In a typical reaction, 1 g (6.10 mmole) of cis-trans isoeugenol and 25 mg of proflavin dihydrochloride were dissolved in 100 ml of methanol. The solution, constantly saturated with a stream of oxygen, was photooxidized by two 300-W incandescent lamps for 24 hr. The ether solution of the photomixture, after extraction with water, yielded 1040 mg of crude photoproduct. Blank runs under nitrogen or under oxygen without any dye gave essentially no reaction. Photooxidation of isoeugenol acetate under the same conditions also produced no products. TLC and column chromatography (silica gel, cyclohexane-ether mixtures) showed the presence of, and partially separated, three major photoproducts--A, B, and C. Separation of B and C was completed by acetylation of the photomixture before column chromatography. In

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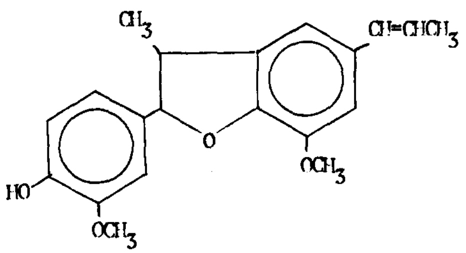
* This is a laboratory of the Northern Marketing and Nutrition Research Division, Agricultural Research Service, U.S. Department of Agriculture.

one run, 540 mg of crude acetylated photomixture gave 95 mg of acetylated A, 110 mg of acetylated B, and 115 mg of acetylated C.

Compounds B and C were catalytically hydrogenated (Pd, C, 1 atm) to eliminate the occurrence of cis,trans isomers. NMR data for compounds B and C, therefore, are given only for the acetylated and hydrogenated compounds.

Major products--A, B, and C--were identified by a combination of chemical and instrumental techniques. Compound A was identified as dehydrodiisoeugenol by comparison of its melting point and that of its p-nitrobenzoyl derivative with reported values.



Compound A, dehydrodiisoeugenol

M.p. 133-5 (cf. 6), p-nitrobenzoyl ester m.p. 155-7 (cf. 6)

λ_{max} (EtOH) 274 nm

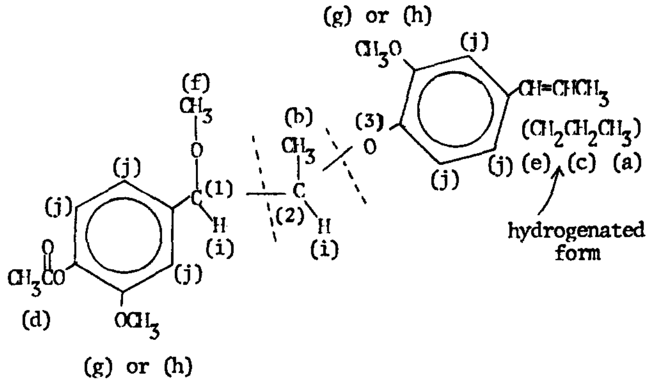
Calc.: C, 73.62; H, 6.75

Found: C, 73.72; H, 6.83

ms. m/e M^+ 326 ($C_{20}H_{22}O_4$)

Elemental analysis and high resolution mass spectroscopy both confirmed the molecular formula $C_{20}H_{22}O_4$. NMR data for A 1.36(3H,d), 1.85(3H,d), 3.44(1H,m), 3.84(3H,s), 3.86(3H,s), 5.08(1H,d), 5.58(1H,s), 6.10(2H,m), 6.82(5H,m) and hydrogenated, acetylated A corresponded to the proposed structure.

Compounds B and C were separated and identified as their acetates. Elemental analysis and mass spectroscopy gave a molecular formula of $C_{23}H_{28}O_6$ for both acetylated B and C. The mass spectra for both acetylated B and C were identical. Catalytic hydrogenation of acetylated B and C gave two compounds, which also fragmented in identical patterns. These fragmentation patterns (Table I), together with elemental analysis and NMR data (Table II), strongly suggested the following structure for both compounds:



(1)-(2) Fragmentation

Frag. (1) 209

Frag. (1) minus CH_3CO 167

Frag. (2) 193

Frag. (2) hydrogenated compound 195

(2)-(3) Fragmentation

Frag. (2) 237

Frag. (2) minus CH_3CO 195

Frag. (3) + H 164

Frag. (3) + H hydrogenated compound 166

B and C (acetylated) 1 methoxy-1-[4-acetoxy-3-methoxyphenyl]-2-[4-propenyl-2-methoxyphenoxyl] propane

TABLE I

Major Mass Spectral Lines for Compounds B and C

m/e[a]	402	237	236	209	195	194	193	167	166	137
Intensity	24	24	18	22	56	40	46	100	8	14
m/e[b]	400	237	236	209	195	194	191	167	164	137
Intensity	28	25	28	9	81	51	21	100	30	18

[a] Acetylated, hydrogenated.

[b] Acetylated.

Differences in NMR and in chromatography between B and C may be explained by the diastereomeric forms possible. The NMR spectra of both B and C fit the proposed general structure well, but it was not possible to fit either one to a specific diastereomeric form. It was also difficult to explain the large shift in the saturated methyl absorption (b) from 1.30 in compound B to 1.09 in compound C. Conformational differences may be responsible, but they are not readily apparent.

TABLE II

NMR Data (ppm) for Compounds B[a] and C[a] ($CDCl_3$)

	B	C		B	C
(a)	0.96(3H,t)	0.92(3H,t)	(f)	3.34(3H,s)	3.30(3H,s)
(b)	1.30(3H,d)	1.09(3H,d)	(g)	3.75(3H,s)	3.79(3H,s)
(c)	1.58(2H,m)	1.61(2H,m)	(h)	3.80(3H,s)	3.81(3H,s)
(d)	2.27(3H,s)	2.28(3H,s)	(i)	4.34(2H,m)	4.35(2H,m)
(e)	2.49(2H,t)	2.51(2H,t)	(j)	6.6-7.1 (6H,m)	6.6-7.1 (6H,m)

[a] Acetylated and hydrogenated.

Formation of dehydrodiisoeugenol and the isomeric β-aryl ethers B and C by dye-sensitized photooxidation suggest that lignin formation could be initiated by a light-dye-O_2 system in the plant. A possible mechanism involves the abstraction of the phenolic hydrogen by an excited dye triplet or singlet oxygen to produce the products via a radical addition involving a quinone methide radical intermediate (7). Recent work by Knowles (8) has implicated the triplet state of flavins in the photooxidation of nucleotides. A number of other workers (9,10) have shown the hydrogen abstracting abilities of singlet oxygen. It is possible that plant pigments and oxygen may function similarly in lignin synthesis.

REFERENCES

1. H. Cousin and H. Herissey, Compt. Rend. 147, 247-9 (1908).
2. H. Cousin and H. Herissey, Bull. Soc. Chim., 3, 1070 (1908).
3. Fr. Fichter and A. Christen, Helv. Chim. Acta, 8, 332-6 (1925).
4. I. Plotnikov, Chem. Ztg., 52, 669-71 (1928).
5. M. Imoto, J. Chem. Soc. Jap., 55, 119-22 (1934).
6. H. Erdtman, Biochem. Z., 258, 172-80 (1933).
7. K. Freudenberg, Fortschr. Chem. Org. Naturst., 11, 43 (1954).
8. A. Knowles, Photochem. Photobiol., 13, 225-6 (1971).
9. A. U. Khan and D. R. Kearns, Advan. Chem. Ser., 77, 143 (1968).
10. T. Matsuura, N. Yoshimura, A. Nishinaga, and I. Saito, Tetrahedron Lett., 1009 (1969).