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THE DIMERIZATION OF ISOEUGENOL BY FREE RADICALS

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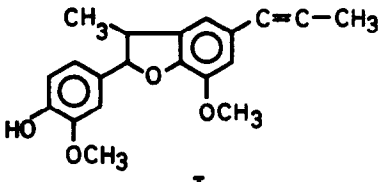
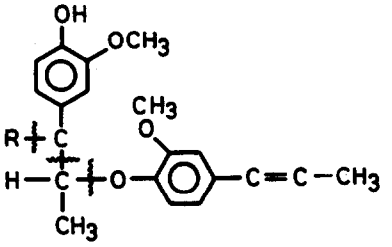
The oxidation of isoeugenol has been studied previously as a model for the observations of the formation of lignin-related dimers during the enzymatic oxidation[1] and the dye sensitized photo-oxidation[2] of isoeugenol. These compounds could be formed by several mechanisms. A free-radical coupling mechanism is frequently proposed[3], but alternative mechanisms include[4] the reaction of a phenol or phenolate ion with a free radical or a phenoxonium ion, which could be formed by two electron oxidation of the phenol. In the present study it has been found that essentially the same products are obtained by oxidation of isoeugenol with the tritertiary-butylphenoxyl radical where free radicals must at least initially be involved. Thus the present study indicates that the biosynthesis of lignin could initially involve the one electron oxidation of phenolic monomers that is frequently postulated.

The tritertiarybutylphenoxyl radical was prepared by oxidation of the corresponding phenol with alkaline ferricyanide and was extracted into benzene. An equivalent amount of this solution in 200ml of benzene was then added over 90 minutes at room temperature, under oxygen-free nitrogen, to a solution of 2g of cis or trans isoeugenol in 100ml of solvent. The solvents, chosen to trap any quinone methides that may have been formed, were benzene with: 30% methanol, 30% acetic acid, and 30% acetic acid + 1g of trichloroacetic acid. The products were separated by chromatography on silica gel (benzene/ether) and by subsequent thick layer chromatography (silica, petrol/ether).



I



II

The dimeric materials obtained, I and the two diastereomeric forms of II, corresponded with compounds formed in the enzymatic oxidation and the photo-oxidation. The yields of these dimeric compounds were about 70% (based on unrecovered starting material) and the ratios of the dimers in acetic acid were similar to those found from the enzymatic studies, except that there was no evidence for a dimer arising from β-β coupling whereas in the enzymatic oxidation this mode of coupling accounted for 13-25% of the products.

Both dimers contain a double bond from the isoeugenol system and as with enzymatic studies it was found that the geometry of the double bonds in the products completely retained the geometry of the starting material. This could be clearly detected as the cis structure gives a strong ir absorption at 710cm^{-1}, and in the pmr spectrum the methyl doublet is further split (J=1.6Hz) by long range coupling. In contrast the trans structure gives a strong ir absorption at 960cm^{-1} and the methyl doublet shows no appreciable long range splitting[5]. This retention of geometry implies that the reactive species, be it radical or ion, must react faster than the double bond can isomerize. As all the products involve the β position, there would seem to be a high charge or spin density at this point and bond isomerization might be expected. As the radical concentration would be low (and this may account for the lack of β-β

coupled products), this may indicate that the reactive intermediate can react with neutral molecules of isoeugenol.

Dehydrodiisoeugenol (I) was identified by pmr and mass spectroscopy, and for the trans isomer by mixed melting point with an authentic sample. Dimer II was separated into two diastereomeric forms, with R = methoxyl or acetate depending on the initial solvent, and was identified by pmr and mass spectroscopy, and by comparison with data in refs. 1 and 2. Thus when R=OAc, there was a parent ion at mass 386 and fragments at 326, 223, 191, 181, and 164 which correspond to fragmentations at the positions marked in the diagram (cf ref.2). The pmr spectrum showed the methyl substituted double bond, two aromatic methoxyl groups, six aromatic protons and an acetate at either 2.13 or 2.03ppm for the two diastereomeric forms. In addition there was a proton (assigned as the β proton) giving a multiplet at 4.3 - 5ppm which, when irradiated, decoupled as 1 proton doublet at 5.9ppm (α proton) and a 3 proton doublet at 1.3ppm (saturated methyl). (Eskins, et al[2], claimed that the α and β protons had the same chemical shift. Apart from this, the pmr and mass spectra were in good accord.)

Apart from the formation of diisoeugenol, which occurs in acid solutions[1], the product ratios did not vary markedly with acidity. This would suggest that the phenolate ion is not important as its concentration should be low in the trichloroacetic acid solutions. Furthermore the product ratio did not vary appreciably, in acetic acid, though the temperature range 10° - 75°, which suggests that the couplings have similar activation parameters. This implies that the slow step in the formation of each dimer is either very similar or involves the formation of a common intermediate.

A preliminary investigation of the more polymeric material has led to some conclusions. One is that structural units of the type I

involving the coumaran system are absent. These could be identified by the doublet of 9.5Hz width at 5.3ppm in the pmr. This might indicate that the further polymerization has not proceeded by the same mechanism as the formation of I and II, as both of these have a phenol system capable of forming a courmaran link.

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