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ANODIC OXIDATION OF E- AND Z-ISOEUGENOL

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Anodic oxidation of E- and Z-isoeugenol (**1** and **2**) in MeOH was carried out at a controlled potential of +800 mV *vs* SCE, using an undivided cell, to afford oxidation products (**3**, **4**, **5**, **6**, **7**, **8**, and **9** from **1**; **3**, **4**, **5**, **6**, **10**, **11**, and **12** from **2**).

Similar treatment of a mixture of Z-isoeugenol (**2**) and 2,6-dimethoxy-4-allylphenol (**13**) gave the arylpropanoid (**14**).

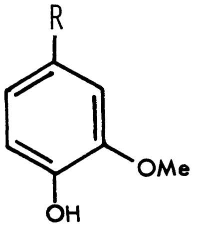
Recent investigations[1] on searching for biologically active substances to insects are quite attractive to us. In the present paper, we wish to describe anodic oxidation of E- and Z-isoeugenol (**1** and **2**) in connection with our interests in the growth inhibitory substances to silkworm larvae, which are dimeric arylpropanoids.[1,2]

An undivided cell with platinum electrodes was used. A solution of E-isoeugenol (2.0 mmoles) in MeOH (100 ml) containing $LiClO_4$ (60 mmoles) as the supporting electrolyte was electrolyzed at a controlled potential of +800 mV *vs* SCE (room temp., 7.5 h), and quenched at 1.5 Faraday/mole. The reaction solution was concentrated under reduced pressure below 40°C, and then separated by column chromatography [Polymer HP-255/MeOH - H_2O (95 : 5)] followed by preparative TLC [Kieselgel PF_{254}/hexane - EtOAc (1 : 1, 3 : 2, or 2 : 1)] to give seven oxidation products (**3**, **4**, **5**, **6**, **7**, **8**, and **9**) in 7, 17, 5.5, 5, 9.5, 8, and 29% isolated yields, respectively.

Of these oxidation products, the compounds (**7** and **8**) were previously reported as photooxidation products of isoeugenol.[3] Although the stereostructures of these isomers have not been mentioned, the former (**7**), whose methyl doublet is observed in lower magnetic field than that of **8** (δ1.32 in **7**; δ1.08 in **8**), is assignable to the erythro isomer.[4] The compound (**9**), which was isolated from *Myristica fragrans* Houtt[2] as well as from *Licaria aritu* Ground,[5] is also an oxidation product of isoeugenol.[3,6] The structures of the remaining oxidation products were determined on the basis of their spectral data [**3**: $C_{12}H_{18}O_4$ (m/e 167(M^+- 59)); ν_{max}(film) 3350br., 1610, and 1520 cm^{-1}; $\delta(CDCl_3)$ 0.94(3H, d, J= 6Hz), 3.23(3H, s), 3.38(1H, quintet, J= 6Hz), 3.42(3H, s), 3.83(3H, s), 3.98(1H, d, J= 6Hz), 5.76(1H, br.s, OH), 6.67 - 6.93(3H, aromatic). 4: $C_{12}H_{18}O_4$ (m/e 167(M^+- 59)); ν_{max}(film) 3325br., 1610, and 1520 cm^{-1}; $\delta(CDCl_3)$ 1.14(3H, d, J= 6Hz), 3.27(6H, s), 3.41(1H, dq, J= 5, 6Hz), 3.90(3H, s), 4.08(1H, d, J= 5Hz), 5.65(1H, s, OH), and 6.19 - 6.95(3H, aromatic). 5: $C_{22}H_{30}O_6$ (m/e 390(M^+) and 167); ν_{max}(film) 3350, 1615sh., 1605, and 1515br. cm^{-1}; $\delta(CDCl_3)$ 0.70(3H, d, J= 7Hz), 0.79(3H, d, J= 7Hz), 1.63 - 2.05(1H, m), 2.34 - 2.72(1H, m), 3.21(3H, s), 3.24(3H, s), 3.41(1H, d, J= 10Hz), 3.82(6H, s), 4.14(1H, d, J= 8Hz), 5.46(2H, br.s, OH), and 5.71 - 6.80(6H, complex). 6: $C_{21}H_{26}O_5$ (m/e 358(M^+) and 326); ν_{max}(film) 3400, 1610, and 1515 cm^{-1}; $\delta(CDCl_3)$ 0.88 (3H, d, J= 6Hz), 1.13(3H, d, J= 6Hz), 1.5 - 1.9(2H, complex), 3.26(3H, s), 3.46(1H, br.d, J= 8Hz), 3.58(3H, s), 3.80(3H, s), 4.27(1H, br.d, J= 8Hz), 5.53(1H, s, OH), 5.59(1H, s, OH), 6.14(1H, s), 6.53(1H, d, J= 2Hz), 6.64(1H, dd, J= 8, 2Hz), 6.86(1H, d, J= 8Hz), and 7.00(1H, s)].

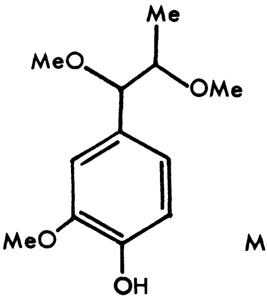
In the case of the two stereoisomers (3 and 4), the former must be the threo isomer, as judged by their chemical shifts of methyl doublets (δ0.94 in 3; δ1.14 in 4).[4]

As shown earlier, the tentative structure of the third compound (5) is particularly supported



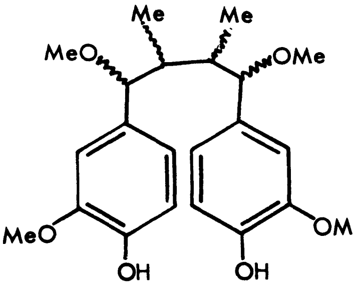
1 R = -CH$\overset{E}{=}$CHMe

2 R = -CH$\overset{Z}{=}$CHMe

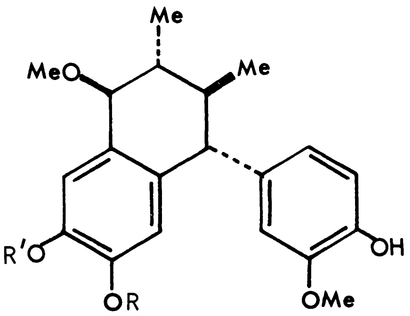


3 (Threo)

4 (Erythro)

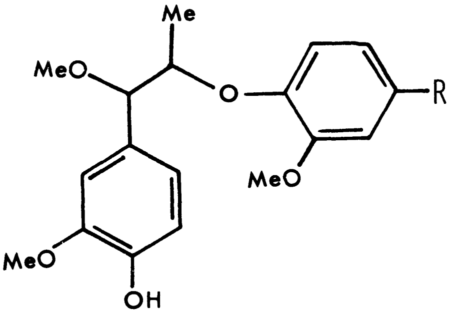


5



6 R = H, R'= Me

or R = Me, R'= H

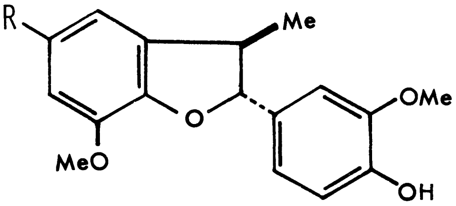


7 R = -CH$\overset{E}{=}$CHMe (Erythro)

8 R = -CH$\overset{E}{=}$CHMe (Threo)

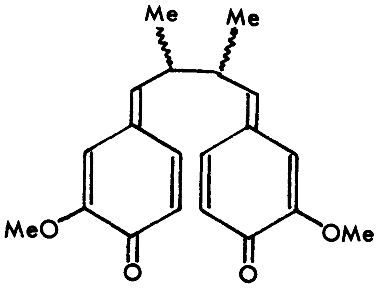
10 R = -CH$\overset{Z}{=}$CHMe (Erythro)

11 R = -CH$\overset{Z}{=}$CHMe (Threo)



9 R = -CH$\overset{E}{=}$CHMe

12 R = -CH$\overset{Z}{=}$CHMe

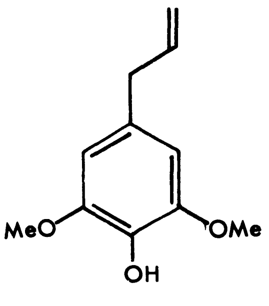


[A]

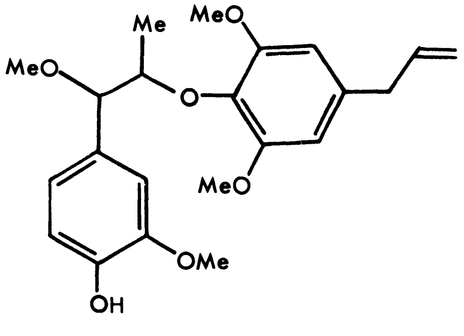
by its NMR spectrum indicating the presence of two environmentally different MeO-CH-CH(Me)- groupings in addition to six aromatic protons (δ5.71 - 6.80), although its stereochemistry remains undecided.[7] The structure of the compound (6) is also based on its spectral data. Particularly, the NMR spectrum of 6 indicates that it has two secondary methyl groups, one MeO-CH-CH- grouping, two methoxyl groups attached to the aromatic rings (δ3.58 - 3.80), and five aromatic protons (δ6.14, 6.53, 6.64, 6.86, and 7.00). Furthermore, its stereostructure may be represented by 6 on the basis of the coupling constants of two methine protons (δ3.46 and 4.27). On dimerization of the two molecules, these two compounds (5 and 6) are produced via C-C bond formation at the side chain, which must take place at the initial stage leading to the formation of a plausible intermediate [A].

We further examined anodic oxidation of Z-isoeugenol (2) under the same conditions as those of the E-isomer. In this case, the same oxidation products (3, 4, 5, and 6) were obtained in addition to three dimers (10, 11, and 12)[8] corresponding to those from E-isoeugenol (7, 8, and 9) [3 (5%); 4 (7%); 5 (3%); 6 (22%); 10 (13.5%); 11 (16%); 12 (4.5%)].[9] However, the relative ratio of these oxidation products in 2 is considerably different from that in 1: total yield of the arylpropanoids (10 and 11) from 2 is higher than that of the corresponding dimers (7 and 8) from 1. Therefore, it seems to be much favorable to use Z-isoeugenol (2) in order to make a cross coupled dimeric arylpropanoid, as described below.

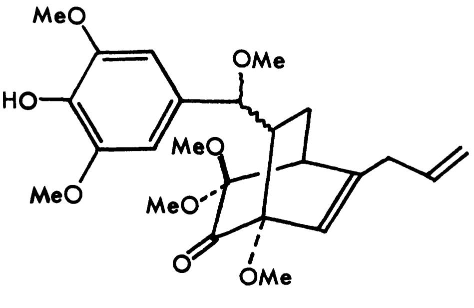
The anodic oxidation of a mixture of 2 and 2,6-dimethoxy-4-allylphenol (13) was carried out under essentially the same conditions as those of 1 and 2 (room temp., 4 h)[10] to afford the desirable arylpropanoid (14) (32%) and two arylpropanoids [10 (11%) and 11 (12%)] in addition to the known minor components (3, 4, 6, and 15[11]).[9] The new arylpropanoid (14) has the following spectral data: $C_{22}H_{28}O_6$ [m/e 388(M$^+$), 221, 195, 194, and 167]; ν_{max}(film) 3400, 1640, 1595br., 1520, and 1510 cm^{-1}; δ(CDCl$_3$) 1.24(3H, d, J= 6.5Hz), 3.27 - 3.36(2H, superimposed on the one methyl singlet), 3.33(3H, s), 3.74(6H, s), 3.82(3H, s), 4.14(1H, m), 4.36(1H, d, J= 4Hz), 5.04(1H,



13



14



15

br.d, J= 11Hz), 5.07(1H, br.d, J= 16Hz), 5.50(1H, br.s, OH), 5.93(1H, m), 6.34(2H, s), and 6.63 - 6.88(3H, complex). Particularly, the structure of 14, which is considered to adopt the erythro form,[12] is supported by its mass and NMR spectra (m/e 221 and 167; δ1.24 and 4.36). Closely related cross dimers have been found in nature.[1]

References and Notes

1. A. Isogai, Nogeikagaku Kaishi, 51, R 47 (1977), and references cited therein.
2. A. Isogai, S. Murakoshi, A. Suzuki, and S. Tamura, Agr. Biol. Chem., 37, 889 (1973); ibid., 37, 1497 (1973); Nogeikagaku Kaishi, 47, 275 (1973).
3. K. Eskins, C. Glass, W. Rohwedder, R. Kleiman, and J. Sloneker, Tetrahedron Lett., 1972, 861.
4. G. H. Schmid, Can. J. Chem., 46, 3415 (1968).
5. C. J. Aiba, R. G. Campos Correa, and O. R. Gottlieb, Phytochemistry, 12, 1163 (1973).
6. H. Erdtman, Biochem. Z., 258, 172 (1933).
7. The relative stereochemistry of the two secondary methyl groups in 5 seems to be the same as that of 6, as expected from their common intermediate [A].
8. Spectral data of these three compounds [10: $C_{21}H_{26}O_5$ (m/e 358(M^+), 326, 195, and 167); ν_{max} (film) 3350br., 1605, 1580, and 1520br. cm^{-1}; $\delta(CDCl_3)$ 1.32(3H, d, J= 6Hz), 1.88(3H, dd, J= 7, 2Hz), 3.31(3H, s), 3.76(3H, s), 3.85(3H, s), 4.28(1H, d, J= 6Hz), 4.40(1H, quintet, J= 6Hz), 5.63(1H, br.s, OH), 5.68(1H, dq, J= 12, 7Hz), 6.37(1H, dq, J= 12, 2Hz), and 6.75 - 6.99(6H, complex). 11: $C_{21}H_{26}O_5$ (m/e 358(M^+), 226, 195, and 167); ν_{max}(film) 3500sh., 3350br., 1605, 1580, and 1620 cm^{-1}; $\delta(CDCl_3)$ 1.09(3H, d, J= 6Hz), 1.90(3H, dd, J= 7, 2Hz), 3.26(3H, s), 3.81 (3H, s), 3.86(3H, s), 4.27(1H, d, J= 6Hz), 4.48(1H, quintet, J= 6Hz), 5.64(1H, br.s, OH), 5.69 (1H, dq, J= 12, 7Hz), 6.36(1H, dq, J= 12, 2Hz), 6.75 - 7.01(6H, complex). 12: $C_{20}H_{22}O_4$ (m/e 326 (M^+), 311, 202, and 149); ν_{max}(film) 3400, 1615, 1600, 1520, and 1500 cm^{-1}; $\delta(CDCl_3)$ 1.39(3H, d, J= 7Hz), 1.93(3H, dd, J= 7, 2Hz), 3.46(1H, dq, J= 10, 7Hz), 3.87(6H, s), 5.11(1H, d, J= 10Hz), 5.63(1H, s, OH), 5.69(1H, dq, J= 11, 7Hz), 6.39(1H, dq, J= 11, 2Hz), and 6.59 - 7.02 (5H, complex)].
9. The yields indicate the isolated ones.
10. This reaction was stopped at 1.7 Faraday/mole.
11. M. Iguchi, A. Nishiyama, Y. Terada, and S. Yamamura, Tetrahedron Lett., 1977, 4511.
12. The doublet at δ4.36 with a small coupling constant (J= 4Hz) indicates that this arylpropanoid is the erythro form, as seen in the following data: coupling constants of the corresponding doublets in the erythro isomers (4, 7, and 10) are 5, 5.5, and 6Hz, respectively, while the corresponding ones are slightly larger than 6Hz in the threo isomers (3, 8, and 11).

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