

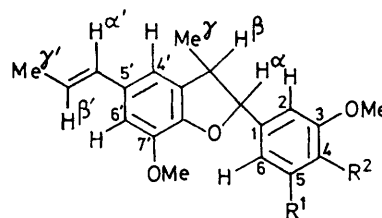
Diarylpropanoids from Nutmeg and Mace (*Myristica fragrans* Houtt.) †

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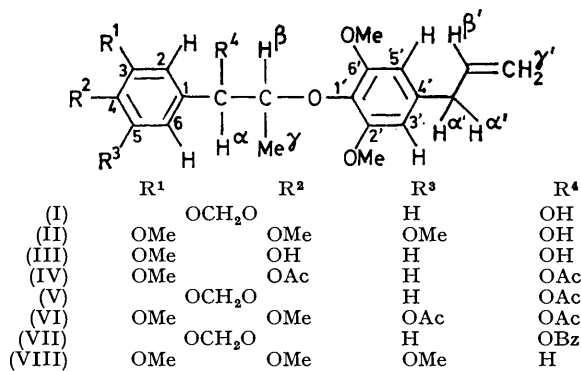
Some diarylpropanoid (bis-C₆-C₃) type compounds have been isolated during the course of a search for the psychoactive components present in the seed (nutmeg) and aril (mace) of the fruit of *Myristica fragrans* Houtt. The presence of two different structural types, analogous to the β-O-4 ether and 2,3-dihydrobenzofuran types of dilignols, has been established. Six examples (I)—(III) and (V)—(VIII) of the former type and two of the latter, dehydrodi-isoegenol (IX) and 5-methoxydehydrodi-isoegenol (X) have been isolated and their structures established. Compounds (I), (II), and (V), have been synthesised and the relative configuration of the β-O-4 ethers has been established as *erythro*.

THE common spices, nutmeg and mace, which are the seed and aril of the fruit of the tree, *Myristica fragrans* Houtt., have been used in folk medicine for many years for their alleged abortifacient, narcotic, and therapeutic properties.¹ This paper presents the results of an examination of some of the lipid soluble aromatic compounds which can be obtained from nutmeg and mace. Eight dimeric phenylpropanoids of two types [cyclic and acyclic ethers, e.g. (IX) and (I)] were isolated from light petroleum extracts of nutmeg and mace by column chromatography and preparative t.l.c. The determination of the structure of a compound isolated from nutmeg, representative of several differently substituted acyclic ethers is outlined below.

C₂₁H₂₄O₆ (precise mass measurement). The presence of a hydroxy-group was indicated by the peak at 3500 cm⁻¹ in the i.r. spectrum (CHCl₃) and the n.m.r. signal at δ ca. 4, variable with concentration and disappearing on



| | R ¹ | R ² |
|-------|----------------|----------------|
| (IX) | H | OH |
| (X) | OMe | OH |
| (XI) | H | OAc |
| (XII) | OMe | OAc |



The molecular formula of this compound (I) was

† Preliminary reports, J. E. Forrest, R. A. Heacock, and T. P. Forrest, *Experientia*, 1973, **29**, 139; *Naturwiss.*, 1973, **60**, 257.

treatment with deuterium oxide (see Table I). Acetylation of (I) yielded a monoacetate (C₂₃H₂₆O₇), the n.m.r. spectrum of which showed a change in the chemical shift of one proton from δ 4.78 to 5.83 indicating the presence of a single proton on the carbon bearing the hydroxy-group. This proton (d, J 2.8 Hz) was coupled to only one other proton, at δ 4.33; this latter proton being also coupled to a methyl group. The n.m.r. spectrum also showed the presence of two methoxy-groups, a methylenedioxy-group, an allyl group, and five aromatic protons. The above data could be accommodated by structure (I) but did not permit the definite placement of the

¹ J. E. Forrest and R. A. Heacock, *Lloydia*, 1972, **35**, 440, and references cited therein.

various substituents on the aromatic rings. Analysis of the mass spectrum (see Table 2) allowed the assignment of the methylenedioxy-group to one ring and the methoxy and allyl groups to the other.

The most likely substitution pattern, based upon biogenetic considerations is that indicated in formula (I).

Reduction of a ketone bearing an α polar group is predicted to yield predominantly the *erythro*-product.^{2,3} The assignment of the *erythro*-configuration to (I) is also consistent with its n.m.r. data. The small coupling constant (J 2.8 Hz) observed between the α - and β -protons indicates that (I) exists predominantly in a

TABLE 1
¹H N.m.r. spectroscopic data (60 MHz spectra) for the β -O-4 type diarylpropanoid ethers ^a

| Compound (I) | Chemical shifts (δ) ^b | | | | | | | | | | | Coupling constants $J_{\alpha,\beta}$ (Hz) | | |
|---------------------|---|----------------|----------------|----------------|---------|---------|----------------------------------|---------------------------------|----------------------------------|-----------------------|-----------------------------------|--|----------------------------------|-----------------------------------|
| | R ¹ | R ² | R ³ | R ⁴ | 2'-OMe | 6'-OMe | H ^{α} | H ^{β} | H ^{γ} | ArH | H ^{α'} | | H ^{β'} | H ^{γ'} |
| (I) | 5.87(s) | | (Arom) | 4.06br(s) | 3.85(s) | 3.85(s) | 4.78(d) | 4.33(qd) | 1.13(d) | 6.87—6.73(m); 6.45(s) | 3.36br(d) | 5.98(m) | 5.10(m) | 2.8 |
| (II) | 3.85(s) | 3.85(s) | 3.85(s) | 4.10br(s) | 3.85(s) | 3.85(s) | 4.80(d) | 4.35(qd) | 1.13(d) | 6.60(s); 6.46(s) | 3.38br(d) | 5.99(m) | 5.11(m) | 3.0 |
| (III) | 3.88(s) | 5.54(s) | (Arom) | 4.10br(s) | 3.83(s) | 3.83(s) | 4.80(d) | 4.35(qd) | 1.10(d) | 6.80—6.56(m); 6.44(s) | 3.35br(d) | 5.96(m) | 5.08(m) | 3.0 |
| (IV) | 3.81(s) | 2.30(s) | (Arom) | 2.18(s) | 3.78(s) | 3.78(s) | 5.91(d) | 4.45(qd) | 1.30(d) | 7.05—6.35(m); 6.40(s) | 3.33br(d) | 5.90(m) | 5.01(m) | 3.5 |
| (V) | 5.90(s) | | (Arom) | 2.15(s) | 3.78(s) | 3.78(s) | 5.83(d) | 4.40(qd) | 1.30(d) | 6.83—6.73(m); 6.40(s) | 3.31br(d) | 5.90(m) | 5.06(m) | 3.5 |
| (VI) ^c | 3.73(s) | 3.73(s) | 2.20(s) | 2.06(s) | 3.73(s) | 3.73(s) | 5.80(d) | 4.30(qd) | 1.16(d) | 7.10—6.43(m); 6.30(s) | 3.25br(d) | 5.90(m) | 5.01(m) | 3.5 |
| (VII) | 5.88(s) | | (Arom) | 8.15—7.33(m) | 3.66(s) | 3.66(s) | 6.00(d) | 4.51(qd) | 1.41(d) | 6.86—6.71(m); 6.35(s) | 3.31br(d) | 5.90(m) | 5.01(m) | 3.5 |
| (VIII) ^d | 3.83(s) | 3.80(s) | 3.83(s) | 2.74(dd) | 3.78(s) | 3.78(s) | 3.10(dd) | 3.82(m) | 1.23(d) | 6.46(s); 6.40(s) | 3.33br(d) | 5.90(m) | 5.06(m) | 5.5 and 7.7 |

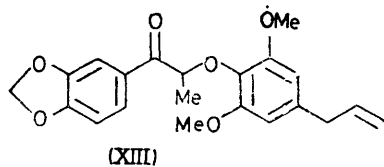
^a The spectra were recorded in CDCl₃ using Me₄Si as internal reference. ^b s = Singlet; d = doublet; m = multiplet; qd = quartet of doublets. ^c Spectrum recorded in CCl₄. ^d Spectrum recorded at 220 MHz; $J_{\alpha,\beta}$ 13.5 Hz.

TABLE 2
Mass spectral fragment ions of β -O-4 ethers *

| Compound | M ⁺ | A | B | C | D | AH † |
|----------|----------------|----------|-----------|----------|-----------|-----------|
| (I) | 372 (25) | 193 (12) | 179 (12) | 221 (27) | 151 (12) | 194 (100) |
| (II) | 418 (10) | 193 (12) | 225 (7) | 221 (7) | 197 (6) | 194 (100) |
| (III) | 374 (1) | 193 (7) | 181 (5) | 221 (8) | 153 (6) | 194 (100) |
| (IV) | 458 (0.3) | 193 (30) | 265 (51) | 221 (9) | 237 (1) | 194 (100) |
| (V) | 414 (5) | 193 (7) | 221 (38) | 221 (8) | 193 (7) | 194 (100) |
| (VI) | 488 (0.1) | 193 (1) | 295 (1) | 221 (1) | 267 (0.3) | 194 (42) |
| (VII) | 476 (1) | 193 (3) | 283 (26) | 221 (4) | 255 (0.1) | 194 (8) |
| (VIII) | 402 (5) | 193 (12) | 209 (100) | 221 (2) | 181 (9) | 194 (21) |

* Figures in parentheses are percentages of the base peak. † The rearrangement ion (AH) at 194 was shown by deuterium labeling of (II) to arise mainly by abstraction of the hydroxy-proton at R⁴ by the phenoxy-group.

That this is correct was proven by synthesis of (I) from the base catalysed reaction of methoxyeugenol with α -bromo-3',4'-methylenedioxypropionophenone, followed by reduction of the intermediate ketone (XIII) with lithium aluminium hydride. The reduction product consisted of mainly one diastereoisomer. Fortunately, this diastereoisomer was of the same relative configuration as the natural product as indicated by their superimposable n.m.r., i.r., and mass spectra. The acetyl (V)

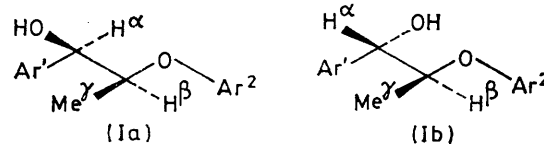


and benzoyl (VII) derivatives of the synthetic and natural products also gave identical spectra.

² K. Koga and S. Yamada, *Chem. and Pharm. Bull. (Japan)*, 1972, **20**, 526.

³ A. F. A. Wallis, *Austral. J. Chem.*, 1973, **26**, 585.

conformation in which these protons are in a *gauche*-orientation with respect to one another. In the *threo*-diastereoisomer (Ib), the most stable conformer, with the bulky aryl groups *trans* to each other, would have the α - and β -protons in a *trans*-orientation, whereas the most stable conformer of the *erythro*-isomer (Ia) would have these protons in a *gauche*-relationship.



Other examples of this β -O-4 dilignol * structural type include (V) and (VIII), found in nutmeg, (VI; R³ = R⁴ = OH instead of OAc), found in mace, and (II) and

* Dilignol nomenclature as given in ref. 4.

⁴ K. V. Sarkanen and C. H. Ludwig, 'Lignins: Occurrence, Formation, Structure and Reactions,' eds. K. V. Sarkanen and C. H. Ludwig, Wiley-Interscience, New York, 1971, ch. 1.

(III) found in both spices. The structures of these compounds follow from the spectral data recorded in Tables 1 and 2.

The structure of (II) was verified by comparison of its n.m.r., i.r., and mass spectral properties with those of a racemic sample synthesised from methoxyeugenol and α -bromo-3',4',5'-trimethoxypropiophenone by an analogous procedure to that used in the synthesis of (I).

A second type of diarylpropanoid having a 2,3-dihydrobenzofuran nucleus was also isolated. Two examples of this class of compound, dehydrodi-isoegenol (IX) and 5-methoxydehydrodi-isoegenol (X) were isolated from both nutmeg and mace. The n.m.r. and mass spectral data of these compounds and of their acetyl derivatives (XI) and (XII) are given in Tables 3 and 4 respectively. The dehydrodi-isoegenol which was isolated from the plant material exhibited solution

which have been isolated from nutmeg and mace have substituents in both positions *ortho* to the ether oxygen and have an allyl side chain. A phenol substituted in this manner can couple only at the oxygen since both *ortho*-positions are blocked and the β -position is not conjugated to the aromatic system. When an *ortho*-position is unsubstituted, a β -C-3 coupling is possible forming the 2,3-dihydrobenzofuran system. The fact that no β -O-4 coupled ethers were found with a free *ortho*-position or a conjugated double bond in the side chain may indicate a preference for coupling at the β or C-3 position when these are available. The deoxy-compound (VIII) is most likely formed by a reduction process after coupling rather than by a non-oxidative coupling mechanism.

Recent examples of the formation of diphenylpropanoids of similar structure by the free radical

TABLE 3
¹H N.m.r. spectroscopic data (60 MHz spectra) for the 2,3-dihydrobenzofuran type dimers ^a

| Compound | Chemical shifts (δ) ^b | | | | | | | | | | Coupling constants (Hz) | | | | | |
|----------|---|----------------|-----------|---------|----------------------------------|---------------------------------|----------------------------------|--------------|-----------------------------------|----------------------------------|-----------------------------------|--|--|---|---|-----|
| | R ¹ | R ² | 3-OMe | 7'-OMe | H ^{α} | H ^{β} | H ^{γ} | ArH | H ^{α'} | H ^{β'} | H ^{γ'} | J _{α,β} | J _{β,γ} | J _{α,β'} | J _{β,γ'} | |
| (IX) | (Arom) | 5.60br(s) | 3.85(s) | 3.87(s) | 5.06(d) | 3.42(m) | 1.37(d) | 6.93—6.74(m) | 6.35(d) | 6.05(m) | 1.85(d) | 9.0 | 7.0 | 15.0 | 5.5 | |
| (X) | (Arom) | 3.83(s) | 5.60br(s) | 3.83(s) | 3.88(s) | 5.03(d) | 3.40(m) | 1.38(d) | 6.80—6.70(m) | 6.35(d) | 6.05(m) | 1.85(d) | 9.0 | 7.0 | 15.0 | 5.5 |
| (XI) | (Arom) | 2.30(s) | 3.81(s) | 3.91(s) | 3.91(s) | 5.16(d) | 3.46(m) | 1.41(d) | 7.05—6.80(m) | 6.35(d) | 6.05(m) | 1.91(d) | 9.0 | 7.0 | 15.0 | 5.5 |
| (XII) | (Arom) | 3.83(s) | 2.33(s) | 3.83(s) | 3.91(s) | 5.11(d) | 3.46(m) | 1.43(d) | 6.79—6.70(m) | 6.35(d) | 6.05(m) | 1.88(d) | 9.0 | 7.0 | 15.0 | 5.5 |

^a The spectra were recorded in CDCl₃ using Me₄Si as internal reference. ^b s = Singlet; d = doublet; m = multiplet.

TABLE 4

Mass spectra of 2,3-dihydrobenzofurans

| Compound | M ⁺ | M - CH ₃ | M - CH ₂ CO | M - (CH ₂ CO + CH ₃) | M - Aryl group * |
|----------|----------------|---------------------|------------------------|---|------------------|
| (IX) | 326 (100) | 311 (10) | | | 202 (10) |
| (X) | 356 (100) | 341 (12) | | | 202 (8) |
| (XI) | 368 (33) | | 326 (100) | 311 (9) | 202 (13) |
| (XII) | 398 (42) | | 356 (100) | 341 (12) | 202 (7) |

* Assigned to the 3-methyl-5-propenyl-7-methoxybenzofuran ion.

spectra identical with those of an authentic racemic sample prepared by treatment of isoegenol with ferric chloride.⁵ The molecular formula of (X), C₂₁H₂₄O₅, suggested the dehydrodi-isoegenol structure with an additional methoxy-group. The n.m.r. spectrum of (X) was identical with that of (IX) with the exception of the presence of an extra methoxy-group at δ 3.83 and one less aromatic proton in the spectrum of (X). The assignment of the extra methoxy-group at C-5 was made on the basis of the superimposition of the peaks due to the 3- and 5-methoxy-groups and of the 2- and 6-aromatic protons (δ 6.70) in the n.m.r. spectrum.

The biogenesis of these compounds probably involves the coupling of two C₆-C₃ units by a free radical mechanism. Analogues of these products, dilignols, such as dehydrodiconiferyl alcohol and guaiacylglycerol- β -coniferyl ether have been observed among the mild acid degradation products of lignin and have been postulated as intermediates in the biosynthesis of lignin.⁶ It is noteworthy that all the open chain (β -O-4 coupled) ethers

oxidative coupling⁷ or dye sensitised photo-oxidation⁸ of isoegenol have been reported. An example of the second class of diarylpropanoid described above (eupomatenoide-8) has been reported to be present as a constituent of the bark of *Eupomatia laurina* R. Br.⁹ Dehydrodi-isoegenol (IX) has very recently been shown to be present in the wood of the Amazonian tree *Licaria aritu* Ducke.¹⁰

EXPERIMENTAL

M.p.s were taken on a Fisher-Johns hot stage apparatus and are uncorrected. N.m.r. spectra were determined with Varian A-60A or T-60 instruments for solutions in deuteriochloroform (unless otherwise indicated) with tetramethylsilane as internal reference. Mass spectra were recorded with Dupont 21-110B and/or 21-491 mass spectrometers. I.r. spectra were measured with a Perkin-Elmer model 237 recording spectrophotometer. Chromatography employed Davison silica gel (100—200 mesh) for columns and Merck silica gel F254 plates, 0.25 mm thick for analytical and 2 mm thick for preparative separations, and anisaldehyde spray reagent for visualisation.

⁹ B. F. Bowden, E. Ritchie, and W. C. Taylor, *Austral. J. Chem.*, 1972, **25**, 2659.

¹⁰ C. J. Aiba, R. G. Campos Correa, and O. R. Gottlieb, *Phytochemistry*, 1973, **12**, 1163.

⁵ B. Leopold, *Acta Chem. Scand.*, 1950, **4**, 1523.

⁶ K. V. Sarkanen in ref. 4, ch. 4.

⁷ I. J. Miller, *Tetrahedron Letters*, 1972, 4955.

⁸ K. Eskins, C. Glass, W. Rohwedder, R. Kleiman, and J. Sloneker, *Tetrahedron Letters*, 1972, 861.

Extraction of Nutmeg.—Freshly ground nutmeg (1 kg) was extracted with light petroleum (b.p. 35–60°) (4 l) for 5 min at room temperature. The extract was refrigerated and the crystalline trimyristin, m.p. 55–56°, which separated was filtered off. The filtrate on concentration gave a brown oil, which was partitioned between hexane and 85% ethanol. The alcohol fraction was concentrated *in vacuo* to give an oil (33.5 g) which was redissolved in ether and extracted successively with 5% aqueous sodium hydrogen carbonate solution, 5% aqueous sodium carbonate solution, and 5% aqueous sodium hydroxide solution. The residual ether fraction was dried (Na₂SO₄) and concentrated *in vacuo* to give a brown oil (19.5 g), *i.e.* the neutral fraction. The sodium hydroxide fraction was acidified with cooling and re-extracted with ether; concentration of the dried (Na₂SO₄) ether extracts gave 3.2 g of an oily phenolic fraction.

The phenolic fraction was chromatographed on a silica gel column giving a series of oily fractions. The column was eluted successively with solvent mixtures of increasing polarity, utilising hexanes, benzene, ethyl acetate, and methanol. The effluent from the column was monitored by t.l.c. [acetone–benzene (5:95)] and similar fractions combined.

Compounds (IV) and (X) were eluted with benzene–ethyl acetate mixtures and further purified after acetylation by preparative t.l.c. [benzene–acetone (98:2)]. Compound (IX) was eluted from the column with benzene–hexane (1:1); this compound was also found in the neutral fraction.

Also isolated from the neutral fraction were (I), (V), and (VIII) by p.l.c. on silica gel using benzene as developing solvent. The main band was removed and further chromatographed in the solvent system light petroleum–diethyl ether–formic acid (700:300:6) which yielded several bands from which, on rechromatography in the solvent system ethyl acetate–cyclohexane (1:1), (I), (V), and (VIII) were isolated.

Freshly ground mace was extracted in a similar manner and column chromatography of the phenolic fraction yielded (III), (VI), (IX), and (X). Compound (II) was isolated by column chromatography of the light petroleum extract of mace on elution from silica gel with benzene–ethyl acetate (9:1).

1-(3,4-Methylenedioxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy)propan-1-ol (I) * was an oil, ν_{\max} (film) 3520, 3080, 3000, 2940, 2850, 2770, 1630, 1590, 1510, 1490, 1330, 1240, 1125, 1060, 1035, 990, 925, 910, 820, and 805 cm⁻¹ (Found: M^+ , 372.1566. C₂₁H₂₄O₆ requires M , 372.1573).

1-(3,4,5-Trimethoxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy)propan-1-ol (II) was an oil, ν_{\max} (CCl₄) 3500, 3080, 3000, 2960, 2940, 2880, 2840, 1750, 1630, 1600, 1325, 1125, and 920 cm⁻¹ (Found: M^+ , 418.1999. C₂₃H₃₀O₇ requires M , 418.1992).

1-(4-Hydroxy-3-methoxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy)propan-1-ol (III) was an oil, ν_{\max} (film) 3500, 3080, 3010, 2970, 2940, 2840, 1605, 1590, 1220, 1120, 820, and 720 cm⁻¹ (Found: M^+ , 374.1732. C₂₁H₂₆O₆ requires M , 374.1729).

1-(4-Acetoxy-3-methoxyphenyl)-2-(4-allyl-2,6-dimethoxy-

phenoxy)propyl acetate (IV) was an oil, ν_{\max} (film) 3100, 3030, 2960, 2860, 1770, 1745, 1680, 1640, 1600, 1590, 1220, 1025, 900, 820, and 750 cm⁻¹ (Found: M^+ , 458.1946. C₂₅H₃₂O₈ requires M^+ , 458.1941).

1-(3,4-Methylenedioxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy)propyl acetate (V) was an oil, ν_{\max} (film) 3080, 3000, 2945, 2850, 2790, 1745, 1640, 1590, 1500, 1230, 1125, 1030, 930, 920, and 810 cm⁻¹ (Found: M^+ , 414.1672. C₂₃H₂₆O₇ requires M , 414.1679).

1-(5-Acetoxy-3,4-dimethoxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy)propyl acetate (VI) was a pale yellow oil, ν_{\max} (film) 3080, 3000, 2950, 2850, 1765, 1740, 1650, 1600, 1580, 1500, 1460, 1420, 1370, 1325, 1125, 1030, 915, 830, and 760 cm⁻¹ (Found: M^+ , 488.2043. C₂₆H₃₂O₈ requires M , 488.2046).

1-(3,4-Methylenedioxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy)propyl benzoate (VII) was an oil, ν_{\max} (film) 3080, 3000, 2945, 2850, 2790, 1720, 1640, 1600, 1590, 1270, 1230, 1120, 1025, 910, and 790 cm⁻¹ (Found: M^+ , 476.1835. C₂₈H₂₈O₇ requires M , 476.1835).

1-(3,4,5-Trimethoxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy)propane (VIII) was an oil, ν_{\max} (film) 3080, 3000, 2970, 2940, 2840, 1590, 1500, 1460, 1420, 1325, 1235, and 1125 cm⁻¹ (Found: M^+ , 402.2044. C₂₃H₃₀O₆ requires M , 402.2042).

Dehydrodi-isoegenol (IX) was a crystalline solid, m.p. 130–132° (lit.,⁵ 132–133°), λ_{\max} (EtOH) 275 nm (Found: M^+ , 326.1515. Calc. for C₂₀H₂₂O₄: M , 326.1518).

5-Methoxydehydrodi-isoegenol (X) was an oil, ν_{\max} (film) 3500, 3080, 3000, 2970, 2940, 2850, 1600, 1240, and 1150 cm⁻¹ (Found: M^+ , 356.1624. C₂₁H₂₄O₅ requires M , 356.1624).

Acetyldehydrodi-isoegenol (XI) was a crystalline solid, m.p. 110° (lit.,¹¹ 112.7–113.7°).

Acetyl-5-methoxydehydrodi-isoegenol (XII) was an oil, ν_{\max} (film) 3020, 2960, 2940, 2880, 2850, 1770, 1600, 1200, 1130, 970, 820, and 750 cm⁻¹ (Found: M^+ , 398.1733. C₂₃H₂₆O₆ requires M , 398.1729).

1-(3,4-Methylenedioxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy)propan-1-one (XIII).— α -Bromo-3',4'-methylenedioxypropionophenone^{12,13} (3.5 g), methoxyegenol (4-allyl-2,6-dimethoxyphenol) (1.8 g), and anhydrous K₂CO₃ (2.4 g) were heated under reflux in anhydrous ethyl methyl ketone (50 ml) for 20 h. The solution was cooled, poured into water, acidified, and extracted with diethyl ether (2 × 200 ml). The combined ether extracts were washed with 1% sodium hydroxide solution (100 ml), water (2 × 100 ml), dried (Na₂SO₄), and evaporated to dryness *in vacuo*. The resulting oil on t.l.c. (5% acetone in benzene) showed two spots, the unchanged bromo-compound (R_F 0.92) and another product (R_F 0.60). The compounds were separated by p.l.c. using benzene as developing solvent (multiple development). The lower band gave the *propanone* (XIII) (2.5 g) as crystals from methanol, m.p. 88–89°, ν_{\max} (CCl₄) 1670 cm⁻¹, δ (CDCl₃) 1.54 (3H, d, J 6.8 Hz), 3.32br (2H, d), 3.74 (6H, s), 5.09 (2H, m), 5.20 (1H, q, J 6.8 Hz), 5.90 (1H, m), 6.00 (2H, s), 6.38 (2H, s), 6.84 (1H, d, J 8 Hz), and 7.84 (4H, m), *m/e* 370 (M^+ ; 15%), 221 (59), 194 (51), 193 (92), and 149 (100) (Found: C, 68.1; H, 5.9. C₂₁H₂₂O₆ requires C, 68.1; H, 6.0%).

Compound (I).—Ketone (XIII) (1.82 g) and LiAlH₄ (2 g) in anhydrous ether (200 ml) were heated under reflux

* The n.m.r. data for products (I)–(XII) are given in Tables 1 and 3.

¹¹ C. H. Ludwig, B. J. Nist, and J. L. McCarthy, *J. Amer. Chem. Soc.*, 1964, **86**, 1186.

¹² R. C. Fuson, R. Gaertner, and D. H. Chadwick, *J. Org. Chem.*, 1948, **13**, 489.

¹³ M. Ohara, *J. Pharm. Soc. Japan*, 1951, **71**, 1244.

(anhydrous conditions) for 7 h. Excess of LiAlH_4 was destroyed by the addition of ethyl acetate and wet ether. The mixture was poured into water (200 ml), acidified, and extracted with ether (2×250 ml). The combined ether extracts were washed with 1% sodium hydroxide solution, dried (Na_2SO_4), and evaporated to dryness *in vacuo* to give an oil, which was purified by p.l.c. using benzene-acetone (98:2) as solvent to give alcohol (I) (1.7 g), m.p. $80-82^\circ$ after recrystallisation from methanol.

1-(3,4,5-Trimethoxyphenyl)-2-(4-allyl-2,6-dimethoxyphenoxy)propan-1-one.— α -Bromo-3',4',5'-trimethoxypropio-phenone^{14,15} (3.02 g), methoxyeugenol (1.94 g), and anhydrous K_2CO_3 (2.8 g) in anhydrous ethyl methyl ketone (50 ml) were heated under reflux for 6 h. The reaction mixture was worked up in the manner employed in the analogous reaction described above and the resulting ketone isolated as a crystalline solid (2.35 g), m.p. $80-82^\circ$ after recrystallisation from methanol, ν_{max} (CCl_4) 1665 cm^{-1} ,

¹⁴ H. K. Iwamoto and W. H. Hartung, *J. Org. Chem.*, **1944**, **9**, 513.

δ (CDCl_3) 1.57 (3H, d, J 6.8 Hz), 3.30br (2H, d), 3.74 (6H, s), 3.90 (3H, s), 5.06 (2H, m), 5.30 (1H, q, J 6.8 Hz), 5.90 (1H, m), 6.41 (2H, s), and 7.54 (2H, s), m/e 416 (M^+ ; 15%), 221 (42), 195 (100), 194 (31), and 193 (75) (Found: M^+ , 416.1828. $\text{C}_{23}\text{H}_{28}\text{O}_7$ requires M , 416.1835).

Compound (II).—The above ketone (1.8 g) and LiAlH_4 (3 g) in anhydrous ether (150 ml) were heated under reflux (anhydrous conditions) for 7 h. The reaction was worked up as for (I), and the products purified by p.l.c. (benzene-acetone 95:5; multiple development) to yield alcohol (II) (1.5 g) as a crystalline solid, m.p. $70-72^\circ$ after recrystallisation from methanol.

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¹⁵ M. J. Hunter, A. B. Cramer, and H. Hibbert, *J. Amer. Chem. Soc.*, **1939**, **61**, 516.