Malabaricones A—D, Novel Diarylnonanoids from *Myristica malabarica* Lam (Myristicaceae)

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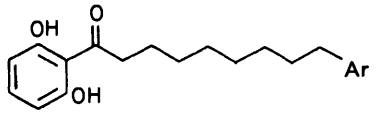
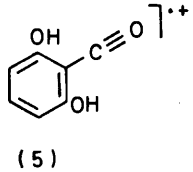
Four novel diarylnonanoids, malabaricones A—D, have been isolated from the fruit rind of *Myristica malabarica* Lam (Myristicaceae) and assigned the structures (1)—(4).

THE plant source of jathipathri, a drug used in the Indian system of medicine, is *Myristica fragrans* Houtt (Myristicaceae). A closely related drug, pasupasi, is often found as an adulterant or a substitute for jathipathri. The botanical source of this is *M. malabarica* Lam (Myristicaceae). The anatomical part of the plant used is the fruit rind. We have investigated the extract of the fruit rind of *M. malabarica* and have isolated four new closely related compounds, malabaricones A—D, whose structures have been established as (1)—(4) by spectroscopic methods.

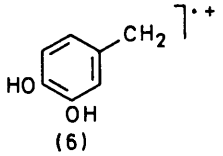
We consider first malabaricone C (3), $C_{21}H_{26}O_5$. The i.r. [$\nu_{max.}$ (KBr) 3 460, 3 390, 3 295, and 1 625 cm^{-1}] and u.v. [$\lambda_{max.}$ 224, 272, and 340 nm (ε 15 000, 11 600, 2 700); $\lambda_{max.}$ (OH^-) 242, 284, and 383 nm; $\lambda_{max.}$ (H^+) as original] spectra were consistent with the presence of an *ortho*-hydroxyacetophenone moiety. The ^1H n.m.r. spectrum revealed that there were two benzene rings, one 1,2,3-substituted [δ ($CDCl_3$–CD_3OD) 6.36 (2 H, d, J 8 Hz) and 7.18 (1 H, t, J 8 Hz)] and the other 1,3,4-substituted [δ 6.54 (1 H, q, J 8 and 2 Hz), 6.67 (1 H, d, J 2 Hz), and 6.74 (1 H, d, J 8 Hz)]. From chemical shift considerations in both the ^1H and ^{13}C spectra it was clear that



(1) Ar = Ph
(2) Ar = 4-HO·C_6H_4
(3) Ar = 3,4-$(HO)_2C_6H_3$
(4) Ar = 3,4-$(CH_2O_2)C_6H_3$



(5)



(6)

malabaricone C contained a 2,6-dihydroxy-substituted acetophenone unit [δ 209.10 (1 C, s), 162.06 (2 C, s), 136.04 (1 C, d), 110.43 (1 C, s), and 107.75 (2 C, d)] and a 1-alkyl-3,4-dihydroxybenzene unit [δ 144.20 (1 C, s), 142.14 (1 C, s), 135.56 (1 C, s), 120.28 (1 C, d), 115.62 (1 C, d), and 115.28 (1 C, d)]. The observed and calculated [1] ^{13}C chemical shifts were in good agreement. The remaining features deduced from the ^1H and ^{13}C spectra were eight methylene groups, one flanking the carbonyl group [δ_H 3.14 (2 H, t, J 7 Hz), δ_C 44.84 (1 C, t)], one benzylic [δ_H 2.46 (2 H, t, J 7 Hz), δ_C 35.33 (1 C, t)], and six others [δ_H 1.6 (4 H, m) and 1.32br (8 H, s), δ_C 31.68 (1 C, t), 29.48 (3 C, t), 29.26 (1 C, t), and 24.66 (1 C, t)]. These data led to the conclusion that the two benzene rings were linked together by the alkyl chain and that malabaricone C had structure (3). Support for this assignment was readily obtained from the mass spectrum, which had prominent peaks resulting from cleavage α to the carbonyl group [*m/e* 137 (5)], loss of carbon monoxide from (5) (*m/e* 109), and benzylic cleavage [*m/e* 123 (6)].

The remaining three compounds shared with malabaricone C the common feature of the polymethylene-substituted 2′,6′-dihydroxyacetophenone: they had the same u.v. absorption, prominent peaks in the mass spectrum at *m/e* 137(5) and 109, and ^1H and ^{13}C (for malabaricone A) resonances similar to those of (3) (see Experimental section). It was apparent that they differed only in the substitution of the second benzene ring. The ^1H n.m.r. data and the mass spectral fragment arising from benzylic cleavage provided a clear indication of the nature of this ring. The simplest member of the series, malabaricone A (1), $C_{21}H_{26}O_3$, lacked oxygenation [δ 7.17 (5 H, m); *m/e* 91]. Malabaricone B (2), $C_{21}H_{26}O_4$, had a hydroxy-group *para* to the point of attachment of the polymethylene chain [δ 6.79 and 7.04 (AA′BB′, both d, J 8 Hz); *m/e* 107]. Malabaricone D (4), $C_{22}H_{26}O_5$, had the same oxygenation pattern as (3) [δ 6.60 (1 H, q, J 8 and 2 Hz), 6.67 (1 H, d, J 2 Hz), and 6.73 (1 H, d, J 8 Hz)] with the addition of a methylenedioxy-group [δ 5.90 (2 H, s); *m/e* 135].

There are many examples of compounds which arise from a cinnamic acid residue extended by acetate or malonate units, *e.g.* gingerol,[2] curcuminoids.[3] It is probable that the biogenesis of the malabaricones involves cinnamate and a hexaketide chain.

EXPERIMENTAL

For general details see ref. 4.

Isolation.—Shade-dried and coarsely powdered fruit rind (2 kg) of *Myristica malabarica* was successively extracted

[1] G. C. Levy and G. L. Nelson, '^{13}C Nuclear Magnetic Resonance for Organic Chemists,' Wiley-Interscience, New York, 1972, p. 81.
[2] D. W. Connell and M. D. Sutherland, *Austral. J. Chem.*, 1969, **22**, 1033.
[3] P. J. Roughley and D. A. Whiting, *J.C.S. Perkin I*, 1973, 2379.
[4] K. K. Purushothaman, S. Vasanth, and J. D. Connolly, *J.S.C. Perkin I*, 1974, 2661.

overnight with hexane, benzene, and chloroform. The hexane extract was chromatographed over silica gel. The early fractions eluted with benzene, gave a yellow solid which was crystallised from ether–hexane to yield *malabaricone A* (1) [1-(2,6-*dihydroxyphenyl*)-9-*phenylnonan*-1-*one*], m.p. 81—82°; *m/e* 326; $\nu_{max.}$ (CCl_4) 3 595 and 1 630 cm^{-1}; $\lambda_{max.}$ 224, 268, and 340 nm (ε 15 000, 11 000, and 2 800); $\lambda_{max.}$ (OH^-) 240, 284, and 384 nm; $\lambda_{max.}$ (H^+) as original; δ_H 1.35br (8 H, s), 1.66 (4 H, m), 2.60 (2 H, t, *J* 7 Hz), 3.10 (2 H, t, *J* 7 Hz), 6.36 (2 H, d, *J* 8 Hz), and 7.17 (1 H, t, *J* 8 Hz); δ_C 208.12 (1 C, s), 161.15 (2 C, s), 135.72 (1 C, d), 110.11 (1 C, s), and 108.50 (2 C, d) (2′,6′-dihydroxyacetophenone), 142.9 (1 C, s), 128.43 (2 C, d), 128.25 (2 C, d), and 125.57 (1 C, d) (alkyl-substituted phenyl ring), 44.80 (1 C, t), 35.98 (1 C, t), 31.48 (1 C, t), 29.68 (3 C, t), 29.38 (1 C, t), and 24 46 (1 C, t) (Found: C, 78.0; H, 8.3. $C_{21}H_{26}O_3$ requires C, 77.3; H, 8.0%). Further elution with benzene afforded a gum which was triturated with hexane. The resulting solid was crystallised from benzene–hexane to give *malabaricone D* (4) [1-(2,6-*dihydroxyphenyl*)-9-(3,4-*methylenedioxyphenyl*)*nonan*-1-*one*], m.p. 90—91°, *m/e* 370; $\nu_{max.}$ (CCl_4) 3 592 and 1 630 cm^{-1}; $\lambda_{max.}$ 224, 272, and 342 nm (ε 15 000, 11 800, and 2 700); $\lambda_{max.}$ (OH^-) 238, 284, and 384 nm; $\lambda_{max.}$ (H^+) as original; δ_H 1.39br (8 H, s), 1.65 (4 H, m), 2.55 (2 H, t, *J* 7 Hz), 3.15 (2 H, t, *J* 7 Hz), 6.40 (2 H, d, *J* 8 Hz), and 7.22 (1 H, t, *J* 8 Hz) (Found: C, 71.6; H, 6.95. $C_{22}H_{26}O_5$ requires C, 71.35; H, 7.0%). The chloroform extract was concentrated and the solid which separated was chromatographed over silica gel. Elution with benzene–chloroform (1 : 1) and crystallisation from benzene afforded *malabaricone B* (2) [1-(2,6-*dihydroxyphenyl*)-9-(4-*hydroxyphenyl*)*nonan*-1-*one*], m.p. 102°, *m/e* 342 and 324; $\nu_{max.}$ (KBr) 3 310br and 1 638 cm^{-1}; $\lambda_{max.}$ 224, 272, and 342 (ε 15 000, 11 300, and 2 600); $\lambda_{max.}$ (OH^-) 240, 286, and 384 nm; $\lambda_{max.}$ (H^+) as original; δ ($CDCl_3$–CD_3OD) 1.36br (8 H, s), 1.64 (4 H, m), 2.54 (2 H, t, *J* 7 Hz), 3.17 (2 H, t, *J* 7 Hz), 6.41 (2 H, d, *J* 8 Hz), and 7.20 (1 H, t, *J* 8 Hz) (Found: C, 74.0; H, 8.1. $C_{21}H_{26}O_4$ requires C, 73.7; H, 7.7%). Further elution with chloroform–ethyl acetate (9 : 1) and crystallisation from chloroform gave *malabaricone* (C) (3) [1-(2,6-*dihydroxyphenyl*)-9-(3,4-*dihydroxyphenyl*)*nonan*-1-*one*] as pale yellow crystals, m.p. 123—124° (*m/e* 358 and 340) (Found: C, 70.6; H, 7.6. $C_{21}H_{26}O_5$ requires C, 70.35; H, 7.25%).

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