The Constitution and Stereochemistry of Obtusafuran

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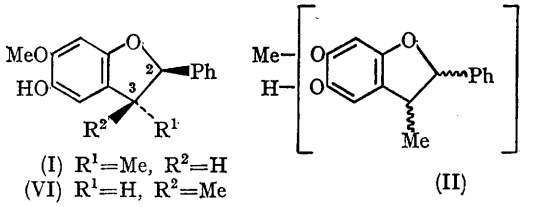
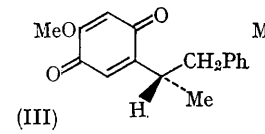
IN addition to two neoflavanoids and two cinnamylphenols,[1] the heartwood of *Dalbergia obtusa* Lecomte (syn. *D. retusa*) has yielded a novel natural product, obtusafuran, which is of interest in that it contains a C_{15}-(1,2-diarylpropanoid)-skeleton associated in a very unusual way with a dihydrobenzofuran residue. This constitution has direct implications regarding our biogenetic proposals.[2] The determination of the constitution and absolute configuration of obtusafuran and the synthesis of its racemate are now reported.

Obtusafuran, $C_{16}H_{16}O_3$, m.p. 110—113°, was optically active, $[\alpha]_D^{20}$ + 47°, and had a u.v. spectrum [λ_{max} (EtOH) 235 (ϵ 2940; infl) and 305 mμ (ϵ 4600)], which suggested an oxygenated benzene chromophore without additional conjugation. The n.m.r. spectrum of obtusafuran indicated the presence of a phenyl group [τ 2·63 (s, 5H)], two *para*-related aromatic protons [τ 3·30

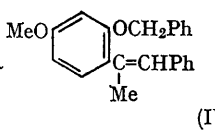


(I) R^1=Me, R^2=H
(VI) R^1=H, R^2=Me

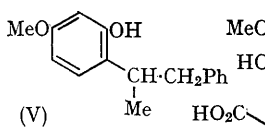
(II)



(III)



(IV)



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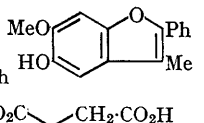
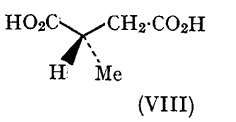


(VII)



(VIII)

(s, 1H), τ 3·53 (s, 1H)], a $>$CH–CH–CH_3 unit [τ_A 4·90 (d, 1H), τ_M 6·4—6·9 (m, 1H), τ_X 8·63 (d, 3H), AMX_3 system, J_{AM} 8·0 c./sec., J_{MX} 7·0 c./sec.], a methoxy-group [τ 6·20 (s, 3H)], and a hydroxy-group [τ 4·77 (broad s, 1H)] (i.r. ν_{max} 3500 cm.$^{-1}$), thus leading to the partial structure (II) for obtusafuran. The relative positions of the hydroxy- and methoxy-substituents were determined by the hydrogenolysis (10% Pd–C catalyst in acetic acid) of obtusafuran followed by aerial oxidation which yielded a yellow quinone (III), m.p. 120°, $[\alpha]_D^{25}$ — 11·0° [τ 2·80 (s, 5H); τ 3·56 (d, 1H), J 1 c./sec.; τ 4·10 (s, 1H); τ 6·4—7·6 (m, 3H); τ 6·20 (s, 3H); τ 8·91 (d, 3H), J 7·0 c./sec.]. This constitution (III) for the optically active quinone was confirmed by synthesis of its racemate. 2-Benzyloxy-4-methoxyacetophenone[3] reacted with benzylidinetriphenylphosphonium ylid to give the olefin (IV) and catalytic reduction (10% Pd–C in acetic acid) of (IV) gave the 1,2-diarylpropane (V) which was oxidised by Frémy's salt giving the racemic quinone (*cf.* III). Obtusafuran must therefore be 2,3-dihydro-5-hydroxy-6-methoxy-3-methylbenzofuran, and the definition of its stereochemistry is now considered.

The relative stereochemistry of obtusafuran was determined by comparison with the synthetic racemic *cis*-2,3-dihydrobenzofuran derivative (VI), prepared by controlled catalytic hydrogenation (10% Pd–C in ethyl acetate) of the benzofuran (VII) which was synthesised by the reaction of 2,5-dihydroxyanisole[4] with 1-bromo-1-phenylpropan-2-one. The *cis*-2,3-dihydrobenzofuran (VI), m.p. 110—111°, had i.r. and n.m.r. spectra different from those of (+)-obtusafuran, particularly with respect to the chemical shifts of the proton on C(2) [τ 4·27 for (VI) and τ 4·90 for (I)] and the methyl group on C(3) [τ 9·26 for (VI) and τ 8·63 for (I)]. The *trans*-2,3-dihydrobenzofuran structure (I) could therefore be assigned to obtusafuran, and this opinion was confirmed by the isomerisation of the *cis*-2,3-dihydrobenzofuran (VI) by heating (100°; 16 hr.) it with potassium t-butoxide in dimethyl sulphoxide. This isomerisation gave racemic obtusafuran (I), whose n.m.r. spectrum was identical with that of natural (+)-obtusafuran.

Ozonolysis of the (—)-quinone (III), from natural (+)-obtusafuran, and decomposition of the ozonide with hydrogen peroxide gave (—)-(*S*)-methylsuccinic acid (VIII).[5] The (—)-quinone therefore has the (*S*)-configuration (III), and it

follows that (+)-obtusafuran has the (2*R*,3*R*)-absolute configuration (I).

This (2*R*,3*R*)-configuration of (+)-obtusafuran may be compared with the (2*S*,3*S*)-configuration recently discussed[6] for melanoxin [2,3-dihydro-5-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-6-methoxy-3-methylbenzofuran] isolated from *Dalbergia melanoxylon*.

The n.m.r. spectral characteristics of the *cis*- and *trans*-2,3-dihydrobenzofurans have the same vicinal coupling (J_{2H-3H} 8 c./sec.). This result is of general interest in relation to considerable recent discussion[7] of the deduction of the stereochemistry of 2,3-dihydrobenzofurans from n.m.r. coupling constants.

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