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AMBOFURANOL - THE FIRST NATURAL 3-METHOXYBENZOFURAN

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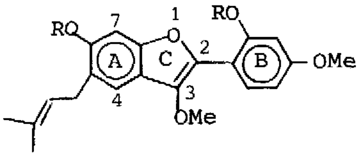
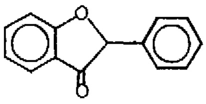
Abstract: The structure of ambofuranol (1), a novel benzofuran, is deter=mined by spectral methods.

Our interest in *Neorautanenia amboensis* Schinz, a species widespread throughout Central and Southern Africa, stems from reports of piscocidal properties[1] and the isolation of insecticidal[2] compounds from members of this genus.

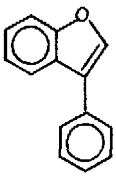
The bulb[2] and the bark[3] independently yield several isoflavonoids and we now report the characterisation of an unique benzofuran, ambofuranol (1), which represents the first natural 2-phenylbenzofuran with oxygen substitution on the heterocyclic ring.[4]



(1) R=H
(2) R=Ac



(3)



(4)

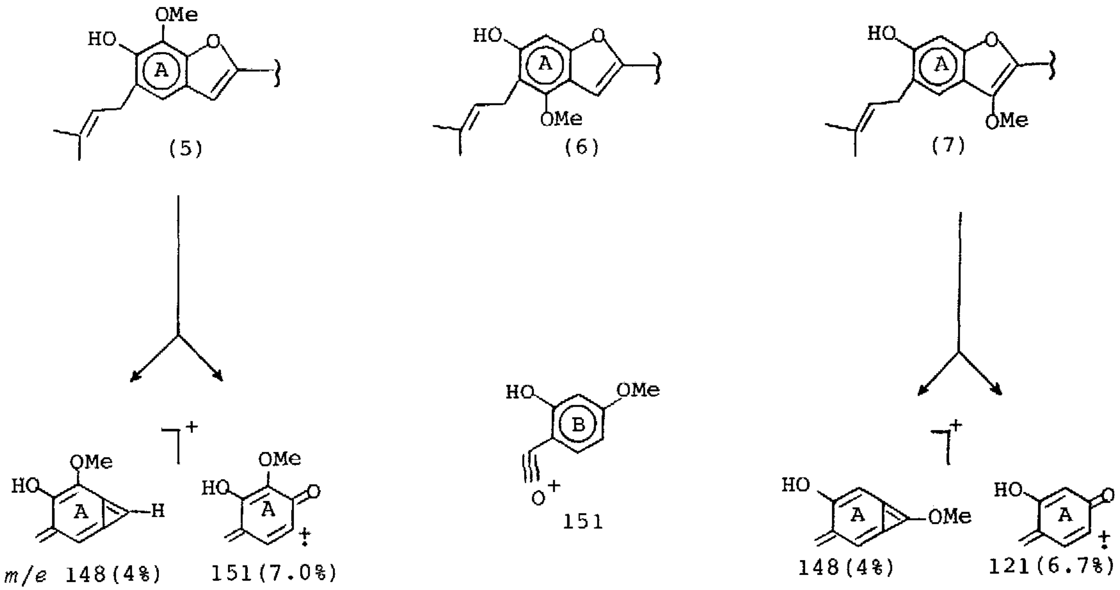
Extensive column and thin layer chromatography of the benzene extract (93 g) of the bark from the bulb yields (1) (9 mg) as colourless needles (benzene or ethanol), m.p. 147-148°, $\nu_{max.}^{CHCl_3}$ 720-850, 1270, 1490, 1520, 1635, 2400 and 3080 cm^{-1}. Reaction with the ironIIIchloride/perchloric acid spray reagent produces a characteristic green spot with a purple edge, R_F 0.41 (benzene:ethyl acetate 9:1) and 0.59 (1,2-dichloroethane:acetone 9:1).

In the PMR spectrum ($CDCl_3$) the resonances of an aromatic ABX system (δ 7.45, doublet, J 8.75 Hz; δ 6.52, quartet, J 8.75 and 2.5 Hz and δ 6.47, doublet, J 2.5 Hz), two aromatic singlets (δ 6.69 and 6.88, the latter slightly split), an isopentenyl group (δ 1.72 and 1.81 for 2 x Me; δ 3.44, broadened doublet, J 7.5 Hz for CH_2 and δ 5.19, triplet, J 7.5 Hz for =CH-) and two methoxyl groups (δ 3.78 and 3.97) are easily discerned. Formation of a diacetate (δ 2.34 and 2.28) with acetic anhydride/pyridine confirms the presence of two hydroxyl groups (δ 5.20, exchangeable with D_2O). Except for the forementioned signals the region δ 3.0 - 6.0 is clear and thus not indicative of the hetero=cyclic nature of ambofuranol (1).

Allocation of the molecular mass of the phenol, M^+ 354, by mass spectro=metry is supported by the presence of a prominent peak at *m/e* 438 (72%) in the spectrum of the diacetate (2) which undergoes consecutive loss of two acetate units, giving rise to fragments at *m/e* 396 $[(M-42)^+, 90\%]$ and 354 $[(M-2 \times 42)^+, 100\%]$. Elementary analysis (C 71.0 and H 6.3%) confirms the $C_{21}H_{22}O_5$ empiri=cal formula indicating the C_6-C_2-C_6 basic skeleton of ambofuranol (1). The ultra-violet spectrum $[\lambda_{max.}^{MeOH}$ (log ε): 220(3.96), 274(4.10), 300(4.41) and 327(3.87)$]$ exhibits the 2-phenylbenzofuran (stilbene type) absorption,[5] thus excluding 3-phenyl analogues, e.g. (3).

The isopentenyl group is placed in position 5 on the basis of NMR evidence and the mass fragmentation pattern. Since the NMR signal of H-4, experiencing long distance coupling ($J < 0.5$ Hz) with the isopentenyl methylene group, is an aromatic singlet, position 6 on the A-ring also bears a substituent which is a hydroxy group as is evident from the chemical shift difference after acetylation ($\Delta\delta$ -0.20 for H-7). This phenomenon ($\Delta\delta$ -0.16 for H-5' and -0.43 for H-3') together with the calculated[6] and observed chemical shifts of the aromatic protons also determine the substitution pattern of the B-ring. This automatically places the remaining methoxyl group in the vacant 3 position.

Supporting differentiation from amongst the three possible[7] substitution patterns, the partial structures (5), (6) or (7), is supplied by the following: in structure (6) protons H-3 and H-7 would experience strong (J *ca* 1.0 Hz)



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mutual long distance coupling,[8] resulting in doublet signals for <u>both</u>. This is not observed. The mass fragmentation pattern[9] of the benzofuran moiety further distinguishes between structures (5) and (7) (Scheme). Both would give rise to fragments *m/e* 148 (4%), but structure (5) would also lead to fragment *m/e* 151, whereas (7) would lead to *m/e* 121. The relative abundance of these fragments is of the same magnitude (*ca* 7%), but as a fragment *m/e* 151 originates from the B-ring (Scheme), the existence of fragment *m/e* 121 apparently supports the structure (7) which is also consistent with the NMR data

Ambofuranol (1) constitutes the first natural 3-oxygenated benzofuran not in the 2-benzyl or 2-benzylidene (aurone) class of compounds,[4] and may be regarded as the enolic form of 2*H*-benzofuran-3-ones (3) trapped by methylation The lastmentioned are known synthetic compounds.[10]

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