Phytochemistry, 1977, Vol. 16, pp. 1017–1018. Pergamon Press. Printed in England.

CIS-AVICENNOL, A NEW PYRANOCOUMARIN FROM THE ROOT BARK OF *ZANTHOXYLUM ELEPHANTIASIS*

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(*Received* 14 *January* 1977)

Key Word Index—*Zanthoxylum elephantiasis*; Rutaceae; pyranocoumarin; *cis*-avicennol; tetrahydroavicennol; lanthanide shift reagent Eu(fod)$_3$.

Abstract—A new pyranocoumarin has been isolated from the root bark of *Zanthoxylum elephantiasis* and identified as *cis*-avicennol (6-(3-hydroxy-3-methyl-*cis*-but-1-enyl)-5-methoxy-2,2-dimethyl-2*H*-benzo [1,2b:3,4b′] dipyran-8-one) on the basis of comparison of spectral data with that of *trans*-avicennol and conversion to tetrahydroavicennol. The usefulness of the lanthanide shift reagent Eu(fod)$_3$ in the assignment of *cis* configuration to the butenyl side-chain is briefly discussed.

INTRODUCTION

The angular pyranocoumarin avicennol (**1**) has, to date, been found to occur only in three species of the rutaceous genus *Zanthoxylum* L: *Z. avicennae* (Lam.) DC. [1], *Z. dipetalum* Mann [2] and *Z. elephantiasis* Macfad. [3]. In the determination of the structure of avicennol [1] considerable use was made of the shifts induced in the PMR spectrum of its *O*-TMSi ether by the lanthanide shift reagent Eu(fod)$_3$. Subsequently the structure of avicennol, with its unusual 3-hydroxy-3-methyl-*trans*-but-1-enyl side-chain, was confirmed by synthesis [4].

We now wish to report the isolation of the corresponding *cis* isomer of avicennol from the root bark of *Z. elephantiasis* and its identification by comparison of spectral data and shift values with Eu(fod)$_3$ with those previously obtained for *trans*-avicennol.

RESULTS AND DISCUSSION

On concentration the petrol extract of the root bark of *Z. elephantiasis* deposited, in high yield, avicennol, xanthoxyletin and canthin-6-one. PLC of the supernatant liquor gave, in addition, dihydrochelerythrine, avicennin, dipetalolactone and triacontanoic acid [3]. Concentration of the supernatant solution from which triacontanoic acid had been obtained yielded 95 mg of a yellow oil, fluorescing dull yellow under UV. The yellow oil, although giving a single spot on TLC using several systems, could not be obtained in crystalline form.

MS of the oil indicated a molecular ion M$^+$ 342.1453 ($C_{20}H_{22}O_5$) with a fragmentation pattern showing only relative abundance variations from that observed for *trans*-avicennol [1]. Likewise, the IR spectrum, apart from a distinct broadening of the OH band, was in close agreement with that previously recorded for *trans*-avicennol.

Conversely the maxima observed in the UV spectrum of the oil (236, 275 and 294 nm; cf. 250, 257 and 301 nm for *trans*-avicennol) and the chemical shifts of some of the protons in the PMR (Table 1) showed distinct differences. With respect to the PMR spectrum, whilst the resonance signals were indicative of a coumarin with similar substituents to *trans*-avicennol, differences in chemical shifts in all signals derived from the 3-hydroxy-3-methylbut-1-enyl side-chain and in the olefinic coupling constant ($J = 13$ Hz; cf. $J = 16$ Hz) were apparent. As the coupling constant of 13 Hz cannot definitely be assigned to either a *cis* or *trans* orientated olefine [5] this new coumarin could, theoretically, have been any one of twenty-three possible isomers of *trans*-avicennol.

Comparison of the Eu(fod)$_3$-induced shifts [1, 6] in the PMR spectrum of the *O*-TMSi derivative of the new

Table 1. Comparison of chemical shifts (δ) of the protons of *trans*-avicennol (**1**) and the 'yellow oil'*

	3-H	4-H	3′-H	4′-H	2′-Me$_2$	OMe	1″-H	2″-H	3″-Me$_2$	OH
trans-Avicennol	6.27	8.06	5.69	6.65	1.48	3.80	6.95	6.81	1.48	2.58
J (Hz)	10	10	10	10			16	16		
'Yellow oil'	6.29	8.05	5.69	6.65	1.49	3.85	6.25	6.01	1.31	2.85
J (Hz)	10	10	10	10			13	13		

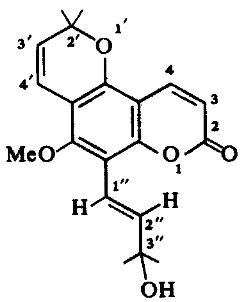
* The non-systematic numbering system adopted (see formula **1**) is used to allow comparison with other coumarin shift data [1, 6].

Table 2. Comparison of induced shift values (relative to 3H = 1.00) for *trans*-avicennol and 'yellow oil' *O*-TMSi ethers with $Eu(fod)_3$*

	3-H	4-H	3'-H	4'-H	$2'$-Me_2	OMe	1''-H	2''-H	$3''$-Me_2	*O*-TMSi
trans-Avicennol	1.00	0.31	0.08	0.13	0-08	0.15	0.40	0.52	0.13	0.11
'Yellow oil'	1.00	0.32	0.09	0.15	0.08	0.16	0.32	0.25	0.28	0.19

* See Table 1.

compound with those of *O*-TMSi-*trans*-avicennol (Table 2) aided the structure assignment. No significant change was noted in shift ratios for protons of the lactone ring, pyran ring or OMe group. On the other hand the olefinic protons of the side-chain of the new compound were less shifted than in *trans*-avicennol but were once again of such a magnitude as to restrict side-chain attachment to C-8 of the coumarin nucleus [1]. The shifts of the *gem*-dimethyl and *O*-TMSi groups were, however, markedly larger than those of the corresponding *trans* side-chain indicating that these groups were closer to the point of complexation. These results are in agreement with those anticipated for the *cis* isomer of *O*-TMSi-avicennol (**2b**).



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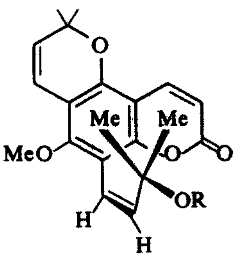
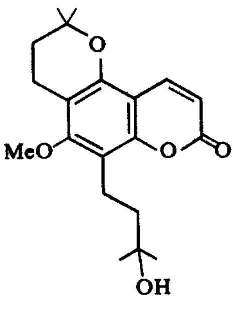


2a R = H
2b R = $Si(Me)_3$



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The substitution pattern of the new coumarin was confirmed by hydrogenation to give the corresponding tetrahydro- derivative which proved identical to the previously synthesised tetrahydroavicennol (**3**) [1], thereby indicating that it was *cis*-avicennol (**2a**).

It has recently come to our notice that synthetically derived 7-methoxy-8-(3-hydroxy-3-methyl-*cis*-but-1-enyl) coumarin showed a high coupling constant ($J = 12$ Hz) for the side-chain olefinic protons and, like *cis*-avicennol, proved impossible to crystallise [7].

EXPERIMENTAL

Plant Material. Root bark of *Zanthoxylum elephantiasis* Macfad. was collected at Falmouth, Trelawny, Jamaica (Voucher: A.I. Gray 3) and at Zalaya, Santo Domingo, Dominican Republic (voucher: J. Jimenez 5972). Vouchers have been deposited at the herbarium of the Royal Botanic Garden, Edinburgh.

Extraction and isolation. The milled bark (800 g from A.I. Gray 3 collection) was extracted with petrol bp 40–60°. The conc petrol extract, after deposition of canthin-6-one, xanthoxyletin and avicennol, was subjected to PLC (1 mm) over Si gel. Elution with EtOAc–hexane (3:2) yielded dihydrochelerythrine, avicennin, dipetalolactone and triacontanoic acid [3]. On concn of the ethanolic supernatant from the recrystallisation of triacontanoic acid a yellow oil (**2a**, 95 mg, R_f 0.55 in PLC system) was obtained.

Cis-*avicennol* (**2a**). The yellow oil could not be obtained in crystalline form. Found M^+ 342.1453; $C_{20}H_{22}O_5$ requires 342.1467. UV λ_{max}^{EtOH} nm: 236, 275, 294. IR ν_{max}^{film} cm^{-1}: 3490, 1725, 1140. PMR (60 MHz, $CDCl_3$, δ): 1.31 (6H, *s*, $3''$-Me_2), 1.49 (6H, *s*, $2'$-Me_2), 2.85 (1H, *br s*, lost on D_2O exchange, 3''-OH), 3.85 (3H, *s*, OMe), 5.69, 6.65 (2H, AB*q*, $J = 10$ Hz, 3'-H and 4'-H), 6.25, 6.01 (2H, AB*q*, $J = 13$ Hz, 1''-H and 2''-H), 6.29, 8.05 (2H, AB*q*, $J = 10$ Hz, 3-H and 4-H). MS *m/e* (rel. int.): 342 (42%, M^+), 327 (100), 324 (19), 309(20).

Cis-*avicennol*-O-*TMSi-ether* (**2b**). **2a** (50 mg) was dissolved in dry C_6H_6 and an excess of BSA added. After 7 hr the mixture was evap. to dryness and the residue chromatographed on Si gel. Elution with EtOAc–hexane (1:1) gave a yellow oil (45 mg, R_f 0.71). UV λ_{max}^{EtOH} nm: 238, 275, 298. PMR (60 MHz, $CDCl_3$, δ): –0.24 (9H, *s*, $SiMe_3$), 1.38 (6H, *s*, $3''$-Me_2), 1.47 (6H, *s*, $2'$-Me_2), 3.81 (3H, *s*, OMe), 5.60, 6.59 (2H, AB*q*, $J = 10$ Hz, 3'-H and 4'-H), 5.78. 6.01 (2H, AB*q*, $J = 13$ Hz, 2''-H and 1''-H), 6.20, 8.00 (2H, AB*q*, $J = 10$ Hz, 3-H and 4-H).

Tetrahydroavicennol (**3**). **2a** (20 mg) in EtOH was hydrogenated over Adams catalyst. The reaction mixture was filtered and evap. to dryness. TLC [1] indicated a single product, R_f 0.4. The residue on recryst. from MeOH as colourless prisms (18 mg) mp 165–165.5°, identical in all respects (UV, IR, PMR, TLC, mmp) with an authentic sample of tetrahydroavicennol [1].

Cis-*avicennol in* Z. elephantiasis—*Jimenez 5972.* A similar extraction and isolation procedure indicated the presence of small amounts of *cis*-avicennol in this material also.

Acknowledgements—The authors wish to express their thanks to Dr. J. Jimenz, Calle Maximo Gomez 34, Santiago de los Caballeros, Dominican Republic, for the collection of plant material in the Dominican Republic. One of us (A.I.G.) extends his thanks to the University of Strathclyde for the award of a scholarship.

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