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DYSOXYSULFONE, A SULFUR RICH METABOLITE FROM THE FIJIAN MEDICINAL PLANT *DYSOXYLUM RICHII*

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Summary *The structure of dysoxysulfone (1), a sulfur rich antibiotic isolated from leaves of the Fijian plant Dysoxylum richii, has been determined by a single crystal x-ray diffraction analysis.*

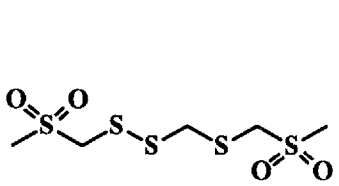
A tea made by adding chopped leaves of *Dysoxylum richii* (Gray) C.D.C. (Meliaceae) to a small amount of boiling water is a traditional Fijian cure for aches and pains.[1] We have been examining the chemistry of *D. richii* as part of an ongoing study of Fijian medicinal plants.[2] Our efforts have resulted in the isolation of four new limonoids from methanol extracts of dried *D. richii* leaves.[3] During the course of the structural work on the new limonoids, we consistently encountered a chromatographic fraction that displayed antimicrobial activity[4] and had an alliaceous (garlic-like) odour. We now wish to report the structure of dysoxysulfone (**1**), the major constituent of this fraction.

Fresh leaves of *D. richii* were collected at Deuba, Fiji in March 1988 and air-dried on site. The dried leaves (230g) were soaked in methanol (1.5L) for 6 days. Concentration of the methanol extract *in vacuo* gave a gum which was suspended in water and extracted sequentially with hexane, dichloromethane and ethyl acetate. The dichloromethane soluble material was fractionated via silica-gel flash (step gradient: hexane to ethyl acetate) and normal phase high performance liquid (isocratic: 3:7 hexane/ ethyl acetate) chromatographies to give pure **1** as a glass. Recrystallization of the glass from chloroform gave colorless prisms of dysoxysulfone (**1**) (mp 97-99°C; 9 X 10^{-4}% dry wt.).

The ^{1}H and ^{13}C nmr spectra of dysoxysulfone were extremely simple. Five singlets, two assigned to methyl protons (400MHz, $CDCl_3$: δ 3.03 and 3.05ppm) and three assigned to pairs of methylene protons (δ 4.04, 4.18 and 4.42ppm) were all that was observed in the ^{1}H nmr spectrum. The ^{13}C nmr spectrum also showed only five resonances (75MHz, $CDCl_3$: δ 38.6(CH_3), 39.3(CH_3), 41.8(CH_2), 51.5(CH_2) and 61.2(CH_2)) and an APT[5] experiment confirmed the presence of two methyl and three methylene carbons. The electron impact high resolution mass spectrum recorded on **1** gave information that was in conflict with the nmr data. An ion at m/z 341.9206 daltons, having an elemental composition of $C_6H_{14}O_4S_6$ (ΔM -1.1mmu), was the highest mass ion observed in the spectrum. Other prominent ions were observed at m/z 171 ($C_3H_7O_2S_3$), 139 ($C_3H_7O_2S_2$) and 93($C_2H_5O_2S$) daltons. It was possible to reconcile the MS and nmr data by assuming that dysoxysulfone was fragmenting in the mass spectrometer to give a stable radical of composition $C_3H_8O_2S_3$ (m/z 171) which was in turn dimerizing to give the ion observed at m/z 342. Reactions of this type are well documented for sulfide containing molecules.[6]

The total lack of connectivity information in the ^{1}H nmr spectrum of **1**, our inability to determine the molecular formula via mass spectrometry, and the small amount of material available prohibited us from determining a complete structure for **1** via spectroscopic[7] or chemical means. Therefore, the structure of

dysoxysulfone was determined by a single crystal x-ray diffraction analysis. Compound **1** crystallized in the monoclinic space group $P2_1/c$ with a=13.347(3), b=5.4820(13), c=8.584(2) Å, and β=102.45°. Since Z=2 for the molecular formula of 1, the molecule had to sit on an inversion center, or a molecular formula of $C_5H_{12}O_4S_5$ required a disordered molecule. X-ray data were collected using Mo $K\bar{\alpha}$ (0.71073 Å) radiation and 1° 2θ:θ scans out to 2θ≤50°. A total of 1049 (96%) of the 1095 unique reflections were judged observed ($|Fo| \geq 4\sigma(Fo)$). The final discrepancy index for a statistically disordered model where S3 and C3 are interchanged is 0.064.[8]



1

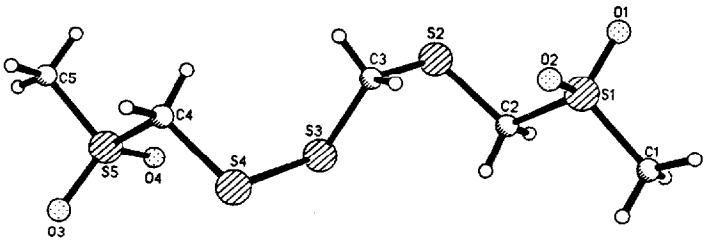


Figure 1. On the left is a conventional chemical drawing of dysoxysulfone (**1**) and on the right, a perspective drawing of the final x-ray model.

Balandrin et al. have recently reported the isolation of a series of volatile di-, tri-, and tetrasulfides of simple alkanes and alkenes from extracts of the neem tree, *Azadiracta indica* (Meliaceae) and they suggested that the sulfur containing compounds may play a role in the plant's uses in traditional medicine.[9] *D. richii* appears to be only the second plant in the family Meliaceae known to elaborate metabolites containing sulfur. It remains to be determined if dysoxysulfone has any useful medicinal properties.

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4. Dysoxysulfone (1) inhibits the growth of *Staphylococcus aureus, Bacillus subtilis, Candida albicans,* and *Rhizoctonia solani* in standard disc (1/4 in) bioassays. The limited quantity of pure dysoxysulfone available to us prohibited determination of accurate minimum inhibitory concentrations.
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8. Archival X-ray crystallographic data have been deposited with and can be ordered from the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, U.K. Please give a complete literature citation when ordering.
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